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Cancer incidence among Swedish pulp and paper mill workers: a cohort study of sulphate and sulphite mills

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Abstract
Purpose Associations between various malignancies and work in the pulp and paper industry have been reported but mostly in analyses of mortality rather than incidence. We aimed to study cancer incidence by main mill pulping process, department and gender in a Swedish cohort of pulp and paper mill workers.
Methods The cohort (18,113 males and 2,292 females, enrolled from 1939 to 1999 with >1 year of employment) was followed up for cancer incidence from 1958 to 2001. Information on the workers' department and employment was obtained from the mills' personnel files, and standardized incidence ratios (SIRs) were calculated using the Swedish population as reference.
Results Overall cancer incidence, in total 2,488 cases, was not increased by work in any department. However, risks of pleural mesothelioma were increased among males employed in sulphate pulping (SIR, 8.38; 95 % CI, 3.37–17) and maintenance (SIR, 6.35; 95 % CI, 3.47–11), with no corresponding increase of lung cancer. Testicular cancer risks were increased among males employed in sulphate pulping (SIR, 4.14; 95 % CI, 1.99–7.61) and sulphite pulping (SIR, 2.59; 95 % CI, 0.95–5.64). Female paper production workers showed increased risk of skin tumours other than malignant melanoma (SIR, 2.92; 95 % CI, 1.18–6.02).
Conclusions Incidence of pleural mesothelioma was increased in the cohort, showing that asbestos exposure still has severe health consequences, and highlighting the exigency of strict asbestos regulations and elimination. Testicular cancer was increased among pulping department workers. Shift work and endocrine disruptors could be of interest in this context.

Keywords Pleural mesothelioma · Skin tumours · Sulphate pulping · Sulphite pulping · Testicular cancer

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Introduction

Various compounds regarded as established or potential carcinogens are present in the pulp and paper industry, *inter alia* asbestos, wood dust, chloroform, organic solvents, mineral oil mist, respirable quartz, formaldehyde, chromium and nickel (Kauppinen et al. 2002; Korhonen et al. 2004; Teschke et al. 1999). Thus, about 20 % of workers employed in the manufacture of paper and paper products are known to be regularly exposed to one or more chemical carcinogens (Kauppinen et al. 2000). In addition to these recognized carcinogens, diverse compounds (e.g. polyaromatic hydrocarbons, pesticides, phthalates, organic

solvents, siloxanes, alkylphenolic compounds; many also present in various pulp and paper mill departments) have been proposed as endocrine disruptors showing carcinogenic effects (Ahrens et al. 2007; Brouwers et al. 2009). In addition, night shift work (common in the pulp and paper industry) is now regarded as being probably carcinogenic to humans by the International Agency for Research on Cancer (IARC) (IARC 2010).

Various malignancies have been associated with work in pulp and paper mills, most consistently lung cancer, for which asbestos and sulphur dioxide are possible contributors (Henneberger and Lax 1998; Langseth and Andersen 2000; Lee et al. 2002; Matanoski et al. 1998; Szadkowska-Stanczyk and Szymczak 2001; Torén et al. 1996), but also pleural cancer/mesothelioma (Andersson et al. 2001; Band et al. 1997, 2001; Carel et al. 2002; Langseth and Andersen 2000). However, most studies of health effects of work in pulp and paper mills have focused on mortality rates. Cancer incidence studies have shown increased risks of lymphohaematopoetical malignancies, stomach cancer, pancreatic cancer, prostate cancer and malignant melanoma (Band et al. 2001; Langseth and Andersen 2000; Rix et al. 1997, 1998). Excess incidences of brain tumour and testicular cancer have also been reported in several case–control or register studies, and in some cohorts (Andersson et al. 1998, 2001, 2002, 2003; Band et al. 1997; Matanoski et al. 1998; Rix et al. 1998). An increased incidence of ovarian cancer has also been found in a cohort study of female pulp and paper mill workers (Langseth and Andersen 1999; Langseth and Kjaerheim 2004).

Cancer mortality rates in a Swedish cohort of sulphate and sulphite pulp and paper mills have been previously analysed and presented together with a Swedish database of exposure measurements by department (Andersson et al. 2010). Increased risks were found for lung cancer among female workers engaged in paper production and for pancreas cancer among female office workers. In the study presented here, we examined cancer incidence stratified by main mill pulping process, department and gender in our cohort.

Materials and methods

The cohort consists of workers from eight pulp and paper mills, four sulphate and four sulphite mills, located in various parts of Sweden, established to permit analyses of associations between cancer incidence and both main mill pulping processes and specific mill departments. The cohort is more extensively described in another paper (Andersson et al. 2007).

Personnel files from the mills provided the name, date of birth, commencement and termination (if applicable) dates of employment, in most cases work history (job titles and/or departments) and the unique personal identification number of the employees. Only workers who had been employed in a mill for more than 1 year, and who were both alive and had not emigrated in 1958 (when the Swedish Cancer Registry started), were included in the cohort. Information on 20,405 workers enrolled from 1939 to 1999 that fulfilled these inclusion criteria was collected from the mills (Table 1). The median year of commencing employment was 1967, the median duration of employment was 12 years, and the median age at employment was 24 years. In the cohort, 141 subjects had worked in more

Table 1 Subjects, person-years at risk and number of cancer cases by gender, main mill pulping process and department in the cohort

