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## Parental Employment at Time of Conception and Risk of Cancer in Offspring

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Studies on the possible association between exposures of parents at the time of conception and cancer in their offspring have provided no clear answer. In this large, population-based, record-linkage study, 1747 childhood cancer cases were identified in the Danish Cancer Registry and matched with 8630 population controls. Specific information on the employment held by each parent at the time of conception and during early pregnancy was obtained through record linkages. The most recent job titles of the parents were also supplied. Significantly increased risks for renal cancer (mainly Wilms' tumour) and for osteogenic and soft tissue sarcomas were observed in children in association with mothers' employment in medical and dental care, based on 15 observations and odds ratios (OR) of 2.5–4.0. The risk for cancers at all sites was significantly elevated in children of female nurses (OR = 1.4;  $n = 75$ ) and of male and female physicians, dentists, dental assistants, veterinarians and pharmacists combined (OR = 1.4;  $n = 53$ ). Handling of drugs, exposure to anaesthetics and infections during pregnancy are suggested to be potential risk factors. Significantly increased risks were also observed for children of fathers employed in the manufacture of iron and metal structures (OR = 2.2;  $n = 16$ ), in machine repair workshops (OR = 2.8;  $n = 6$ ), as machinists (OR = 1.6;  $n = 47$ ) and as smiths (OR = 1.5;  $n = 28$ ). The suggestion in earlier studies that exposures to hydrocarbons and lead are risk factors for childhood cancer could not be supported by our analysis. Overall, few associations were observed; it was therefore concluded that parental occupation is not likely to be a major risk factor for childhood cancer.

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### INTRODUCTION

THE INITIAL peak of cancer incidence during the first 5 years of life can plausibly be explained as the result of prenatal mutagenic exposures such as those of parents during the working day. Accordingly, many studies have been conducted to evaluate potential associations between the occupational activities of the parents and the risk for cancer among their offspring [1–25]. A number of occupational exposures, particularly of men, have been suggested as potential risk factors [1–16], and a few general tendencies appear: an increased risk for cancer among offspring of fathers occupied as mechanics, machinists or painters, and of

fathers employed in subsections of the iron and metal industries [1–4, 6, 9, 12, 13]. Exposure of mothers to "chemicals" during work has also been cited as a risk factor for childhood cancer [4, 8]. Exposures of parents to hydrocarbons, lead, solvents, paints and exhaust gases from motor engines have been hypothesised as specific causes, but, other studies have not substantiated this association [3, 10, 17, 20, 21, 24].

Thus, the results reported to date on the association between childhood cancer and parental occupation are largely inconsistent. This may be due to the hypothesis-generating nature of most of the studies or to variation in the terminology of occupations applied in the different studies. Furthermore, in all of the studies, the numbers of specific types of childhood cancer are relatively small and often insufficient for detailed analyses.

We report the findings of a large, population-based record linkage, which was set up specifically to investigate the possible importance of parental employment at the time of conception for the risk that their offspring will develop cancer before the age of 15.

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### MATERIAL AND METHODS

The cases in this study were children conceived after 1 April 1964 who were newly diagnosed with a cancer during the period 1 April 1968 to 31 December 1984. They were identified through the files of the Danish Cancer Registry which provided the name, sex and unique personal identity number. This nationwide cancer registration system, which was set up in 1942, was described and evaluated in previous publications on cancers of adulthood [26] and cancers of childhood [27]. The registration includes histologically benign tumours of the brain and papillomas of the lower urinary tract.

The diagnoses of all childhood cancers notified to the Cancer Registry have recently been reviewed and recoded according to the International Classification of Diseases for Oncology (ICD-O). The tumour entities were further aggregated into a classification scheme proposed by the International Agency for Research on Cancer in their study on childhood cancer worldwide [28].

Controls were drawn from the files of the Danish Central Population Register, established in Denmark on 1 April 1968 and were identified by name, sex and identity number. 5 controls per case were selected at random but matched for sex and date of birth (within 1 year) and had to have survived without cancer until the date of diagnosis of the case. Children born outside Denmark were excluded as cases or controls.

In 1985 parents of cases and controls were identified through the files of the Central Population Register. This is feasible because the register contains a system of cross-references between the identity numbers of children and their parents. The name, sex and identity number of each parent was obtained, with a verification code for the validity of the registered family relationship; in addition, the most recent job titles of the parents were available, on the basis of information supplied on annual income tax forms.

