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Incidence of lymphohematopoietic malignancies among styrene-exposed workers of the reinforced plastics industry

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OBJECTIVES — The goal of this study was to determine the risk of lymphohematopoietic malignancies for workers exposed to styrene.

METHODS — This was a historical cohort study. The observed numbers of newly diagnosed cases of lymphohematopoietic malignancies in the study population were compared with expected numbers based on the national rates. The study took place in the Danish reinforced plastics industry, in which high exposure levels of styrene occur frequently in an environment free of most other suspected carcinogens. Altogether 36 525 male employees of 386 companies producing reinforced plastics and 14 254 nonstyrene exposed employees of similar industries were studied.

RESULTS — An insignificantly increased standardized incidence ratio (SIR) of 1.22 [95% confidence interval (95% CI) 0.88-1.65] was found for leukemia among all employees of the reinforced plastics industry. Workers employed in the 1960s (the period with the highest recorded styrene levels) or in companies with the highest exposure probability showed increased SIR values of 1.54 (95% CI 1.04-2.19) and 1.38 (95% CI 0.75-2.32), respectively. Both estimates increased when a 10-year latency period was considered.

CONCLUSIONS — An increased risk of leukemia was shown for workers in the early phase of the reinforced plastics industry in Denmark. If this association is not due to chance or confounding, the most likely cause is styrene exposure.

KEY TERMS — cohort study, Hodgkin's disease, leukemia, lymphoma, neoplasms, occupational exposure.

Styrene is a major component of plastics and synthetic rubbers. Small amounts of styrene are found in foods kept in plastic containers and also in the urban atmosphere (1), while high exposure levels occur in the plastics industry (2). Increased mortality from non-Hodgkin's lymphoma, Hodgkin's disease, and leukemia has been indicated in some studies (3-7) but has not been found in all (8-12). The objective of this study was to evaluate the incidence of lymphohematopoietic malignancies among employees exposed to styrene in the reinforced plastics industry, in which particularly high styrene levels are recorded in an environment free of most other suspected carcinogens.

Subjects and methods

Companies

All companies producing reinforced plastics in Denmark at any point between the early 1960s and 1988 were traced with assistance from the Work Inspection Service, the National Institute of Occupational Health, the Danish Plastic Federation, the Unskilled and Semiskilled Worker's Union, local authorities for protection of the external environment, and the Central Bureau of Statistics and from an examination of telephone books (13). Altogether 552 companies were identified.

On the basis of independent reviews of the production by two dealers of plastic raw materials, the companies were classified as ever or never producing reinforced plastics. The companies unknown to the dealers were classified as having unknown production. The two dealers agreed independently on the production in all but 4 of 328 companies known by both of them (kappa 0.94).

The companies were classified in a similar manner according to information on production given by 368 employers responding to a postal questionnaire, to which 184 employers did not reply. The employers and dealers agreed on the production for 281 out

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of the 309 companies known by the dealers and mentioned in the questionnaires (kappa 0.72) (table 1).

Most of the companies producing reinforced plastics were boat yards or manufacturers of containers produced by hand lamination. According to the dealers the companies not involved in the production of reinforced plastics were producing wooden boats ($N = 17$) or thermoplastics ($N = 19$) or were within the metal industry ($N = 17$) or were dealers of reinforced plastics goods ($N = 31$).

The companies were all rather small. Fifty percent had an average work force of fewer than five employees. Fifty percent of the companies were closed by the end of the study (1989).

Subjects

All employees of the 552 companies were identified by means of unique personal identification numbers in the Supplementary Pension Fund, which has administered a pension system for all Danish wage earners since 1964. A total of 53 720 male workers employed at any point between 1964 and 1988 and resident in Denmark after 1 January 1970 was included in the study. (Six employees with invalid personal identification numbers were not included.) According to the dealers this figure represented over 90% of all reinforced plastics workers in Denmark between 1964 and 1988. Female workers ($N = 10 799$) were excluded from the study since the majority were not involved in the production of reinforced plastics.

