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Occupational **risk factors** for multiple myeloma among Danish men

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A large population-bared rase-contml study evaluated occupational exposures in 1,098 Danish males diagnosed with multiple myeloma from 1970 to 1984 and in 4,369 age- and gender-matched controls alive at the time of case-diagnosis. Industrial histories were obtained from the Supplementary Pension Fund which, since 1964, has recorded employments of adult Danes; occupation came from subjects' most recent tax records. Four industrial hygienists created a job-exposure matrix for 47 substances based on 15,000 unique industry/occupation combinations in subjects' histories. Risk of myeloma was significantly elevated among mad and railroad workers. precision metalworkers, and workers in the transportation and communication industries. Risk increased significantly with duration of employment in: production of synthetic yarns, plastic packaging, and miscellaneous chemical compounds; fabricating structural metal and stationary tanks; body factories; electrical plants; and retail sale of paint and wallpaper. Risks of myeloma were elevated, though statistically nonsignificantly, in all categories of exposure to gasoline and engine exhausts. Risks rose with likelihood and duration of exposure to phthalates, and were statistically significant and nearly fivefold witb probable exposure to vinyl chloride for five or more years. After adjusting for multiple exposures and disregarding exposures within 10 years of diagnosis (or selection as a control), probable exposure to vinyl chloride was associated with increased risk of myeloma, which rose to fivefold with longer exposure. Associations with gasoline, engine exhausts, and phthalates persisted, but were inconsistent with duration and probability of exposure. Previously reported associations with agriculture were not confirmed by these data,

Key words: Denmark, industry, metalworking, multiple myeloma, occupation, phthalates, risk factors, vinyl chloride,

Introduction

Multiple myeloma (MM), a tumor of well-differentiated plasma cells, is responsible for about one to two percent of the cancers diagnosed in the United States[1] and in Denmark.[2] The incidence in Danish men, 2.7/100,000, is similar to that of men in Finland, the United Kingdom, and US Whites.[2] Myeloma incidence increased between 1943 and 1962 in Denmark, then stabilized or decreased slightly.[3] The etiology of MM is largely unknown.[4]

Studies of occupational risk factors for myeloma have shown few consistent patterns. Apart from exposure to ionizing radiation and an excess risk among farmers,[4] few specific associations have been observed consistently. Prior studies of occupational

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factors in myeloma have been hampered by relatively small size (given the rarity of the disease) and by lack of detailed information on potential exposures. In this collaborative study, we attempted to overcome some of the limitations of prior studies by amassing a large number of incident cases and employing industrial hygienists to assess exposures in subjects' jobs. This paper, which evaluates occupational exposures and MM among men, is a companion report to an earlier publication on women.[5]

Methods and materials

Subjects

Men diagnosed with MM in Denmark between 1970 and 1984 and reported to the Danish Cancer Registry were eligible for the study. Of all malignancies diagnosed in Denmark since 1943, an estimated 95 to 98 percent are included in the Registry.[6] Subjects born before April 1897 or under age 18 at date of diagnosis were excluded, because they were not included in the Danish Supplementary Pension Fund (SPF), the primary source of employment information for this study. Ninety-two percent of cases had been verified histologically.

Four live controls were chosen randomly from the Danish Central Population Registry for the year in which the case was diagnosed, matched to the case on sex and year of birth. Subjects were excluded if they were diagnosed with a malignancy other than myeloma for a case or any malignancy for a control, 91 or more days prior to an index date—the date of diagnosis of the case.

Data collection

Information on employment histories was obtained by linking Cancer Registry records to those of the SPF, using subjects' unique Danish identity number and name. Established in 1964, the SPF contains information on all wage-earners aged 16 to 66 who are employed at least 10 h per week by any one employer. Information is kept for pensioners and deceased persons. Type of industry was identified for jobs held by subjects from 1964 to the index date, except for a small number of jobs (8.8 percent) for which the employer was not in business after 1977. No data were available for jobs held while self-employed.

Occupation was determined by the job title recorded on subjects' most recent tax records. Norm-od of earlier occupations was available. occupation and industry were classified using Danish codes, which are based on the 1968 International Standard Industrial Classification of all Economic Activities (ISIC).[7]

Exposure assessment

The 15,000 unique combinations of occupation and/or industry codes for the study subjects were divided among four Danish industrial hygienists, who assessed exposure (none, possible, probable, or unknown) to 20 major categories of substances and 27 specific stances. In their assessment, the hygienists gave primary weight to industry. Occupation was used primarily to determine whether or not a subject was likely to be a 'blue-collar' worker (exposed to processes of production) within an industry, with two exceptions. For job/industry combinations in which the study subjects were employed for less than one year, exposures were coded based on occupation alone. In the case of farming occupations, an industrial hygienist judged whether the industry was one in which a person was likely to be employed while also farming. If so, that industry/occupation combination was assigned exposures typical for both the industry and the farming occupation.

Analyses

Of the 1,222 cases and 4,888 controls, no information available on either occupation or industry for 124 cases (10 percent) and 719 controls (15 percent). These subjects were omitted from further consideration.

Maximum likelihood estimates of the odds ratio (OR) and 95 percent confidence intervals (CI) were calculated according to Gart,[8] adjusting for age in four categories (<60, 60-69, 70-79, and 80+ years). CIs which excluded one (before rounding to one decimal) were considered statistically significant.

Risks for each occupation were calculated compared with all other occupations combined. Men lacking occupation information and those with uninformative entries for occupation (e.g., pensioner, student, worker 'not otherwise specified') were excluded from analyses ... specific occupations, leaving 835 cases and 2,979 controls. Risk for employment in specific industries was evaluated among subjects for whom the Pension Fund recorded at least one industry (791 cases, 3,070 controls). For each industry, subjects never employed in that industry comprised the referent group. For analyses of specific substances, the referent group consists of subjects judged never to have been exposed to the substance. Subjects lacking any industrial history were excluded from these analyses, as were subjects with unknown exposure to a given substance.

Analyses of duration, whether for industries or agents, were restricted to men with at least five years of employment recorded on the file. Trends of risk with duration of employment (less than five years, five years or more) in industries were tested for linearity using the Mantel extension test for trend,[9] as were trends with duration of exposure (*i.e.*, employment in jobs judged to entail possible or probable exposure to an agent). Risks allowing for latency period were calculated by lagging exposure data, that is, by disregarding employment or exposures within five or 10 years of the index date (the date of diagnosis of the case).

Logistic regression was used to adjust simultaneously for exposure to multiple agents (categorically, by probability and duration), controlling for age as a continuous variable.

Results

The 1,098 cases and 4,169 controls with information on occupation and/or industry were mostly in their 60s and 70s at diagnosis. Of the 843 excluded subjects with information on neither, 87 percent had been more than 55 years of age in 1964, when the Pension Fund began recording information, compared with 47 percent of included subjects. Among the 3,964 subjects with employment records in the Pension Fund (75 percent), the majority (2,982, 75 percent) had one to three jobs listed.

