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Ahti Anttila · Eero Pukkala · Riitta Riala
Markku Sallmén · Kari Hemminki

Cancer incidence among Finnish workers exposed to aromatic hydrocarbons

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Abstract ***Objectives***: To assess whether occupational exposure to aromatic hydrocarbons increases carcinogenic risk. ***Methods***: We followed cancer incidence among 3,922 male and 1,379 female workers monitored for exposure to styrene, toluene, or xylene. The follow-up after the first personal measurement comprised 66,500 person-years at risk over the period 1973–1992. We computed the indirectly standardized incidence ratios (SIR) with 95% confidence interval (CI) with regard to age-, gender-, and period-specific incidence rates of cancer in the Finnish general population. ***Results***: The overall rate of cancer incidence for the total cohort was fairly similar to that of the general population. The risk for nervous system tumors was increased at 10 years after the first personal measurement (SIR 2.80, CI 1.03–6.08). For styrene there was an excess risk for rectal cancer (SIR 3.11, CI 1.14–6.77), and risks for pancreatic and nervous system tumors were increased nonsignificantly. For toluene and xylene, no clear increase in cancer risk was found. ***Conclusions***: The data are not supportive of an overall increase in the cancer risk for these solvents, even though we cannot rule out site-specific associations with the rectum, pancreas, and nervous system. There is supporting evidence in the epidemiology literature for pancreatic cancer risk and heavy exposure to styrene. More studies are warranted on solvents, with detailed information on lifetime exposures and habits being collected whenever possible.

A. Anttila (✉) · E. Pukkala
Finnish Cancer Registry, Liisankatu 21 B,
FIN-00170 Helsinki, Finland
Tel.: +358 9 135 33 240; Fax: +358 9 135 5378
e-mail: ahti.anttila@cancer.fi

A. Anttila · R. Riala · M. Sallmén · K. Hemminki
Finnish Institute of Occupational Health, Helsinki, Finland

K. Hemminki
Center for Nutrition and Toxicology,
Karolinska Institute, Huddinge, Sweden

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Introduction

Three aromatic hydrocarbons (styrene, toluene, and xylene) belong to the most commonly used solvents in industrial and manual applications. The three compounds are substituted benzenes and resemble each other both chemically and toxicologically [14, 15]. Only styrene is known to have some genotoxic activity, and only styrene has shown some evidence of carcinogenic activity in animal experiments [14, 15, 23]. The central nervous system is the target organ of toxicity for all these compounds. As cytotoxicity may sometimes be related to carcinogenicity, the central nervous system is one hypothetical site of cancer induced by these three solvents [34].

The carcinogenicity of styrene, toluene, and xylene has been examined in several epidemiology studies, with inconclusive results [14, 15, 22]. In at least two independent study populations the sites that have emerged most consistently are lymphohematopoietic tissues and the pancreas for exposure to styrene [17, 19, 20] and the lung [32, 35], gastrointestinal tract [30, 32, 35, 36], brain [7, 31], and lymphohematopoietic tissues [5, 25, 32, 36] for exposure to toluene or xylene.

The aim of the present study was to assess whether exposure to aromatic hydrocarbons would increase the risk for cancer. The study was based on a follow-up of cancer incidence among workers biologically monitored for exposure to any one of these solvents. We consider this worker population to be a particularly suitable study source [3, 4]. As biologic measurements are usually done because the exposure is considered substantial and reasonably well documented at the workplace, some of the common weaknesses of the retrospective cohort studies in the selection of the cohort members, exposure ascertainment, and completeness of the follow-up were avoided. However, the present study population was relatively small. Therefore we wanted to examine cancer

primarily at those sites for which hypotheses are available from prior studies.

