

Mortality and morbidity of workers exposed to acrylonitrile in fiber production

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This study assessed the risk of cancer mortality and incidence among 2559 employees exposed to acrylonitrile in the production of Orlon® at 2 plants in 1944–1991. Latency, duration of exposure, highest level of exposure ever experienced, and cumulative exposure were used as indicators of exposure. The average duration of exposure for the workers was 7.6 years with an average cumulative exposure of 57.6 ppm-years. Overall mortality was lower than expected in a comparison with the United States population and all DuPont employees [454 deaths, standardized mortality ratios (SMR) of 69 and 91, respectively]. All the cancer death ratios were lower than expected in a similar comparison. The SMR values for specific sites did not differ significantly from the expected values. Mortality from all cancers and from prostate, respiratory, and digestive cancer did not show any significantly associated increases or a consistent pattern suggestive of a dose-response. The cancer morbidity patterns were similarly unremarkable.

Key terms chemical exposures, epidemiology, industry studies, morbidity studies, mortality studies, occupational studies.

Acrylonitrile is a widely used, commercially important industrial chemical. At DuPont, increased interest in the potential adverse health effects of exposure to acrylonitrile dates to the late 1970s, approximately the same time when Maltoni demonstrated the carcinogenic activity of acrylonitrile in experimental animals (1). O'Berg conducted an epidemiologic study on acrylonitrile exposure among DuPont employees who worked from 1950 to 1967 in Orlon® production at the May plant in Camden, South Carolina (2). A preliminary analysis of cancer morbidity, as reported using DuPont register data, 1956–1975 (N=470 active and retired employees), showed excesses of colon and lung cancer incidence. The increased rate of colon cancer incidence did not persist when data for the entire cohort (N=1345) were analyzed (3). However, lung cancer incidence remained elevated, although the difference was not statistically significant. This cohort study was updated in 1985 by O'Berg et al (4) to include exposure through 1980 and to evaluate cancer incidence through 1983 and mortality through 1981. The results of this update revealed a nonsignificant elevation of lung cancer morbidity and mortality. In this update a

significant elevated incidence of prostate cancer (6 cases observed versus 1.8 expected) was observed based on DuPont incidence rates; however, no excess mortality from prostate cancer was observed. Exposure assessment in the O'Berg studies was based upon a qualitative indicator due to limited quantitative data. For this qualitative exposure measure, relative levels of exposure were estimated by a panel of knowledgeable employees.

A second DuPont epidemiologic investigation was conducted by Chen for 1083 employees exposed to acrylonitrile in Orlon® production at the Waynesboro, Virginia, plant from 1944 to 1970 (5). The development of Orlon® began at the Bengel laboratory in Waynesboro in 1944; production began in 1957 (5). Cancer incidence was assessed using the DuPont register for the years 1956–1983, and mortality was assessed through 1981. No cause-specific mortality rates were significantly higher than expected based upon either DuPont or United States (US) rates. A significant deficit of total cancer mortality among both wage and salaried employees was observed; however, the incidence for prostate cancer was significantly elevated (5 observed versus 1.9 expected).

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Quantitative exposure data were not available for the Waynesboro cohort. Therefore, an assessment of exposures estimated by a panel of knowledgeable long-term employees was used. Data were not shown by exposure level.

In response to the lingering question of health effects of acrylonitrile exposure, DuPont decided to update these investigations. Furthermore, since 1975 industrial hygiene monitoring data for acrylonitrile have been collected at both sites; an exposure assessment analysis was developed to estimate potentially exposed jobs at both plants.

The objectives of the study were as follows: (i) to assess overall and cause-specific mortality patterns among workers with a potential for exposure to acrylonitrile compared with mortality patterns of the DuPont (1957–1991) and US general populations (1940–1989); (ii) to determine whether cause-specific mortality patterns are associated with indices of exposure to acrylonitrile, for example, duration of exposure and cumulative exposure estimated as ppm-years; (iii) to assess site-specific cancer incidence patterns among workers with potential for exposure to acrylonitrile in comparison with the total DuPont work force for 1956–1991; (iv) to determine whether site-specific cancer incidence patterns show an association with indices of exposure to acrylonitrile, for example, duration of exposure and cumulative exposure estimated as ppm-years.

Methods

Cohort identification

The cohorts of employees potentially exposed to acrylonitrile at the 2 processing plants had been previously identified for the periods 1950–1980 (May plant) and 1944–1970 (Waynesboro plant). These 2 exposure cohorts were updated to include all employees who worked in exposed areas until the plants were closed in 1991 and 1990, respectively. Rosters from the medical surveillance program and historical seniority rosters were used to identify additional employees.