Main mill process	Included males			Included females		
Department	Subjects	Person-years	Cancer cases	Subjects	Person-years	Cancer cases
Sulphate mills	10,108	271,548	1,114	1,253	35,110	166
<10 years employment	4,768	119,283	382	633	16,460	78
≥10 years employment	5,340	152,265	732	620	18,650	88
Sulphite mills	8,005	206,769	1,095	1,039	25,611	113
<10 years employment	3,324	82,741	312	651	15,656	73
≥10 years employment	4,681	124,028	783	388	9,955	40
Wood preparation	1,349	36,247	222	39	956	5
Sulphite pulping	1,873	52,035	274	59	1,445	4
Sulphate pulping	1,800	47,414	206	48	1,171	7
Paper and related production	3,190	78,833	290	571	17,495	93
Maintenance	4,531	127,234	589	121	2,757	13
Steam and power generation	227	5,630	28	0	–	–
Office	1,927	5,2310	267	822	20,469	85
Others and/or unknown	4,681	123,627	538	722	19,164	83

than one mill. Vital status was determined for all cohort members; 14,272 were alive and 319 had emigrated at the end of follow-up. None was lost to follow-up, and at the end of the inclusion period, 3,808 sulphate and 2,337 sulphite workers were still employed.

Start of follow-up was 1958 or (if later) the commencement date of first included employment. Cancer incidence was followed up from first inclusion year to 31 December 2001, until death, emigration or last observed date, whichever came first. The cohort was linked to the Swedish Cancer Registry, and cancer diagnoses given here are according to the 7th revision of the International Classification of Diseases (ICD-7). The study was approved by the Ethical Committees in Göteborg and Uppsala.

Exposure assessment

Subjects were first categorized by the main pulping (sulphite or sulphate) process of the mill in which they worked. For each period of their employment, the department and job title were defined. In the present study, data were analysed by department and department was used as a proxy for exposure. Wood preparation and ground wood pulping were merged and named wood preparation. Paper- and paper-board production and paper and paperboard products manufacture (converting operations) were entitled paper production. Subjects included and person-years in each category along with number of cancer cases are presented by department (Table 1). One subject could contribute person-years to more than one department; accordingly, 1,449 subjects were employed in two different departments and 127 in three or more. Measurements from the mills from 1971 to 1991 were included in the Swedish exposure measurements database for pulp and paper mills presented by Andersson et al. (2007, 2010) that comprehensively covered all chemical exposures, including quantitative data on most of the potential carcinogens present in the pulp and paper industry.

Statistical analysis

Person-years at risk were calculated and stratified according to gender, 5-year age groups and 1-year calendar periods. The expected numbers of cases for these strata were calculated using the general Swedish population as reference. In addition, since the mills are located in rural areas, we compared total cancer and lung cancer incidence in the cohort and the Swedish population apart from inhabitants of the three main Swedish cities from 1970 to 2001. Standardized incidence ratios (SIRs) with 95 % confidence intervals (CI) were calculated assuming a Poisson distribution of the observed numbers. Risks by main mill pulping process, department, gender and duration of employment ($\geq$10 years was defined as long-term) were also calculated for cancers for which there were at least 20 cases. In addition, a 10-year latency period was applied in the calculations, and for certain sites, SIRs were calculated for two separate time periods: 1958–1979 and 1980–2001. For female workers, the analysis only addressed risks associated with the main mill pulping process, paper production and office work as there were too few female workers in the other departments. All the analyses were performed using STATA software (STATA Corp 2005).

Results

The cohort was followed up from 1958 and encompassed 539,038 person-years at risk, 11 % of them from female workers and 43 % from sulphite mills (Table 1). The included workers were employed, in total, for 317,031 years in the mills, 47 % of those years in the sulphite mills. During the period 1958–2001, 2,305 of the workers developed 2,488 diagnosed cancers reported to the Swedish Cancer Registry. In the entire cohort, the overall cancer incidence was lower among male workers than in the reference population (SIR, 0.93; 95 % CI, 0.89–0.97); no difference was seen among the females (SIR, 1.00; 95 % CI, 0.89–1.13).

The risk estimates by main mill pulping process and gender were increased for pleural mesothelioma among male sulphate workers, especially long-term employed, and for male sulphite mill workers long-term employed (Table 2). No cases of pleural mesothelioma were reported among females. No association between excess brain tumours (not even glioma) and either of the pulping processes was detected. Testicular cancer was increased among sulphate workers with short employment. The incidence of skin cancers other than melanoma was increased for females, especially among sulphite mill workers. Ovary cancer was not increased among female workers of any considered category (Table 3).

Cancer incidence rates by department and gender are presented in Table 4. No single department was associated with any increased risk of overall cancer incidence. Cancer of the lip was increased, especially among sulphite pulping male workers. Pleural mesothelioma was increased among male workers employed in sulphate pulping, maintenance and (non-significantly) sulphite pulping. Among steam and power generation workers, there were two cases compared to 0.11 expected cases (data not shown in table). However, lung cancer incidence was not increased in any department (and decreased among all male workers), although it was slightly increased among females engaged in paper