Occupation

Men whose most recent tax record listed either no occupation or 'pensioner' had a significantly lower risk of MM than other Danish men (81 cases, OR = 0.4, CI = 0.3-0.5; and 169 cases, OR = 0.8, CI = 0.6-0.9, respectively). Inclusion of these men in the referent group for analyses of occupation would have inflated estimates for all other occupations. The other excluded men (worker 'not otherwise specified,' student) were similar in risk to the remaining subjects (137 cases, OR = 1.0, CI = 0.9-1.3).

In 13 broad occupational categories (Table 1), risk of myeloma was increased only among Danish men in the military. Among more narrowly defined occupations, risks were elevated significantly among 'other specialty

Table 1. Age-adjusted odds ratios (OR) and 95% confidence interval (CI) for risk of multiple myeloma for most recent occupation[a] among Danish men

Occupation	Cases (*n* = 835)	Controls (*n* = 2,979)	OR	(CI)
Managerial/professional	130	491	0.9	(0.8-1.2)
Doctor/dentist/pharmacist	4	34	0.5	(0.1-1.2)
Veterinarian/assistant	2	11	0.6	(0.1-3.1)
Teacher	19	63	1.1	(0.6-1.9)
Sculptor/artist/photographer	7	16	1.6	(0.6-4.1)
Technical/sales/administrative support	147	494	1.1	(0.9-1.3)
Wholesaler	7	[illegible]	2.B	(0.9-8.3)
Grocer	2	[illegible]	15	(0.8-2.6)
Service	38	152	0.9	(0.6-1.3)
Cook/caterer	1	3	1.2	(0.0-12.4)
Protective service	5	36	0.5	(0.2-1.3)
Janitor, drycleaning	7	25	1.0	(0.4-2.4)
Military	5	8	2.2	(0.6-7.5)
Agriculture	192	647	11	(0.9-1.3)
Farm owner	84	290	1.0	(0.8-1.3)
Tenant farmer, agricultural garden worker	98	310	1.1	(0.9-1.5)
Herdsman	4	8	1.8	(0.5-6.6)
Nurseryman	3	8	1.3	(0.3-5.5)
Other specialty farm worker	5	4	1.6	(1.1-20.3)
Forestry/fishing	4	34	0.4	(0.1 - 13)
Foreman/technical leader/contractor	31	113	1.0	(0.6-1.5)
Contractor	4	5	2.8	(0.6-12.1)
Construction trades	52	204	0.9	(0.7-1.3)
Bricklayer/brickworker	12	63	0.7	(0.3-1.3)
Electrician/electrical installer	9	18	1.8	(0.8-4.3)

Continued...

Table 1. *Continued*

Occupation	Cases (n = 831)	Controls (n = 2,979)	OR	(CI)
Carpenter/joiner	10	57	0.6	(0.3-1.3)
Printer	11	38	1.0	(0.5-2.1)
Mine/other extractive workers	0	2	—	—
Precision mechanic/repair	6	46	0.5	(0.2-1.1)
Precision production	96	330	1.0	(0.8-1.3)
Fabricator/assembler	31	138	0.8	(0.5-1.2)
Food/alcohol/tobacco worker	19	75	0.9	(0.5-1.6)
Butcher/slaughterhouse	7	40	0.6	(0.3-1.5)
Baker/confectioner	2	22	0.3	(0.1-1.4)
Grain miller	1	2	1.9	(0.1-26.3)
Tailor/cutter	4	12	1.2	(0.3-4.0)
Textile fabrication	4	16	0.9	(0.3-2.8)
Precision shoe/leather	2	20	0.4	(0.1-1.6)
Leather tanning	0	6	—	—
Precision wood worker	26	74	1.3	(0.8-2.0)
Furniture maker	19	55	1.2	(0.7-2.1)
Sawmill/other wood worker	8	27	1.1	(0.4-2.5)
Paper and cardboard worker	2	6	1.2	(0.2-6.4)
Print/graphics fabrication	14	46	1.1	(0.6-2.0)
Typographer/compositor	4	22	0.6	(0.2-2.0)
Precision stone worker	6	11	2.0	(0.6-5.7)
Glass/ceramic worker/glazier	6	8	2.7	(0.8-8.7)
Glass blower/maker	1	2	1.8	(0.1-25.1)
Ceramic and porcelain worker	2	4	1.8	(0.2-11.5)
Glazier	3	2	5.4	(0.7-46.6)
Rubber/plastic worker	0	4	—	—
Precision metal/machinist	1	105	1.4	(1.0-2.1)
Smith	3	25	1.9	(0.9-3.8)
Machine fitter	7	10	1.6	(0.6-4.1)
Machinist/engine mechanic	6	52	1.1	(0.6-2.0)
Other precision metalworker	3	4	2.6	(0.5-13.8)
Toolmaker, skilled and unskilled metalworker	6	18	1.2	(0.4-32)
Insulator/pipefitter/boilermaker	1	13	0.3	(0.0-2.0)
Welder	6	11	2.0	(0.6-5.7)
Transportation and material handling	5	119	1.2	(0.9-1.6)
Road/railroad worker	2	19	2.3	(1.0-4.9)
Chauffeur	1	123	1.2	(0.8-1.7)
Other transportation worker	1	2	7.4	(1.2-58.0)

[a] Occupation is that listed on subjects' most recent tax record. For each occupation, the unexposed consists of all other occupations. Subjects with missing or noninformative occupation codes were excluded from the analysis.

farm workers' (e.g., bee keeper, kennel worker), precision metalworkers, road and railroad workers, and other transportation workers.

Industry

Men who worked in transportation or communication had a statistically significant 30 percent excess of MM (Table 2), an excess seen among those employed particularly in the railroad, bus/taxi/freight, and communication industries. None of the other eight broad industry-categories showed a significantly elevated risk. Among narrower industries, a significant deficit of myeloma was observed among workers in the food/alcohol/tobacco industry. Also significant were a nearly threefold risk for workers in cement plants and a twofold risk associated with employment in fabricating structural metal and stationary tanks (with similar risks found in both subdivisions of the industry). Although not statistically significant, ORs were two- to threefold in: wool spinning and weaving; manufacture of synthetic yarns; 'other' chemical compounds

Table 2. Risk of multiple myeloma among Danish men employed in selected industries (Danish industrial code); age-adjusted odds ratios (OR) and 95% confidence interval (CI)

