A Retrospective Cohort Study of Mortality and Cancer Incidence Among Chemists

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This retrospective cohort study examines mortality and cancer incidence among 3,686 men and 75 women who were employed as chemists in 1959. During the period 1964 to 1977, the male chemists experienced lower overall mortality than other salaried employees of the chemical company (198 deaths observed, 241.0 expected, SMR = 82). Large deficits are seen in lung cancer and arteriosclerotic heart disease deaths. The chemists appear to be at slightly higher risk for death from malignancies of the colon (12 observed, 6.7 expected, SMR = 178) and from cerebrovascular disease (15 observed, 10.8 expected, SMR = 138). The low overall mortality resulted in a larger than expected proportion of deaths due to cancer. Fewer than expected cases were diagnosed of cancer of all sites combined (61 observed, 86.5 expected, SIR = 71) and of the lung (8 observed, 20.0 expected, SIR = 40). The incidence rates of melanoma and of cancer of the prostate are slightly higher than expected, relative to the Third National Cancer Survey and the experience of nonchemists, respectively. Among female chemists, deaths due to all causes and suicide occurred more frequently than expected. Possible explanations for the lack of anticipated excess risks and for the observed deficits are presented.

Reports from the United States, Sweden, and Great Britain suggest there is excess mortality from certain types of cancer among chemists.[1-9] However, the designs of the studies reported have some limitations. First, the populations were not restricted to persons employed as chemists. The American and British studies of chemical society members may include persons who were not occupationally exposed to chemicals, for example, administrators for chemical companies.[1,2,8] Secondly, several of the studies were based on proportional mortality rates, not absolute mortality rates.[1-4,7,8] Apparent excesses in proportional mortality from cancer may reflect deficits in other causes of death.[10] Thirdly, the Swedish study which was based on absolute mortality and attempted to identify subjects who worked in a laboratory included too few deaths to be conclusive.[6]

E. I. du Pont de Nemours and Company, Inc., employs many chemists and was concerned over these reports. Du Pont had data available to identify many persons employed as chemists and to generate cancer incidence and mortality rates. This paper describes an absolute mortality and cancer incidence study of chemists employed by that company.

Materials and Methods

The Du Pont Company maintains a computerized personnel file which includes records of all salaried persons who were active employees on or after January 1, 1964. Records of hourly wage roll workers are not included in the file. The file contains demographic information and work histories retroactive to 1959. From this file, the authors identified 3,713 men and 75 women who were employed in 1959 as chemists, chemical engineers, or research associates, or in occupations with similar job titles. Because of the small number of nonwhites, the cohort was restricted to 3,686 male and 75 female white chemists.

It is difficult to define the job title "chemist" and to characterize occupational exposure. Most chemists are exposed to numerous substances that change constantly in quantity and in quality. Different chemists rarely sustain the same exposures. This is especially true for a cohort of Du Pont chemists. Du Pont is an international company with many different processes, products, and locations, and chemists are employed throughout the company. A large number are employed in research and development at the Experimental Station in Wilmington,

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Supported by grants from E I. du Pont de Nemours and Co., Inc., the Exxon Corporation, and the United States National Cancer Institute (5 P01 06373).

Reprinted from Journal of Occupational Medicine
July, 1981, Volume 23, No. 7
pp. 485-501

Table 1. — Du Pont Department Groups and Products.

Name	Examples of Products or Exposures
Plastic resins, fibers and products	Plastic resins, filaments, sheetings, photographic papers, chemicals and equipment, textile fibers
Basic chemicals and finishes	Paints, pigments, chromates, finishes, tetraethyl lead, fluorinated compounds, dyes, solvents, polymers for non-plastic uses, dry cleaning fluid, sodium products, electronic products, plant protection chemicals, feed supplements, pharmaceuticals, basic chemicals and intermediates
Petrochemicals	Acrylonitrile, explosives, industrial diamonds
Elastomers	Neoprene, accelerators, antioxidants and miscellaneous chemicals for natural and synthetic rubber, coated fabrics
Research, development and engineering	
Atomic energy	Low-level radiation
Administration	

Del., while others work in research and development at the plants. Some are involved with pilot plants or semiworks operations for new products and processes, and others serve in engineering or quality control positions at the production plants. This variety is further complicated by rotation of some chemists from plant to plant or to the Experimental Station.

The same job title and code number can represent different tasks at different company locations. For instance, "technical investigator" could be a laboratory research position at one location, but an administrative position at another. A chemical engineer could do laboratory work at one site, but design work on a computer at another. A few tasks are consistent across locations. For example, a "patent chemist" is always an office job, but the position may be held by someone who was once a laboratory research chemist.

Du Pont is organized into industrial and administrative departments. Within a department, the types of processes and products have some similarity. Because most employees stay within the same department throughout their careers despite transfers to several locations, exposures were characterized by usual and "ever" department affiliation. A Du Pont industrial hygienist identified the seven major department groups that existed during the study years, combining those that had undergone name changes and reorganization (Table 1).[11]

The authors also identified 19,262 male and 673 female white "nonchemists" who were active salaried employees in 1959 and were listed in the computerized personnel file on January 1, 1964. Persons ever employed by Du Pont as chemists were excluded from the nonchemist group.