Table 2 Cancer incidence among pulp and paper mill workers, 1958–2001

Cancer site (ICD-7)	Sulphate mills males <10 years			Sulphate mills males ≥10 years			Sulphite mills males <10 years			Sulphite mills males ≥10 years		
	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI
Lip (140)	3	1.02	0.21–2.98	7	0.98	0.39–2.02	4	1.60	0.43–4.08	12	1.55	0.80–2.72
Oesophagus (150)	4	0.82	0.22–2.10	4	0.39	0.10–0.99	5	1.30	0.42–3.04	6	0.57	0.21–1.25
Stomach (151)	10	0.55	0.26–1.02	56	1.17	0.88–1.52	15	0.97	0.54–1.59	59	1.12	0.85–1.45
Colon (153)	25	0.92	0.60–1.36	65	1.10	0.85–1.41	21	0.96	0.60–1.47	55	0.91	0.68–1.18
Rectum (154)	20	1.07	0.65–1.65	46	1.14	0.83–1.52	20	1.34	0.82–2.07	37	0.90	0.63–1.24
Liver, primary (155.0)	3	0.62	0.13–1.81	5	0.46	0.15–1.07	4	1.02	0.28–2.60	11	0.95	0.47–1.70
Pancreas (157)	13	1.18	0.63–2.01	24	0.94	0.60–1.40	5	0.55	0.18–1.29	20	0.74	0.45–1.14
Lung and bronchus, primary (162.1)	48	1.30	0.96–1.73	51	0.64	0.48–0.84	24	0.81	0.52–1.21	69	0.85	0.66–1.08
Pleural mesothelioma (162.2)	5	3.00	0.98–7.01	15	5.17	2.89–8.52	0		(1.25)	7	2.59	1.04–5.33
Breast (170)	0		(0.68)	2		(1.58)	1		(0.56)	1		(1.63)
Prostate (177)	67	0.80	0.62–1.02	182	0.95	0.82–1.10	67	1.00	0.77–1.27	195	0.99	0.85–1.14
Testis (178)	13	1.87	1.00–3.20	6	0.84	0.31–1.83	5	1.12	0.36–2.60	2		(5.30)
Kidney (180)	16	1.06	0.60–1.71	23	0.73	0.46–1.10	14	1.16	0.64–1.95	32	1.01	0.69–1.43
Bladder, ureter, urethra (181)	30	1.11	0.75–1.59	50	0.88	0.66–1.16	25	1.16	0.75–1.71	63	1.10	0.85–1.41
Malignant melanoma of skin (190)	12	0.70	0.36–1.22	24	0.95	0.61–1.41	11	0.92	0.46–1.64	19	0.89	0.53–1.39
Other skin (191)	12	0.69	0.36–1.21	24	0.64	0.41–0.95	7	0.50	0.20–1.04	36	0.93	0.65–1.28
Brain (193.0)	15	1.07	0.60–1.76	21	0.93	0.57–1.41	7	0.68	0.27–1.40	19	0.92	0.55–1.43
Glioma (193.0, histology code 475–476)	7	0.87	0.35–1.78	14	1.10	0.60–1.85	3	0.51	0.11–1.50	11	0.98	0.49–1.74
Non-Hodgkin lymphoma (200, 202)	20	1.33	0.81–2.06	23	0.87	0.55–1.31	12	1.07	0.55–1.88	13	0.52	0.28–0.90
Multiple myeloma, plasmocytoma (203)	2		(5.78)	9	0.73	0.33–1.38	8	1.73	0.73–3.40	16	1.26	0.72–2.05
Myeloid leukaemia (205)	6	1.25	0.46–2.72	4	0.46	0.13–1.18	6	1.66	0.61–3.61	12	1.45	0.75–2.53
Cancer site (ICD-7)	Sulphate mills females <10 years			Sulphate mills females ≥10 years			Sulphite mills females <10 years			Sulphite mills females ≥10 years		
	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI
Lip (140)	0		(0.11)	0		(0.15)	1		(0.10)	0		(0.09)
Oesophagus (150)	1		(0.26)	0		(0.39)	1		(0.25)	0		(0.25)
Stomach (151)	1		(1.59)	3	1.17	0.88–1.52	2		(1.58)	2		(1.67)
Colon (153)	5	1.16	0.38–2.71	9	1.42	0.65–2.69	5	1.20	0.39–2.81	4	1.00	0.27–2.55
Rectum (154)	3	1.33	0.27–3.88	0		(3.32)	3	1.39	0.29–4.05	1		(2.03)
Liver, primary (155.0)	0		(0.44)	2		(0.64)	0		(0.43)	2		(0.42)
Pancreas (157)	4	2.66	0.72–6.80	2		(2.22)	1		(1.46)	1		(1.47)
Lung and bronchus, primary (162.1)	4	1.34	0.36–3.42	6	1.42	0.52–3.09	3	1.10	0.23–3.23	3	1.34	0.28–3.92
Pleural mesothelioma (162.2)	0		(0.05)	0		(0.07)	0		(0.05)	0		(0.04)
Breast (170)	27	1.32	0.87–1.92	20	0.73	0.45–1.13	26	1.41	0.92–2.06	8	0.55	0.24–1.07

Table 2 continued

Cancer site (ICD-7)	Sulphate mills females <10 years			Sulphate mills females ≥10 years			Sulphite mills females <10 years			Sulphite mills females ≥10 years		
	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI
Kidney (180)	0		(1.52)	2		(2.22)	2		(1.48)	0		(1.39)
Bladder, ureter, urethra (181)	0		(1.39)	2		(2.05)	2		(1.32)	1		(1.26)
Malignant melanoma of skin (190)	1		(2.66)	6	1.82	0.67–3.96	5	2.10	0.68–4.90	0		(1.74)
Other skin (191)	1		(1.54)	3	1.28	0.26–3.75	2		(1.44)	5	3.42	1.11–7.99
Brain (193.0)	2		(2.21)	3	1.04	0.21–3.03	1		(2.06)	2		(1.62)
Glioma (193.0, histology code 475–476)	0		(0.89)	1		(1.16)	0		(0.84)	1		(0.64)
Non-Hodgkin lymphoma (200, 202)	2		(1.69)	4	0.87	0.55–1.31	2		(1.58)	0		(1.38)
Multiple myeloma, plasmocytoma (203)	0		(0.69)	1		(1.02)	0		(0.66)	0		(0.65)
Myeloid leukaemia (205)	1		(0.61)	0		(0.84)	0		(0.58)	2		(0.50)

