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Mortality of United Kingdom acrylonitrile workers — an extended and updated study

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The mortality experience of 2763 men employed between 1950 and 1978 for at least 1 year at 6 factories involved in the polymerization of acrylonitrile and the spinning of acrylic fiber was followed to the end of 1991. Overall, cancer deaths did not exceed the expected numbers. There were, however, excess cancer deaths among the workers in the jobs more highly exposed to acrylonitrile. The excesses did not reach conventional levels of statistical significance apart from an excess of lung cancer among workers under 45 years of age. Detailed analyses provided no consistent support for a causal association between acrylonitrile exposure and carcinogenesis. The limitations of the study, including a lack of information on smoking habits and very limited estimates of acrylonitrile exposure, need to be borne in mind.

Key terms acrylic fiber, cancer occupational cohort, polymerization.

In 1978, following consultation between the Health and Safety Executive (HSE) and the Chemical Industries Association, a study was set up to investigate whether a carcinogenic risk existed for workers exposed to acrylonitrile in the United Kingdom (1). Exposures of workers to acrylonitrile have always been controlled because of its acute toxicity. The study was prompted by findings that acrylonitrile was carcinogenic in rats (2, 3) and by an epidemiologic study at a Du Pont plant in the United States which reported excesses of cancer, particularly lung cancer, for exposed workers (4).

The first phase of the study in the United Kingdom, reported by Werner & Carter (1) in 1981, looked at the mortality (up to 1978) of 1111 men employed at some time between 1950 and 1968 in either the polymerization of acrylonitrile or the spinning of acrylic fiber at 6 major sites. It found significant excesses of stomach cancer overall and also for men 55—64 years of age, and lung cancer was increased among men 15—44 years of age. Since the results of this study were judged to be inconclusive, it was resolved to extend the study both by enlarging the study population to include more recently exposed workers and by extending the period of follow-up. The present paper reports the results of the extended study.

Subjects and methods

The study population was enlarged by the addition of workers employed in polymerization or as spinners at some time between 1969 and 1978 (shown as "phase 2" in table 1). The factories (2 in England, 2 in Wales, 1 in Scotland, and 1 in Northern Ireland) provided work histories with dates of starting and leaving each job, the jobs being classified by the companies into the following categories: (i) polymerization worker, (ii) spinner, (iii) craftsman with possible acrylonitrile exposure (PAE), (iv) control laboratory worker, (v) other — possible acrylonitrile exposure, and (vi) other — no acrylonitrile exposure (AE).

However, the initial analysis of mortality in the combined populations of phases 1 and 2 showed a marked deficit of deaths for men who had worked in factory 5 (the biggest factory in terms of the number of men recruited into the study). This finding raised concern as to whether the population at this factory had been correctly ascertained. The factory was therefore visited by HSE staff, and the worker records were reviewed. Details of another 785 eligible workers first exposed in 1969—1978 came to light, and these were added to the study population. (They are included in the "phase 2" column of

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table 1. There was no obvious explanation for their being overlooked initially.) In addition, after discussions with the company, the jobs were recoded at this factory to a revised set of categories. The main change was that the majority of the workers originally coded as spinners (and therefore presumed to have had relatively high acrylonitrile exposure) were reclassified into a group called "end of line" workers (comprising dry finishers, plaiters, plaiter/packagers and quality assessors) with minimal or no exposure.

So that comparisons could be made of mortality by exposure across all factories, it was necessary to equate the revised job categories of factory 5 with the original classification used at the other factories. The *assumed* grouping is shown in table 2, but it is emphasized that the grouping had not been validated in comparisons of exposure measurements across factories. Indeed for the earlier years of the study there were no measurements available.

Table 3 shows the number of workers in each category by factory. (Some workers who did more than 1 job appear in more than 1 category). All workers in factories 1, 2, and 4 had some experience as polymer workers (a high-exposure job), as did 240 out of the 242 workers at factory 3. Not so clear from the table is that all the workers at factory 6 also had had some high acrylonitrile exposure, either as a polymer worker or as a spinner. This finding is in contrast to the total of 283 out of 2208 workers (12.8%) at factory 5 who had held both of these jobs.

Table 1. Study population by factory and phase of recruitment to the study.