Demographic data were obtained for each employee from Du Pont corporate files and plant personnel records. Work history data were obtained from hard copy personnel records maintained at the plants. For employees added to the cohort, the beginning and ending date for the work area and job title of each unique job assignment were entered into the work history data base. For employees included in the earlier studies, the work history was reviewed for accuracy, and additional job assignments were added to the data base as appropriate. Vital status of prior employees was determined by a review of the National Death Index (1979–1991 deaths) and Social Security Administration files (all years). The vital status of living

prior employees was confirmed using DuPont pension records, motor vehicle records, and credit bureau reports. Death certificates were obtained from the DuPont Mortality Registry and the bureaus of vital records of states where reported deaths occurred. DuPont's cancer register was used to identify cancer cases diagnosed among cohort members during employment. The cancer register is maintained by the DuPont corporate offices and contains data on primary cancer diagnoses among *active* US employees. Accident and health insurance claims (1956–1989) and physician reports of cancer diagnosis (1977 to present) acted as sources of data.

Job classification and exposure assessment

A single exposure assessment procedure was developed with the objective of standardizing exposure classifications across work areas and job titles in the 2 plants. The process of manufacturing Orlon® was essentially the same at both plants, but there was greater distance between the process areas at Waynesboro. In each case acrylonitrile monomer was received by tank car and stored in the recovery tank farm. It was transferred to the polymer area, where it was polymerized and the final product (the Orlon® fiber) was made and packaged.

The following data were used for exposure assessment: (i) a general history of the plant, (ii) process descriptions of where acrylonitrile was used and engineering or operating changes in the process which would impact potential sources of exposure, (iii) a matrix of work area names and job titles held in the relevant production areas during the years that acrylonitrile was used, (iv) documentation of personal protective equipment used, (v) air sampling data, both area and personal, (vi) plant production records, and (vii) details of the work conditions and practices, as described by long-term employees (including retirees) in panel meetings held to assist with the exposure assessment. After the relevant job titles at each plant were standardized, a panel of long-term employees reviewed all the job title and work area designations for their respective plants to discuss the appropriateness of the assumptions made by the industrial hygienists and to elaborate further on workplace conditions, such as whether or not the odor from acrylonitrile was detectable during normal operations (exposure concentration approximately 20 ppm) or workers experienced symptoms of exposure, such as headaches and nausea (exposure concentration ≥ 20 ppm) (6, 7). The procedures and data used to develop the job- and area-specific exposure assessment were fully documented (Nelson & Whatley, "Exposure Assessment for Acrylonitrile: Final Report", report submitted to the DuPont Haskell Laboratory in 1993, unpublished results).

As has already been stated, area and personal air monitoring data were routinely collected from 1975 on. These data, with consideration of requirements for the use of

personal protective equipment, were the principal factors used to estimate the parts per million (ppm) levels of job assignments at the 2 plants after 1975. Changes in the processes, engineering, and ventilation were confirmed to be reflected in the monitoring data. So that the exposure levels could be estimated prior to 1975, data related to the changes and the panel of knowledgeable employees (and prior employees), who could detail work conditions, formed the primary sources of information. An estimate of acrylonitrile exposure was made in parts per million for a 40-hour workweek for each potentially exposed job title-work area combination by time period. The exposure estimates were then ranked into the 4 groups of low, moderate, high, and very high, based on the distribution of all jobs at both plants. The arithmetic mean midpoints for the categories were 0.11 ppm (low), 1.10 ppm (medium), 11.0 ppm (high), and 30.0 ppm (very high). The estimated ranges for each exposure level are shown in table 1.

No data were available regarding periods or levels of simultaneous exposure to other chemical agents in the workplace. Furthermore, no data regarding the smoking status of employees were available.

Data analysis

Since the exposure assessment was standardized and data regarding exposure-related characteristics at the 2 plants were comparable, the data from the 2 plants were combined. The overall and cause-specific mortality patterns of the cohort were evaluated with the standardized mortality ratio (SMR) as the measure of association using both DuPont mortality rates and US mortality rates. The DuPont rates were derived from company records of deaths among retirees and active employees. It was anticipated that a comparison of this subcohort with the experience of all DuPont employees would mitigate the influence of the healthy worker effect found in comparisons with the US general population. The reporting of deaths among retirees and active employees is believed to be complete, as a copy of the death certificate must be filed with the company before death benefits are paid.