Subjects and methods

Ascertainment of the cohort

The study was based on the follow-up for cancer among workers biologically monitored at the Finnish Institute of Occupational Health (FIOH) for occupational exposure to any of three aromatic hydrocarbons [1, 21, 33]. The measurements ($n = 10,336$; see Table 1) recorded in the data base were the mandelic acid concentration in the urine (U-ManA) for exposure to styrene (5,549 postshift samples performed during the years 1973–1983), the methylhippuric acid concentration in the urine (U-MetHippA) for exposure to xylene (1,855 postshift samples during the years 1976–1983), and the concentration of toluene in the blood (B-Tol; 2,932 samples during the years 1978–1983). The recording of the monitoring data from laboratory logbooks and other documents into a computer was done during the years 1983 and 1984. The personal identification code could be traced from laboratory documents, from population registers, and from employers for 10,237 samples (99.0%) comprising 5,301 workers. The numbers of the untraced samples were 6 samples in the toluene data (0.2%), 9 samples in the xylene data (0.5%), and 84 samples in the styrene data (1.5%). Information on the detailed methods of the analyses, their validation, and quality control has been published elsewhere [11, 26, 27].

There were 3,922 men and 1,379 women in the study. The mean age at the time of the first personal measurement was 31.4 years for the men and 37.7 years for the women. For styrene measurements the employees were on average about 2 years younger than for measurements of the other two solvents.

Concentrations

The overall median U-ManA value was 2.3 mmol/l (range 0–47 mmol/l) through the monitored period. The levels were higher among women (median 4.8 mmol/l) than among men (median 1.8 mmol/l), possibly because of selection in the monitored work tasks [1]. No overall temporal decrease was seen in the U-ManA concentrations measured for 1973–1983. Since then, the concentrations have been roughly halved at the Finnish workplaces [26]. On average there were 2.1 U-ManA samples per individual worker. Only one sample was analyzed for 56.7% of the workers, and three samples or more were analyzed for 25.8% of the workers. As the half-life of mandelic acid in the urine is short, about a couple of hours, the number of repeated samples was generally too small for reliable distinguishment of the variability in the yearly or lifetime solvent burden between individuals [3, 9, 10]. The job monitored was usually lamination of reinforced plastics products.

The average styrene concentrations measured during the lamination of reinforced plastics products had been around 220 ppm in the 1960s, according to the registry of hygienic measurements of the FIOH. The average 8-h daily exposure of laminators had been 150–200 ppm in the 1950s and 1960s [17]. In the 1970s the 8-h daily exposure decreased to < 100 ppm [16, 28]. The Finnish standard for occupational exposure to styrene was lowered from 100 to 50 ppm in 1981 and was further lowered to 20 ppm in 1987. The 8-h average of 20 ppm corresponds roughly to 2.9 mmol U-ManA/l [27].

The median B-Tol concentration was 0.2 μmol/l among both genders (range 0–18.4 μmol/l), and for xylene the median U-MetHippA concentration was below the detection limit (< 1 mmol/l; range 0–14.0 mmol/l). Toluene and xylene were typically used in mixtures, e.g., in paints, lacquers, thinners, and glues. Other main components in these mixtures, along with toluene or xylene, included mineral spirits (mainly aliphatic hydrocarbons, boiling range 140–200 °C, aromatic hydrocarbon concentration less than 20%), butanol, *n*-hexane, propanol, acetone, butyl acetate, and glycol compounds [29]. Thus, biologic monitoring took into account only a compartment of the total solvents burden in these uses. Besides its use in mixtures, xylene was occasionally used as a laboratory solvent [29]. Only a very small proportion of the workers was exposed permanently to very high levels of toluene or xylene, e.g., to toluene in the rotogravure printing shops or to toluene or xylene in paint manufacture or in painting. For both toluene and xylene the Finnish hygienic standard has been 100 ppm throughout the study period.

Follow-up for cancer

The follow-up for cancer incidence was done through the files of the Finnish Cancer Registry between 1973 and 1992. The follow-up was started on January 1, 1973, or at the date of the first personal measurement, whichever was later. The calculation of person-years ended at emigration, at death, or on December 31, 1992, whichever occurred first. There was no loss to follow-up among those whose personal identifier had been traced.