Factory	Phase 1[a]	Phase 2[b]	Total
1	14	24	38
2	118	2	120
3	228	14	242
4	61	30	91
5	534	1674	2208
6	154	160	314

[a] First exposed in 1950—1968.
[b] First exposed in 1969—1978.

Table 2. Job category descriptions. (PAE = possible acrylonitrile exposure, AE = acrylonitrile exposure)

Job category	Exposure to acrylonitrile	Job description (factories 1,2,3,4,6)	Job description (factory 5)
1	High	Polymer worker	Control room worker
2	High	Spinner	Spinner
3	Other PAE	Craftsman	Maintenance
4	Other PAE	Control laboratory worker	Chemists (staff status)
5	Other PAE	Other PAE	Other PAE
6	Little or no AE	Other - no AE	Other - no AE
7	Little or no AE	Not applicable	End of line worker

Table 3. Number of workers who worked in each job category (1—7) by factory.[a] (PAE = possible acrylonitrile exposure, AE = acrylonitrile exposure)

Factory	Total	High[a]		Other PAE[a]			No or little AE[a]	
		1	2	3	4	5	6	7
1	38	38	-	-	2	2	5	-
2	120	120	-	-	-	94	44	-
3	242	240	-	-	-	2	108	-
4	91	91	-	-	-	4	4	-
5	2208	143	140	687	55	180	250	1367
6	314	159	199	1	16	29	79	-
Total	3013	791	339	688	73	311	490	1367

[a] For a description of the job category see the corresponding number in table 2.

Ascertainment of vital status and coding of causes of deaths

Identification details for the 3013 men were sent for tracing to the National Health Service Central Register (NHSCR) maintained by the Office of Population Censuses and Surveys in England and Wales, the General Register Office for Scotland, or to the Central Services Agency in Northern Ireland. Altogether 2928 (97%) were successfully traced, although a small proportion of these (under 2%) had emigrated. For these men the determination of vital status was limited to the knowledge that they were alive at the date of emigration. For those who had died, a copy of the death certificate, giving the date of death and the underlying cause, coded according to the International Classification of Diseases (ICD), was sent to HSE. The coding was done according to the ICD revision that was in force for national statistical purposes at the time of death, except that the small number of deaths (approximately 5%) that occurred before 1968 were retrospectively coded to the 8th rather the 7th revision (consistently with the national rates used in this study to calculate expected deaths). Thus the deaths of workers in this study were coded by the 8th revision up to the end of 1978 and by the 9th revision from 1979 onwards. For those workers who were alive at the time of tracing, records in the national registers were marked so that details of subsequent deaths could be forwarded to HSE.

Ascertainment of length of employment and analysis population

The employment details for each worker were used to calculate the length of time spent in each job category. However almost half (49.9%) of the workers had no known leaving date. In most cases, this lack of data stemmed from their having been employed at the time they were recruited into the study, and no arrangements were made to update their employment histories. Therefore leaving dates, where not recorded, were assigned as follows: (i) 31 December 1978, 65th birthday, or date of death or emigration, whichever came first, for workers exposed prior to 1969 (phase 1) and (ii) 31 December 1980, 65th birthday, or date of death or emigration,

whichever came first, for workers first exposed between 1969 and 1980 (phase 2).

As a result, 22 workers were assumed to have retired on reaching 65 years of age, 12 to have died during employment, and 3 to have terminated employment on emigration. The remaining workers were given fixed leaving dates of 31 December 1978 or 31 December 1980 according to their phase of recruitment into the study. For workers actually employed longer, this procedure was effectively equivalent to assuming that acrylonitrile exposure from around 1980 on was negligible when compared with earlier exposure. The plausibility of this assumption in relation to the reduction of control limits is discussed in the Discussion section. The effects of an alternative set of assumptions with later leaving dates are described in the Results section.

Of the initial sample population, 85 cases could not be traced and were excluded from the mortality analysis. In addition 165 workers with an actual or estimated length of employment of less than 1 year were also excluded, leaving an analysis population of 2763 workers.

Calculation of expected deaths

National death rates for England and Wales derived from mortality and population data provided by the Office of Population Censuses and Surveys were used to calculate expected deaths at all of the factories except the Scottish factory, for which Scottish rates were used. (No rates were available for Northern Ireland to allow a more local analysis for the factory there.) The number of deaths expected for each cause was calculated by applying these rates to the person-years at risk in each 5-year age group during the periods 1968—1972, 1973—1978, 1979—1984, and 1985—1991. Mortality rates for 1968—1972 (8th revision ICD) were applied for periods prior to 1968.