According to the dealers' classification of the companies each worker was categorized into one of the following exposure categories (in order of priority): (i) exposed: ever employed in a company producing reinforced plastics during a period of production, (ii) unexposed: employed in a company never producing reinforced plastics or in a company producing reinforced plastics but only outside years of production, (iii) exposure unknown: employed in a company with unknown production only. According to this

classification 36 525 male workers were classified as exposed (table 1). Similar categories were constructed from the employers' classifications.

For the exposed employees the first and last year of exposed employment was recorded, and for all the other workers the first and last year of any employment was recorded. Duration of employment was calculated from the amount paid each year by the employers to each employee's account in the Supplementary Pension Fund. For the exposed workers only payments recorded during exposed employment were included. For 60% of the workers the payments corresponded to less than 12 months of employment.

For each company the dealers estimated the proportion of all employees working in the production of reinforced plastics. For 99 companies the estimate was between 1 and 49% of a work force of 23 688 employees, and for 287 companies it was between 50 and 100% of a work force of 12 837 employees. If a mean proportion of 25% is applied for the companies employing less than 50% reinforced plastics workers and a mean proportion of 75% is applied for the companies employing 50% or more, then an estimated total of 15 550 $[(0.25 \cdot 23 688) + (0.75 \cdot 12 837)]$ reinforced plastics workers is obtained, corresponding to 43% of all employees of companies producing reinforced plastics.

A total of 292 employers reported the proportion of all workhours spent producing reinforced plastics in their company. This measure was assumed also to indicate the employees' probability of working with reinforced plastics. The dealers' estimates correlated well with the employers' reports (figure 1).

The 12 837 male workers of companies with an estimated proportion of reinforced plastics workers above 50% were included in an international cohort study of cancer mortality among workers of the reinforced plastics industry (14).

In the Central Population Register, vital status for all workers was reported by 31 December 1989 (table 2). In the Danish Cancer Register 1915 newly diagnosed cancer cases, including 161 cases of lym-

Table 1. Exposure classification of 53 720 male employees in the Danish reinforced plastics industry and similar industries according to reports from employers and dealers on the production of 552 employing companies.

Production according to dealers	Production according to employers ^a							
	Reinforced plastics		No reinforced plastics		No reports		Total	
	Companies (N)	Employees (N)	Companies (N)	Employees (N)	Companies (N)	Employees (N)	Companies (N)	Employees (N)
Reinforced plastics	233	26 784	14	1 774	139	7 967	386	36 525
No reinforced plastics	14	1 013	48	12 357	22	884	84	14 254
Company unknown	30	721	29	1 716	23	504	82	2 941
Total	277	28 518	91	15 847	184	9 355	522	53 720

^a Companies were classified according to ever or never producing reinforced plastics; employees were classified according to ever or never employment during the period of production of reinforced plastics.

Figure 1. Proportion of reinforced plastics workers, as estimated by two dealers of plastic raw materials, and the proportion of all workhours spent on production of reinforced plastics, as reported by the employers of 292 companies.

Table 2. Vital status of 53 720 male employees in the Danish reinforced plastics industry and similar industries in 1970–1989, as of 31 December 1989.

Vital status	Male employees (N)
Alive	48 454
Deceased	4 281
Emigrated	937
Disappeared	48
All included in follow-up	53 720
Employees with a lymphohematopoietic diagnosis	
Non-Hodgkin's lymphoma	61
Hodgkin's disease	24
Leukemia	61
Multiple myeloma	15

phohematopoietic malignancies, classified according to the seventh revision of the International Classification of Diseases (ICD-7) by the codes 200–205, were identified between 1 January 1970 and 31 December 1989.

Years at observation were counted from 1 January 1970 or 1 January the year following the first year of employment if 1970 or later to ensure that only cancer cases occurring after the start of exposure were included, as no information on day or month of employment was available. Follow-up continued until the date of death, emigration, disappearance, or the end of the study on 31 December 1989, whichever came first. A mean follow-up of 10.9 years with a range of 0 to 20 years and a total of 584 556 person-years were observed.