We calculated the indirectly standardized incidence ratios (SIR) with regard to gender, 5-year age group, and calendar-period-specific rates in the Finnish general population. For all SIRs, 95% confidence intervals (95% Cls) were computed on the assumption that the number of observed cases followed a Poisson distribution.

The follow-up comprised 49,112 person-years at risk for the men and 17,464 person-years for the women. The length of follow-up was 12.6 years on average. Of the person-years, 30% were within the age groups above 44 years and 22% were in the follow-up category of ≥ 10 years after entry. About 34,300 person years were accrued for styrene; 22,200, for toluene; and 15,700, for xylene (Table 1). Because 8.8% of the employees had been monitored for

Table 1 Aromatic hydrocarbons monitored, years of monitoring, number of samples, and number of persons and person-years at risk by solvent type. (*U-ManA* Mandelic acid in the urine – postshift samples, *B-Tol* toluene in the blood, *U-MetHippA* methylhippuric acid in the urine – postshift samples)

Solvent category	Measurement	Years of monitoring	Number of samples collected	Number of samples with the personal identifier traced	Number of persons traced[a]	Person-years at risk[a,b]
Styrene	U-ManA	1973–1983	5,549	5,465	2,580	34,288
Toluene	B-Tol	1978–1983	2,932	2,926	1,856	22,169
Xylene	U-MetHippA	1976–1983	1,855	1,846	1,358	15,676
Total cohort	–	1973–1983	10,336	10,237	5,301	66,576

[a] The same person may have measurements of various solvent types. Includes only those persons whose identifier had been completely traced

[b] Follow-up of cancer incidence initiated at the first personal measurement and ended at emigration, death, or on December 31, 1992, whichever was earlier

Table 2 Observed and expected numbers of cancer cases and SIRs in 1973–1992 for exposure to aromatic hydrocarbons, both genders combined, by years since the first measurement[a] (*Obs* observed, *Exp* expected)

Primary site (ICD-7)	Years since the first measurement											
	0–9				10+				Whole follow-up			
	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI
All sites (140–204)	**66**	**87.6**	**0.75**	**0.58–0.96**	45	42.6	1.06	0.77–1.41	111	130.3	0.85	0.70–1.01
Stomach (151)	6	5.2	1.16	0.42–2.52	3	2.5	1.22	0.25–3.55	9	7.7	1.18	0.54–2.23
Colon (153)	2	3.9	0.52	0.06–1.87	0	2.1	0.00	0.00–1.75	2	6.0	0.34	0.04–1.21
Rectum (154)	4	2.7	1.47	0.40–3.75	4	1.5	2.65	0.72–6.77	8	4.3	1.88	0.81–3.71
Liver (155.0)	0	0.9	0.00	0.00–4.34	1	0.5	2.02	0.05–11.2	1	1.4	0.74	0.02–4.13
Pancreas (157)	1	2.5	0.40	0.01–2.20	4	1.5	2.77	0.75–7.08	5	4.0	1.26	0.41–2.93
Lung, bronchus (162.0–1)	**5**	**12.0**	**0.42**	**0.13–0.97**	9	6.2	1.45	0.66–2.75	14	18.2	0.77	0.42–1.28
Breast (170)	8	13.1	0.61	0.26–1.21	7	5.9	1.18	0.47–2.42	15	19.0	0.79	0.44–1.30
Female genital organs (171–176)	9	6.3	1.42	0.65–2.69	2	0.8	0.75	0.09–2.69	11	9.0	1.22	0.61–2.18
Cervix uteri (171)	2	0.9	2.20	0.27–7.94	0	0.3	0.00	0.00–13.1	2	1.2	1.69	0.20–6.09
Prostate (177)	1	3.0	0.33	0.01–1.83	2	2.4	0.84	0.10–3.02	3	5.4	0.55	0.11–1.61
Kidney (180)	5	3.33	1.50	0.49–3.50	0	1.9	0.00	0.00–1.97	5	5.2	0.96	0.31–2.24
Bladder, ureter, urethra (181)	3	2.8	1.09	0.23–3.19	1	1.6	0.62	0.02–3.44	4	4.4	0.92	0.25–2.34
Nervous system (193)	6	5.5	1.08	0.40–2.36	**6**	**2.2**	**2.80**	**1.03–6.08**	12	7.7	1.56	0.81–2.72
Lymphohematopoietic tissue (200–204)	5	7.5	0.67	0.22–1.56	2	3.1	0.64	0.08–2.31	7	10.6	0.66	0.27–1.36
Non-Hodgkin lymphoma (200, 202)	1	2.6	0.40	0.01–2.17	1	1.3	0.79	0.02–4.38	2	3.8	0.52	0.06–1.88
Hodgkin's lymphoma (201)	3	1.6	1.90	0.39–5.55	0	0.4	0.00	0.00–8.68	3	2.0	1.49	0.31–4.36
Multiple myeloma (203)	1	0.9	1.09	0.03–6.06	0	0.5	0.00	0.00–7.16	1	1.4	0.70	0.02–3.88
Leukemia (204)	0	2.4	0.00	0.00–2.54	1	0.9	1.07	0.03–5.97	1	3.3	0.30	0.01–1.67