The calculation of expected deaths and the comparison of observed and expected mortality was carried out using the Occupational Cohort Mortality Analysis Program (5). The person-years at risk or period of follow-up was calculated for each person from 1 year after the start of employment until date of emigration, date of death or 31 December 1991, whichever was the earliest. There was a total of 63 058 person-years at risk in the study, of which 72% were from factory 5. The majority (53%) of the person-years was at ages <45, with 26%, 15%, and 6% falling into the 45—54, 55—64, and ≥65 age groups, respectively.

The standardized mortality ratios (SMR) were calculated in the normal manner and 95% confidence intervals (95% CI) for the SMR values were calculated under the assumption that the observed number of deaths followed a Poisson distribution. The results were described as "significant" when the SMR of 100 was outside the 95% CI. A comparison of the SMR values was carried out using the method described by Berry (6)

Possible trends were examined for the SMR by fitting linear regression functions to the log of the SMR using the GLIM modeling package (7), the statistical significance of the slope parameter being tested in the usual way by comparing the reduction in the scaled deviance with a chi-square distribution with 1 degree of freedom.

Exposure to acrylonitrile

No exposure measurements were available for the earlier years covered by the study. Up to 1979, acrylonitrile exposure was subject to a threshold limit value of 20 ppm [8-hour time-weighted average (TWA)]. In that year the Health and Safety Commission, in view of concern about possible carcinogenicity, issued a statement that, in accordance with general policy on toxic substances, exposure should be reduced to a level as low as reasonably practicable, with the objective of working within a control limit of 2 ppm (8-hour TWA) by about 1981. The statement provided for a staged reduction of limits in the interim period, with a control limit of 5 ppm immediately and 4 ppm from the first quarter of 1980.

The earliest measured exposures referred to the late 1970s and gave mean values ranging from 0.4 to 2.7 ppm (8-hour TWA) for polymer workers and spinners at the various factories in this study, with minimums ranging from nil to 0.2 ppm and maximums from 2 to 20 ppm (8-hour TWA).

At factory 5, for the period before personal exposure measurements were available, the works' chemist prepared estimates of exposure levels using recorded measurements of concentrations of unreacted monomer in the spinning dope, adjusting the estimates to match personal monitoring measurements taken from 1978 on. This admittedly approximate method was believed by him to be the best available way of estimating earlier exposures. It gave mean estimates of from 2 to 7 ppm (8-hour TWA) for spinners in the period from 1958 to 1977.

Results

Overall there was a deficit in mortality for the combined analysis population, reflecting a significant deficit in circulatory disease deaths and deficits for most other causes (table 4). All cancers combined showed a deficit, and for most individual cancer sites (including lung and stomach) the observed numbers were close to the expected.

An analysis by factory (tables 5 and 6) showed that there was still a deficit in overall mortality at factory 5, even after the reascertainment of the study population at this factory (table 6). Indeed the deficit in the total study population appeared to be almost entirely determined by the deficit at this factory, the all-cause mortality at the other factories combined being close to the expected number. For all cancers combined, there was a significant deficit

Table 4. Mortality of the total analysis population by cause. (O = observed number of deaths, E = expected number of deaths, SMR = standardized mortlity ratio)

Cause of death	O	E	SMR
All causes	409	485.5	84.2**
All malignant neoplasms	121	137.12	88.2
Stomach	11	11.44	96.2
Large intestine - not rectum	11	8.75	125.7
Rectum	6	5.99	100.2
Trachea, bronchus & lung	53	51.54	102.8
Genitourinary organs	12	14.85	80.8
Lymphatic & hematopoietic	5	10.02	49.9
Endocrine,nutritional & metabolic diseases	5	5.79	86.4
Circulatory disease	200	232.2	86.1*
Ischemic heart disease	151	167.6	90.1
Cerebrovascular disease	27	33.86	79.7
Respiratory disease	31	41.43	74.8
Bronchitis	13	12.15	107.0
Diseases of the digestive system	8	13.8	58.0
Suicides & violence	11	12.87	85.5

*Significant at 5% level, ** significant at 1% level.

at factory 5 (SMR 76.3, 95% CI 59.5—96.4), compared with a nonsignificant excess at the other factories combined (SMR 112.2, 95% CI 83.5—147.5). These factories combined also showed nonsignificant excesses of lung and stomach cancer, although it was difficult to interpret the figures at individual factories because of the smallness of the numbers.