Standardized incidence ratios by site of cancer, main mill pulping process, gender and duration of employment

O observed cases, *ICD* International Classification of Diseases

[a] Standardized incidence ratios for pulp and paper mill workers compared with the general population in Sweden, when <3 cases the expected numbers are shown in parenthesis

production. For males employed in wood preparation, stomach cancer and lung cancer incidences were significantly decreased. Testicular cancer was more common among sulphate pulping workers than among Swedish males in general and tended to be more common also in sulphite pulping. Liver cancer among men working in paper production showed a doubled, but not significantly increased, risk. Among employees of some departments the SIR for glioma incidence exceeded 1.0, but not statistically significant. For female paper production workers, there was an increased risk of skin tumours other than malignant melanoma and the risk of melanoma was doubled. Male workers in other and/or unknown departments had an increased risk of myeloid leukaemia. Restricting department analyses to an employment time of 10 years or more did not change the main results (data not shown in table).

The cancer incidence risks described above were calculated using the entire Swedish population as reference. But for analyses of all cancer sites and lung cancer, the Swedish population outside the three biggest cities was used as reference (Table 5). The risk estimates increased, as expected, but only marginally.

Risks of cancer at certain sites—e.g. prostate, testis and the subgroup seminoma, breast and non-Hodgkin lymphoma (NHL)—were further analysed with regard to duration of employment and latency time (Table 6). The risks of all testicular cancers and seminoma among male workers and of breast cancer among female workers were highest when the latency time was restricted to less than 10 years, and for NHL the risk was entirely associated with short latency to disease.

Comparison of the cancer incidence and employment data for two time periods, 1958–1979 and 1980–2001, did not reveal any significant trends or changes, even for pleural mesothelioma (data not shown), indicating that there were no significant changes in exposure over time.

Discussion

No increase in overall cancer incidence was found in the examined cohort of Swedish pulp and paper mill workers. However, pleural mesothelioma was increased among male workers in certain departments without any corresponding increase in lung cancer. An increased risk of skin tumours other than malignant melanoma, along with a slightly increased risk of melanoma, was found for female paper production workers. Lip cancer was increased among sulphite pulping males, and the incidence of testicular cancer was increased among workers in both sulphate and sulphite pulping departments. For some cancer sites, for example testis, breast and NHL, the risks were consistently highest in the strata with less than 10 years latency.

Table 3 Cancer incidence (less than 20 cases) among pulp and paper mill workers, 1958–2001

Cancer site (ICD-7)	Sulphate mills males			Sulphite mills males			Sulphate mills females			Sulphite mills females		
	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI
All cancer sites	1114	0.91	0.86–0.96	1095	0.96	0.90–1.01	166	1.03	0.88–1.20	113	0.96	0.79–1.16
Buccal cavity (141–144)	9	0.61	0.28–1.16	7	0.54	0.22–1.11	3	2.37	0.49–6.93	0	–	(0.93)
Pharynx (145–148)	6	0.61	0.22–1.32	7	0.82	0.33–1.68	1	–	(0.47)	0	–	(0.34)
Gall bladder (155.1)	5	0.80	0.26–1.87	9	1.41	0.64–2.67	1	–	(1.76)	0	–	(1.44)
Nose and nasal sinuses (160)	2	–	(2.81)	5	1.88	0.61–4.39	1	–	(0.19)	0	–	(0.15)
Larynx (161)	8	0.65	0.28–1.27	7	0.60	0.24–1.24	0	–	(0.24)	0	–	(0.17)
Cervix uteri (171)	–	–	–	–	–	–	7	1.08	0.44–2.23	4	0.84	0.23–2.15
Corpus uteri (172)	–	–	–	–	–	–	6	0.61	0.22–1.32	4	0.57	0.15–1.45
Ovary (175)	–	–	–	–	–	–	7	0.74	0.30–1.52	4	0.58	0.16–1.49
Thyroid gland (194)	9	1.34	0.61–2.54	1	–	(5.79)	2	–	(2.14)	2	–	(1.57)
Pituitary (195.3)	8	1.51	0.65–2.97	7	1.63	0.66–3.36	0	–	(0.95)	1	–	(0.39)
Bone (196)	2	–	(2.80)	1	–	(2.29)	0	–	(0.25)	0	–	(0.19)
Connective tissue (197)	6	0.64	0.23–1.38	6	0.73	0.27–1.58	1	–	(1.05)	0	–	(0.78)
Hodgkin disease (201)	9	0.99	0.45–1.87	7	0.90	0.36–1.86	0	–	(0.67)	0	–	(0.54)
Lymphatic leukaemia (204)	5	0.30	0.10–0.71	13	0.84	0.44–1.43	2	–	(1.16)	0	–	(0.88)
Other haematological (206–209)	2	–	(9.09)	8	0.94	0.41–1.85	1	–	(0.95)	0	–	(0.73)

Standardized incidence ratios by site of cancer, main mill process and gender

O observed cases, *ICD* International Classification of Diseases

[a] Standardized incidence ratios for pulp and paper mill workers compared with the general population in Sweden, when <3 cases the expected numbers are shown in parenthesis

With regard to the numbers of cancer cases, this is one of the largest published studies of a cohort of pulp and paper mill workers. As in many cohort studies, information on potential lifestyle confounders was rare. However, for part of the cohort, we have questionnaire data on smoking habits (Andersson et al. 2007). Occupational exposure was assessed only by department and not by specific agents. Anyhow, the complex chemical exposures in pulp and paper mills make assessments of specific agents intricate, even more on a worker level and misclassification can be introduced. Departments might also have been misclassified, and changes in department may not have been recorded. However, many of the workers were skilled, so changes in jobs were more likely to have occurred within than between departments. In this study, we regarded potential exposure misclassifications as non-differential. Outcomes may also have been misclassified, but registers of Scandinavian countries, including the Swedish Cancer Registry, are considered to have high quality (Barlow et al. 2009). It should also be recognized that some of the reported results of the analysis of multiple outcomes may have been due to chance.