Industry	Cases (n = 791)	Controls (n = 3,070)	OR	(CI)
Agriculture/hunting/forestry/fishing (1)	69	266	1.0	(0.8-1.4)
Agriculture (11101)	45	162	1.1	(0.8-1.5)
Truck garden/orchard/nursery (11102)	10	30	1.3	(0.6-2.8)
Forestry (12)	10	39	1.0	(0.5-2.1)
Extraction of raw material (2)	11	28	1.5	(0.7-3.2)
Manufacturing (3)	319	1323	0.9	(0.8-1.1)
Food/alcohol/tobacco (31)	71	368	0.7	(0.6-1.0)
Slaughter/meat (3111)	21	94	0.9	(0.5-1.4)
Dairies (31121)	15	45	1.3	(0.7-2.4)
Grain/bakery (31160-31174)	5	34	0.6	(0.2-1.5)
Textile manufacture (321)	17	57	1.2	(0.7-2.1)
Wool spinning/weaving (32111)	6	8	2.9	(0.9-9.3)
Cotton spinning/weaving (32112)	2	6	1.3	(0.2-7.2)
Synthetic yarns (32113)	3	4	2.9	(0.5-15.4)
Leather/shoe (32310-32409)	5	24	0.8	(0.3-2.3)
Wood/wood products (33)	34	138	1.0	(0.6-1.4)
Lumber (33111-33114)	12	68	0.7	(0.3-1.3)
Miscellaneous wood products (33121-33197)	8	19	1.6	(0.7-4.0)
Paper/printing (34)	25	135	0.7	(0.5-1.1)
Chemical/rubber/plastic (35)	50	208	0.9	(0.7-1.3)
Other chemical compounds (35119)	5	9	2.2	(0.6-7.2)
Paint (35210)	3	5	2.3	(0.4-11.1)
Rubber (355)	6	23	1.0	(0.4-2.7)
Plastic (356)	9	38	0.9	(0.4-2.0)
Plastic packaging (35601)	5	8	2.5	(0.7-8.3)
Stone/clay/glass (36)	49	187	1.0	(0.7-1.4)
Porcelain and glass (36101-36202)	11	37	1.1	(0.6-2.4)
Porcelain/ceramics (36101-36102)	5	13	1.5	(0.5-4.4)
Cement plant (36921)	9	13	2.7	(1.1-6.7)
Concrete products (36993)	19	75	1.0	(0.6-1.7)
Other stone/clay/glass, including asbestos (36999)	4	8	2.0	(0.5-7.3)
Primary metal (37)	13	61	0.8	(0.4-1.6)
Fabricated metal/shipbuilding/machinery (38)	132	529	1.0	(0.8-1.2)
Structural metal/tanks (38131-2)	15	29	2.0	(1.0-4.0)
Body factory excluding auto (38432)	8	17	1.8	(0.7-4.5)
Electricity/gas/heat/water (4)	18	44	1.6	(0.9-2.9)
Elec/gas/heating supply (41)	16	39	1.6	(0.9-3.0)
Electrical plants (41010)	12	31	1.5	(0.7-3.1)
Other utilities (41020-42000)	6	13	1.8	(0.6-5.1)
Building/planning (5)	140	560	1.0	(0.8-1.2)
General contracting (50121)	82	335	0.9	(0.7-1.2)
Painting/wallpapering (50150)	3	22	0.5	(0.1-1.9)
Trade/restaurant/hotel (6)	188	715	1.0	(0.9-1.3)
Wholesale trade (61)	133	498	1.0	(0.8-1.3)
Grain (61161)	21	68	1.2	(0.7-2.0)
Wood/lumber/building materials (61168)	20	66	1.2	(0.7-2.0)
Fuel/oil/gas (61192)	12	56	0.8	(0.4-1.6)
Retail trade (62)	55	223	1.0	(0.7-1.3)
Paint (62131)	2	5	1.5	(0.2-9.0)
Restaurants/hotel (63)	21	90	0.9	(0.5-1.5)
Transportation/communication (7)	127	399	1.3	(1.0-1.6)
Transportation (71)	100	320	1.3	(1.0-1.6)
Railroads (71110)	34	96	1.4	(0.9-2.1)

Continued ...

Table 2. *Continued*

Industry	Cases (n = 791)	Controls (n = 3,070)	OR	(CI)
Bus/taxi/freight (71120-49)	29	88	1.3	(0.8-2.0)
Communication (72)	28	88	1.2	(0.8-2.0)
Banking/finance/real estate/administration (8)	154	520	1.2	(1.0-1.5)
Service (9)	253	1051	0.9	(0.8-1.1)
Chimney sweeping (92023)	1	2	2.0	(0.1-27.6)
Health care (933)	4	19	3.8	(0.2-2.6)
Repair/laundry/personal services (95)	21	71	1.1	(0.7-1.9)
Repair (951)	12	31	1.5	(0.7-3.1)
Auto painting (95133)	2	2	5.9	(0.4-38.0)

(including emulsifiers, enzymes, tanning extracts, dyes, sulfonamides, and pesticides as single compounds); plastic packaging; 'other' stone, clay and glass (including asbestos) products; and body factories excluding automobiles (e.g., trailers, camping, and farm vehicles). Risk of myeloma was elevated in paint manufacture, retail sale of paint, and auto painting, but not among painting and wallpapering contractors. Smaller risk increases were evident in both electrical plants and other utilities. Risk of myeloma was not elevated in agriculture (except for a nonsignificant 30 percent increase in truck gardening, orchards, or nurseries) or forestry, the leather or *shoe*, paper or printing, or rubber industries.

Among men for whom five or more total years of employment were recorded, risk of myeloma did not increase with duration in the broad industrial categories, except for a small, statistically significant increase for employment in banking, finance, and real estate (Table 3). Risk of myeloma increased significantly with duration of employment in manufacture of synthetic yarns, 'other' chemical compounds, plastic packaging, fabricated structural metal and stationary tanks, body factories, and retail sale of paint and wallpaper. Employment in the food, alcohol, and tobacco industry of either more or less than five years was associated with the same reduced risk (OR = 0.6), though the test for trend was significant. Compared with men employed for less than five years, risk of myeloma was higher, though not significantly so, among men employed longer in dairies, in manufacture of miscellaneous wood products, chemical raw materials, paint, porcelain and glass, in electrical plants, in wholesale trade in grain, and in real estate.

In most industries, disregarding employment within five years of the index date (not shown) had little effect *on* the ORs. The only significant individual risk was that for five or more years' employment in retail sale of paint and wallpaper. Statistically significant increases with duration of employment were apparent for: manufacture of synthetic yarns (OR = 1.9 for less than five years [based on one case]; OR = ∞ for more than five years [two cases, no controls]); fabricated structural metal and stationary tanks (OR = 2.3 [10 cases], and 3.9 [three cases]): body factory (2.9 [five cases] and 2.6 [two cases]); and retail sale of paint and wallpaper (1.3 [two cases] and 15.5 [four cases]). Risk elevations with increased duration were enhanced and trends were statistically significant for manufacture of miscellaneous wood products (OR = 1.1 [three cases] and 6.0 [three cases]), and wholesale trade in grain (1.4 [12 cases], 2.1 [seven cases]). The increase *with* duration was nearly significant for employment in electric plants (1.2 [five cases] and 2.4 [five cases]). Longer employment in manufacture of plastic packaging was still associated with increased risk of myeloma (1.9 [two cases] and 3.9 [one case]) but the trend was no longer significant.