Extracts of the personnel records were created and missing demographic data were obtained from noncomputerized employee rosters stored by the Du Pont Epidemiology Section.

Cancer Incidence. — Cancer cases were ascertained by review of the Medical Division cancer registry. The registry consists of cases gleaned from the Accident and Health Insurance (AHI) claims and life insurance claims. The AHI claims are submitted for any disability of eight or more consecutive days. The diagnosis on the disability claim is certified by the attending physician. About 97% of employees with at least six months of service are enrolled in the AHI plan and all employees are enrolled in the life insurance plan. The registry and insurance plan have been described in detail in other studies.[12]

Cancer incidence data are available only during the subjects' years of active employment at Du Pont. Illnesses that occur after termination from the Company, or during retirement, are not recorded in the registry.

Using a computer program developed by Monson,[13] the observed number of cancer cases diagnosed during the period 1964 to 1977 was compared with the estimated expected number based on the experience of the nonchemists and on the Third National Cancer Survey (TNCS) rates.[14] Standardized incidence ratios (SIRs), the ratios of the incidence rates of the chemists and the comparison group, standardized to the age and calendar year distribution of the person-years of the chemists, were calculated. Ninety-five percent confidence intervals were constructed, assuming a Poisson distribution of the observed number of events.[15]

The TNCS rates were used to detect excess risks occurring in both the chemist and the nonchemist cohorts which would not be apparent from internal comparisons.

A third comparison group, all Du Pont salaried employees from each year of the study observation period, was considered. The more inclusive Du Pont salaried group was larger than the nonchemist group, but less comparable to the chemists with respect to year hired and socioeconomic status. The results based on all Du Pont salaried employees were similar to the nonchemist-based analysis and will not be presented.

For all sites combined and for any site with three or more chemist cases, the authors examined the effects of age and decade hired, and usual and ever department affiliation. For each value of the factors, the expected number of cases was generated by consideration of the nonchemists with the same value for the factor.

The effects of alcoholism were also examined. A subject was classified as an alcoholic if he had a cause of death or disability due to alcoholic cirrhosis of the liver or to alcoholic psychoses, or had been identified in a company-wide survey of plant physicians conducted in 1964.[16] An AHI claim for alcoholism can be filed for an episode of illness or for a 30-day treatment course at an alcoholism rehabilitation center. Referral to a rehabilitation center may be made by either the employee or by management.

Mortality. — The chemist and nonchemist cohorts were followed to December 31, 1977, regardless of employment status. The mortality data were obtained from two sources, Du Pont records and the Social Security Administration (SSA). The Medical Division maintains a mortality file which records all deaths among active employees and among pensioners. The file contains the life insurance claim data, supplemented by information

Table 2. — Vital Status, as of December, 1977, of the Chemists and Nonchemist Cohorts, by Sex.

Vital Status	Chemists		Nonchemists	
	Men	Women	Men	Women
Total	3,686	75	19,263	673
Alive	3,488(95)*	69(92)	17,243(90)	653(97)
Active employees	2,722(74)	41(55)	10,867(56)	454(67)
Pensioners	448(12)	13(17)	5,465(28)	170(25)
Terminated from company, not pensioned	318(9)	15(20)	911(5)	29(4)
Deceased	198(5)	6(8)	2,020(10)	20(3)
Active employees	111(3)	4(5)	897(5)	9(1)
Pensioners	76(2)	1(1)	1,071(6)	10(1)
Terminated from company, not pensioned	11†	1(1)	52†	1†

*Percent of total for the sex-cohort group
†Less than 1%

from the employees' medical records and from the plant physicians. As of December 31, 1977, 187 male and 5 female chemists and 1,979 male and 19 female nonchemists were known to have died while actively employed or after having retired. Of the 329 male chemists who left the company before retirement or death, the SSA identified 260 as alive, 11 as deceased, and 58 as status unknown. Persons not known to be dead were assumed to be alive until the end of the study. One female chemist and one female and 51 male nonchemists were known to have died after termination from Du Pont (Table 2).

The authors requested copies of death certificates from state departments of health, but did not try to obtain certificates for 11 nonchemists and one chemist who died outside the United States. Certificates were obtained for 185 (93%) of the male and 6 (100%) of the female deceased chemists and for 1,863 (92%) of the male and 15 (79%) of the female deceased nonchemists. When a certificate was unobtainable, the cause of death from the life insurance claim was utilized. Ninety percent of the available certificates contained the same cause of death as the life insurance claim. Ninety-nine percent of the deaths attributed to cancer on the death certificate were also attributed to cancer on the life insurance claim.

Cause of death was coded according to the *International Classification of Diseases, Adapted for Use in the United States.*[17,18] The Seventh Revision was used from

Table 3. — Observed and Expected Cancer Cases* Among Male Chemists, Aged 20-64, Diagnosed in 1964-1977, Based on the Nonchemist Cohort Rates.