Employment histories of parents were established by record linkage with the files of the nationwide Supplementary Pension Fund [29]. The Pension Fund, which is a supplement to the Danish state pension, was established by law on 1 April 1964 as a compulsory scheme for wage earners 18–66 years of age and since September 1978 those aged 16–66. The supplement is paid from monthly contributions from the wage earners themselves and from their employer. The money is retained in the Pension Fund in the account of the employee, together with a specification of the calendar period of the contribution and the name, address and a unique seven-digit identification number of the company. The industrial category of the company is also recorded, as a five-digit, hierarchically formed number that corresponds closely to the International Standard Industrial Classification (ISIC) [30].

On the basis of the job titles of the parents, each family was allocated to one of five socioeconomic groups, similar to those used by the Registrar General for England and Wales for social class definitions [31].

Table 1 gives an overview of the information obtained from the Cancer Registry, the Central Population Register and the Pension Fund.

#### Analysis

The employment held by the parent 270 days (i.e. approximately 9 months) before the birth of the child was chosen *a priori* to be that of greatest interest. If more than one job was held at this time, that held longest was chosen as the potential risk factor. The most recent job of the mother and of the father

Table 1. Sources of information on child and parents in the linked data file\*, 1968–1984

Item	Source		
	Cancer registry (index child)	Population register (child and parent)	Pension fund (parent)
Identification number of child†	+ >>>>>> +		
Cross-reference between child and parent		+	
Identification number of parent†		+ >>>> +	
Company name			+
Date of start of employment			+
Date of end of employment			+
Industry			+
Job title		+	
Cancer diagnosis	+		
Date of diagnosis	+		
Basis of diagnosis	+		
Vital status		+	
Date of death		+	

\*>>> = basis of linkage.

†Includes information on date of birth and sex.

was also included in the analysis. Analyses were performed for mothers and fathers independently but for girls and boys jointly.

Statistical associations between parental employment or job title and cancer among their offspring were estimated on the basis of cross-classification of data in multiple  $2 \times 2$  tables; thus, in the present analysis, the odds ratio (OR) for the specific occupational activity among case and control parents was the measure of the degree of association. When analyses were performed on subgroups of cases, only the corresponding controls were included. In addition, 95% and 99% confidence intervals (CI) were calculated as outlined by Miettinen [32]. As a stratified analysis based on the age of parents and/or children did not change the results, all ORs and CIs were derived from unstratified analyses. To allow for the large number of tests of significance performed in this study, most attention was devoted to the results which were significant on a 1% level.

### RESULTS

Initially, 1840 cases and 9200 controls were selected for study, i.e. a total of 6324 boys and 4716 girls. Of these, 91 cases and 560 controls born before 1 January 1965 were excluded since no information was available on parental employment 9 months prior to birth (starting date of Pension Fund, 1 April 1964). 2 cases and 10 controls were excluded because the diagnosis of malignancy could not be maintained. Thus, 1747 cases and 8630 controls remained for study (Table 2).

All except 497 fathers (4.8%) and 52 mothers (0.6%) were successfully traced. The case children of untraced parents were excluded from the analysis, together with the associated controls and their parents; so were eligible controls and their parents when the corresponding case was born before 1 January 1965 (758 fathers and 261 mothers). 3 cases lost all 5 controls and were accordingly excluded. Those remaining for analysis were 9119 fathers (1613 case fathers) and 10061 mothers (1721 case mothers) (Table 2).

Table 2. Exclusion of parents prior to analysis and descriptive characteristics of children and parents

Characteristics	Fathers		Mothers	
	Cases	Controls	Cases	Controls
Parents of eligible children	1747	8630	1747	8630
Parents not traced	131(7.5%)	366(4.2%)	23(1.3%)	29(0.3%)
Parents of controls of excluded cases	—	758(8.8%)	—	261(3.0%)
Cases for which all controls excluded	3(0.2%)	—	3(0.2%)	—
Parents included in analysis	1613	7506	1721	8340
Sex of child (%)				
Male	57.1	57.2	57.4	57.3
Female	42.9	42.8	42.6	42.7
Year of birth of child (%)				
1965–1969	41.7	40.4	41.0	39.6
1970–1974	32.7	33.7	33.1	34.2
1975–1979	19.7	20.7	20.2	21.3
Since 1980	5.9	5.2	5.8	5.0
Average age of parents (S.D.)	29.1(6.2)	28.8(6.1)	25.9(5.0)	25.8(5.0)

Table 3 shows the distribution of cases by the 12 main diagnostic groups used in this study. Leukaemia, tumours of the sympathetic and central nervous system, malignant lymphomas and renal tumours were the five most important diagnostic groups, constituting almost 85% of the diagnoses.