[a] Statistically significant results are indicated in boldface type

more than one solvent, mainly for both toluene and xylene, the follow-up time as well as the number of persons in the whole cohort were slightly lower than the sums recorded for the individual solvents.

Results

In all, 111 incident cancer cases were observed and 130.3 were expected for the three aromatic hydrocarbons combined; the SIR of overall cancer was 0.85 (95% CI 0.70–1.01; Table 2). The risks for overall and lung cancers were decreased in the study base for the shorter follow-up period (SIR 0.75, 66 cases of any cancer, and SIR 0.42, 5 cases of lung cancer for the follow-up group <10 years from entry). Corresponding risk estimates were close to unity after 10 years from entry (SIRs 1.06 and 1.45 for the prolonged follow-up group, respectively). There was an increased risk for nervous system tumors for the combined cohort in the prolonged follow-up group as based on six cases.

There was no clear difference in the SIRs of overall cancer observed between men and women (SIR 0.82, 63 cases among the men, and SIR 0.90, 48 cases among the women). The rectal cancer incidence was slightly higher among the women, as was the incidence of pancreatic and nervous system tumors among the men (data not shown).

For styrene we found a pattern in the incidence of overall and lung cancers very similar to that observed within the whole cohort. The only significant increase for exposure to styrene was seen in the incidence of rectal cancer (Table 3). There were nonsignificant increases in the incidence of pancreatic and nervous system tumors for the follow-up of >10 years. The incidence of lymphohematopoietic malignancies was not in excess. There were two cases of Hodgkin's lymphomas, whereas the expected number was 1.06. There was no clear difference in the overall incidence pattern between women and men for exposure to styrene (data not shown).

We grouped the styrene data according to the lifetime mean U-ManA results into three groups: <1 mmol/l, 1–2.9 mmol/l, and 3.0 mmol/l or more. We did not detect any clear difference in the risk estimates of any of the primary sites for the U-ManA groups. SIRs of overall cancer incidence were 1.03 (21 cases observed), 0.79 (9 cases), and 0.77 (18 cases) for these three U-ManA groups. The site-specific SIRs in the lowest group (<1 mmol/l) were 4.30 (3 cases) in the rectum, 3.55 (3 cases) in the pancreas, 0.62 (2 cases) in the lung, and 1.59 (2 cases) in the nervous system, and those in the highest group (≥ 3.0 mmol/l) were 2.76 (2 cases), 0.00 (0.8 expected), 0.35 (1 case), and 2.07 (3 cases), respectively.