In this study, we used SIR to analyse the risk comparing the mill workers and different departments with the Swedish population. Another possibility is to use internal analyses especially if the purpose is to compare the departments or trying to establish dose–response relationship for particular agents. The exposure intensity could be semi quantitatively estimated by time period and department and serve as a basis for individual dose estimates. We are planning to update the cohort soon and then internal comparison by department or by more specific and refined exposure measures could be performed using Cox regression analysis and even a nested case referent study within the cohort could be done for some diagnoses.

The risk of pleural cancer or mesothelioma has not been analysed in all pulp and paper mill cohort studies, but increased rates have often been detected when analysed. An exposure assessment of mesothelioma cases among pulp and paper workers found asbestos exposure to be the most important cause (Järvholm et al. 1988). The IARC carried out a collaborative epidemiological study regarding the pulp and paper industry and created an international database of exposure measurements (Kauppinen et al. 1997). Subsequent analyses of the exposure assessments (Kauppinen et al. 2002) and the associations between asbestos exposure and mortality due to lung cancer and pleural cancer (Carel et al. 2002) showed increased risks of pleural cancer, but not lung cancer. Also in our study, we found no increased risk of lung cancer, even relative to the general population outside big cities. The risk of lung cancer among paper production female workers was

Table 4 Cancer incidence among pulp and paper mill workers, 1958–2001

Cancer site (ICD-7)	Wood preparation males			Sulphite pulping males			Sulphate pulping males			Maintenance males		
	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI
All cancer sites	222	0.85	0.75–0.97	274	0.95	0.84–1.07	206	0.87	0.76–1.00	589	0.98	0.90–1.06
Lip (140)	3	1.26	0.26–3.69	7	2.77	1.11–5.70	3	1.49	0.31–4.34	5	0.98	0.32–2.28
Oesophagus (150)	4	1.23	0.34–3.15	1	–	(3.61)	1	–	(2.95)	5	0.67	0.22–1.55
Stomach (151)	8	0.49	0.21–0.97	19	1.15	0.69–1.79	16	1.18	0.67–1.91	38	1.14	0.81–1.57
Colon (153)	17	0.90	0.52–1.44	15	0.73	0.41–1.20	16	0.95	0.54–1.55	54	1.27	0.95–1.66
Rectum (154)	16	1.25	0.71–2.03	15	1.06	0.60–1.76	7	0.61	0.24–1.25	35	1.20	0.84–1.67
Liver, primary (155.0)	4	1.11	0.30–2.84	3	0.78	0.16–2.27	1	–	(3.10	9	1.14	0.52–2.17
Pancreas (157)	10	1.20	0.57–2.20	8	0.89	0.38–1.76	4	0.55	0.15–1.41	15	0.82	0.46–1.35
Lung and bronchus, primary (162.1)	14	0.56	0.30–0.94	34	1.21	0.84–1.69	19	0.84	0.51–1.32	47	0.81	0.60–1.08
Pleural mesothelioma (162.2)	1	–	(0.84)	3	2.92	0.60–8.53	7	8.38	3.37–17	14	6.35	3.47–11
Breast (170)	1	–	(0.49)	0	–	(0.54)	0	–	(0.45)	0	–	(1.13)
Prostate (177)	60	0.96	0.73–1.23	58	0.88	0.67–1.14	51	0.95	0.71–1.25	128	0.95	0.79–1.13
Testis (178)	1	–	(1.48)	6	2.59	0.95–5.64	10	4.14	1.99–7.61	6	0.96	0.35–2.10
Kidney (180)	10	1.03	0.49–1.89	17	1.54	0.89–2.46	6	0.67	0.25–1.45	19	0.82	0.50–1.28
Bladder, ureter, urethra (181)	13	0.73	0.39–1.24	20	1.00	0.61–1.55	17	1.06	0.62–1.70	48	1.16	0.86–1.54
Malignant melanoma of skin (190)	5	0.77	0.25–1.79	8	0.92	0.40–1.81	4	0.53	0.14–1.36	16	0.81	0.46–1.32
Other skin (191)	8	0.65	0.28–1.27	8	0.61	0.27–1.21	4	0.38	0.10–0.97	18	0.67	0.40–1.06
Brain (193.0)	5	0.81	0.26–1.88	3	0.38	0.08–1.10	8	1.19	0.51–2.34	20	1.13	0.69–1.75
Glioma (193.0, histology code 475–476)	5	1.49	0.48–3.47	2	–	(4.43)	7	1.85	0.74–3.80	11	1.11	0.55–1.98
Non-Hodgkin lymphoma (200, 202)	7	0.91	0.37–1.88	7	0.76	0.31–1.57	3	0.39	0.08–1.15	20	1.01	0.61–1.55
Multiple myeloma, plasmocytoma (203)	3	0.76	0.16–2.23	6	1.38	0.51–3.00	2	–	(3.53)	9	1.00	0.46–1.89
Myeloid leukaemia (205)	0	–	(2.54)	2	–	(3.01)	1	–	(2.53)	6	0.92	0.34–2.00
Cancer site (ICD-7)	Paper production males			Office males			Others males			Total males		
	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI
All cancer sites	290	0.98	0.87–1.10	267	0.92	0.81–1.03	538	0.92	0.84–1.00	2209	0.93	0.89–0.97
Lip (140)	3	1.28	0.26–3.73	4	1.58	0.43–4.06	4	0.81	0.22–2.06	26	1.28	0.84–1.88
Oesophagus (150)	1	–	(3.66)	2	–	(3.65)	5	0.69	0.22–1.60	19	0.64	0.39–1.00
Stomach (151)	21	1.37	0.85–2.10	15	0.90	0.50–1.48	35	1.07	0.74–1.49	140	1.04	0.88–1.23
Colon (153)	22	1.08	0.67–1.63	14	0.67	0.37–1.13	35	0.85	0.59–1.18	166	0.99	0.84–1.15
Rectum (154)	20	1.42	0.87–2.19	11	0.77	0.39–1.38	28	0.99	0.66–1.43	123	1.07	0.89–1.27
Liver, primary (155.0)	8	2.15	0.93–4.23	1	–	(3.91)	5	0.65	0.21–1.52	23	0.74	0.47–1.10
Pancreas (157)	9	1.04	0.48–1.98	8	0.89	0.38–1.75	14	0.79	0.43–1.32	62	0.85	0.65–1.09
Lung and bronchus, primary (162.1)	19	0.68	0.41–1.07	26	0.93	0.60–1.36	49	0.88	0.65–1.16	192	0.85	0.73–0.97
Pleural mesothelioma (162.2)	0	–	(1.14)	2	–	(1.03)	4	1.89	0.51–4.83	27	3.17	2.09–4.61
Breast (170)	0	–	(0.54)	1	–	(0.55)	1	–	(1.10)	4	0.90	0.24–2.30
Prostate (177)	62	0.98	0.75–1.25	79	1.16	0.92–1.45	120	0.91	0.75–1.09	511	0.95	0.87–1.03