In contrast, after lagging exposures, risk of myeloma was higher among men who worked fewer than five years, but lower among men employed longer in manufacture of other chemical compounds (OR = 4.0 [four cases] and 1.9 [one case]) and paint (OR = 1.9 [two cases] and 0 [no cases, one control]). For industries in which at least five cases were available, results for analyses allowing for a 10-year latency period (not shown) were similar *to* those presented above.

Agents

Risk of myeloma from potential exposure to specific substances is shown in Table 4. Only men employed in jobs which entailed possible exposure to engine exhausts or to raw milk had a significantly increased risk of myeloma. Risk of MM was higher among men probably exposed than among those possibly exposed

Table 3. Risk of myeloma by duration of employment in selected industries (Danish industrial code), among Danish men with at least five years' employment recorded in the Supplementary Pension Fund (SPF), age-adjusted odds ratios (OR) and 95% confidence intervals (CI)

Industry	Employed 1 month to < 5 years				Employed 5 + years				*P* for trend
	Cases	Controls	OR	(CI)	Cases	Controls	OR	(CI)	
Agriculture/hunting/forestry/fishing (1)	37	128	1.1	(0.8-1.7)	17	78	0.8	(0.5-1.5)	0.82
Agriculture (11101)	24	78	1.2	(0.8-1.9)	9	43	0.8	(0.4-1.7)	0.95
Truck garden/orchard/nursery (11102)	7	15	1.8	(0.7-4.7)	1	8	0.5	(0.0-3.8)	0.80
Extraction of raw material (2)	9	16	2.2	(0.9-5.3)	1	8	0.5	(0.0-3.8)	0.49
Manufacturing (3)	91	339	1.0	(0.8-1.3)	177	734	0.9	(0.7-1.1)	0.37
Food/alcohol/tobacco (31)	25	143	0.6	(0.4-1.0)	28	163	0.6	(0.4-1.0)	0.005
Dairies (31121)	6	23	1.0	(0.4-2.6)	5	13	1.5	(0.5-4.5)	0.52
Textile manufacture (321)	6	28	0.8	(0.3-2.1)	a	22	14	(0.6-3.3)	0.49
Wool spinning/weaving (32111)	5	5	2.3	(0.4-11.1)	1	3	13	(0.1-13.9)	0.38
Synthetic yarns (32113)	0	3	—	(—)	3	1	11.9	(1.1-297.2)	0.03
Wood/wood products (33)	16	54	1.1	(0.6-1.9)	11	47	0.9	(0.4-1.8)	0.86
Miscellaneous wood products (33121-33197)	3	13	0.9	(0.2-3.4)	3	3	3.9	(0.6-24.4)	0.19
Chemical raw materials (351)	12	40	1.0	(0.5-1.9)	9	23	1.5	(0.7-3.5)	0.40
Other chemical compounds (35119)	3	5	2.4	(0.4-11.3)	2	2	3.9	(0.4-38.8)	0.06
Paint (35210)	I	4	0.9	(0.0-9.0)	1	I	3.8	(0.1-139.7)	0.44
Rubber (355)	2	10	0.8	(0.1-3.7)	2	I0	0.8	(0.1-3.8)	0.64
Plastic (356)	6	25	1.0	(0.4-2.6)	3	9	1.3	(0.3-5.2)	0.74
Plastic packaging (35601)	3	4	2.9	(0.5-15.6)	2	2	3.9	(0.4-38.2)	0.04
Porcelain/glass (36101-36202)	3	9	1.3	(0.3-5.2)	7	19	1.4	(0.5-3.6)	0.38
Cement plant (36921)	3	3	3.9	(0.6-24.0)	5	7	1.7	(0.3-7.1)	0.18
Other stone/clay/glass including asbestos (36999)	3	3	3.9	(0.6-24.3)	1	4	1.0	(0.0-9.2)	0.39
Fabricated metal (381)	17	86	0.8	(0.4-1.3)	15	36	1.6	(0.8-3.1)	0.50
Structural metal/tanks (38131-2)	7	20	1.4	(0.5-3.4)	7	5	5.5	(1.6-19.9)	0.003
Body factory excluding auto (38432)	6	8	224	(0.9-9.2)	2	2	39	(0.4-38.7)	0.01
Electricity/gas/heat/water (4)	8	19	1.6	(0.7-4.0)	7	20	1.4	(0.5-3.4)	0.25
Electrical plants (41010)	4	12	13	(0.3-4.3)	6	15	1.5	(0.5-4.3)	0.32
Other utilities (41020-42000)	4	7	2.3	(0.6-$6)	1	5	0.8	(0.0-6.8)	0.58
Building/planning (5)	70	231	1.2	(0.9-1.6)	48	225	0.8	(0.6-1.2)	0.55
Painting/wallpapering (50150)	1	8	0.5	(0.0-3.8)	1	9	0.4	(0.0-32).	0.29
Trade/restaurant/hotel (6)	70	255	1.1	(0.8-1.5)	84	298	1.1	(0.8-1.5)	0.39
Grain (61161)	12	36	1.3	(0.6-2.6)	7	14	2.0	(0.7-5.2)	0.10
Wood/lumber/building materials (61168)	11	34	1.3	(0.6-2.6)	6	19	1.2	(0.4-3.3)	0.48
Paint/wallpaper (retail) (62131)	1	5	as	(0.0-6.8)	5	3	64	(1.3-33.8)	0.01
Transportation/communication (7)	41	142	11	(0.8-1.6)	59	197	1.2	(0.9-1.6)	0.24
Railroads (71110)	9	24	1.4	(0.6-3.3)	17	67	1.0	(0.5-1.7)	0.95
Banking/finance/real estate/administration (8)	73	241	1.2	(0.9-1.6)	60	182	1.3	(1.0-1.8)	0.03
Real estate (83)	59	205	1.1	(0.8-1.6)	39	109	1.4	(0.9-2.1)	0.07
Service (9)	66	237	1.0	(0.8-1.4)	143	597	a9	(0.7-1.1)	0.43
Repair (951	9	17	2.0	(0.8-4.9)	2	8	1.0	(0.1-4.9)	0.29

to gasoline, oil products, textile dyes, phthalates, and vinyl chloride. Although ORs were 1.3 or greater with possible exposure to benzene, hair dyes (based on one case), manufacture of rubber. leather dust, furred animals and products, living farm animal, raw milk, and ionizing radiation, risks were nor elevated among men probably exposed to these agents.