Site (ICD)†	Obs	Exp	SIR‡	C.I. of SIR§
All sites (140-239)	61	86.5	71	54-91
Buccal cavity (140-149)	1	2.1	48	2-235
Stomach (151)	2	2.4	83	14-275
Small and large intestine (152-153)	7	11.6	60	26-119
Rectum (154)	3	4.4	68	17-185
Liver and biliary passages (155-156)	1	0.9	—	—
Pancreas (157)	2	1.1	181	30-598
Lung (162)	8	20.0	40	19-76
Melanoma (172)	8	8.3	97	45-184
Prostate (185)	7	4.5	156	68-308
Bladder (188)	3	2.0	150	38-407
Kidney (189)	4	3.7	108	34-261
Brain (191)	2	3.0	67	11-221
Endocrine glands, excluding thyroid (194)	1	0.5	—	—
Lymphatic and hematopoietic system (200-209)	12	10.0	120	65-203
Lymphosarcoma (200)	3	2.1	142	36-385
Hodgkin's disease (201)	2	1.6	127	21-419
Other lymphomas (202)	1	1.5	67	3-332
Multiple myeloma (203)	1	0.9	—	—
Leukemia (204-207)	3	3.5	85	22-231
Other neoplasms of the lymphopoietic system (208)-209)¶	2	0.4	—	—
All other sites	0	12.0	—	—

*Excluding non-melanotic skin cancer
†Eighth Revision, International Classification of Diseases[18]
‡Standardized incidence ratio (SIR) = (observed/expected) x 100
§95% confidence intervals[15]
¶Polycythemia vera and adenogenic myeloid metaplasia

Table 4. — Observed and Expected Cancer Cases* Among Male Chemists, Aged 20-64 Years, Diagnosed in 1964-1977, Based on the Third National Cancer Survey, 1969-1971.

Site	Obs	Exp	SIR†	C.I. of SIR‡
All sites	61	112.0	54	42-70
Buccal cavity	1	8.5	12	1-58
Stomach	2	3.8	53	9-175
Small and large intestine	7	9.9	71	31-140
Rectum	3	5.7	53	14-145
Liver and biliary passages	1	1.6	62	3-306
Pancreas	2	3.7	54	9-178
Lung	8	28.4	28	13-54
Melanoma	8	3.3	239	111-454
Prostate	7	5.6	124	54-246
Bladder	3	6.6	45	12-123
Kidney	4	3.8	105	33-253
Brain	2	3.4	59	10-196
Endocrine glands, excluding thyroid	1	0.3	—	—
Lymphosarcoma	3	2.7	111	28-303
Hodgkin's disease	2	2.1	97	16-322
Other lymphomas	1	1.0	97	5-479
Multiple myeloma	1	1.2	81	4-397
Leukemia	3	3.3	91	23-249
All other sites	2	17.1	—	

*Excluding non-melanotic skin cancer
†Standardized incidence ratio (SIR) = (observed/expected) x 100
‡95% confidence intervals[15]

Table 5. — Observed and Expected Numbers of Deaths Due to Selected Causes Among Male Chemists, 1964-1977, Based on the Nonchemist Cohort.

Cause (ICD)*	Obs	Exp	SMR‡	C.I. of SMR‡
All causes	198	241.0	82	71-94
Malignant neoplasms (140-209)	43	62.4	69	51-92
Stomach (151)	2	2.2	90	15-300
Large intestine (153)	12	6.7	178	97-305
Rectum (154)	2	0.9	—	—
Liver and biliary passages (155-156)	1	1.7	59	3-290
Pancreas (157)	2	1.7	120	20-389
Lung (162)	9	21.9	41	20-75
Prostate (185)	2	2.8	72	12-236
Bladder (188)	0	1.1	—	—
Kidney (189)	2	2.3	86	15-287
Brain (191)	1	3.0	33	2-164
Thyroid (193)	1	0.2	—	—
Lymphatic and hematopoietic cancer (200-209)	9	7.5	120	59-220
Lymphosarcoma and reticulosarcoma (200)	1	1.2	85	4-411
Hodgkin's disease (201)	2	0.7	—	—
Leukemia (204-207)	4	3.7	109	34-261
Other lymphatic cancer (208-209)	2	2.0	102	17-337
Diabetes mellitus (250)	1	3.2	32	2-154
Circulatory system diseases (390-458)	96	128.1	75	61-92
Arteriosclerotic heart disease (410-414)	75	103.3	73	57-91
Cerebrovascular disease (430-438)	15	10.8	138	81-224
Pneumonia (480-486)	3	1.1	281	69-742
Gastric and duodenal ulcer (531-533)	1	0.6	—	—
Cirrhosis of the liver (571)	5	5.7	88	32-194
Accidents (E800-E949)	14	13.5	104	59-170
Suicide (E950-E959)	8	5.6	144	66-271
Residual	27	20.8	—	—

*Eighth Revision, International Classification of Diseases[18]
†Standardized mortality ratio = (observed/expected) x 100
‡95% confidence intervals[15]

1964 through 1969, and the Eighth Revision, from 1969 through 1977.