Measurements of styrene exposure

The Work Inspection Service collected 2473 personal air samples containing styrene from work sites in

Denmark between 1964 and 1988 as part of their surveillance routines (2). During 1964–1970, 1971–1975, and 1976–1988 the mean styrene levels were 180, 88, and 43 ppm, respectively. The level thus decreased significantly over time. Of the measurements, 1814 were sampled from 128 companies included in the study, but the identity of the sampled workers was not available. The mean annual level of styrene was therefore calculated for each of the 128 companies.

Altogether 9335 workers were employed in these companies during the year of measurement. These workers were selected for a separate analysis.

Statistics

Standardized incidence ratios (SIR) were calculated from a comparison of the number of malignancies observed in the study population with the number of expected cases according to the national incidence rates, standardized for gender, age, and year of diagnosis. Ninety-five percent confidence intervals (95% CI) were calculated according to the Poisson distribution (15). Internal comparisons were made for the incidence rates with Poisson regression models (16). In tests for linear trend, the exposure variables were treated as continuous variables.

Results

The overall cancer incidence for the 53 720 male employees equaled the expected number based on national incidence rates (observed 1915, SIR 1.02, 95% CI 0.97–1.07). The SIR values for Hodgkin's disease (observed 24, SIR 1.09, 95% CI 0.70–1.63) and multiple myeloma (observed 15, SIR 0.81, 95% CI 0.46–1.34) were close to 1. Non-Hodgkin's lymphoma and leukemia showed slightly nonsignificantly increased SIR values (observed 61, SIR 1.29, 95% CI 0.99–1.66 and observed 61, SIR 1.17, 95% CI 0.90–1.51, respectively).

In table 3, the SIR values are presented for lymphohematopoietic malignancies by the production and proportion of reinforced plastics workers of each company according to the dealers' reports. Among the exposed workers of companies producing reinforced plastics the SIR values for non-Hodgkin's lymphoma and leukemia were slightly higher than those obtained for the total study population (observed 42, SIR 1.33, 95% CI 0.96–1.80 and observed 42, SIR 1.22, 95% CI 0.88–1.65, respectively). Non-Hodgkin's lymphoma showed a significantly increased risk among employees of companies with 1–49% reinforced plastics workers. The increase was seen in particular during the first 10 years after the start of employment. For both Hodgkin's disease and leukemia the SIR values were higher for employees of companies with 50–100% reinforced plastics workers, but none of these risk estimates significantly exceeded 1. For Hodgkin's disease the in-

crease was confined to the first 10 years after start of employment, while for leukemia the increase was confined to the period of 10 years or more after the start of employment (observed 10, SIR 1.92, 95% CI 0.92—3.52). All lymphohematopoietic malignancies, except multiple myeloma, showed increased risks for workers of companies assumed to produce reinforced plastics but the production was unknown to the dealers. The estimates were based on small numbers and only non-Hodgkin's lymphoma showed a significantly increased SIR value, however, during the first 10 years of follow-up.

The risk of leukemia was significantly increased among the exposed workers starting employment in companies producing reinforced plastics during the 1960s. This was in particular the case among employees followed 10 years or more after the start of employment (observed 25, SIR 1.69, 95% CI 1.09—2.49) (table 4). Among the workers starting employment in the 1960s in a company with 50% or more reinforced plastics workers, an SIR of 2.02 (observed 6, 95% CI 0.74—4.40) was found (data not presented). The risk pattern for Hodgkin's disease by year of first employment was similar to that of leukemia,

but not significant. The occurrence of non-Hodgkin's lymphoma showed little difference across the three time periods. In the Poisson model the incidence ratio for leukemia showed a significantly declining trend during subsequent periods 1964—1970, 1971—1975, and 1976—1988 ($P = 0.02$). When time since first employment was included in the model, the slope was reduced to an insignificant value.