Employment of the labour market had been recorded in the

Table 3. Cases\* of cancer included in the case-control analysis, according to whether parents were traced (%)

Main diagnostic group	Parents included in analysis	
	Father	Mother
Leukaemias	570 (93)	603 (99)
Lymphomas and other reticuloendothelial neoplasms	133 (91)	142 (97)
Central nervous system neoplasms†	386 (92)	416 (99)
Sympathetic nervous system tumours	137 (90)	150 (98)
Retinoblastoma	47 (90)	52 (100)
Renal tumours	128 (96)	132 (99)
Hepatic tumours	23 (96)	23 (96)
Malignant bone tumours	45 (94)	47 (98)
Soft tissue sarcomas	62 (89)	68 (97)
Germ-cell, trophoblastic and other gonadal neoplasms	39 (98)	40 (100)
Carcinomas and other malignant epithelial neoplasms	34 (92)	37 (100)
Other and unspecified malignant neoplasms	9 (82)	11 (100)
All malignant tumours	1613 (92)	1721 (99)

No. (%)

\*Notified in Denmark during 1968–1984 among children (aged 14 years or less) born after 1 January 1965.

†Including benign tumours.

Table 4. Control parents with known employment status at the time of conception of the index child

Main industry	Fathers	Mothers
Agriculture, forestry and fishery	216 (3)	49 (1)
Mining and quarrying	10 (0)	2 (0)
Manufacturing	1532 (20)	848 (10)
Electrical, gas, heating and water supplies	26 (0)	7 (0)
Construction industry	744 (10)	44 (0)
Trade, restaurant and hotel industry	872 (12)	764 (9)
Transportation, storage and communication	514 (7)	187 (2)
Banking, finance, insurance, real estate and business	507 (7)	515 (6)
Community, social and personal service	1193 (16)	2220 (27)
Unspecified trades	401 (5)	217 (3)
Total employed	6015 (80)	4853 (58)
Total not employed*	1491 (20)	3487 (42)
Total	7506 (100)	8340 (100)

No. (%)

\*Includes self-employed persons, housewives and students.

records of the Pension Fund for 96% of the fathers and 95% of the mothers in the control series, but for only 80% of fathers and 58% of mothers at the time of conception (Table 4). Manufacturing was the most common employment among fathers, and community, social and personal services the most common among mothers. Employment in mining and quarrying and work in electricity, gas and water supply were too rare to provide sufficient observations for risk analyses.

#### Cancers at all sites

Table 5 gives the risks for childhood cancer at any site associated with employment of fathers and mothers at the time

Table 5. Type of employment (main industry) of parents at the time of conception and odds ratio (OR) for cancers at all sites among the offspring

Main industry	Fathers		Mothers	
	OR	95% CI	OR	95% CI
Farming, forestry and fishery	0.79	0.56–1.13	0.89	0.44–1.81
Manufacturing activity	1.15	1.01–1.31	1.03	0.87–1.22
Construction industry	0.96	0.80–1.16	0.88	0.41–1.87
Trade, restaurant and hotel industry	0.97	0.82–1.15	0.76	0.62–0.92
Transportation, storage and communication	0.83	0.66–1.05	0.91	0.63–1.30
Banking, finance, insurance, real estate and business services	1.03	0.83–1.27	1.01	0.81–1.25
Community, social and personal services	1.11	0.96–1.28	1.05	0.93–1.18
Unspecified trade	0.84	0.65–1.08	0.96	0.69–1.34
Not employed	0.95	0.82–1.08	1.05	0.95–1.17

**Table 6. Industries of fathers and mothers that were significantly associated with increased risks for cancer at all sites**

ISIC code	Industry of employment	Cases	OR	P
<b>Fathers</b>				
3511	Production of chemical raw materials and compounds	6	3.1	<0.05
3691	Tile works	9	3.0	<0.01
3813	Manufacture of iron and metal structures*	16	2.2	<0.01
61179	Wholesale trade in some raw materials and semi-manufacture†	6	3.1	<0.05
83111	Administration of property	39	1.6	<0.05
83245	Technical and chemical laboratories	5	3.3	<0.05
91050	Municipal administration	84	1.3	<0.05
92012	Refuse removal activities‡	5	3.9	<0.05
9331	Health department	12	2.2	<0.05
94	Amusements, sports etc.	12	2.2	<0.05
<b>Mothers</b>				
38329	Other manufacture of communication material§	7	4.3	<0.01
91040	County administration	122	1.2	<0.05

\*Includes doors, windows, facade elements, mechanical ventilators, hotwater tanks, steam boilers, and tanks for compressed gases.

†Includes packaging material and bakery, butchering and flower-shop articles.

‡Includes cleaning companies, dumps and incinerators.