Through the use of the Monson program, the observed number of deaths among the chemists was compared with the estimated expected number based on the experience of the nonchemists and on the U.S. mortality rates. Standardized mortality ratios (SMRs) and 95% confidence intervals were calculated in the manner described previously.

An analysis based on all Du Pont salaried personnel employed during the study observation period yielded results similar to those of the nonchemist-based analysis and will not be presented.

Proportional mortality ratios (PMRs) also were calculated, comparing the mortality patterns of the chemists with those of white male population of the United States.

Results

Cancer Incidence. — While employed as chemists at Du Pont, the 3,686 men accrued 44,656.8 person-years of observation. With the exclusion of non-melanotic skin cancer, 61 cases of cancer were diagnosed during the period 1964 to 1977. The expected numbers of cancer of all sites were 86.5 (SIR = 71) and 112.0 (SIR = 54), based on the nonchemist and the TNCS rates, respectively. Table 3 shows the observed and the expected numbers, the SIRs, and the 95% confidence intervals of the SIRs, based on the nonchemist experience, for all combined and for selected cancer sites. Approximately one-half of the deficit in overall cancer morbidity was attributable to the low lung cancer morbidity. Slight excesses, based on small numbers, were seen for cancers of the pancreas, the prostate, the urinary bladder, and the lymphatic and hematopoietic system.

A slight excess of prostatic cancer is seen among chemists ever and usually employed in basic chemicals and finishes (3 observed, 1.0 expected). All the chemists diagnosed with kidney cancer were employed in basic chemicals and finishes (ever: 4 observed, 0.6 expected; usual: 4 observed, 0.4 expected). Slight excesses were seen in the plastic resins and fibers chemists for lymphosarcoma (ever: 2 observed, 0.3 expected; usual: 2 observed, 0.2 expected) and leukemia (ever: 3 observed, 1.1 expected; usual: 2 observed, 0.4 expected). The number of cases is too small for multiple breakdowns to be meaningful.

The comparison of the chemists with the TNCS population was generally consistent with the nonchemist-based analysis (Table 4). However, melanoma was more common among the chemists than expected (8 cases observed, 3.3 expected, SIR = 239), an association that does not appear in the nonchemist-based analysis. An excess of melanoma is observed in the nonchemists themselves in comparison with the TNCS population (38 cases observed, 17.1 cases expected, SIR = 223). In the internal comparison with the nonchemists, the chemists do not appear to have excess melanoma risk.

The female chemists accrued 747.0 person-years of observation. During the period 1964 to 1977, five cancers were diagnosed: one each of the breast, uterus, and ovary, one case of leukemia, and one cancer of unknown primary site. The expected number of cancers of all sites was 2.7 (SIR = 185), based on both the nonchemist and the TNCS rates. Because of the small number of cases, no further analysis of the women's experience will be presented.

Table 6. — Observed and Expected Number of Deaths Due to Cancer of the Large Intestine Among Male Chemists, 1964-1977, by Work History Characteristics, Based on the Nonchemist Cohort.

	Obs	Exp
Age hired		
20-24	3	2.1
25-29	4	3.2
30-34	4	0.6
35-44	1	0.4
Decade hired		
1920-1929	0	1.1
1930-1939	4	2.3
1940-1949	4	1.2
1950-1959	4	2.1
Usual department group		
Plastic resins and fibers	3	3.4
Basic chemicals and finishes	4	2.0
Petrochemicals	2	0.3
Elastomers	0	0.2
Research, development and engineering	2	0.5
Atomic energy	1	0.0
Total	12	6.7

Mortality. — From 1964 to the earlier of either the date of death or the end of the study, the male chemists accrued 50,538.7 person-years of observation and 198 deaths. The expected numbers of deaths were 241.0 (SMR = 82) and 418.3 (SMR = 47), on the basis of the experience of the male nonchemists and of the U.S. white male population, respectively.

In comparison with the experience of the nonchemists, deaths due to malignant neoplasia were less frequent than expected (43 observed, 62.4 expected, SMR = 69) (Table 5). An elevated SMR was seen for cancer of the large intestine (12 observed, 6.7 expected, SMR = 178). A large deficit was observed for deaths due to carcinoma of the lung. Nine lung cancer deaths occurred, 21.9 were expected (SMR = 41). Slight excesses were observed for deaths due to Hodgkin's disease, to all lymphatic and hematopoietic cancer, and to cerebrovascular disease, pneumonia, and suicide. A low SMR was seen for arteriosclerotic heart disease.

Table 6 presents the observed and expected numbers for cancer of the large intestine according to work history characteristics. Deaths occurred among chemists usually employed in plastic resins and fibers, basic chemicals and finishes, petrochemicals, research and engineering, and atomic energy.

The associations seen in the total cohort were generally found in each department. Chemists usually employed in the elastomers department experienced slightly more deaths than expected (13 observed, 11.8 expected, SMR = 110); chemists in the other departments had SMRs well below 100. The elastomers department's relative excess was due to deaths from coronary heart disease and suicide. However, for most departments and most causes of death, the number of deaths was too small for any meaningful comparisons.