In table 5 the SIR values for lymphohematopoietic malignancies in exposed workers is presented according to the time since first employment and the duration of employment, as calculated from the contributions to the Supplementary Pension Fund. Non-Hodgkin's lymphoma showed increased SIR values within the first 10 years after the start of employment, while no increase in risk was seen when 10 years of latency was taken into account. A statistically significant increased risk of leukemia was found after 10 years of latency (observed 32, SIR 1.57, 95% CI 1.07—2.22). The increase was confined to workers employed for less than one year.

Direct comparisons with the unexposed population by Poisson regression modeling showed rate ratios close to the results presented.

Table 3. Standardized incidence ratios (SIR) of lymphohematopoietic malignancies in 1970—1989 for 53 720 male employees, by production of employing companies and the proportion of reinforced plastics workers within each company and time since first employment. (O = observed number of cases, E = expected number of cases, 95% CI = 95% confidence interval)

Production	Non-Hodgkin's lymphoma				Hodgkin's disease				Multiple myeloma				Leukemia				All lymphohematopoietic malignancies			
	O	E	SIR	95% CI	O	E	SIR	95% CI	O	E	SIR	95% CI	O	E	SIR	95% CI	O	E	SIR	95% CI
Companies not producing reinforced plastics																				
<10 years since first employment	5	5.27	0.95	0.31—2.21	4	3.71	1.08	0.29—2.76	1	1.78	0.56	0.01—3.13	5	5.81	0.86	0.28—2.01	15	16.73	0.90	0.50—1.48
≥10 years since first employment	10	8.04	1.24	0.60—2.29	2	2.32	0.86	0.10—3.11	2	3.68	0.54	0.07—1.96	8	9.30	0.86	0.37—1.70	22	23.55	0.93	0.59—1.41
Total	15	13.30	1.13	0.63—1.86	6	6.03	1.00	0.37—2.17	3	5.46	0.55	0.11—1.61	13	15.11	0.86	0.46—1.47	37	40.28	0.92	0.65—1.27
Companies producing reinforced plastics																				
1—49% of employees in reinforced plastics production																				
<10 years since first employment	19	8.08	2.35	1.42—3.67	5	5.71	0.88	0.28—2.04	4	2.83	1.41	0.39—3.62	6	9.09	0.66	0.24—1.44	34	25.96	1.31	0.91—1.83
≥10 years since first employment	17	13.77	1.23	0.71—1.98	4	4.10	0.98	0.27—2.50	4	5.88	0.68	0.19—1.74	22	15.16	1.45	0.91—2.20	47	39.3	1.20	0.88—1.59
Total	36	21.86	1.65	1.15—2.28	9	9.80	0.92	0.42—1.74	8	8.72	0.92	0.40—1.81	28	24.25	1.15	0.77—1.67	81	65.26	1.24	0.99—1.54
50—100% of employees in reinforced plastics production																				
<10 years since first employment	2	4.60	0.43	0.05—1.57	6	3.34	1.80	0.66—3.91	2	1.43	1.40	0.17—5.05	4	4.92	0.81	0.22—2.08	14	14.41	0.97	0.53—1.63
≥10 years since first employment	4	5.06	0.79	0.22—2.02	1	1.62	0.62	0.02—3.44	2	1.97	1.02	0.12—3.67	10	5.22	1.92	0.92—3.52	17	14.00	1.21	0.71—1.94
Total	6	9.66	0.62	0.23—1.35	7	4.96	1.41	0.57—2.91	4	3.39	1.18	0.32—3.02	14	10.14	1.38	0.75—2.32	31	28.41	1.09	0.74—1.55
All companies producing reinforced plastics																				
Total	42	31.52	1.33	0.96—1.80	16	14.76	1.08	0.62—1.76	12	12.11	0.99	0.51—1.73	42	34.39	1.22	0.88—1.65	112	93.67	1.20	0.98—1.44
Production of company unclassified																				
<10 years since first employment	4	1.04	3.86	1.05—9.85	1	0.76	1.31	0.03—7.33	—	0.31	0.00	0.00—11.90	2	1.10	1.82	0.22—6.57	7	3.23	2.16	0.87—4.47
≥10 years since first employment	—	1.34	0.00	0.00—2.75	1	0.40	2.50	0.06—13.92	—	0.54	0.00	0.00—6.83	4	1.43	2.78	0.76—7.16	5	3.76	1.33	0.43—3.10
Total	4	2.38	1.68	0.46—4.30	2	1.17	1.71	0.21—6.17	—	0.86	0.00	0.00—4.29	6	2.53	2.37	0.87—5.16	12	7.00	1.71	0.89—2.99