When the workers were grouped according to the highest of the 3 exposure categories (high, other, and little or no exposure) (table 7), mortality from each of the examined causes other than respiratory disease was higher in the high-exposure group than in the other 2 groups. However, only stomach cancer showed a clear and statistically significant trend across the 3 groups, and the excesses of cancer in the high-exposure group were not significant when considered in isolation. For lung cancer the SMR was lowest in the middle ("other exposure") group. (Workers were grouped into the high or other group if they had worked at least a year in the relevant jobs; 12 workers who had worked for less than a year in any group individually were entered into the lowest category.)

Because of the way in which the job categories in the study cohort were very unevenly distributed across the factories (which would lead to likely confounding of job and factory differences), the analyses which follow have been restricted to the "high-exposure" group (those who had worked for at least a year as polymer workers or spinners). There were still some differences in mortality between factory 5 and the group of the other factories combined (table 8). The "other factories" group showed overall mortality close to expected, and a not statistically significant excess of cancer (50 observed compared with 40.5 expected deaths from all cancers, 23 observed compared with 15.7 expected deaths from lung cancer). Factory 5

Table 5. Mortality by factory. (O = observed number of deaths, E = expected number of deaths, SMR, standardized mortality ratio)

Cause of death	Factory 1			Factory 2			Factory 3			Factory 4			Factory 5			Factory 6			P-value[a]
	O	E	SMR	O	E	SMR	O	E	SMR	O	E	SMR	O	E	SMR	O	E	SMR	
All causes	3	5.7	52.6	26	24.8	104.8	89	83.1	107.1	10	6.5	153.4	246	319.1	77.1**	35	46.3	75.6	0.034*
All malignant neoplasms	2	1.7	118.3	9	7.0	128.2	23	22.8	101.1	1	1.8	55.2	70	91.7	76.3*	16	12.2	131.6	0.334
Stomach	-	0.1	0.0	2	0.6	339.0	4	2.1	188.7	-	0.1	0.0	4	7.5	53.4	1	1.0	104.2	0.317
Tachea, bronchus & lung	-	0.6	0.0	2	2.6	75.8	12	9.0	132.9	-	0.6	0.0	30	33.8	88.8	9	4.9	185.6	0.237
Circulatory disease	1	2.8	36.1	10	11.9	83.8	51	41.0	124.5	5	3.0	168.9	120	151.7	79.1**	13	21.9	59.4	0.036*
Respiratory disease	-	0.5	0.0	-	2.2	0.0	9	9.4	96.2	1	0.5	222.2	18	25.9	69.5	3	3.1	95.8	0.348

[a] For test of homogeniety.
*Significant at 5% level, ** significant at 1% level.

Table 6. Comparison of mortality at factory 5 with that of the other factories. (O = observed number of deaths, E = expected number of deaths, SMR = standardized mortality ratio)

Cause of death	Factory 5			Other factories			P-value[a]
	O	E	SMR	O	E	SMR	
All causes	246	319.1	77.1**	163	166.4	97.9	0.019*
All malignant neoplasms	70	91.7	76.3*	51	45.4	112.2	0.039*
Stomach	4	7.5	53.4	7	4.0	177.2	0.05*
Trachea, bronchus & lung	30	33.8	88.8	23	17.8	129.4	0.178
Circulatory disease	120	151.7	79.1**	80	80.5	99.3	0.118
Respiratory disease	18	25.9	69.5	13	15.6	83.4	0.617

[a] For test of homogeniety.
*Significant at 5% level, ** significant at 1% level.

had a deficit in overall mortality, with cancer deaths near the expected numbers.

The analysis by age group (table 9) did not show any obvious trends, but there was a significant excess of lung cancer in the 15- to 44-year age group (5 deaths, 0.8 expected, SMR 609.8, 95% CI 198.0—1423.0). The 5 deaths from lung cancer in relatively young men were not all from 1 factory. There were 2 from each of factories 3 and 6 and 1 from factory 2.