We next evaluated risk of myeloma with duration of exposure within probability categories among men with five or more years recorded in the Pension Fund. When exposures were not lagged (Table 5, columns 1 and 2), all categories of exposure to gasoline and to engine exhausts showed a similar 20 to 50 percent increase in risk of myeloma. Although tests for trend

Table 4. Risk of myeloma among Danish men with possible or probable exposure to agents as assessed by industrial hygienists, based on work history; age-adjusted odds ratios (OR) and 95% confidence intervals (CI)

Agent[a]	Possible exposure to agent				Probable exposure to agent			
	Cases	Controls	OR	(CI)	Cases	Controls	OR	(CI)
Products of coal and oil	199	766	1.0	(0.8-1.3)	134	523	1.0	(0.8-1.3)
Coal	58	214	1.1	(0.8-1.5)	12	45	1.1	(0.5-2.1)
Tar/asphalt/soot	49	173	1.1	(0.8-1.6)	17	113	0.6	(0.3-1.0)
Cutting oils	178	679	1.0	(0.8-1.3)	48	191	1.0	(0.7-1.4)
Gasoline	146	500	1.2	(1.0-1.5)	41	123	1.4	(0.9-2.1)
Oil products	200	771	1.1	(0.9-1.3)	57	171	1.4	(1.0-1.9)
Engine exhausts	125	395	1.3	(1.0-1.6)	89	267	1.3	(0.9-1.6)
Organic solvents	214	719	1.1	(0.9-1.4)	119	489	0.9	(0.7-1.2)
Benzene	137	415	1.3	(1.0-1.6)	52	253	0.8	(0.6-1.1)
White spirit	151	506	1.1	(0.9-1.4)	70	264	1.0	(0.8-1.4)
Halogenated organic solvents	150	500	1.1	(0.9-1.4)	39	154	1.0	(0.6-1.4)
Methylethylketone	110	352	1.2	(1.0-1.6)	41	192	0.8	(0.6-1.2)
Anaesthetic gases	4	19	0.8	(0.2-7.4)	0	12	—	—
Paints and lacquers	69	253	1.0	(0.8-1.4)	38	174	0.8	(0.6-1.2)
Pigments	58	216	1.0	(0.7-1.4)	17	101	0.6	(0.4-1.1)
Textile dyes	8	26	1.2	(0.5-2.7)	7	21	1.3	(0.5-3.1)
Printing ink	11	39	1.0	(0.5-2.1)	5	32	0.6	(0.2-1.6)
Hair dyes	1	1	3.6	(0.1-132.1)	0	7	—	—
Manufacture of rubber and vulcanization of rubber	5	5	2.3	(0.4-11.0)	3	13	0.9	(0.2-3.3)
Plastic materials and adhesives except those based on formaldehyde and phenol	126	440	1.1	(0.9-1.4)	60	221	1.1	(0.8-1.5)
Styrene	79	265	1.2	(0.9-1.5)	6	44	0.5	(0.2-1.3)
Phthalates	34	99	1.3	(0.9-2.0)	11	21	2.0	(0.9-4.4)
Vinyl chloride	22	83	1.0	(0.6-1.7)	4	20	1.7	(0.7-4.0)
Acrylonitrile	102	336	1.2	(0.9-1.5)	18	81	0.9	(0.5-1.5)
Isocyanates	110	387	1.1	(0.9-1.4)	9	46	0.8	(0.3-1.5)
Formaldehydes	144	527	1.0	(0.8-1.3)	41	142	1.1	(0.7-1.6)
Phenols	117	435	1.0	(0.8-1.3)	33	138	0.9	(0.6-1.3)
Metals	170	592	1.1	(0.9-1.4)	78	330	0.9	(0.7-1.2)
Lead	46	204	0.9	(0.6-1.3)	11	53	0.7	(0.4-1.5)
Mercury	31	100	1.2	(0.8-1.8)	3	15	0.7	(0.2-2.6)
Soldering	72	248	1.1	(0.8-1.5)	10	45	0.8	(0.4-1.7)
Wood dust	110	360	1.2	(0.9-1.5)	49	222	0.8	(0.6-1.2)
Leather dust	3	8	1.4	(0.3-5.9)	0	7	—	—
Other biologic organic dust	123	406	1.1	(0.9-1.4)	137	615	0.8	(0.7-1.0)
Asbestos	135	443	1.2	(1.0-1.5)	19	79	1.0	(0.6-1.7)
Silica dust	97	320	1.2	(0.9-1.5)	18	61	1.2	(0.7-2.0)
Other inorganic dust	206	693	1.2	(0.9-1.4)	118	467	1.0	(0.8-1.3)
Animals or products of	40	133	1.1	(0.8-1.6)	87	366	0.9	(0.7-1.1)
Furred animals[b]	11	26	1.6	(0.7-3.4)	10	66	0.6	(0.3-1.2)
Farm animals (living)	26	76	1.3	(0.8-2.1)	59	217	1.0	(0.7-1.4)
Raw meat	31	126	0.9	(0.6-1.4)	29	162	0.7	(0.4-1.0)
Raw milk	17	31	2.1	(1.1-4.0)	60	222	1.0	(0.8-1.4)
Pesticides	113	391	1.1	(0.9-1.4)	105	394	1.0	(0.8-1.3)
Fungicides (wood)	106	353	1.1	(0.9-1.3)	20	83	0.9	(0.5-1.5)
Pesticides in agriculture, forestry or gardening	24	78	1.2	(0.7-1.9)	88	307	1.0	(0.8-1.4)
Ionizing radiation	15	37	1.5	(0.8-2.9)	0	10	—	—
Non-ionizing radiation	17	70	0.9	(0.5-1.6)	3	26	0.4	(0.1-1.5)

[a] For each agent, the referent group consists of men considered by the industrial hygienist to have never been exposed to that substance.
[b] Principally 'fur-farmers' (e.g., of mink, ermine) and workers handling furs or hides of these or other animals.