SMR values and 95% confidence intervals (95% CI) were computed for the entire cohort and for specific causes of death (of special interest because of earlier DuPont reports) by latency, duration of exposure, highest level of exposure, and cumulative exposure using Monson's program (8). The person-years of observation for the

mortality analysis began 6 months after the starting date of the first job with potential for exposure to acrylonitrile and ceased with the date of death or the date the study ended or the last date known to follow-up. Latency was divided into <20 years since first exposure and ≥20 years since first exposure. The level of exposure indicated the highest level ever experienced by an employee, regardless of the duration of the job. Cumulative exposure was divided into the 4 strata of <10, 10–49, 50–99, and ≥100 ppm-years. In this calculation the first 9.9 ppm-years of an individual's exposure history was attributed to the lowest category, the 10–49 ppm-years were attributed to the second category, and so forth.

The overall and site-specific cancer incidence patterns of the cohort were evaluated in the same manner using the standardized incidence ratio (SIR) as the measure of association. The expected numbers of cases were based on the DuPont cancer incidence rates, and the Monson program was used. The person-years of observation for morbidity analysis began 6 months after the starting date of the first job with a potential for exposure to acrylonitrile and ceased with the last date employed or the study cut-off date for those employed at that time. [As has already been stated, a register of cancer incidence among active employees is maintained by DuPont. When an employee terminates for any reason (including retirement) information on any cancer is no longer collected by the company.]

Results

Since tax records were not available to verify the completeness of the cohort, face validity was confirmed by an evaluation of the completeness of the work force of each plant by job activities over time. The acrylonitrile-exposed cohorts identified at each plant had similar demographic and exposure-related characteristics, although the Waynesboro cohort was initially exposed somewhat later. The median year of birth was 1929 for the May plant and 1930 for Waynesboro (table 2). The mean exposure duration was 7.5 years at the May plant and 7.7 years at Waynesboro (table 3). The mean cumulative exposure was 61.4 ppm-years at the May plant, 52.1 ppm-years at Waynesboro, and 57.6 ppm-years for the total cohort. More than 50% of the May plant cohort was exposed prior to 1956 in Orlon® production, while slightly less than one-fourth (23.2%) of the Waynesboro cohort was exposed prior to 1956 at the Bengel laboratory operation before Orlon® production commenced in 1957 (table 4).

Vital status was unknown for only 17 (1.2%) of the May cohort and 6 (0.5%) of the Waynesboro cohort. Approximately 18% of the combined cohort was deceased at

Table 1. Acrylonitrile exposure level categories.

Level	Range (ppm)	Mean (ppm)
Low	≥0.0001—<0.20	0.11
Moderate	≥0.20—<2.00	1.10
High	≥2.00—<20.0	11.0
Very high	≥20.0—<100.0	30.0

the time of the follow-up, for a total of 454 deaths. Death certificates were obtained for all but 2 of the 454 identified decedents. The May plant cohort contributed a total of 42 622 person-years of follow-up and the Waynesboro plant cohort contributed 29 461 person-years of follow-up to the mortality analysis. Morbidity observation, which was maintained only for active employees, was shorter than mortality. A total of 49 577 person-years of observation was available from both cohorts for the morbidity analysis (table 5). The cohort for both the mortality and morbidity analyses was restricted to men who were potentially exposed to acrylonitrile for at least 6 months. (Women are not included in the analysis because only 25 exposed female employees were identified.) The distribution of the study subjects by cumulative exposure (ppm-years) for the 2 plants by 3 time periods of initial exposure (initial exposure prior to 1956, initial exposure 1956–1970, and initial exposure after 1970) is shown in table 6.

At the May plant, more than one-third of those initially exposed before 1956 attained ≥ 100 ppm-years of exposure. At Waynesboro, one-half of these early exposed employees attained ≥ 100 ppm-years of exposure. In contrast, at both plants nearly 90% of those first exposed after 1971 accrued less than 10 ppm-years of exposure.

Table 2. Exposed workers at the DuPont plants by year of birth and plant.

Year of birth	May plant		Waynesboro plant		Both plants ^a	
	N	Cumulative %	N	Cumulative %	N	Cumulative %
<1910	27	1.9	49	4.3	75	2.9
1910–1919	172	14.0	185	20.5	355	16.8
1920–1929	579	54.6	330	49.3	904	52.1
1930–1939	366	80.2	265	72.5	629	76.7
1940–	282	100.0	314	100.0	596	100.0
Total	1426	.	1143	.	2559 ^a	.

^a Ten study subjects worked at both plants.

Table 3. Exposed workers by duration of acrylonitrile exposure and plant.

Duration (years)	May plant ^a		Waynesboro plant ^b		Both plants ^{c,d}	
	N	Cumulative %	N	Cumulative %	N	Cumulative %
0.5 - <1 year	163	11.4	129	11.2	292	11.4
1 - <5	504	46.8	460	51.5	964	48.9
5 - <10	328	70.0	197	68.8	525	69.3
10 - <20	305	91.2	231	89.0	536	90.2
20 - <30	96	97.9	104	98.1	200	98.0
≥ 30	30	100.0	22	100.0	52	100.0
Total	1426	.	1143	.	2559 ^d	.