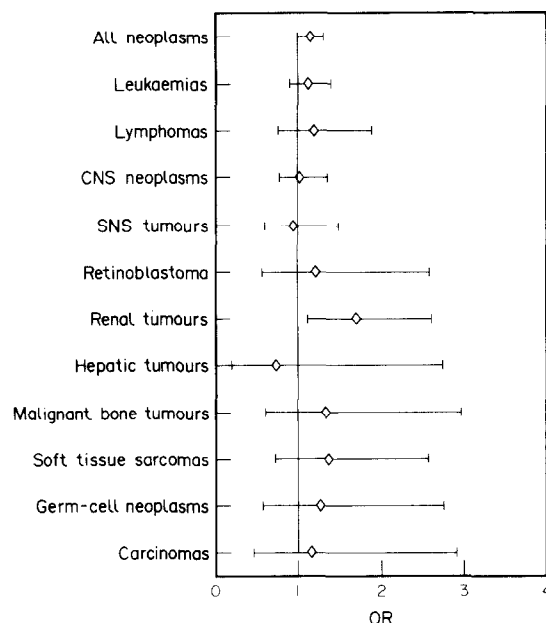
§Includes radiotelephone and telegraph equipment, wire telephone and telegraph transmitters, radar, traffic signals, alarm equipment, radio tubes and X-ray equipment.

of conception in the main industries of the country. A significant positive association was found for fathers in manufacturing (OR = 1.15), based on 368 observed childhood cancer cases; a negative one was found for mothers employed in the trade, restaurant and hotel industry (OR = 0.76) based on 122 observed cases. The latter finding was due to a decreased proportion of mothers of cases in wholesale trade (OR = 0.67), based on 34 cases.

Table 6 identifies the specific industries that were significantly associated with an excess number of childhood cancers, excluding results based on fewer than 5 observed cases. The increased risk associated with fathers' employment in all types of manufacturing activities was thus due mainly to the fact that more fathers of cases were employed in production of chemical raw materials ( $P < 0.05$ ), in tile works ( $P < 0.01$ ) and in the manufacture of iron and metal structures ( $P < 0.01$ ) than were fathers of controls. Mothers' employment in other manufacture of communication material was associated with an increased risk for cancers at all sites among the offspring.

#### Specific tumour types

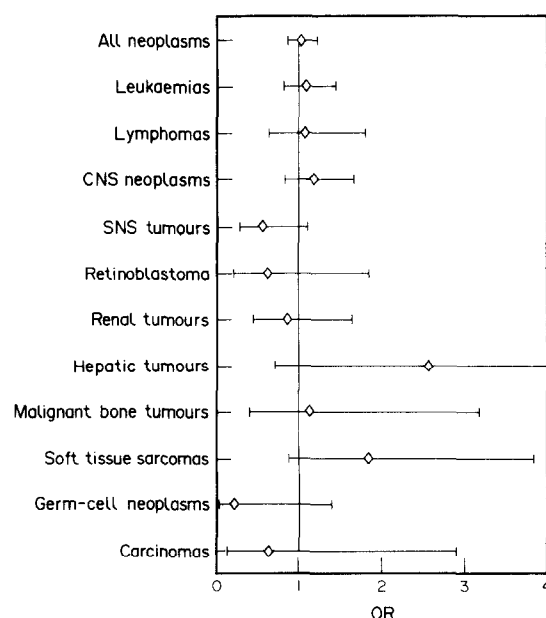
Figures 1 (fathers) and 2 (mothers) show the estimated ORs and associated 95% CIs for subgroups of tumours among parents employed in manufacturing. The observed increased risk for cancers at all sites in children of fathers employed in this industry (Table 5) was due mainly to a significant excess of renal tumours. Figures 3 (males) and 4 (females) give the equivalent risk



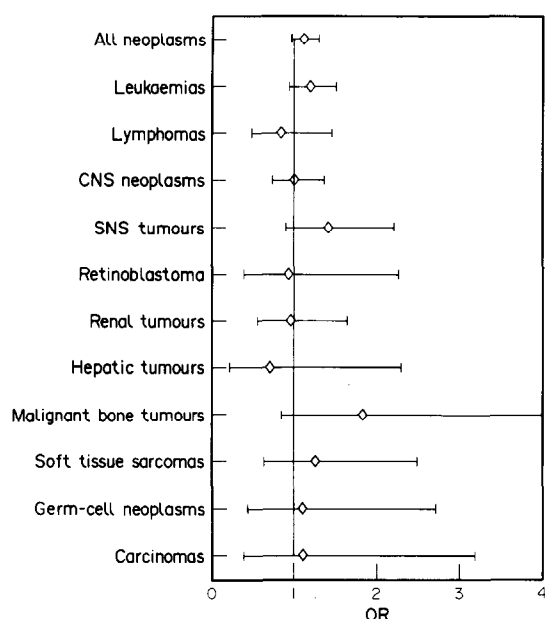
**Fig. 1. Estimated relative risks (◇) and associated 95% confidence intervals (—) for subgroups of tumours among children of fathers employed in manufacturing at the time of conception. CNS = central nervous system, SNS = sympathetic nervous system.**

estimates for parents who were employed in service occupations at the time of conception.