The analysis by period when first exposed to high levels showed a tendency for the men more recently exposed to have lower SMR values for all causes and for circulatory disease mortality (table 10). However the SMR values for all cancers showed some indication of an opposite trend, being higher for those with more recent first exposure. There was a statistically significant excess of lung cancer for the most recent exposure group (those first exposed in 1969 or later). Of the 5 workers who died of lung cancer at under 45 years of age, one was first exposed in the pre-1960 period, 2 in 1960—1968, and 2 in the post-1968 period.

The analysis by time interval from first exposure to death showed a significant tendency for the SMR values for all causes and circulatory diseases to increase with time

Table 7. Mortality by highest level of exposure. (PAE = possible acrylonitrile exposure, AE = acrylonitrile exposure, O = observed number of deaths, E = expected number of deaths, SMR = standardized mortality ratio)

Cause of death	Highest exposure level									Regression analysis		
	High			Other PAE			No or little AE					
	O	E	SMR	O	E	SMR	O	E	SMR	P-value	Estimate of slope	Standard error
All causes	170	181.2	93.8	97	124.7	77.8*	142	179.6	79.1**	0.126	-0.088	0.058
All malignant neoplasms	58	50.1	115.8	22	35.9	61.2*	41	51.12	80.2	0.058	-0.202	0.107
Stomach	7	4.2	166.3	3	2.9	102.7	1	4.31	23.2	0.028*	-0.845	0.425
Trachea, bronchus & lung	27	19.1	141.1	7	13.3	52.6	19	19.1	99.5	0.201	-0.205	0.162
Circulatory disease	81	86.9	93.2	49	59.1	83.0	70	86.25	81.2	0.392	-0.070	0.082
Respiratory disease	11	15.7	70.2	7	10.0	69.9	13	15.76	82.5	0.687	0.083	0.207

*Significant at 5% level, ** significant at 1% level.

Table 8. Comparison of mortality in factory 5 with that of the other factories for the workers employed in high-exposure jobs for ≥1 year. (O = observed number of deaths, E = expected number of deaths, SMR = standardized mortality ratio)

Cause of death	Factory 5			Other factories		
	O	E	SMR	O	E	SMR
All causes	23	32.3	71.1	147	148.9	98.7
All malignant neoplasms	8	9.6	83.6	50	40.5	123.5
Stomach	-	0.7	0.0	7	3.4	205.9
Trachea, bronchus & lung	4	3.4	117.6	23	15.7	146.5
Circulatory disease	13	15.4	84.6	68	71.5	95.1
Respiratory disease	-	2.1	0.0	11	13.6	80.9

Table 9. Mortality of the workers exposed to high levels of acrylonitrile by age group. (O = observed number of deaths, E = expected number of deaths, SMR = standardized mortality ratio)

Cause of death	Age group												P-value[a]
	15—44 years			45—54 years			55—64 years			≥65 years			
	O	E	SMR	O	E	SMR	O	E	SMR	O	E	SMR	
All causes	18	19.0	94.0	35	41.4	84.5	62	59.5	104.2	55	59.8	91.9	0.786
All malignant neoplasms	8	3.8	213.3	9	11.0	81.5	25	18.5	134.9	16	16.5	97.2	0.188
Stomach	1	0.3	357.1	1	0.9	107.5	4	1.6	256.4	1	1.4	69.9	0.502
Trachea, bronchus & lung	5	0.8	609.8**	3	4.1	73.7	9	7.8	115.1	10	6.4	157.0	0.029*
Circulatory disease	8	6.3	127.8	16	20.5	78.2	26	29.8	87.2	31	30.0	103.4	0.641
Respiratory disease	1	1.0	102.0	2	2.4	84.7	6	4.8	126.3	2	7.5	26.7	0.207

[a] For test of homogeniety.
*Significant at 5% level, ** significant at 1% level.