^a Average years of exposure per person was 7.5 years.

^b Average years of exposure per person was 7.7 years.

^c Average years of exposure per person was 7.6 years.

^d Ten study subjects worked at both plants.

Table 4. Exposed workers by year of first exposure and plant.

Year of first exposure	May plant		Waynesboro plant		Both plants ^a	
	N	Cumulative %	N	Cumulative %	N	Cumulative %
1947–1950	84	5.9	167	14.6	251	9.8
1951–1955	658	52.0	98	23.2	756	39.2
1956–1960	191	65.4	217	42.2	408	55.1
1961–1965	134	74.8	189	58.7	323	67.7
1966–1970	192	88.3	181	74.5	373	82.2
1971–1975	37	90.9	74	81.0	111	86.5
1976–	130	100.0	217	100.0	347	100.0
Total	1426	.	1143	.	2559 ^a	.

^a Ten study subjects worked at both plants.

Table 5. Person-years of follow-up and number of employees included in the mortality and morbidity analyses by plant.

	Mortality analysis	Morbidity analysis
May plant		
Person-years	42 622	27 526
Number of subjects	1426	1428 ^a
Waynesboro plant		
Person-years	29 461	22 300
Number of subjects	1143	1148 ^b
Both plants ^c		
Person-years	71 763	49 577
Number of subjects	2559 ^c	2566 ^c

^a Two subjects reported more than 1 cancer incident.

^b Five subjects reported more than 1 cancer incident.

^c Ten study subjects worked at both plants.

Table 6. Exposed workers by cumulative exposure (ppm-years) to acrylonitrile by year of initial exposure by plant.

Cumulative exposure	May plant		Waynesboro plant		Both plants ^a	
	N	Cumulative %	N	Cumulative %	N	Cumulative %
<i>Initial exposure 1947–1955</i>						
<10 ppm-years	124	16.7	22	8.3	146	14.5
10 - <50 ppm-years	208	44.7	69	34.3	277	42.0
50 - <100 ppm-years	143	64.0	41	49.8	184	60.3
≥ 100 ppm-years	267	100.0	133	100.0	400	100.0
Total	742	.	265	.	1007	.
<i>Initial exposure 1956–1970</i>						
<10 ppm-years	144	27.9	185	31.5	329	29.8
10 - <50 ppm-years	199	66.3	223	69.5	422	68.0
50 - <100 ppm-years	99	85.5	101	86.7	200	86.1
≥ 100 ppm-years	75	100.0	78	100.0	153	100.0
Total	517	.	587	.	1104	.
<i>Initial exposure 1971 and later</i>						
<10 ppm-years	147	88.0	257	88.3	404	88.2
10 - <50 ppm-years	17	98.2	30	98.6	47	98.5
50 - <100 ppm-years	3	100.0	4	100.0	7	100.0
≥ 100 ppm-years	-	.	-	.	-	.
Total	167	.	291	.	458	.
<i>Total, all time periods of initial exposure</i>						
<10 ppm-years	415	29.1	464	40.6	879	34.2
10 - <50 ppm-years	424	58.8	322	68.8	746	63.3
50 - <100 ppm-years	245	76.0	146	81.5	391	78.5
≥ 100 ppm-years	342	100.0	211	100.0	553	100.0
Total	1426	.	1143	.	2559 ^a	.

^a Ten study subjects worked at both plants.

Table 7. Standardized mortality ratios (SMR) for the acrylonitrile-exposed workers by plant, with the United States mortality rate as reference. (O = observed number of deaths, 95% CI = confidence interval, CNS = central nervous system)