Table 7 presents significant associations between industrial employments of parents and the risk of leukaemia, based on 3 or more cases. The excess number of leukaemias associated with fathers' employment in administration of property (OR = 1.8) and with mothers' employment in county administration (OR = 1.4) and in other manufacture of communication material (OR = 14.5) partly explain the increased risk for cancer at all sites associated with these industries (Table 6). All 5 cases of leukaemia that were linked with fathers' employment in the



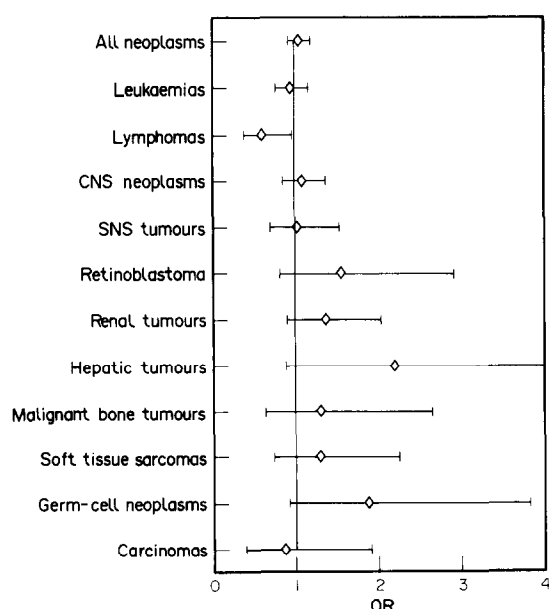
**Fig. 2. Estimated relative risks (◇) and associated 95% confidence intervals (—) for subgroups of tumours among children of mothers employed in manufacturing at the time of conception.**



**Fig. 3.** Estimated relative risks ( $\diamond$ ) and associated 95% confidence intervals (—) for subgroups of tumours among children of fathers employed in rendering of services at the time of conception.

rubber industry were of the acute lymphatic type (OR = 18). The observed associations between childhood leukaemia and fathers' employment in the rubber industry and mothers' employment in the porcelain industry, in wholesale trade in raw materials, and in other manufacture of communication material were significant at the 1% level.

Similarly, Table 8 presents significant associations found between tumours of the central nervous system and parental employment. The excess risk observed for cancer at all sites among children of fathers employed in the production of chemical raw materials and compounds (Table 6) was explained mainly by the observed risk for brain tumours (OR = 7.0). The



**Fig. 4.** Estimated relative risks ( $\diamond$ ) and associated 95% confidence intervals (—) for subgroups of tumours among children of mothers employed in rendering of services at the time of conception.

**Table 7.** Leukaemia cases significantly associated with parental employment at the time of conception of index child

ISIC code	Industry of employment	Parent	Cases	OR	P
355	Rubber industry*	Father	5	5.8	<0.01
36101	Porcelain industry	Mother	3	14.5	<0.01
38251	Manufacture of office machines	Father	3	7.0	<0.05
38280	Machine repair workshops	Father	6	2.8	<0.05
38329	Other manufacture of communication material	Mother	3	14.5	<0.01
50	Construction industry†	Mother	7	3.1	<0.05
6116	Wholesale trade in raw materials	Mother	8	3.9	<0.01
61181	Wholesale in agricultural machinery	Father	3	4.6	<0.05
83111	Administration of property	Father	17	1.8	<0.05
83210	Legal services	Mother	4	3.9	<0.05
91040	County administration	Mother	47	1.4	<0.05
92	Refuse removal and cleaning‡	Father	3	4.6	<0.05

\*3 cases observed in rubber factories and 2 cases in vulcanising plants.

†2 cases observed in painting firms.

‡Includes chimney sweeps.

observed excess risk in carpentry firms was mainly due to 5 cases of astrocytoma (OR = 4.7,  $P < 0.01$ ). The excesses of brain tumours associated with mothers' employment in department stores and in organisations of economic interest, and with fathers' occupation in soap factories and in car repair, etc. were all significant at the 1% level (Table 8).