Table 10. Mortality of the workers exposed to high levels of acrylonitrile by year of first exposure. (O = observed number of deaths, E = expected number of deaths, SMR = standardized mortality ratio)

Cause of death	Year of first exposure									P-value[a]
	Pre-1960			1960—1968			1969 on			
	O	E	SMR	O	E	SMR	O	E	SMR	
All causes	71	70.1	101.3	75	82.3	91.1	24	27.3	88.0	0.756
All malignant neoplasms	20	19.1	104.8	27	23.3	116.0	11	7.4	148.6	0.659
Stomach	4	1.8	224.7	2	1.9	107.0	1	0.6	181.8	0.674
Trachea, bronchus & lung	10	7.6	132.3	10	8.9	112.0	7	2.6	270.3*	0.220
Circulatory disease	37	34.7	106.8	35	39.6	88.3	9	12.2	73.6	0.523
Respiratory disease	5	8.0	62.3	6	6.0	100.8	-	1.6	0.0	0.222

[a] For test of homogeniety.
*Significant at 5% level.

Table 11. Mortality of the workers exposed to high levels of acrylonitrile by time since first exposure. (O = observed number of deaths, E = expected number of deaths, SMR = standardized mortality ratio)

Cause of death	Time since first exposure												Regression analysis		
	<5 years			5—10 years			10—15 years			>15 years			P-value	Estimate of slope	Standard error
	O	E	SMR	O	E	SMR	O	E	SMR	O	E	SMR			
All causes	6	12.8	47.0	10	19.6	50.9*	30	29.3	102.4	124	118.0	105.1	0.004**	0.263	0.098
All malignant neoplasms	3	2.9	103.1	7	4.9	142.0	7	7.9	88.5	41	34.0	120.4	0.905	0.018	0.149
Stomach	2	0.3	769.2	-	0.5	0.0	1	0.7	142.9	4	2.8	144.4	0.303	-0.361	0.333
Trachea, bronchus & lung	1	1	101.0	4	1.9	215.1	5	3.1	160.8	17	13.1	129.7	0.665	-0.092	0.207
Circulatory disease	2	5.1	38.9	1	8.9	11.2**	15	14.0	107.0	63	58.5	107.8	0.004**	0.436	0.172
Respiratory disease	1	0.9	114.9	-	1.4	0.0	3	2.2	134.5	7	11.1	63.3	0.847	-0.064	0.327

*Significant at 5% level, ** significant at 1% level.

Table 12. Mortality of the workers exposed to high levels of acrylonitrile by length of exposure. (O = observed number of deaths, E = expected number of deaths, SMR = standardized mortality ratio)

Cause of death	Length of exposure												Regression analysis		
	<5 years			5—10 years			10—15 years			>15 years			P-value	Estimate of slope	Standard error
	O	E	SMR	O	E	SMR	O	E	SMR	O	E	SMR			
All causes	52	69.8	74.5	53	50.0	106.1	49	42.6	115.1	16	16.8	95.4	0.082	0.131	0.075
All malignant neoplasms	19	19.0	100.3	17	13.7	123.9	16	12.1	132.6	6	4.9	122.2	0.468	0.093	0.128
Stomach	5	1.6	316.5	-	1.2	0.0	1	1.0	101.0	1	0.4	243.9	0.361	-0.374	0.429
Trachea, bronchus & lung	10	7.0	142.2	7	5.3	131.6	6	4.7	127.4	4	2.0	204.1	0.765	0.056	0.188
Circulatory disease	24	32.6	73.6	23	24.2	95.0	25	20.9	119.4	9	8.4	106.8	0.120	0.168	0.107
Respiratory disease	3	5.8	51.5	3	4.4	68.5	4	3.7	108.7	1	1.6	61.0	0.513	0.191	0.289

(table 11), but there was no clear trend for cancer. The workers dying from lung cancer at ages under 45 years had intervals of 6, 7, 9, 12, and 13 years between first exposure and death.

The analysis by length of exposure (subject to the assumptions noted earlier in respect to workers whose leaving dates were not recorded) (table 12) did not show any clear SMR trends for any of the causes examined.

To examine further the lengths of exposure of the younger men with lung cancer, we compared them with matched referents, drawn from the study cohort and born in the same years as the corresponding cases, alive at the time of the deaths of the cases; their employment subsequent to the case deaths was discounted in the comparisons to avoid bias. Of the 5 workers who died of lung cancer and had been employed in high-exposure jobs, 3

had longer exposures and 2 had shorter exposures than the means of their corresponding matched reference groups. The mean length of employment in the high-exposure jobs was 6.4 years for these 5 cases, compared with a mean of 5.0 years for their matched referents.