Table 4 continued

Cancer site (ICD-7)	Paper production males			Office males			Others males			Total males		
	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI
Testis (178)	3	0.66	0.14–1.92	1	–	(2.42)	4	0.64	0.17–1.63	26	1.10	0.71–1.60
Kidney (180)	11	0.97	0.49–1.74	4	0.36	0.10–0.93	25	1.12	0.73–1.66	85	0.94	0.75–1.17
Bladder, ureter, urethra (181)	16	0.80	0.46–1.30	20	0.99	0.61–1.54	43	1.08	0.78–1.45	168	1.04	0.88–1.20
Malignant melanoma of skin (190)	12	1.05	0.54–1.83	5	0.57	0.19–1.33	18	0.94	0.56–1.49	66	0.87	0.67–1.11
Other skin (191)	19	1.48	0.89–2.31	11	0.81	0.41–1.46	14	0.53	0.29–0.89	79	0.74	0.58–0.92
Brain (193.0)	9	0.92	0.42–1.75	4	0.51	0.14–1.30	22	1.29	0.81–1.95	62	0.92	0.70–1.17
Glioma (193.0, histology code 475–476)	3	0.54	0.11–1.57	2	–	(4.36)	11	1.15	0.57–2.05	35	0.92	0.64–1.28
Non-Hodgkin lymphoma (200, 202)	10	0.95	0.46–1.75	11	1.19	0.59–2.12	11	0.57	0.28–1.02	68	0.88	0.68–1.11
Multiple myeloma, plasmocytoma (203)	2	–	(4.35)	4	0.91	0.25–2.34	10	1.15	0.55–2.11	35	0.99	0.69–1.37
Myeloid leukaemia (205)	2	–	(3.44)	2	–	(3.02)	14	2.21	1.21–3.71	28	1.10	0.73–1.59
Cancer site (ICD-7)	Paper production females			Office females			Other females			Total females		
	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI
All cancer sites	93	1.01	0.82–1.24	85	0.95	0.76–1.18	83	1.04	0.83–1.29	279	1.00	0.89–1.13
Lip (140)	0	–	(0.15)	0	–	(0.14)	1	–	(0.13)	1	–	(0.46)
Oesophagus (150)	1	–	(0.40)	1	–	(0.35)	1	–	(0.32)	3	2.61	0.54–7.61
Stomach (151)	2	–	(2.48)	3	1.37	0.28–4.00	3	1.52	0.31–4.45	8	1.12	0.48–2.21
Colon (153)	5	0.77	0.25–1.80	8	1.38	0.60–2.72	10	1.91	0.91–3.50	23	1.22	0.77–1.83
Rectum (154)	3	0.90	0.19–2.62	2	–	(3.05)	2	–	(2.74)	7	0.72	0.29–1.47
Liver, primary (155.0)	1	–	(0.66)	2	–	(0.59)	1	–	(0.54)	4	2.08	0.57–5.33
Pancreas (157)	1	–	(2.31)	4	1.95	0.53–4.99	3	1.63	0.34–4.76	8	1.20	0.52–2.37
Lung and bronchus, primary (162.1)	7	1.76	0.71–3.63	4	1.03	0.28–2.62	4	1.15	0.31–2.93	16	1.32	0.75–2.14
Pleural mesothelioma (162.2)	0	–	(0.07)	0	–	(0.07)	0	–	(0.06)	0	–	(0.21)
Breast (170)	19	0.74	0.44–1.15	28	1.06	0.70–1.53	27	1.15	0.75–1.67	81	1.00	0.79–1.24
Kidney (180)	0	–	(2.25)	3	1.46	0.30–4.26	0	–	(1.84)	4	0.61	0.17–1.55
Bladder, ureter, urethra (181)	1	–	(2.07)	1	–	(1.86)	2	–	(1.67)	5	0.83	0.27–1.94
Malignant melanoma of skin (190)	6	2.00	0.73–4.35	2	–	(3.39)	4	1.31	0.36–3.34	12	1.19	0.62–2.08
Other skin (191)	7	2.92	1.18–6.02	4	1.96	0.53–5.03	1	–	(1.93)	11	1.62	0.81–2.61
Brain (193.0)	1	–	(2.76)	5	1.73	0.56–4.05	1	–	(2.59)	8	0.91	0.39–1.80
Glioma (193.0, histology code 475–476)	0	–	(1.10)	2	–	(1.15)	0	–	(1.04)	2	–	(0.57)
Non-Hodgkin lymphoma (200, 202)	3	1.28	0.26–3.75	1	–	(2.24)	2	–	(2.02)	8	1.13	0.49–2.24
Multiple myeloma, plasmocytoma (203)	1	–	(1.05)	0	–	(0.94)	0	–	(0.83)	1	–	(0.33)
Myeloid leukaemia (205)	2	–	(0.83)	0	–	(0.81)	0	–	(0.73)	3	1.18	0.24–3.46