Cause of death ^a	May plant			Waynesboro plant			Total cohort		
	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI
All causes of death	271 ^b	76	67—86	185 ^b	60	51—69	454	69	62—75
All malignant neoplasms (140—209)	77	88	69—110	50	66	49—87	126	78	64—93
Buccal cavity & pharynx (140—149)	2	78	..	1	47	..	2	43	5—155
Digestive system (150—159)	12	57	29—99	15	81	45—133	27	69	45—100
Esophagus (150)	-	0	..	3	164	33—480	3	75	15—219
Stomach (151)	2	66	..	1	37	..	3	53	11—154
Large intestine (153)	5	67	22—156	6	90	33—196	11	78	39—140
Rectum (154)	1	55	..	2	124	..	3	89	18—259
Liver (155—156)	1	61	..	1	68	..	2	65	7—233
Pancreas (157)	3	69	14—200	2	53	..	5	62	20—144
Respiratory system (160—163)	35	101	71—141	12	41	21—72	47	74	55—99
Larynx (161)	-	0	..	1	98	..	1	45	..
Lung (162)	35	106	74—147	11	40	20—71	46	76	56—102
Genital organs (180—187)	5	110	35—236	6	124	45—269	11	118	59—210
Prostate (185)	5	123	40—286	6	132	48—288	11	129	64—230
Urinary system (188—189)	5	123	40—287	2	54	..	7	90	36—186
Bladder (188)	3	172	35—503	1	57	..	4	115	31—295
Kidney (189)	2	86	..	1	52	..	3	71	14—207
Brain & CNS (191—192)	6	199	73—433	-	0	..	6	113	41—247
Lymphatic and hematopoietic (200—209)	4	46	12—119	5	70	22—163	9	57	26—109
Lympho- and reticulosarcoma (200)	1	72	..	2	176	..	3	121	24—353
Hodgkin's disease (201)	1	110	..	-	0	..	1	65	..
Leukemia (204—208)	2	62	..	1	37	..	3	51	10—148
Other lymphoma (202—203)	-	0	..	2	75	..	2	35	3—127
Other & unspecified	8	88	38—173	9	156	71—297	17	101	59—161

^a Code of the International Classification of Diseases, 9th revision, in parentheses.^b Two deaths occurred among the 10 employees who worked at both plants.**Table 8.** Standardized mortality ratios (SMR) for the acrylonitrile-exposed workers, with United States and DuPont mortality rates as reference. (O = observed number of deaths, 95% CI = 95% confidence interval, CNS = central nervous system)

Cause of death ^a	O		US		DuPont ^b	
			SMR	95% CI	SMR	95% CI
All causes of death	454	69	62—75	91	84—99	
All malignant neoplasms (140—209)	126	78	65—93	86	71—102	
Buccal cavity & pharynx (140—149)	2	43	5—155	67	8—241	
Digestive system (150—159)	27	69	45—100	72	48—105	
Respiratory system (160—163)	47	74	55—99	89	65—181	
Prostate (185)	11	129	64—230	106	53—189	
Urinary system (188—189)	7	91	36—187	90	36—185	
Lymphatic & hematopoietic (200—209)	9	57	26—109	55	25—105	

^a Code of the International Classification of Diseases, 9th revision, in parentheses.^b DuPont includes brain and CNS cancer with other and unspecified sites.

Approximately one-fifth of the employees (21.5%) in the cohort contributed to the ≥ 100 ppm-year category and close to two-thirds of the cohort (65.8%) experienced more than 10 ppm-years. Given that this exposure measure incorporates exposure level and duration, this distribution reflects the fairly long observation time for the cohort, and it was weighted by high exposures (> 10 ppm) estimated for a large proportion of the workers first exposed prior to 1956 (table 6).

Mortality patterns among acrylonitrile-exposed workers are shown in table 7 for all causes of death and selected cancer sites for the 2 cohorts and the combined cohort using US rates as the comparison. The all-cause SMR for the May plant was higher than that for the Waynesboro plant (SMR 76 versus 60). Elevated cancer site-specific SMR values were observed for prostate, bladder, brain and central nervous system (CNS) cancer, lymphosarcoma and reticulosarcoma, but the 95% CI values for these sites embraced 100.

The mortality ratios for the sites of interest for the combined cohort were compared using both the DuPont and US populations as reference in table 8. The overall SMR for all causes of death using the US comparison was 69, a value significantly lower than expected. When the DuPont population was used as the basis of comparison, an SMR of 91 was observed, a value slightly lower than expected. The SMR for all cancer deaths (86 using the DuPont comparison and 78 using the US population) was not affected by the healthy worker effect to the same extent as the overall SMR. The 95%CI values for all site-specific cancer embraced 100 when the DuPont population was used as the reference group. Unfortunately, the DuPont rates for brain and CNS cancers [International Classification of Diseases (ICD) 191—192] and the site-specific categories of bladder (ICD 188) and reticulosarcoma and lymphosarcoma (ICD 200) were not available. In the DuPont mortality register CNS and brain are included with "other and unspecified" cancer sites, bladder

Table 9. Standardized mortality ratios (SMR) for selected cancer sites among the acrylonitrile-exposed workers by exposure indices, with the DuPont mortality rate as reference. (O = observed, 95% CI = 95% confidence interval)