Table 7. — Observed and Expected Numbers of Deaths Due to Selected Causes Among Male Chemists, 1964-1977, Based on U.S. Mortality Rates.

Cause	Obs	Exp	SMR*	C.I. of SMR†
All causes	198	418.3	47	41-54
Malignant neoplasms	43	86.0	50	37-660
Stomach	2	3.6	55	9-184
Large intestine	12	6.9	174	94-296
Rectum	2	2.4	85	14-275
Liver and biliary passages	1	1.3	78	4-379
Pancreas	2	4.7	43	7-141
Lung	9	30.7	29	14-54
Prostate	2	2.8	70	12-236
Bladder	0	1.9	—	—
Kidney	2	2.4	83	14-275
Brain	1	3.5	29	1-141
Thyroid	1	0.2	—	—
Lymphatic and hematopoietic system	9	9.1	99	48-182
Lymphosarcoma and reticulosarcoma	1	2.2	46	2-224
Hodgkin's disease	2	1.3	150	26-508
Leukemia	4	3.4	119	37-284
Other lymphatic cancer	2	2.1	94	16-315
Diabetes mellitus	1	5.8	17	1-85
Diseases of nervous system and sensory organs	2	3.9	51	9-169
Diseases of the circulatory system	96	198.9	48	39-59
Arteriosclerotic heart disease	75	151.5	50	39-62
Cerebrovascular disease	15	20.0	75	44-121
Respiratory diseases	7	20.9	33	15-66
Pneumonia	3	7.3	41	11-112
Digestive system diseases	11	26.5	41	22-72
Gastric and duodenal ulcer	1	2.5	40	2-193
Cirrhosis of the liver	5	17.1	29	11-65
External causes	22	54.2	41	26-60
Accidents	14	34.7	40	23-66
Suicide	8	13.6	59	27-112
Residual	16	22.1		

*SMR = Standardized mortality ratio = (observed/expected) x 100
†95% confidence intervals[15]

In comparison with the U.S. white male general population, 86.0 deaths due to cancer were expected, yielding an SMR of 50 (Table 7). An excess was observed for deaths due to cancer of the large intestine (12 observed, 6.9 expected, SMR = 174). Two Hodgkin's disease deaths occurred; 1.3 were expected (SMR = 150). Four leukemia deaths occurred; 3.4 were expected (SMR = 119). Deficits are seen in numbers of deaths due to carcinoma of the lung (9 observed, 30.7 expected, SMR = 29), arteriosclerotic heart disease, respiratory and digestive system diseases, accidents, and suicide.

The deaths and person-years of exposure were categorized by employment status. Active employees had the lowest SMRs, pensioners had the highest, and terminated, nonpensioned employees had intermediate SMRs. The last group, the most difficult to trace, did not reveal any associations not seen in the active employees or the pensioner group. Risk of cancer of the large intestine was elevated relative to the overall SMR in both active and pensioned employees, but particularly among the pensioners. Only the active employees had slight excesses in deaths due to cancer of the kidney and to Hodgkin's disease. Only the pensioners had excesses in deaths due to prostatic cancer, cerebrovascular disease, diseases of the digestive system, cirrhosis of the liver, and suicide (Table 8).

In the proportional mortality analysis, the method used in several of the previous chemist studies, deaths due to malignant neoplasia were found to be more frequent than expected (Table 9). A larger than expected proportion of deaths among active employees was due to lung cancer, but deficits were seen among the pensioned and other terminated employees. Colon cancer, arteriosclerotic heart disease, and cerebrovascular disease were responsible for larger proportions of deaths than expected. Deaths attributable to prostatic cancer occurred more frequently than expected among pensioners. The risk of deaths from accidents was lower than expected, and among terminated employees, suicide accounted for a larger than expected proportion of deaths.

Among the female chemists, six deaths occurred during 994.7 person-years of observation. The expected numbers were 1.8 (SMR = 327) and 4.8 (SMR = 125), on the basis of the experience of the female nonchemists and of the U.S. white female population, respectively. The causes of death were lung cancer, leukemia, abscess of the lung, house fire, and in two cases, suicide. Compared to the U.S. rates, only 0.1 deaths due to suicide were expected.

Discussion

The Du Pont male chemists experienced lower overall mortality and lower cancer morbidity and mortality than

Table 8. — Observed and Expected Numbers of Deaths Due to Selected Causes Among Male Chemists, 1964-1977, by Employment Status, Based on U.S. Mortality Rates.