Table 9 presents significant associations observed between parental employment and risk for renal tumours, bone tumours and soft tissue sarcomas in the offspring. The excess risk for renal tumours in children of fathers in manufacturing (Fig. 1) was due mainly to employment in the wood and furniture

**Table 8.** Cases of tumours of CNS significantly associated with parental employment

ISIC code	Industry of employment	Parent	Cases	OR	P
31111	Slaughterhouses and meat packers	Mother	3	7.3	<0.05
31121	Dairies	Father	4	3.8	<0.05
321	Textile industry	Mother	10	2.2	<0.05
3511	Production of chemical raw materials and compounds*	Father	3	7.0	<0.05
35231	Soap factories	Father	3	14.1	<0.01
50140	Carpentry firms	Father	11	2.3	<0.05
62114	Department stores	Mother	6	3.7	<0.01
62121	Butcher shops	Father	3	7.0	<0.05
83111	Administration of property	Father	12	2.3	<0.05
93101	Institutions of higher education	Father	4	4.7	<0.05
935	Organizations of economic interest	Mother	7	3.4	<0.01
9513	Auto repair, etc.†	Father	5	5.9	<0.01

\*2 observed cases in production of industrial gases.

†3 cases in car repair shops and two in car painting shops.

industry (OR = 2.9) and in the manufacture of iron and metal structures (OR = 7.1). A noteworthy observation is the association between mothers' employment in the health department and increased risks for renal, bone and soft tissue tumours among the offspring. A similar association was observed for fathers in relation to bone tumours in the offspring, which fully explains the observed increased risk for cancers at all sites associated with this trade (Table 6). An additional, highly significant observation (which is not included in the tables) was five hepatic tumours in children of mothers employed in education, health and welfare (OR = 4.6).

#### Job title

We observed significant associations between childhood cancer and certain specific job titles held most recently by the parents (Table 10). Fathers' jobs as machinists and mothers' jobs as owners of laundry or dry-cleaning establishments were associated with an increased risk in their children for cancers at all sites at the 1% level.

Jobs within the medical and social services of the community covered a large proportion of the observed associations. The odds ratios for tumours of the central nervous system among male carpenters, joiners and insulation workers was significant at the 1% level.

### DISCUSSION

Our main findings were increased risks for renal tumours, bone tumours and soft tissue sarcomas in children of mothers who were employed in medical and dental services at the time of conception and in early pregnancy. We also found increased risks for liver tumours associated with mothers' occupation in the main service section of education, health and welfare

Table 9. Cases of renal tumours, bone tumours and soft tissue sarcoma significantly associated with parental employment

ISIC code	Industry of employment	Parent	Cases	OR	P
<b>Renal tumours</b>					
3	Manufacturing	Father	39	1.7	<0.05
33	Wood and furniture industry	Father	6	2.9	<0.05
3813	Manufacture of iron and metal structures	Father	3	7.1	<0.05
50170	Electrical contracting firms	Father	3	4.7	<0.05
93	Education, health and welfare	Mother	13	2.2	<0.05
9331	Health department*	Mother	7	2.5	<0.05
93313	Practising dentists	Mother	3	7.5	<0.01
<b>Bone tumours</b>					
93	Education health and welfare	Father	5	6.1	<0.01
93	Education, health and welfare	Mother	8	3.9	<0.01
9331	Health departments	Mother	4	4.0	<0.05
<b>Soft tissue sarcomas</b>					
38411	Iron shipyards	Father	3	4.9	<0.05
91050	Municipal administration	Father	7	3.3	<0.05
9331	Health department	Mother	4	3.5	<0.05

\*Includes hospitals, practising physicians and dentists, maternity clinics and physiotherapy clinics.

Table 10. Observed associations between childhood cancer and parental job

Job	Tumour type	Parent	Cases	OR	P
Machinists	All	Father	47	1.6	<0.01
Smiths	All	Father	28	1.5	<0.05
Laundry/dry cleaner owners	All	Mother	6	3.7	<0.01
Weighers, shipping agents etc.	All	Father	7	3.0	<0.05
	All	Mother	3	5.0	<0.05
Unskilled workers, unspecified	CNS	Father	14	2.1	<0.05
	Bone	Father	5	5.1	<0.05
Carpenters, joiners and insulation workers	CNS	Father	19	2.8	<0.01
Nurses*	All	Mother	75	1.4	<0.05
	Retino-blastoma	Mother	4	3.3	<0.05
Male nursing aid	All	Father	7	3.0	<0.05
Physicians, dentists, dental assistants, veterinarians and pharmacists	All	Both sexes, combined	53	1.4	<0.05
Physicians	Retino-blastoma	Father	2	10.2	<0.05
Childcare workers	CNS	Mother	23	1.7	<0.05
Kindergarten heads	SNS	Mother	19	1.7	<0.05

CNS = central nervous system, SNS = sympathetic nervous system.