Table 5. Risk of myeloma associated with duration and probability of exposure to selected agents among Danish men with at least 5 years of employment recorded in the Supplementary Pension Fund; age-adjusted odds ratios (OR) and 95% confidence intervals (CI)

Agent	No lagging of exposure								Lagging exposure 10 years[a]							
	Possible exposure to agent				Probable exposure to agent				Possible exposure to agent				Probable exposure to agent			
	Cases	Controls	OR	(CI)	Cases	Controls	OR	(CI)	Cases	Controls	OR	(CI)	Cases	Controls	OR	(CI)
Gasoline																
1 month - < 5 years	48	156	1.3	(0.9-1.9)	14	40	1.5	(0.8-2.9)	51	190	1.1	(0.8-1.6)	18	40	1.9	(1.0-3.5)
5 + years	85	307	1.2	(0.9-1.5)	24	71	1.4	(0.9-2.4)	36	93	1.6	(1.0-2.5)	6	31	0.6	(0.3-2.1)
P for trend[b]		0.09				0.04				0.02				0.24		
Oil products																
1 month - < 5 years	57	212	1.1	(0.8-1.6)	19	54	1.5	(0.8-2.6)	71	294	1.0	(0.7-1.3)	20	60	1.4	(0.8-2.4)
5 + years	131	490	1.1	(0.9-1.4)	32	99	1.4	(0.9-2.1)	48	162	1.2	(0.8-1.7)	7	35	0.8	(0.3-2.0)
P for trend		0.20				0.04				0.26				0.42		
Engine exhausts																
1 month - < 5 years	52	147	1.5	(1.0-2.1)	25	71	1.4	(0.9-2.4)	56	163	1.4	(1.0-2.0)	29	94	1.3	(0.8-2.1)
5 + years	76	242	1.3	(1.0-1.7)	52	169	1.3	(0.9-1.8)	30	73	1.7	(1.0-2.7)	19	75	1.1	(0.6-1.9)
P for trend		0.02				0.05				0.002				0.24		
Benzene																
1 month - < 5 years	58	147	1.5	(1.1-2.1)	22	67	1.2	(0.7-2.1)	51	162	1.2	(0.9-1.8)	25	72	1.4	(0.8-2.3)
5 + years	68	246	1.1	(0.8-1.5)	25	148	0.7	(0.4-1.1)	23	79	1.1	(0.7-1.9)	6	59	0.4	(0.2-1.0)
P for trend		0.16				0.07				0.14				0.12		
Textile dyes																
1 month - < 5 years	5	7	2.7	(0.7-9.4)	4	8	1.9	(0.5-6.8)	2	9	0.8	(0.1-4.2)	1	7	3.5	(0.0-4.4)
5 + years	4	21	0.7	(0.2-2.2)	1	8	0.5	(0.0-3.7)	1	11	0.3	(0.0-2.6)	0	5	—	
P for trend		0.50				0.46				0.15				0.10		
Phthalates																
1 month - < 5 years	12	41	1.1	(0.6-2.3)	3	6	1.9	(0.4-8.5)	7	41	0.6	(0.3-1.5)	4	7	2.1	(0.5-8.1)
5 + years	17	54	12	(0.7-2.2)	7	11	2.5	(0.9-7.0)	7	14	1.9	(0.7-5.2)	1	6	0.7	(0.0-5.4)
P for trend		0.21				0.02				0.30				0.38		
Vinyl chloride																
1 month - < 5 years	9	39	0.9	(0.4-2.0)	2	9	0.9	(0.1-4.3)	3	36	0.3	(0.1-1.1)	4	7	2.2	(0.5-8.6)
5 + years	7	37	0.7	(0.3-1.7)	7	6	4.6	(1.4-15.4)	2	13	0.6	(0.1-2.8)	3	4	2.9	(0.5-15.6)
P for trend		0.22				0.004				0.04				0.03		
Asbestos																
1 month - < 5 years	53	170	1.3	(0.9-1.8)	1	23	0.2	(0.0-1.2)	56	165	1.4	(1.0-2.0)	7	30	1.0	(0.4-2.3)
5 + years	65	222	1.2	(0.9-1.6)	13	47	1.1	(0.6-2.2)	25	83	1.2	(0.7-2.0)	6	22	1.1	(0.4-3.0)
P for trend		0.08				0.42				0.04				0.44		
Pesticides in agriculture, forestry or gardening																
1 month - < 5 years	8	31	1.0	(0.4-2.2)	18	79	0.8	(0.5-1.5)	8	39	0.8	(0.3-1.8)	32	83	1.5	(1.0-2.3)
5 + years	19	55	1.3	(0.7-2.3)	45	142	1.2	(0.8-1.7)	3	16	0.8	(0.2-2.8)	12	60	0.8	(0.4-1.6)
P for trend		0.20				0.22				0.24				0.36		

[a] Disregarding employment within 10 years of the index date (date of diagnosis of the case).
[b] Trend over duration within each probability group.

with duration were significant, risk estimates were slightly lower among those probably exposed for five or more years to gasoline, oil products, and engine exhausts than men exposed for shorter periods. When employment within 10 years of the index date was disregarded (Table 5, columns 3 and 4), myeloma risks among men exposed to gasoline were significantly elevated, and were higher in the intermediate categories (possibly exposed for five or more years; probably exposed for less than five years), than in analyses without lagging. However, risk fell among those probably exposed for five or more years to gasoline. Among men possibly exposed to engine exhausts, risks increased with duration, and CIs just excluded one, but risks fell among those probably exposed.

Risks increased with duration of exposure to phthalates in both probability groups when latency was not considered, rising significantly to 2.5 among those probably exposed for five or more years. When exposures were lagged 10 years, risks increased in intermediate categories (possible/longer and probable/shorter duration) of exposure but fell in the probable/longer category, compared with analyses without lagging.

Among men probably exposed to vinyl chloride, risk of myeloma increased significantly with duration

Table 6. Risk of myeloma for exposure to four agents, adjusting for age and other agents by logistic regression, among Danish men with at least 5 years of employment recorded; odds ratios (OR) and 95% confidence intervals (CI)

Agent[a]	Probability	Duration	No lagging OR	No lagging (CI)	Lagging 10 years[a] OR	Lagging 10 years[a] (CI)
Gasoline	Possible	< 5 years	0.9	(0.6-1.5)	0.9	(0.6-1.3)
	Possible	5 + years	0.9	(0.6-1.2)	1.3	(0.7-2.2)
	Probable	< 5 years	1.0	(0.5-2.1)	1.6	(0.8-3.2)
	Probable	5 + years	1.1	(0.6-1.9)	0.7	(0.2-1.9)
Engine exhaust	Possible	< 5 years	1.5	(1.0-2.3)	1.5	(1.0-2.3)
	Finable	5 + years	1.3	(1.0-1.9)	1.5	(0.9-2.7)
	Probable	< 5 years	1.2	(0.7-2.1)	1.0	(0.6-1.7)
	Probable	5 + years	112	(0.8-1.9)	1.0	(0.5-2.0)
Phthalates	Possible	< 5 years	1.2	(0.6-2.4)	0.7	(0.3-1.8)
	Possible	5 + years	1.4	(0.8-2.5)	2.2	(0.8-6.0)
	Probable	< 5 years	2.2	(0.5-10.5)	3.5	(0.7-17.3)
	Probable	5 + years	1.6	(0.5-5.5)	0.3	(0.0-4.2)
Vinyl chloride	Possible	< 5 years	0.8	(0.3-1.7)	0.3	(0.1-1.0)
	Possible	5 + years	0.6	(0.2-1.5)	0.5	(0.1-2.4)
	Probable	< 5 years	0.7	(0.1-3.7)	1.5	(0.3-6.4)
	Probable	5 + years	3.6	(1.0-13.1)	5.1	(0.8-32.3)

[a] Disregarding employment within 10 years of the index date (date of diagnosis of the case).

to nearly fivefold (CI = 1.4-15.4) among those probably exposed fox more than five years. The intermediate categories showed slight risk deficits. Disregarding employment within 10 years of the index date, the increase of risk with duration of employment among men probably exposed to vinyl chloride remained statistically significant, but risks in most categories were lower than without lagging.