To test the effect of the assumptions about unknown leaving dates on the SMR analysis by length of employment, an alternative analysis was carried out that assumed the unknown leaving dates to be 31 December 1991, 65th birthday, date of death, or date of emigration, whichever was the soonest. (The entire study cohort with all 3 job-exposure subgroups was included in this analysis.) Although the average length of employment was appreciably increased by these assumptions, the analysis still did not show any clear trends or significant excesses of cancer mortality for workers with longer employment periods. These results are therefore not given in this report.

Discussion

The conclusions that can be drawn from this study are restricted by the limitations of the data. National mortality rates were used to compute expected deaths, and the use of local rates for the areas in which the factories were located would have led to some differences in the figures.

No information was collected on smoking habits although the absence of excess respiratory or circulatory disease mortality suggested that the levels of smoking were unlikely to have been markedly above average.

The available information on exposures was very limited. While it seems reasonable to assume a general downward trend in exposure, the lack of precise information and the fact that work histories were not updated after the workers were recruited into the study meant that length of employment up to 1978 or 1980 was used as a proxy measure of exposure. (An alternative model incorporating longer assumed employment made little difference to the pattern of the results of the mortality analyses.) It is difficult to say, on the basis of the available information, whether there were any major differences in exposure between factories, and the way in which the revised job-exposure categories at factory 5 were equated to the original classification used elsewhere has not been validated by cross-factory comparisons.

The excess of cancer in the high-exposure jobs was unfortunately confounded by the differences in the distribution of jobs between the different factories, making it difficult to determine whether the cancer excess was genuinely related to exposure or to other factors which varied between the sites. (Some analyses, see tables 8—12, have been restricted to the high-exposure job group to reduce the effects of such confounding, and because this group is one of the most intrinsic interest.) The tendency for factory 5 to have a lower SMR (both for cancer and other causes of death) than the other factories was apparent in the initial analyses with the phase 1 and 2 populations before the factory 5 population was reascertained; it continued to be apparent after the reascertainment and was also seen in the analyses restricted to workers in high-exposure jobs (table 8). This result suggests that the difference in mortality between factories was influenced by some factor or factors independent of acrylonitrile exposure, and it was not an artifact of the reascertainment of the cohort or the revision of the job classification for factory 5. The difference could have been connected with different patterns of recruitment over time; over three quarters of the study population in factory 5 had starting dates after 1968, compared with a quarter of those at other factories. It is therefore plausible that there could be a "healthy worker effect" among the more recently recruited workers at factory 5, while any such effect in the other factories would have had longer to wear off.

Since controls on acrylonitrile exposure have become more stringent over time, one would have expected any consequent effect on cancer mortality to have been more marked for workers first employed in the earlier time periods. In fact there were no clear trends, the all cancer and lung cancer SMR values being highest for workers first employed from 1969 on (table 10).

The analysis by time since first high exposure similarly did not show evidence of a carcinogenic effect since the SMR values did not increase with time; if anything the trends for lung and stomach cancer were in the opposite direction (table 11). Likewise, the analysis by length of employment in high-exposure jobs showed no clear indication of a cumulated dose-effect (table 12).

There was a noticeable excess of lung cancer for the men under 45 years of age in the high-exposure jobs, but these cases did not have their times of first exposure predominantly in the earliest periods when exposure was presumed to be higher. Their mean length of employment was only slightly longer than that of matched referents drawn from the study cohort. The excess of lung cancer among the younger men would have been slightly increased by the use of national death rates in 1968—1972 to estimate the expected number of deaths in earlier periods, as lung cancer mortality had slightly fallen for younger men between 1950 and 1968. The underestimate would, however, have been trivial, less than 0.1 case. Chance is a credible explanation, as an excess in this age group was not a priori hypothesis, and the finding results from a post hoc subgroup analysis.

Overall, this cohort of United Kingdom acrylonitrile workers did not appear to have been at increased mortality risk. Although there were indications of excess cancers in the more highly exposed jobs, more detailed analyses did not give consistent support to the hypothesis of a causal relationship between acrylonitrile exposure and cancer. The limitations of this study should be borne in mind, particularly the lack of information on smoking

habits and the very limited exposure data. The results should be seen in the context of those of other epidemiologic studies of workers exposed to acrylonitrile.

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