Cause	Actives			Pensioners		
	Obs	Exp	SMR*	Obs	Exp	SMR
All causes	111	309.7	36	76	91.5	83
Malignant neoplasms	25	61.8	40	16	21.0	76
Large intestine	5	4.7	106	6	2.0	307
Lung	7	22.0	32	2	7.5	27
Prostate	0	1.2	—	2	1.6	125
Kidney	2	1.8	110	0	0.5	—
Lymphatic and hematopoietic cancer	6	7.0	86	3	1.7	172
Hodgkin's disease	2	1.2	174	0	0.1	—
Circulatory system diseases	49	141.0	35	42	50.7	83
Arteriosclerotic heart disease	40	108.7	37	31	37.2	83
Cerebrovascular disease	5	12.6	40	9	6.8	133
Respiratory diseases	2	13.5	15	5	6.8	74
Digestive system diseases	7	21.6	32	4	3.6	111
Cirrhosis of the liver	3	14.4	21	2	1.8	114
Suicide	4	11.9	34	2	0.9	—
Residual	24	59.9	—	7	8.5	—

*SMR = Standardized mortality ratio = (observed/expected) x 100

expected on the basis of the experience of the industrial and general population comparison groups. Deaths due to cancer of the large intestine and to cerebrovascular disease occurred more frequently than expected. Small excesses of cases of prostatic cancer and of melanoma were observed. Sharply decreased rates of lung cancer incidence and mortality and of arteriosclerotic heart disease mortality were observed. The female chemists experienced greater than expected mortality from all causes combined and from suicide.

Among the men, the finding of excess mortality from cancer of the large intestine is based on 12 observed deaths, a number larger than that for any other cancer site. Relative to the experience of the U.S. population, the excess of colon cancer was highest among pensioners. The deaths were distributed throughout all but two major Du Pont department groups.

Larger than expected proportions of deaths due to cancer of the intestine and the rectum occurred among deceased ACS and British RIC members and among chemists dying in the state of California during the years 1959 to 1961.[1,4,11] Among the Swedish chemistry graduates the number of deaths due to malignancies of the digestive system was approximately that which was expected.[6] A recent update of the Swedish cohort showed a slight deficit of digestive system cancer deaths.[19] Among chemists dying in the state of Washington there was one death due to cancer of the large intestine; two deaths were expected.[3]

The incidence of cancer of the large intestine was not elevated with respect to the comparison groups. However, the incidence data are limited to active employees who are under age 65. If the excess frequency appears after age 64, as suggested by the U.S.-based mortality analysis, no excess in incidence would be expected.

The Du Pont chemists show an excess of prostatic cancer relative to nonchemist salaried employees. The occurrence of prostatic cancer increases directly with age,[14] so the Du Pont incidence data, restricted to cases diagnosed before the age of 65, may underestimate the

Table 9. — Observed and Expected Numbers and Proportional Mortality Ratios for Deaths Due to Selected Causes Among Male Chemists, 1964-1977, by Employment Status, Based on U.S. Proportional Mortality Rates.

Cause	Actives			Pensioners			Total		
	Obs	Exp	PMR*	Obs	Exp	PMR	Obs	Exp	PMR
All causes	111	111.0	100	76	76.0	100	198	198.0	100
Malignant neoplasms	25	18.3	137	16	17.9	89	43	37.2	116
Large intestine	5	1.3	377	6	1.5	398	12	2.8	426
Lung	7	5.6	125	2	6.9	29	9	12.7	71
Prostate	0	0.2	—	2	0.8	—	2	0.6	—
Kidney	2	0.5	—	0	0.5	—	2	1.1	187
Lymphatic and hematopoietic cancer	6	2.8	213	3	1.5	196	9	4.7	192
Hodgkin's disease	2	0.6	—	0	0.1	—	2	0.9	—
Leukemia	3	1.1	284	1	0.6	—	4	1.7	230
Arteriosclerotic heart disease	40	29.8	134	31	30.4	102	75	61.9	121
Cerebrovascular disease	5	3.8	132	9	4.1	221	15	7.5	201
Respiratory diseases	2	3.9	51	5	4.6	109	7	8.0	87
Digestive system diseases	7	8.2	85	4	4.0	100	11	13.9	79
Cirrhosis of the liver	3	5.6	54	2	2.4	83	5	9.4	53
Accidents	12	19.2	62	1	3.0	34	14	25.8	54
Suicide	4	7.1	56	2	1.3	158	8	9.9	81

*PMR = Proportional mortality ratio = (observed/expected) x 100

Table 10. — Proportional Mortality Ratios and Estimated Standardized Mortality Ratios for Selected Causes of Death Among Male Chemists.

Cause	Du Pont (Overall SMR = 47)		Li et al[1] < 65 Years		Li et al[1] ≥65 Years		Milham[9] Washington St.		Peterson et al[4] California St.		Registrar General[7] England and Wales	
	PMR_{obs}*	SMR_{obs}†	PMR_{obs}	SMR_{est}‡	PMR_{obs}	SMR_{est}	PMR_{obs}	SMR_{est}	PMR_{obs}	SMR_{est}	PMR_{obs}	SMR_{est}
All cancers	116	50	125	59	115	54	99	47	91	43	96	45
Large intestine	426	174	115	54	134	63	43	20	207	97	N/A§	N/A
Lung	71	29	116	54	80	38	63	30	64	30	63	30
Leukemia	230	119	132	62	178	84	213	100	116	55	320	150
Suicide	81	59	117	55	100	47	195	92	248	117	378	178

*PMR_{obs} = Cause-specific proportional mortality ratio
†SMR_{obs} = Cause-specific standardized mortality ratio
‡SMR_{est} = Cause-specific estimated standardized mortality ration= PMR_{obs} x overall SMR (from Du Pont data)[22]
§N/A = Data not available in published report

risk. Both of the chemists who died from prostatic cancer were pensioners, again suggesting that the greatest risk is in the oldest age groups, for whom incidence data are unavailable. The problem would be compounded if undetected cancer were associated with retirement or with employment termination. An excess of prostatic cancer is also seen among the Swedish chemistry graduates and among the Californian chemists.