Standardized incidence ratios by site of cancer, gender and department

O observed cases, *ICD* International Classification of Diseases

[a] Standardized incidence ratios for pulp and paper mill workers compared with the general population in Sweden, when <3 cases the expected numbers are shown in parenthesis

Table 5 Cancer incidence among pulp and paper mill workers from 1970 to 2001 compared with the general population in Sweden and the population outside the three main cities

Cancer site (ICD-7)	Sulphate mills males			Sulphite mills males			Sulphate mills females			Sulphite mills females		
	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI
All cancer sites/total population	993	0.91	0.85–0.96	981	0.97	0.91–1.04	156	1.03	0.88–1.21	103	0.96	0.78–1.16
All cancer sites/population outside 3 cities	993	0.94	0.88–1.00	981	1.01	0.95–1.08	156	1.05	0.90–1.23	103	0.98	0.80–1.19
Lung (162.1)/total population	91	0.88	0.71–1.08	88	0.92	0.73–1.13	10	1.42	0.68–2.61	5	1.05	0.34–2.45
Lung (162.1)/population outside 3 cities	91	0.97	0.78–1.19	88	1.02	0.82–1.26	10	1.54	0.74–2.83	5	1.15	0.37–2.68

O observed cases, *ICD* International Classification of Diseases

[a] Standardized incidence ratios for pulp and paper mill workers compared with the general population in Sweden

non-significant; in contrast to the significant risk, we found in our previous mortality study (Andersson et al. 2010). Only a small number of measurements of asbestos have been performed in the Swedish mills, all indicating very low levels of asbestos (Andersson et al. 2010). In a Nordic register study of cancer incidence by occupational category, increased risks among chemical process workers (mainly pulp and paper mill workers) were found for lung cancer, for both genders (but not among males in Sweden) and for mesothelioma among males (Pukkala et al. 2009). These findings from various studies indicate that low intensity asbestos exposure is causal for mesothelioma. A recent estimation also found that asbestos contributed to over half of the occupational attributable deaths in Great Britain (Rushton et al. 2008), emphasizing the importance of eliminating asbestos exposure. The incidence of ovarial cancer reported from Norway was hypothesized, but not confirmed, to be causally linked to asbestos (Langseth and Andersen 1999; Langseth and Kjaerheim 2004; Langseth et al. 2007). However, we found no such increase of ovarial cancer among our cohort.

Among male pulp and paper mill workers in Norway, an increased incidence of malignant melanoma has been reported, but not for females (Langseth and Andersen 1999, 2000). Increased incidence of melanoma has also been found in Canadian, but not Danish, incidence studies (Band et al. 2001; Rix et al. 1997, 1998). Non-melanoma skin cancer is not always reported, but was not increased in the subjects considered in the cited Norwegian or Danish studies. Thus, the increased incidence among female paper production workers in our cohort could be a random finding, and males had a low incidence except those working in paper production. The non-melanomas were predominantly facial, and the melanomas were located on the trunk. Occupational skin cancers may be due to chemical carcinogens, but some cases may be attributable to burns (Gawkrodger. 2004). Sun exposure does not seem to increase the risk of non-melanoma skin cancer (unlike lip cancer) among outdoor workers (Kenborg et al. 2010). We found an increased incidence of lip cancer among male sulphite pulping department workers. This could, of course, be a chance finding, but the SIR for lip cancer among chemical process workers was not less than one for any country mentioned in the cited Nordic register study (Pukkala et al. 2009). If the increased rates reflect real associations, they could be due to well-known risk factors, such as farming and sun exposure when not working, and more hypothetically in sulphite pulping exposure to sulphur dioxide could be a contributory factor. In the Swedish measurement database, 57 % of the sulphur dioxide measurements exceeded the Swedish occupational exposure limit (5 mg/m^3) (Andersson et al. 2007).