Without lagging, for oil products and rubber manufacture and vulcanization (not shown), risk was higher among the probably than among the possibly exposed, but without consistent patterns with duration. For benzene, textile dyes, silica (not shown), and raw milk (not shown), risk was lowest among men exposed longer with higher probability. Similarly, for asbestos, paints and lacquers (not shown), and wood dust (not shown), risk was highest among those possibly exposed for five or fewer years. For oil products, benzene, textile dyes, asbestos, and agricultural pesticides, when exposures within 10 years of the index date were disregarded, risk of myeloma changed only slightly, and decreased among men probably exposed for more than five years.

Because exposures overlapped, we excluded men with a potentially confounding exposure in stratified analyses. In the highest exposure category (men considered probably exposed for five or more years), those exposed to phthalates but never to vinyl chloride (OR = 2.0, CI = 0.1-27.5 [one case]) and those exposed to vinyl chloride bur never phthalates (OR = 2.6, CI = 0.3-19.2 [two cases]) both experienced an elevated risk of myeloma compared with men never exposed to either. Men probably exposed to both phthalates and vinyl chloride for five or more years had yet higher risks (OR = 5.2, CI = 1.0-29.5 [four cases]). A similar analysis considering gasoline and engine exhausts (not shown) yielded results similar to those from the logistic regression presented below. Too few cases were available for these analyses to consider latency by lagging exposures.

We also used logistic regression to evaluate risks for exposure to gasoline, engine exhausts, phthalates, and vinyl chloride simultaneously (Table 6). When latency was not considered, men exposed to gasoline had no increased risk of mydoma, but with lagging, risk rose slightly in the intermediate categories of exposure. Risks were elevated for men in all categories of exposure to engine exhausts when all employment was considered; the risks rose slightly for those possibly exposed, and fell for those probably exposed when jobs within 10 years of the index date were disregarded. For phthalates, without lagging, men probably exposed had higher risk of my-duma than those possibly exposed. When exposures were lagged, no clear patterns with duration and probability of exposure were observed, though risks rose in the intermediate categories. Rink of myeloma was highest among men judged at high probability of exposure to vinyl chloride far five or more years, with a statistically significant OR of 3.6 without lagging and a fivefold risk when the employment within 10 years of the index date was disregarded.

Discussion

We conducted this population-based case-control study among Danish men to evaluate previously reported associations of occupational factors and MM and to generate new hypotheses. Because of the large number of comparisons, some observed associations may be due to chance. However, exposure-response relationships and the consistency of these findings with previous reports suggest that a few associations may be worthy of further evaluation. The most interesting associations were between MM and potential exposures to vinyl chloride, phthalates and certain metal industries.

Men probably exposed to vinyl chloride for five or more years had a statistically significant fourfold excess risk. With consideration of a 10-year latency and exposures to other agents, risk rose to fivefold, although it was no longer significant. Those possibly exposed had no excess risk of myeloma. Men considered probably exposed to vinyl chloride were predominately electricians or electrical installers, line and cable workers, or employed in plastics manufacturing. In the only cohort study[12] of vinyl chloride workers in which data are reported separately for myeloma, no elevated risk for myeloma incidence or for mortality from myeloma and other lymphatic neoplasms (ICD-8 codes 202-203) was observed. Electric cable manufacture was associated with a nonsignificant risk (approximately threefold (calculated by authors]) in one case-control study of myeloma.[11] Vinyl chloride is carcinogenic in humans and experimental animals; target sites in humans include the liver, and perhaps brain, lung, and lymphatic and hematopoetic system in humans.[12]

Risk of myeloma increased significantly with duration among Danish men probably exposed to phthalates, rising to 2.5 among men exposed for five or more years. After consideration of latency and adjustment for exposure to vinyl chloride, risk of myeloma from exposure to phthalates no longer displayed a duration of exposure effect. However, if duration of employment is a poor surrogate for cumulative exposure, the resulting exposure misclassification would tend to dilute exposure-response gradients.[13] Nearly all men considered probably exposed to phthalates worked in plastics manufacturing, or were painters (including building, auto, and machine painters); over one-third were considered also to have been exposed to vinyl chloride.

Phthalate ester plasticizers are used widely, primarily in plastics, rubber, and as a substitute for PCBs in electric capacitors.[14,15] They are also used in paints (including alkyd resins used on cars), hydraulic fluids, vinyl floor coverings, aircraft jet engine lubricants, and pesticides.[14,15] The most common, di-2-ethylhexyl phthalate (DEHP), causes peroxisome proliferation,[14] and is an animal hepatocarcinogen and teratogen.[14] Butyl benzyl phthalate and diallyl phthalate increased the incidence of leukemia in female rats.[16]

Although the numbers of cases and controls exposed to phthalates is small and the excesses may be chance findings, some characteristics of phthalates suggest the associations may deserve a second look. Phthalic anhydrides induce an immunologically mediated hypersensitivity response.[14,17,19] Workers who manifest allergic symptoms to a phthalate compound have elevated levels of IgE and/or IgG specific to that phthalate;[17,19,20] highly exposed workers have higher levels of specific IgG than workers with lower exposure, irrespective of allergic symptoms.[17] Increases in MM have been observed in workers with potential exposure to occupational allergens, such as farmers,[21] and grain[22] and textile workers.[23] Immune stimulation, defined variously as chronic infections,[24] autoimmune disorders,[24-26] asthma,[25] hay fever,[25,27] and allergies,[24,25] has been evaluated in previous studies but results are not consistent.[11,26,28,29] However, risk of myeloma has not been evaluated in populations with quantified exposure to specific occupational allergens, independent of allergic symptoms.[30]

Little evidence is available to evaluate an association of mydoma and phthalate exposure. A population-based caw-coned study[31] of incident myeloma found twofold risks (borderline statistical significance) with exposure to "organically high polymers." A cohort in a polyamide-polyester factory,[32] whose exposures included terephthalic acid and dimethylterephthalate, suffered no excess of lymphatic and hematopoietic cancers other than leukemia (two observed, 4.4 expected [calculated by authors]). No risk estimates were provided for hematopoietic tumors in a cohort of Swedish men[33] exposed to both vinyl chloride and phthalic acid esters. Although DEHP is readily leached from flexible plastic medical devices,[14,35] patients on dialysis have no excess risk of myeloma.[35-37] However, idlop-up time in dialysis cohorts is typically short (usually less than five years)[36,37] or myeloma is excluded *a priori* because chronic renal failure may indicate early stages of myeloma.[38] Previous studies have reported significant excesses of myeloma in a Swedish cohort in paint manufacturing, particularly with higher and among painters.[31,40] Two studies[11,41] reported nonsignificant excesses with paints or painting. Higher risks have been observed among car/spray/signwriter painters (OR = 2.8) than construction/general painters (OR = 1.8).[31] In this study, Danish men employed in paint manufacturing (OR = 2.3) or auto painting (OR = 3.9) had higher risk of myeloma than those employed by (construction) painting contractors (OR = 0.5).