The incidence of melanoma was greater than expected among the chemists and the nonchemists, based on the experience of the TNCS population. A similar excess was seen among all Du Pont employees in the period 1956 to 1974.[12] A possible explanation may be occupational exposure to chemicals, some of which are suspected of causing non-melanotic skin cancer.[20] Another putative cause is exposure to solar radiation. The majority of Du Pont plants are located in the southeastern United States where exposure to the sun is high. Fifteen southern states have the highest mortality rates for melanoma, accounting for 37% of the melanoma deaths in the United States.[21] Sixty-five percent of the Du Pont salaried employees are located in these same states.

Excess deaths due to cerebrovascular disease were seen in the Du Pont chemist cohort and among chemists dying in the state of Washington during 1950 to 1971.[3]

Among the men and women, slightly more deaths than expected were due to suicide. Reports from the ACS, from the states of Washington and California, and from the Registrar General of England and Wales also mentioned excess numbers of deaths due to suicide.[2,3,4,7] An excess of suicide among female physicians suggests that a sociological phenomenon may account for the excess among female chemists.[22]

Other excesses were anticipated on the basis of the previous studies of chemist populations. Almost all of the previous studies reported excess deaths due to all sites of cancer combined and to lymphatic and hematopoietic malignancies. Several studies reported excesses in deaths due to bladder and pancreatic cancers.

There are several possible reasons why the Du Pont experience was not consistent with the earlier reports of excesses. First, the outcome measures differed: this study is based on cancer incidence and absolute mortality, while most of the earlier studies were based on proportional mortality. Decouflé et al[23,24] recently discussed the bias of PMR analyses when the overall death rate differs from that of the comparison group. Low overall mortality can cause PMRs to overstate risk. For deaths due to cancer, the Du Pont male chemists had an SMR of 50 and a PMR of 116, relative to the appropriate U.S. comparison population. The earlier chemist populations with excess proportional cancer mortality also may have had low absolute cancer mortality. Table 10 presents the observed PMRs and the estimated SMRs for selected causes of death from the previous chemist cohorts and from the Du Pont chemists. The SMRs were estimated by multiplying each cause-specific PMR by the Du Pont overall SMR. Few of the elevated PMRs are converted into elevated SMRs. In each study, the observed or estimated SMR for leukemia is greater than the SMR for deaths due to all cancers. Conversely, the observed or estimated SMR for lung cancer is smaller than the SMR for all cancers. The Swedish absolute mortality study[6] showed greater cancer mortality than expected, inconsistent with the Du Pont results.

Second, the follow-up period may be too short to permit detection of the anticipated excesses. Slight excesses of deaths due to lymphatic and hematopoietic malignancies and of cases of bladder and of pancreatic cancer were seen, but the observed numbers of events rarely exceeded the expected numbers by more than one. Further follow-up and reanalysis may yield enough cases to confirm the earlier reports of increased risk of these diseases among chemists.

The Du Pont subjects were hired as early as the 1920s, were actively employed in 1959, and were followed until December 31, 1977. The length of follow-up, 19 years, was thought to be adequate for investigation of lymphatic and hematopoietic diseases; the average incubation period for leukemia associated with benzene exposure has been estimated at between 6 and 14 years.[25] The number of persons in the cohort was greater than in the Swedish study, the other absolute mortality study of chemists. However, the chemists were younger and the events fewer than estimated. Approximately three-fourths of the chemists were active employees at the close of the study. The numbers of cases and deaths are small.

Third, associations may have been obscured by exposure misclassification. The Du Pont cohort was restricted to persons employed as chemists who were thought to have had more exposures than either the previously studied chemist cohorts or the nonchemists. However, if

only a small subgroup of the chemists were exposed to hazardous substances, the excess risk would be diluted by the larger unexposed group at low risk. Also, some of the Du Pont nonchemists sustained exposure to hazardous chemicals, contributing to the misclassification problem.

Finally, the cancer incidence data are limited to cases diagnosed before employment termination. No cancers detected after age 65, the mandatory retirement age during the observation period, are identified. This restriction reduces the study's ability to detect excesses of disease increasing directly with age.

Large deficits in overall mortality and in cancer morbidity and mortality rates were observed among the chemists. Deficits were anticipated in the comparisons with the U.S. general population because of the "healthy worker effect,"[26] but not in the comparisons with the Du Pont nonchemist group.