Table 4. Standardized incidence ratios (SIR) of lymphohematopoietic malignancies in 1970–1989 for 36 525 male employees of companies producing reinforced plastics, by year of first employment. (O = observed number of cases, E = expected number of cases, 95% CI = 95% confidence interval)

First year of employment	Non-Hodgkin's lymphoma				Hodgkin's disease				Multiple myeloma				Leukemia				All lymphohematopoietic malignancies			
	O	E	SIR	95% CI	O	E	SIR	95% CI	O	E	SIR	95% CI	O	E	SIR	95% CI	O	E	SIR	95% CI
1964–1970																				
< 10 years since first employment	7	3.48	2.01	0.81–4.14	4	2.56	1.56	0.42–4.00	3	1.62	1.85	0.38–5.41	5	4.70	1.06	0.35–2.48	19	12.51	1.52	0.91–2.37
≥ 10 years since first employment	14	12.93	1.08	0.59–1.82	5	3.64	1.37	0.45–3.21	3	5.89	0.51	0.11–1.49	25	14.83	1.69	1.09–2.49	47	37.65	1.25	0.92–1.66
Total	21	16.40	1.28	0.79–1.96	9	6.20	1.45	0.66–2.76	6	7.51	0.80	0.29–1.74	30	19.53	1.54	1.04–2.19	6	50.16	1.32	1.02–1.67
1971–1975																				
< 10 years since first employment	5	3.51	1.42	0.46–3.32	3	2.61	1.15	0.24–3.36	3	1.31	2.29	0.47–6.69	2	4.22	0.47	0.06–1.71	13	11.76	1.11	0.59–1.89
≥ 10 years since first employment	5	4.93	1.01	0.33–2.37	—	1.63	0.00	0.00–2.26	3	1.70	1.76	0.36–5.16	7	4.79	1.46	0.59–3.01	15	13.16	1.14	0.64–1.88
Total	10	8.44	1.19	0.57–2.18	3	4.24	0.71	0.15–2.07	6	3.01	1.99	0.73–4.34	9	9.01	1.00	0.46–1.90	28	24.92	1.12	0.75–1.62
1976–1988																				
< 10 years since first employment	9	5.71	1.58	0.72–2.99	4	3.88	1.03	0.28–2.64	—	1.32	0.00	0.00–2.79	3	5.10	0.59	0.12–1.72	16	16.10	0.99	0.57–1.61
≥ 10 years since first employment	2	0.98	2.04	0.25–7.37	—	0.78	0.00	0.00–4.73	—	0.26	0.00	0.00–14.19	—	0.76	0.00	0.00–4.85	2	2.49	0.80	0.10–2.90
Total	11	6.69	1.64	0.82–2.94	4	4.33	0.92	0.25–2.37	—	1.59	0.00	0.02–3.50	3	5.85	0.51	0.11–1.50	18	18.59	0.97	0.57–1.53

Table 5. Standardized incidence ratios (SIR) of lymphohematopoietic malignancies in 1970–1989 for 36 525 male employees of companies producing reinforced plastics, by duration of employment^a and time since first employment. (O = observed number of cases, E = expected number of cases, 95% CI = 95% confidence interval)