	All cancer			Prostate cancer			Respiratory cancer			Digestive cancer		
	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI
Latency												
<20 years	26	65	42–95	3	221	44–645	5	52	21–107	6	56	21–123
≥20 years	100	71	58–87	8	83	36–163	40	79	56–108	21	59	37–91
Duration												
<5 years	48	102	75–135	6	200	73–435	17	99	58–158	10	84	40–155
5–9 years	14	60	33–100	2	118	-	5	60	19–141	4	67	18–171
≥10 years	64	84	65–107	3	57	11–165	25	91	59–135	13	66	35–113
Highest exposure level (mean values)												
Low (0.11 ppm)	-	0	..	-	0	..	-	0	..	-	0	..
Moderate (1.10 ppm)	12	102	53–178	2	286	..	3	70	14–203	2	67	..
High (11.0 ppm)	63	75	58–96	7	123	49–253	21	71	44–109	15	70	39–151
Very High (30.0 ppm)	51	101	75–133	2	56	..	23	123	80–185	10	79	38–145
Cumulative exposure ^a												
<10 ppm-years	25	90	58–133	4	280	75–716	10	103	49–189	3	43	86–125
10–<50 ppm-years	34	81	56–114	4	149	40–381	12	79	41–139	10	96	46–176
50–<100 ppm-years	25	87	57–129	2	48	..	9	88	40–167	6	81	30–176
≥100 ppm-years	42	86	62–116	2	54	..	16	90	51–146	8	64	27–125

^a Sum of number of years at specified concentration in parts per million.

(ICD 188) is combined with kidney (ICD 189) in the urinary system category, and lymphosarcoma and reticulosarcoma (ICD 200) are included in the lymphatic and hematopoietic category (ICD 200–209).

Four indicators of acrylonitrile exposure were used to evaluate further mortality from all cancer and from prostate, respiratory, and digestive cancers. The indicators included the following: (i) latency (<20 and ≥20 years of observation), (ii) duration of exposure (<5, 5–9, and ≥10 years), (iii) highest exposure level ever attained (low, moderate, high, and very high), and (iv) cumulative exposure (<10, 10–<50, 50–<100, and ≥100 ppm-years). SMR values using DuPont mortality rates for comparison are shown on table 9. Of the deaths from all cancer sites combined, none of the exposure indicators showed an increased risk. The results of the exposure analysis for prostate, respiratory, and digestive cancers were similarly unremarkable except for the consistent inverse relationship of prostate cancer with exposure, namely, lower SMR values observed for higher values of exposure-related measures.

SIR values for all cancer and for specific sites are shown in table 10 using DuPont register rates as the comparison. The incidence ratios of all digestive cancers combined, respiratory cancer, and total cancer were slightly lower than expected. Within the digestive category, the incidence of intestine and rectum cancers was slightly higher than expected (SIR 112 and 125, respectively). Elevated SIR values, based on ≥5 deaths, were also noted for larynx, prostate, and lymphosarcoma and reticulosarcoma. However, the 95% CI values embraced 100 for all the SIR values showing elevation.

Using the same exposure-related measures of latency, duration of exposure, highest exposure level ever attained,

Table 10. Standardized incidence ratios (SIR) for selected cancer sites among the acrylonitrile-exposed workers, with the DuPont employee population as reference. (O = observed, 95% CI = 95% confidence interval)

Cancer site ^a	O	SIR	95% CI
All cancers	101	97	79–118
Buccal cavity & pharynx (140–149)	5	132	42–307
Digestive organs (150–159)	22	89	56–134
Esophagus (150)	1	59	..
Stomach (151)	1	44	..
Small & large intestine (152–153)	13	112	60–192
Rectum (154)	6	125	46–272
Liver (155–156)	-	0	..
Pancreas (157)	1	33	..
Respiratory system (160–163)	22	86	54–130
Larynx (161)	5	192	62–449
Lung, bronchus & trachea (162)	17	81	48–128
Malignant melanoma (172)	7	89	36–183
Male genital organs (185–187)	15	0	..
Prostate (185)	12	158	82–276
Testis (186)	2	125	14–451
Other male genital (187)	1	333	..
Urinary organs (188–189)	8	0	..
Bladder (188)	4	69	19–177
Kidney (189)	4	98	26–250
Eye (190)	1	250	..
Brain & other CNS (191,192)	4	111	30–285
Thyroid (193)	2	143	..
Lymphatic & hematopoietic (200–209)	10	0	..
Lymphosarcoma & reticulosarcoma (200)	5	227	73–530
Hodgkin's disease (201)	3	150	30–438
Other lymphoma (202 excluding 202.1)	1	40	..
Multiple myeloma (203)	-	0	..
Leukemia (204–208)	1	28	..
Residual	5	55	18–128

^a Code of the International Classification of Diseases, 9th revision, in parentheses.