The incidence of testicular cancer is increasing in industrialized countries, so rapidly that the rise must be attributed to environmental factors (Huyghe et al. 2007; Jørgensen et al. 2011). Postulated contributory factors include both factors related to modern living and occupational exposure (Garner et al. 2008; Jørgensen et al. 2011). The latter may include endocrine disruptors, which (*inter alia*) could have adverse effects on foetal gonads (Auharek et al. 2010), which may be relevant in the context of this study. Chemicals with such potential effects are applied in the pulp and paper mills, including phthalates and siloxanes used in coating paper products. Actually, a study based on the Swedish Cancer Environment Registry found that maintenance workers, paper product workers and packers in paper mills have increased risks of testicular cancer (Andersson et al. 2003). It has been proposed that exposure-related risks of testicular cancer may be particularly strong during certain developmental periods, such as prenatal and puberty (Richiardi et al. 2007). Our findings that risks were highest among those with less than 10 years latency might be related to the puberty association, since 70 % of the workers diagnosed with testicular cancer had started their mill work before they were 21 years old.

Breast cancer and prostate cancer are also regarded as hormonally dependent malignancies; accordingly, endocrine-disrupting compounds are suspected to contribute to

Table 6 Cancer incidence among pulp and paper mill workers, 1958–2001, for selected cancer forms by duration of employment and latency periods of < and ≥10 years

Cancer site (ICD-7)/latency	Sulphate mills males <10 years			Sulphate mills males ≥10 years			Sulphite mills males <10 years			Sulphite mills males ≥10 years		
	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI
Prostate (177)												
<10 years	5	1.03	0.33–2.41				3	1.10	0.23–3.22			
≥10 years	62	0.79	0.61–1.01	182	0.96	0.83–1.11	64	0.99	0.77–1.27	195	0.99	0.86–1.15
Testis (178)												
<10 years	7	2.65	1.07–5.46				4	2.50	0.68–6.39			
≥10 years	6	1.39	0.51–3.03	6	1.19	0.44–2.60	1		(2.87)	2		(3.54)
Seminoma (178, histology code 066)												
<10 years	2	1.75	0.21–6.33				3	4.41	0.91–12.9			
≥10 years	5	1.75	0.57–4.08	6	1.79	0.70–3.61	1		(1.88)	2		(2.40)
Non-Hodgkin lymphoma (200, 202)												
<10 years	9	4.69	2.14–8.88				6	5.46	2.00–11.9			
≥ 10 years	11	0.84	0.42–1.51	23	0.92	0.59–1.39	6	0.60	0.22–1.30	13	0.55	0.29–0.94
Cancer site (ICD-7)/latency	Sulphate mills females <10 years			Sulphate mills females ≥10 years			Sulphite mills females <10 years			Sulphite mills females ≥10 years		
	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI	O	SIR[a]	95 % CI
Breast (170)												
<10 years	6	2.04	0.75–4.43				7	2.91	1.17–5.99			
≥10 years	21	1.20	0.74–1.83	20	0.82	0.50–1.27	19	1.18	0.71–1.85	8	0.63	0.27–1.24

O observed cases, *ICD* International Classification of Diseases

[a] Standardized incidence ratios for pulp and paper mill workers compared with the general population in Sweden, when <3 cases, the expected numbers are shown in parenthesis

their development (Muir 2005; Fenton 2006; Prins 2008), and vulnerability may be most pronounced in certain developmental phases, notably during foetal development, puberty and pregnancy (Fenton 2006; Prins 2008; Agalliu et al. 2005). Analogously to our findings regarding testicular cancer among the male workers in our cohort, the increased risk of breast cancer for females with less than 10-year latency time is interesting. The authors of a study of mortality and cancer incidence in New Zealand pulp and paper mill workers reported non-statistically significant excess risks of breast cancer mortality and incidence (McLean et al. 2002). For prostate cancer, we found no increased risks, even when our latency time restrictions were applied.

Employment in the pulp and paper industry frequently involves working at night, which is classified as probably carcinogenic by the IARC, and may be particularly influential in relation to breast and prostate cancers and NHL (Costa et al. 2010; Wang et al. 2011). The underlying mechanisms are complex and multifactorial, but it has been suggested that exposure to light at night suppresses nocturnal melatonin secretion and perturbs sex hormone homoeostasis (Wang et al. 2011). Our findings and the current exposure in pulp and paper mills are interesting even in the light of this mechanistic pathway.

An increased risk of NHL among those with a latency time of less than 10 years appeared in this study. A short latency time for NHL is also reported secondary to cancer therapy, with an increased risk appearing within the first 5 years following completion of chemotherapy (Krishnan and Morgan 2007). Previous studies have found increased risks of NHL among pulp and paper industry workers (Band et al. 1997; Torén et al. 1996). Indeed, a dose–response relationship between NHL and cumulative SO_2 exposure in pulp and paper work has been reported (Lee et al. 2002). In addition, mycosis fungoides, a chronic T-cell cutaneous lymphoma, has been associated, among women, with employment in pulp and paper manufacture (Morales-Suárez-Varela et al. 2004), and exposure to atmospheric pollutants from paper, pulp and board industries has been linked to excess NHL mortality among local residents (Ramis et al. 2009).

Conclusions

In this study, we found not only evidence of well-known effects of exposures linked to pulp and paper mill work, such as pleural mesotheliomas related to asbestos exposure, but also indications of other malignancies where the causing exposure is ambiguous. Certain hormonally related malignancies are example of this where shift work and endocrine-disrupting compounds might be involved. Further studies with particular focus on specific exposures, exposure time windows and latency time probably are required to elucidate the mechanisms involved.

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