Malignancy	Time since first employment							
	< 10 years				≥ 10 years			
	O	E	SIR	95% CI	O	E	SIR	95% CI
Non-Hodgkin's lymphoma								
< 1 year of employment	12	7.38	1.62	0.84–2.84	11	8.65	1.27	0.63–2.28
≥ 1 year of employment	9	5.30	1.70	0.78–3.22	10	10.18	0.98	0.47–1.81
Total	21	12.68	1.68	1.03–2.53	21	18.83	1.12	0.69–1.70
Hodgkin's disease								
< 1 year of employment	7	5.86	1.19	0.48–2.46	3	3.08	0.97	0.20–2.85
≥ 1 year of employment	4	3.20	1.25	0.34–3.20	2	2.64	0.76	0.09–2.74
Total	11	9.06	1.21	0.61–2.17	5	5.72	0.87	0.28–2.04
Multiple myeloma								
< 1 year of employment	2	2.18	0.92	0.11–3.17	5	3.09	1.62	0.53–3.78
≥ 1 year of employment	4	2.08	1.92	0.52–4.92	1	4.76	0.21	0.01–1.17
Total	6	4.26	1.41	0.52–3.07	6	7.85	0.76	0.28–1.66
Leukemia								
< 1 year of employment	7	7.93	0.88	0.35–1.82	20	8.55	2.34	1.43–3.61
≥ 1 year of employment	3	6.07	0.49	0.10–1.44	12	11.84	1.01	0.52–1.77
Total	10	14.00	0.71	0.34–1.31	32	20.33	1.57	1.07–2.22
All lymphohematopoietic malignancies								
< 1 year of employment	28	23.56	1.19	0.79–1.72	39	23.57	1.65	1.18–2.26
≥ 1 year of employment	20	16.80	1.19	0.73–1.84	25	29.72	0.84	0.54–1.24
Total	48	40.36	1.19	0.88–1.58	64	53.29	1.20	0.92–1.53

^a Duration of employment was estimated from the payment records of the Supplementary Pension Fund.

In the subpopulation of employees of companies for which styrene measurements were available, Hodgkin's disease showed an SIR of 2.48 (observed 5, 95% CI 0.80–5.78) for employees of companies with a recorded mean styrene level above 50 ppm and an SIR of 1.37 (observed 2, 95% CI 0.17–4.95) for employees of companies with a mean level below 50 ppm. The SIR values of the other lymphohematopoietic malignancies were not increased in

this population and did not correlate with increasing styrene level (data not shown).

Discussion

A slightly increased incidence of leukemia was found among male employees in the reinforced plastics industry. The incidence was significantly increased among employees in the early years of production.

When account was taken for an appropriate latency period, a significantly increased risk was also observed. The estimates were slightly higher for workers employed in companies where the majority worked with reinforced plastics than in companies where less than 50% were employed in this production. No increase was, on the other hand, seen in the subpopulation of workers of companies with available measurements of styrene. The risk patterns of non-Hodgkin's lymphoma and Hodgkin's disease were less consistent. No indications of an increased risk of multiple myeloma were found.

Among the workers of the 82 companies unknown to the dealers, increased risks for leukemia and lymphomas were observed. We traced the owners of 59 of these companies, and 30 verified a production of reinforced plastics, while 29 denied ever having produced this material. The risk of lymphomas and leukemia was increased for the exposed workers in the 30 companies (observed 4, SIR 3.33, 95% CI 0.91—8.46), which may have been due to higher exposure levels of styrene in less known companies. On the other hand, an increased risk for leukemia (observed 5, SIR 3.63, 95% CI 1.18—8.46), but no excess for lymphomas, was found for the presumably unexposed workers of the 29 companies. This finding could indicate an aggregation of nonoccupational risk factors for leukemia among workers in less known companies.

Only a few women took part in the production of reinforced plastics according to both the employers and the dealers of plastic raw materials, and female employees were not included. We have earlier presented a significantly reduced risk of non-Hodgkin's lymphoma (observed 1, SIR 0.16, 95% CI 0.00—0.88) for the women of this population, while the observed number of cases of Hodgkin's disease, multiple myeloma, and leukemia among the women were close to the expected values based on the national rates (13).