Selection bias is an unlikely explanation for the deficits. The chemist and nonchemist subjects were selected in the same manner from preexistent records that were created without regard for future disease or death.

Observation bias is also unlikely although incomplete ascertainment of deaths may have occurred. Deaths and cancer cases were identified through the Du Pont epidemiologic surveillance system which was established for all employees prior to the initiation of this cohort study. The SSA identified deaths among the employees who terminated employment prior to retirement. Subjects were classified as dead, alive, or status unknown. The subjects not known to be dead were assumed to be alive until the end of the study. If all the chemists whose status was unknown had been deceased, but all such nonchemists were alive, the observed number of deaths would increase by 58 to 256. The expected number would decrease slightly because of fewer chemist person-years of observation, being at most 241.0, yielding an SMR of 106. It is unlikely that this extreme situation occurred. More than half of the chemists whose status was unknown and who had been last employed by Du Pont in the Delaware area had private or business phones listed in their names in the local 1978 phone books. The SSA also may have erred in classifying as alive people who were deceased. In previous studies as many as 6% of persons known to be dead were classified as alive by the SSA.[27]

The most likely explanation for the deficits in the morbidity and mortality experience of the chemists is confounding. Factors associated with cancer may be distributed unequally between the chemist and the comparison groups. The significant deficit in lung cancer morbidity and mortality among the chemists suggests smoking habits different from those of the comparison groups. The chemists also had low mortality from cardiovascular disease and low incidence for several other cancers thought to be related to smoking: cancer of the buccal cavity, esophagus, stomach, and larynx.[28,29] The chemists had only one more case than expected of cancers of the bladder and of the pancreas, which also are associated with cigarette smoking.

It was not possible to obtain smoking histories for past or present Du Pont chemists. Questionnaires and interviews could not be administered, and the smoking histories recorded in the annual medical examinations are unreliable. However, some information on smoking is known. The Du Pont chemists are prohibited from smoking in the research laboratories, while persons in many of the nonchemist occupations, such as lawyers and accountants, have the freedom to smoke during the workday. On-the-job smoking behavior may influence smoking habits outside of work. Data on smoking and occupation from the National Center for Health Statistics 1970 Household Interview Survey showed that the smoking habits of chemists differed from those of other professional and technical workers and from those of other business management employees, such as accountants and auditors.[30] Only 29% of chemists are current smokers, while 33% of accountants and auditors, 36% of professional, technical and kindred workers, and 37% of personnel and labor relations workers are current smokers. The percentage of smokers who smoked one pack or more per day was 59% for the chemists, 66% for professional, technical and kindred workers, 69% for accountants and auditors, and 71% for personnel and labor relations workers. A recent National Health Survey[31] stated that 41% of managers and administrators were current smokers while only 30% of professionals, such as chemists, presently smoked.

The deficits observed in mortality from all causes, from all cancers, and from lung cancer are compatible with the differences in smoking habits reported in the surveys, but there may be other confounding factors also. For example, the chemists probably have a higher socioeconomic status than the comparison groups. The nonchemists include persons, such as foremen, who began employment on the hourly wage roll.

Summary

In this study, Du Pont male employees with the job title chemist or with associated titles experienced lower rates of overall mortality and of overall cancer morbidity and mortality than other salaried employees of the company. A large deficit is seen in lung cancer and arteriosclerotic heart disease. The chemists appear to be at slightly higher risk of death from malignancies of the colon and from cerebrovascular disease. The incidence rates of melanoma and of cancer of the prostate are slightly higher than expected, relative to the TNCS and the experience of nonchemists, respectively. Among female chemists, deaths from all causes combined and from suicide occurred more frequently than expected.

The low overall mortality among the male chemists resulted in a larger than expected proportion of deaths due to cancer. The cancer excesses in the previous proportional mortality reports on chemists may also reflect low absolute mortality and not absolute excesses.

Anticipated excesses of certain types of cancers were not observed, possibly because of the use of absolute mortality rates, inadequate length of follow-up, exposure to hazardous chemicals by the referent group, or restriction of case identification to active employees.

Deficits in overall mortality rates and in lung cancer rates were observed. These findings may have been due to lower prevalence of smoking among the chemists, or to disparate socioeconomic status or other factors.

The authors wish to thank Dr. Bruce W. Karrh, Corporate Medical Director of Du Pont for his support of the study, Drs. Brian MacMahon, Richard R. Monson, and David H. Wegman for epidemiologic advice, Dr. Alan S. Morrison for his review of the manuscript, Dr. Vann C. Brewster for his administrative assistance, and Audrey E. L. Gidney for her programming assistance. William E. Fayerweather, Brian H. Wright, and George W. Zervas also provided programming assistance. Ann D. Monson was the nosologist. Clerical duties were performed by Mary Donahue, Louise Mowbray, Geni A. Nardo, Lisa P. Ranken, and Delores Saunders. Kathryn C. Buchanan, Doris Carmo, Gertrude M. Crowley, Martha DiDomenicis, and Mary O'Loughlin provided secretarial services.

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