Risk of myeloma was elevated also among Danish men with possible and probable exposure to gasoline and engine exhausts. Consideration of latency and overlapping exposures dampened these risks. ORs remained slightly elevated among men possibly exposed for more than five years, or probably exposed for shorter periods to gasoline and among those possibly, but not probably, exposed to engine exhausts. Previous studies have reported significant excess risks of myeloma with engine exhausts (considering a five-year latency period)? with self-reported exposure to petroleum products,[26] and carbon monoxide (including diesel, jet, and auto exhaust, as well as coal fumes; and smoke).[14] In a case-control study nested in the American Cancer Society Prospective study,[27] risks were nonsignificantly increased for self-reported exposure to diesel exhaust (OR = 1.4) but not gasoline exhaust (OR = 0.9). A recent case-control study in Northern Sweden[43] found a slight elevation of risk with exposure to engine exhausts (OR = 1.4, 90 percent CI = 0.9-2.1 [61 cases]); this risk fell in the multivariate analysis when numerous agriculture-related variables were included. Although the evidence for an association of myeloma with gasoline or engine exhausts in these data is weak, neither exposure should be dismissed until studies with more precise exposure assessments are available.

An association with agriculture[21,24,25,27,43] was not confirmed by these data. We saw no increase in myeloma among subjects whose most recent tax form listed occupation as farm owner, tenant farmer, or agricultural or garden worker. Self-employed farmers are not included in the Pension Fund, but farm owner is generally a lifelong occupation in Denmark, so results based on the recent tax form may reflect a true lack of excess risk of myeloma among farmers in Denmark. In a recent population-based case-control study,[7] farmers who reported tractor-driving had a higher risk of MM than ones who did not (OR = 2.3, 90 percent CI = 0.8-7.1). Farmers may be exposed to engine exhausts[42] and gasoline, though it seems unlikely that these exposures would entirely explain farmers' excess risk observed elsewhere. No association was observed with pesticides, in contrast to an association with self-reported exposure in one study.[27] Specific classes of pesticides or individual compounds were not evaluated.

Our data did not confirm previously suggested associations with asbestos[11,25] and solvents,[11,19,43,44] particularly benzene,[45] which have been contradicted by other studies.[27,42,43] Although risks were elevated slightly among precision wood-workers (OR = 1.3) and rose to nearly fourfold among men employed in miscellaneous wood-product fabrication, results did not confirm possible associations with wood dust[27] or fresh wood.[42] Several occupations and industries associated with higher risk of myeloma in previous studies, such as cooks,[11] leather tanners,[11] and the food,[11] shoe or leather,[46] paper,[47] or rubber[11,47,48] industries, had a detectable excess of MM in this population.

Without additional information about the employers and jobs, we could not attribute a nearly 12-fold risk (based on three cases) among men employed for five or more years in the manufacture of synthetic yarn to any specific exposure. The association may warrant future investigation. A parallel study of Danish women[5] observed a slight elevation of risk among spinners and weavers (OR = 1.6, CI = 0.3-6.8). Others have reported a risk of 2.7 ($P < 0.01$) for myeloma among female textile workers in the Swedish wool industry,[25] and a nearly twofold increase (CI = 0.8-4.4 [eight cases])[7] with self-reported exposure to textile fibers and dusts in the US. Counties in the US with a higher proportion of the population employed in synthetic fiber manufacture had significantly higher rates of myeloma.[49] A nearly threefold risk of death from myeloma (standardized mortality ratio = 2.7, CI = 0.7-6.9 [4 cases]) was observed in a cohort of cotton textile workers in the US.[50]

Precision metal workers and machinists, smiths, machine fitters, and welders all had slightly elevated risks. Risks among men employed in manufacture of structural metal or stationary tanks and in body factories (excluding automobiles) rose significantly with duration of employment to 5.5 and 3.9, respectively. Several studies have reported slight or nonsignificantly elevated risks in metal-working occupations and industries (smelter and metallurgy workers,[21] compositors,[21] foundry workers,[52] in diesel engine manufacture[53]) or with exposure to metals.[11] No specific exposure clearly explains these risks; risks were not elevated for exposure to metals or metal dusts, lead, or mercury.

A nearly fourfold risk in Danish stokers (based on four cases) is unlikely to entirely explain the myeloma excess observed among electrical workers, but the stokers could not be identified separately in this study.[54] Electricians were at significantly lower risk of myeloma in a recent case-control study in Sweden.[43]

The strengths of this study were: its large size, allowing the examination of a greater number of specific occupations and industries; the availability of accurate industrial employment histories after 1964; and assessment of exposure by industrial hygienists, based on job titles and employment history of subjects. However, the occupational histories have limitations. Because myeloma is predominately a disease of older people, most subjects had spent at least two decades of their working lives before 1964, when the SPF began recording employment histories. Risks considering latency, in particular, were difficult to interpret due to small numbers. For many substances, for example, CIs often encompassed hoth the risks and Cis calculated without consideration of latency. We therefore did not dismiss otherwise suggestive findings that were weakened in the latency analyses. Jobs in which subjects were self-employed were excluded, which made it difficult to evaluate risk for farmers and with agricultural exposures in detail. Occupational title, limited io that recorded on the tax form, reflected only the most recent occupation. However, job mobility, at least for farmers and skilled workers, is very low in Denmark compared wirb that of, *e.g.*, *the* US, reducing some of the likely misclassification. We also attempted to reduce misclassification by using occupation primarily to distinguish between production ('blue collar') and managerial ('white collar') jobs, eliminating pensioners (more likely to be surviving controls) from all analyses, omitting subjects with only occupation from analysts of specific substances, a d restricting analysts of duration to subjects with at least five years recorded in the Pension Fund.

These limitations would tend to reduce statistical power, and to misclassify men employed (in an industry) or exposed (*to* a substance) before 1964 as unexposed. This misclassification, nondifferential with respect to case status, most likely would result in diminution of true risks. Associations corroborated by previous studies therefore may be stronger than indicated by these data alone.

The lack of strong and consistent associations in these and other data, and the low attributable risk for most occupational exposures probably reflect a relatively minor role for occupation" in the *etiology* of this tumor. Nonetheless, improvements in exposure assessment are likely *to* better our understanding of the importance of widespread exposures such as solvents and engine exhausts in the *development* of myeloma.

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