Almost all of the employees of the Danish reinforced plastics industry between 1964 and 1988 were included in this study, and it can be assumed that virtually all diagnosed cancers were involved. Selection bias was unlikely since the loss to follow-up was negligible (less than 2%) and mainly due to emigration.

Exposure data was available only at a company level, and even though most of the companies were small, not all employees were exposed. The dealers estimated that an average of about 40% of the workers classified as exposed actually had worked producing reinforced plastics, and from this estimate we can expect to detect only about 40% of the "true" excess rate ratios (17). Exposure data were collected from several independent sources, and agreement was good. However, a threefold excess risk for non-Hodgkin's lymphoma and leukemia was seen for 1774 employees of companies producing reinforced plastics according to the dealers but not according

to the employers. This finding may indicate differential reporting of exposure by a few employers. For this reason the analysis was restricted to the exposure data obtained from the dealers.

Few causes of lymphohematopoietic malignancies are known. Benzene and radiation cause leukemia but are not used in the reinforced plastics industry. Confounding by factors related to occupational career and the life-styles of the employees is a possibility (18), but perhaps unlikely, since internal comparisons among workers within the enrolled companies did not change the results very much.

The finding of an increased risk of leukemia among short-term employees (<1 year) but not among long-term employees (≥ 1 year) does not appear to corroborate a causal association, given that duration of employment calculated from the payment records in the Supplementary Pension Fund indicates dose of exposure. The phenomenon of high risk for short-term workers is well known from other occupational cancer studies and is explained by a higher mobility among short-term workers. This higher mobility increases their probability for attracting carcinogenic exposures in other industries or for having more unfavorable life-styles (19). Although this explanation is a possibility, it is perhaps less likely since a comparison between the exposed and unexposed short-term employees did not yield lower rate ratios for leukemia (observed 27, rate ratio 1.89, 95% CI 0.78—4.59).

The contributions to the Supplementary Pension Fund were assumed to give the most precise estimates of duration of employment, as no exact employment dates were known. When we instead estimated duration of employment by the extent of employment (the difference between last and first year of employment), the risk difference between the short-term and long-term employees diminished, but the same pattern was found. However, the estimates of duration of employment from the Supplementary Pension Fund did not correlate well with information on duration of employment obtained in a questionnaire from a sample of 671 employees of eight companies. According to the data, as much as 40% of the workers classified as short-term workers by the Supplementary Pension Fund were classified as long-term workers in the questionnaire, while 13% of the long-term workers were classified as short-term workers.

The risk estimates observed for employees of companies with available measurements of styrene showed inconsistency with the results obtained for the total exposed population, except for Hodgkin's disease. The findings could be due to random variation, as the wide confidence interval indicates, or they could be a result of a high proportion of long-term workers (according to the Supplementary Pension Fund) in the cross-sections of workers employed during years of recorded measurements (length-biased sampling). The short-term workers showed an

SIR value for leukemia of 2.63 (observed 3, 95% CI 0.54—7.69) when a 10-year latency period was considered.

The mean follow-up of 10.9 years limited the ability to elucidate fully the risks of lymphohematopoietic malignancies and may in part explain why increased rate ratios were found mainly among the exposed in the early years.

The reinforced plastics industry is free of most suspected carcinogens other than styrene, which was the reason for selecting this industry for the study. During the 1960s the exposure levels to styrene were high, and the year of first exposure is probably the best indicator of exposure level to styrene. A small but significantly increased risk of leukemia was found for workers of the 1960s, and the risk estimate increased when an appropriate latency period was implemented. On the other hand, the data did not fit the expected dose-response pattern based on duration of employment, perhaps because of an inappropriate proxy measure of "dose."

In conclusion, the study shows an increased risk of leukemia for workers in the early phase of the reinforced plastics industry in Denmark. If this association is not due to chance or confounding, the most likely cause is styrene exposure. The lack of individual work histories weakens, however, the strength of the conclusions to be drawn. Efforts should be made to collect individual exposure histories in large-scale studies to clarify the presented findings.