Table 11. Standardized incidence ratios (SIR) for selected cancer sites among the acrylonitrile-exposed workers by exposure indices, with the DuPont employee population as reference. (O = observed, 95% CI = 95% confidence interval)

	All cancer			Prostate cancer			Respiratory cancer			Intestinal cancer		
	O	SIR	95% CI	O	SIR	95% CI	O	SIR	95% CI	O	SIR	95% CI
Latency												
<20 years	55	71	54—93	4	83	22—212	13	73	39—124	6	74	27—160
≥20 years	46	57	42—76	8	134	58—263	9	46	21—87	7	78	31—160
Duration												
<5 years	28	106	70—153	2	108	..	7	113	45—233	4	144	39—370
5—9 years	16	96	55—155	1	88	..	2	49	..	2	110	..
≥10 years	57	93	71—121	9	197	90—375	13	84	45—144	7	77	31—159
Highest exposure level (mean values)												
Low (0.11 ppm)	4	187	50—479	-	0	..	-	0	..	..	0	..
Moderate (1.10 ppm)	8	74	32—146	1	133	2—912	2	79	..	1	88	..
High (11.0 ppm)	62	99	76—126	7	152	61—312	13	86	46—147	9	127	58—240
Very high (30.0 ppm)	27	95	62—138	4	192	52—492	7	92	37—189	3	89	19—277
Cumulative exposure ^a												
<10 ppm-years	21	89	55—137	3	210	42—613	6	119	44—259	2	86	..
10 - <50 ppm-years	34	116	81—162	1	48	..	7	99	40—205	6	189	69—412
50 - <100 ppm-years	19	95	57—148	2	81	..	3	58	12—171	1	43	..
≥100 ppm-years	27	85	56—124	6	232	85—506	6	71	26—154	4	105	28—269

^a Sum of number of years at the specified concentration in parts per million.

Table 12. Comparison of year of first exposure to acrylonitrile between the fiber plants studied by the National Cancer Institute (NCI) (N=3) and the DuPont fiber plants (N=2).

Year of first exposure or entry into the study ^{a, b}	Fiber plants in NCI study ^c		DuPont plants	
	N	Cumulative %	N	Cumulative %
-1955	1136	9.0	1007	39.2
1956—1960	1908	24.2	408	55.1
1961—1965	2880	47.1	323	67.7
1966—1970	2864	70.0	373	82.2
1971-	3788	100.0	458	100.0
Total	12 576	.	2559 ^b	.

^a The NCI data show year of entry of all study subjects including the unexposed workers. The DuPont data show year of first acrylonitrile exposure.

^b Prior to 1978 the permissible exposure limit (PEL) of the Occupational Safety and Health Administration was 20 ppm; in 1978 the PEL was lowered to 2 ppm with a 10 ppm excursion limit.

^c Plants 1, 4, and 5.

Table 13. Comparison of person-years of follow-up of the workers exposed to acrylonitrile in the fiber plants studied by the National Cancer Institute (NCI) and the DuPont fiber plants.

	Fiber plants in NCI study	DuPont plants
Fiber plants	3	2
Person-years of follow-up among exposed workers ^a	198 345	71 763
Study subjects in fiber plants	12 576 ^b	2 559

^a The exposed subcohort of the NCI includes all the exposed workers, whereas the DuPont cohort was restricted to workers exposed for ≥6 months. This restriction reduced the person-years in the DuPont cohort from 75 009 to 71 763.

^b Includes an unknown number of unexposed employees who contributed an additional 75 075 person-years of follow-up.

and cumulative exposure in ppm-years, the morbidity analysis was repeated for all cancer, prostate cancer, respiratory cancer, and cancer of the small and large intestine (table 11). For all cancer sites combined, respiratory

cancers, and intestinal cancers, there was no apparent relationship with level of exposure and cancer incidence. For prostate cancer, based on 12 cases, the SIR values increased in the analyses of latency, duration of exposure, highest exposure level, and cumulative exposure dose. Once again, however, the 95% CI values for site-specific cancer embraced 100 for all the elevated SIR values.

Discussion

This study provided an opportunity for a more-detailed evaluation of mortality patterns in a combined cohort of workers exposed to acrylonitrile at 2 plants involved in the production of Orlon® beginning approximately 45 years ago. Although a modest difference was observed in the overall SMR values for the workers at the 2 plants, both plants showed a healthy worker effect. Reasons for the differences in the overall and all-site cancer mortality for workers at the 2 plants may have been due to differences in the demographic characteristics of the 2 locales: South Carolina for the May plant and Virginia for the Waynesboro plant. South Carolina had a higher proportion of blacks in the total population than Virginia, 29.8% versus 18.8% (1990); South Carolina had a lower per capita income than Virginia [USD 16 923 versus USD 21 634 (1993)]; and South Carolina had higher mortality rates for all causes and all-cancer sites than Virginia, 9.1 versus 8.0 per 1000, respectively, for all deaths in 1995 and 202 versus 191 per 100 000, respectively, for all cancer deaths in 1995 (as shown by reference 9 and personal communications from MS Barnes of the South Carolina Office of Public Health Statistics and Information Systems and NL

Ruckner of the Virginia Department of Vital Records and Health Statistics). Information on the race or ethnicity of the employees at the 2 plants was not available to allow for a more-specific evaluation of black:white differentials in overall mortality. However, we were able to identify overall demographic differences and establish the comparability of the exposure-related characteristics of the 2 plants.