\*Elevated risk for almost all subgroups of tumours.

combined and of bone tumours where fathers had held similar employments. It is impossible to point out any specific candidates for risk factors within this broad trade; however, the analysis of parental job titles indicated that children of nurses were at risk in particular (Table 10). The risk for cancers at all sites was increased for parents in the combined group of physicians, dentists, dental assistants, veterinarians and pharmacists. Except for an association reported in an earlier Finnish study between the mother's job as a pharmacist and risk for childhood cancer [4], no report has been made of increased risk in children of parents in medical or dental services. Handling of drugs, exposure to fumes from or direct contact with sterilising agents, inhalation of anaesthetics, ionising and non-ionising radiation and infections are potential risk factors. The observed increase in risk for tumours of the central and sympathetic nervous system among children of female childhood care workers and kindergarten heads, respectively (Table 10), may again point to infections during pregnancy as a potential risk factor for childhood cancer.

We also observed significantly elevated numbers of cancers in children of fathers employed in the manufacture of iron and metal structures (Table 6), in machine repair workshops (Table 7) and as machinists and smiths (Table 10). Three of the four observations were based on a substantial number of cancer cases. If any association with specific tumour types exists, it seems to be with leukaemia, lymphomas and renal tumours. In a Canadian study from 1974 [1], which was the first epidemiological study on parental occupation and childhood cancer to be published, prenatal paternal exposure to hydrocarbons was associated with mortality due to cancer in offspring below the age of 5. This suggestion was based mainly on an observed excess number of case fathers who were engaged as motor vehicle mechanics, machinists, miners and painters. Although we found increased risks associated with some of these job categories, we found no

overall elevated risk in association with fathers' employment which had been defined as hydrocarbon-related occupations and industries. Other studies have also failed to reproduce this specific association [3, 14, 17–19, 20, 22, 24]; however, in one of the studies paternal employment as a mechanic or machinist at the time of birth of the child was significantly associated with tumours of the urinary tract, mainly Wilms' tumour [3], and in two others an association was seen between Wilms' tumour and the father's employment as a machinist, car body repairman or welder [12, 14]. A Finnish study reported an association between fathers' jobs as machine repair men (partly equivalent to smiths) and brain tumours in the offspring, and a US study between paternal employment in the metal industries and intracranial neoplasms of childhood [4, 13]. Thus, fathers' employment within certain areas of the iron and metal industries and with machinery or with manufacturing of machinery, including repair, are areas of specific interest for future research into paternal exposures at the time of conception that may give rise to cancer among the offspring.

Lead has also been proposed as a significant cause of childhood cancer. A relatively large case-control study from Connecticut, on Wilms' tumour reported that more case fathers than controls had been employed in what were defined *a posteriori* as lead-related occupations, i.e. drivers, motor vehicle mechanics, service station attendants, welders, solderers, metallurgists and scrap metal workers [2]. We were not able to demonstrate any consistent association between such occupations or industries and risk for Wilms' tumour (or any other cancer), in agreement with recent hospital-based case-control studies on this tumour [14, 21].

In a recent study from the UK, leukaemia in children aged 0–14 was associated with preconceptional exposure of fathers to wood dust [16]. In our survey we observed a non-significant 50% increased risk for this malignancy associated with fathers' employment in the wood and furniture industries; in particular, this could be identified as a significant 2-fold increased risk in the industrial subgroups of wooden furniture factories and manufacturers of building materials. No increased risk for childhood leukaemia was detectable in association with fathers' employment in carpentry firms, or as carpenters or joiners. However, employment as a carpenter or joiner was significantly linked with tumours of the central nervous system in the children (Tables 8 and 10).

As our study was based on record linkage between pre-existing registries, we had no information on exposures other than industrial employment and job of the parents. We could therefore not adjust for confounding factors such as non-occupational ionising radiation, air pollution, traffic density and socioeconomic level of the family, which have been shown or proposed as risk factors for childhood cancer [19, 33, 34]. Classification of families into five socioeconomic groups on the basis of job titles, however, showed no consistent positive or negative association with socioeconomic gradient, either for total childhood cancer or for any of the defined 12 subgroups. Socioeconomic status, and thus possibly the other non-occupational risk factors mentioned, are likely to be of minor importance as confounding factors and probably cannot explain our findings. The use of multiple tests to analyse the data for the different subgroups increases the probability of obtaining false positive results, and some of the significant results reported here may have occurred simply by chance.