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References

1. World Health Organization (WHO). Styrene. Geneva: WHO, 1983. Environmental health criteria, no 26.
2. Jensen AA, Breum NO, Bacher J, Lynge E. Occupational exposures to styrene in Denmark 1955—88. *Am J Ind Med* 1990;17:593—606.
3. Nicholson WJ, Selikoff IJ, Seidman H. Mortality experience of styrene-polystyrene polymerization workers: initial findings. *Scand J Work Environ Health* 1978;4 suppl 2:247—52.
4. Meinhardt TJ, Lemen RA, Crandall MS, Young RJ. Environmental epidemiologic investigation of the styrene-butadiene rubber industry: mortality patterns with discussion of the hematopoietic and lymphatic malignancies. *Scand J Work Environ Health* 1982;8:250—9.
5. Hodgson JT, Jones RD. Mortality of styrene production, polymerization and processing workers at a site in northwest England. *Scand J Work Environ Health* 1985;11:347—52.
6. Bond GG, Bodner KM, Olsen GW, Cook RR. Mortality among workers engaged in the development or manufacture of styrene-based products — an update. *Scand J Work Environ Health* 1992;18:145—54.
7. Santos-Burgoa C, Matanoski GM, Zeger S, Schwartz L. Lymphohematopoietic cancer in styrene-butadiene polymerization workers. *Am J Epidemiol* 1992;136:843—54.
8. Frentzel-Beyme R, Thiess AM, Wieland R. Survey of mortality among employees engaged in the manufacture of styrene and polystyrene at the BASF Ludwigshafen works. *Scand J Work Environ Health* 1978;4 suppl 2:231—9.
9. Matanoski GM, Santos-Burgoa C, Schwartz L. Mortality of a cohort of workers in the styrene-butadiene polymer manufacturing industry (1943—1982). *Environ Health Perspect* 1990;86:107—17.
10. Okun AH, Beaumont JJ, Meinhardt TJ, Crandall MS. Mortality patterns among styrene-exposed boatbuilders. *Am J Ind Med* 1985;8:193—205.
11. Coggon D, Osmond C, Pannett B, Simmonds S, Winter PD, Acheson ED. Mortality of workers exposed to styrene in the manufacture of glass-reinforced plastics. *Scand J Work Environ Health* 1987;13:94—9.
12. Wong O. A cohort mortality study and a case-control study of workers potentially exposed to styrene in the reinforced plastics and composites industry. *Br J Ind Med* 1990;47:753—62.
13. Kolstad HA, Lynge E, Olsen J. Cancer incidence in the Danish reinforced plastics industry. In: Sorsa M, Peltonen K, Vainio H, Hemminki K, editors. Health hazards of butadiene and styrene. Lyon: International Agency for Research on Cancer (IARC), 1993. IARC scientific publications, no 127.
14. Kogevinas M, Ferro G, Andersen A, Bellander T, Biocca M, Coggon D, et al. Cancer mortality in a historical cohort study of workers exposed to styrene. *Scand J Work Environ Health* 1994;20:251—61.
15. Ispen J, Feigl P. Bancrofts introduction to biostatistics. 2nd ed. New York, NY: Harper and Row 1970:73—5.
16. Breslow NE, Day NE. Statistical methods in cancer research; vol II (The design and analysis of cohort studies). Lyon: International Organization for Research on Cancer (IARC), 1987. IARC scientific publications, no 82.
17. Plato N, Steineck G. Methodology and utility of a job-exposure matrix. *Am J Ind Med* 1993;23:491—502.
18. Brownson RC, Novotny TE, Perry MC. Cigarette smoking and adult leukemia. *Arch Intern Med* 1993;153:469—75.
19. Gilbert ES. Some confounding factors in the study of mortality and occupational exposures. *Am J Epidemiol* 1982;116:177—88.

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