Although the combined study cohort was small ($N=2559$), relative to the larger cohort in the study of the National Cancer Institute (NCI) ($N=25\,460$), the DuPont cohort was limited to workers exposed for at least 6 months to acrylonitrile, whereas the NCI cohort included unexposed workers. In addition, extended follow-up, very high completeness of follow-up, the high proportion of deceased persons in the cohort [ie, 17.7% versus 8% in the NCI study by Blair et al (10)], and the high proportion of workers exposed prior to 1956 (39% versus 9% in the NCI study) made the DuPont cohort extremely useful in the assessment of exposure effects (table 12).

This investigation had the advantage of being able to assess cancer morbidity and mortality patterns. Important occupational risk factors may be observed in morbidity patterns earlier than mortality, particularly as cancer survival rates increase. However, in this case, there were no remarkable findings in either the morbidity or mortality analyses.

One strength of the exposure assessment protocol developed for this investigation was a standardized approach that would allow estimates of cumulative exposure for all workers at the 2 plant sites. The range of levels for each exposure estimate was useful in grouping the data. As with most retrospective cohort studies, the exposure assessment process was limited by the lack of monitoring data from the earliest time period. This data gap raises specific concerns regarding the accuracy of the cumulative acrylonitrile exposure estimates (ppm-years), which appeared to be higher in this cohort than what one might predict using the symptoms perception method for estimation proposed by Esmen (11). However, given the high proportion of workers initially exposed prior to 1971 in this cohort (82.2%), when workplace acrylonitrile exposures often exceeded 5–10 ppm, estimates of cumulative exposures of 100 ppm-years in this cohort may not be unrealistic, even though considerably higher than levels observed in more recently exposed cohorts, such as that reported by Blair et al (10).

An additional useful analysis could be made by comparing the 3 fiber plants studied by NCI (plants 1, 4 and 5) with the DuPont fiber plants since these are the facilities with potential for higher acrylonitrile exposure. The person-years of follow-up for exposed workers in the fiber plants studied by NCI were 198 345, whereas there were 71 763 ppm-years observed in this study (table 13). The person-years of observation for the DuPont cohort were

restricted to those occurring after the first 6 months of exposure, but no such criterion was employed in the NCI study.

As has already been indicated, the ability to evaluate cancer incidence was an important advantage in the assessment of risk from occupational carcinogens. Data from the DuPont cancer register are limited in that the register only contains data reported during active employment. When a worker terminates employment, follow-up is discontinued. In addition, the reporting of cancer diagnoses among DuPont employees has diminished in recent years due to changes in reporting requirements and health insurance benefits. The pattern of risk for prostate cancer incidence suggests an association with exposure (table 11), but not for mortality due to prostate cancer (table 9). Only 4 of the incident cases were included among the 11 prostate cancer deaths. This discrepancy suggests that the association of prostate cancer seen with incidence data may be more a function of duration of employment than one of exposure.

The DuPont mortality rates have the important advantage of controlling for the healthy worker effect. The reporting system includes only deceased pensioners and employees (who died while employed). However, employees who neither retire from DuPont nor die while employed and who may experience a different mortality risk are not included in the denominator, whereas, if they were exposed for at least 6 months, they are included in the numerator. Smoking, race, and other possible risk factor data were not available for analysis.

Concluding remarks

This study assessed the risk of mortality from specific causes and cancer morbidity among DuPont employees with potential exposure to acrylonitrile during the production of Orlon® at 2 plants. The combined cohort numbered 2559 employees. An exposure assessment was conducted for the jobs potentially exposed to acrylonitrile, and the estimated levels of exposure (ppm) were assigned to each job title and work area.

A total of 454 deaths was observed. The overall mortality was lower than expected when compared with that of the DuPont population and with the US mortality rates. The 95% CI values for the SMR values for all site-specific cancers embraced 100. A total of 101 incident cancer cases was observed, and the overall and cause-specific morbidity ratios (SIR values) similarly embraced 100.

Earlier DuPont studies (2, 3) suggested a possible association of acrylonitrile exposure with colon and lung cancer outcomes. Mortality and morbidity analyses by exposure indicators in this more-complete evaluation of the cohort did not show an elevated risk or an apparent association with exposure indicators.

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