As in most earlier studies on occupational causes of childhood cancer, the job titles of the parents were used as a risk factor.

Table 11. Risks of childhood cancers associated with job of parents compared with earlier findings

Job title	Tumour type	Parent	n	OR	Ref.	Confirms /not
Machinists	All	Father	47	1.6	1,3,4,12	C
Smiths*	All	Father	28	1.5	4	C
Car repair mechanics	All	Father	6	0.6	1–4,6	NC
Motor vehicle drivers†	All	Father	75	0.9	2,4,6	NC
	Leukaemia	Father	27	0.9	4,6	NC
	Kidney	Father	6	1.1	2	NC
House painters	All‡	Father	23	1.0	1,4	NC
Spray painters§	All‡	Father	2	0.6	9	NC
Welders	All‡	Father	11	1.0	6,12	NC
Printers	All‡	Father	8	1.0	10	NC
Electricians	All	Father	21	0.8	11	NC
	CNS	Father	5	0.8	11	NC
Farmers	All	Father	19	1.0	4	NC

\*Compared with machine repair men in reference 4.

†A marginally significant observation of six tumours was observed among female drivers (OR = 2.7).

‡No significant result in any subgroup of tumour.

§Automobile and machinery painters.

||References 4, 6–9 and 12 concern prenatal parental occupations and references 1–3 and 10–11 concern occupation at birth.

C = confirms and NC = does not confirm findings in these references.

Table 11 gives our findings for each job category reported in other studies as significantly associated with childhood cancer. We were able to confirm only the associations reported between childhood cancer and fathers' job as machinist or smith, and mothers' job as a laundry or dry cleaning establishment owner. Other earlier reported associations include brain tumours and employment as a painter or in jobs with exposure to solvents and paints [1, 4, 5], leukaemias and occupations with exposure to gasoline exhaust [4, 6], central nervous system tumours and employment as paper and pulp mill workers [3] or occupations that involve the use, repair or manufacture of electrical and electronic equipment [11], and childhood tumours and farming [4]. One simple explanation might be that such associations do not exist; however, for several reasons, the present study may not have the power to reproduce fully earlier findings of associations between parental occupation and childhood cancer. Firstly, the familial relationship between parents and children born before 1 April 1968 was not fully verified through the Central Population Register but for some 15% of the individuals was based on a link-up of persons living in the same household. Secondly, although the information on employment of the parents concerns the period of conception, this was not the case for the job title. Thirdly, definitions of occupational groups and industries are related to national and local traditions, which make them more or less incomparable internationally. Fourthly, the industrial classification used by the Danish authorities are based on information delivered by companies, and the quality of the allocation is not checked in any way. This may give rise to misclassification. There is no reason to suppose that such misclassification would be different among cases and controls, so the resulting bias would tend to reduce any deviation in risk towards unity. This could lead to us missing some of the associations found in other studies. Moreover, because there were relatively small numbers of cases in many of the subgroups

included in the analysis, the power to detect moderately increased risks in those groups was very low.

With the inclusion of 1747 childhood cancer cases and 8630 controls, however, our study on parental employment at the time of conception and the risks for cancer among the offspring is one of the largest carried out to date. Cases were ascertained through the files of a high-quality, nationwide cancer registry, and controls were selected at random from a complete central population register. Approximately 90% of the tumours were verified microscopically. All tumours were classified according to the ICD-O and further aggregated into 12 main diagnostic groups based mainly on the morphology of the tumour. The records of parental employment from 9 months prior to the birth of the case or control child up to the date of cancer diagnosis were assembled independently of the case-control status and completed before notification of the cases, which implies that any observational and/or recall bias can be disregarded.

In conclusion, we observed relatively consistent associations between childhood cancer, most notably sarcomas and renal tumours, and mothers' occupation in medical and dental care, and we were able to confirm earlier reports of a link between childhood cancer and fathers' work as machinists. Although the use of industrial employment and job titles may be only a substitute for the exposure of importance and thus result in an unknown degree of attenuation of risk, many fewer associations were found in this childhood cancer study than in similar studies on adults, even in one based on the same data linkage [29]. This result is in agreement with the major finding of a recent descriptive study on trends in childhood cancer in Denmark [27], i.e. that the overall incidence of childhood cancer since the beginning of nationwide registration in 1943 has been influenced hardly at all by the profound changes in Danish society that have occurred over the same period. The increasing time trends specifically observed for lymphomas in boys and neuroblastomas in both sexes in the descriptive study could not be explained in the present study by any particular employment of the parents at the time of conception. The combined results of the two studies suggest that environmental exposures associated in modern society play no major role in the aetiology of most childhood cancers.

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