No clear increase was seen in the risk estimates specific for toluene or xylene (Table 4). Very small numbers of cases were observed in the primary cancer sites for these solvents. Three cases of lung cancer were observed for the prolonged follow-up period for toluene (SIR 1.62), as were two cases for xylene (SIR 1.83). Among the lymphohematopoietic malignancies were one case of

Table 3 Observed and expected numbers of cancer cases and SIRS in 1973–1992 for exposure to styrene, both genders combined, by years since the first measurement[a] (*Obs* observed, *Exp*, expected)

Primary site (ICD-7)	Years since the first measurement											
	0–9				10+				Whole follow-up			
	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI
All sites (140–204)	25	35.4	0.71	0.46–1.04	23	24.4	0.94	0.60–1.41	48	59.8	0.80	0.59–1.06
Stomach (151)	3	2.2	1.40	0.29–4.08	2	1.4	1.40	0.17–5.06	5	3.6	1.40	0.45–3.26
Colon (153)	1	1.5	0.65	0.02–3.62	0	1.2	0.00	0.00–3.07	1	2.7	0.36	0.01–2.03
Rectum (154)	3	1.1	2.80	0.58–8.19	3	0.9	3.49	0.72–10.2	**6**	**1.9**	**3.11**	**1.14–6.77**
Liver (155.0)	0	0.3	0.00	0.00–11.2	1	0.3	3.54	0.09–19.7	1	0.6	1.63	0.04–9.08
Pancreas (157)	0	1.0	0.00	0.00–3.76	3	0.8	3.64	0.75–10.6	3	1.8	1.66	0.34–4.85
Lung, bronchus (162.0–1)	1	4.8	0.21	0.01–1.16	4	3.6	1.11	0.30–2.84	5	8.4	0.59	0.19–1.38
Breast (170)	3	4.8	0.62	0.31–1.81	2	3.1	0.63	0.08–2.28	5	8.0	0.62	0.20–1.45
Female genital organs (171–176)	5	2.4	2.08	0.68–4.86	0	1.4	0.00	0.00–2.62	5	3.8	1.31	0.43–3.06
Kidney (180)	1	1.3	0.76	0.02–4.25	0	1.1	0.00	0.00–3.40	1	2.4	0.42	0.01–2.32
Nervous system (193)	2	2.4	0.82	0.10–2.96	4	1.3	3.11	0.85–7.95	6	3.7	1.61	0.59–3.50
Lymphohematopoietic tissue (200–204)	2	3.3	0.61	0.07–2.20	0	1.9	0.00	0.00–1.97	2	5.2	0.39	0.05–1.40
Hodgkin's lymphoma (201)	2	0.8	2.53	0.31–9.15	0	0.3	0.00	0.00–13.7	2	1.1	1.89	0.23–6.84

[a] Statistically significant results are indicated in boldface type

Table 4 Observed and expected numbers of cancer cases and SIRs in 1976–1992 for exposure to toluene or xylene, both genders combined, by years since the first measurement[a] (*Obs* observed, *Exp* expected)

Primary site (ICD-7)	Years since the first measurement										
	0–9				10+				Whole follow-up		
	Obs	Exp	STR	95% CI	Obs	Exp	STR	95% CI	Obs	Exp	STR	95% CI
Toluene:												
All sites (140–204)	32	37.0	0.86	0.59–1.22	13	13.0	1.00	0.53–1.70	45	50.1	0.90	0.66–1.20
Gastrointestinal (150–154)	5	5.3	0.94	0.30–2.19	2	2.0	1.00	0.12–3.59	7	7.4	0.95	0.38–1.96
Lung, bronchus (162.0–1)	4	5.1	0.79	0.22–2.02	3	1.9	1.62	0.33–4.73	7	6.9	1.01	0.41–2.08
Nervous system (193)	2	2.2	0.93	0.11–3.34	1	0.6	1.66	0.04–9.24	3	2.8	1.09	0.22–3.18
Lymphohematopoietic tissue (200–204)	3	2.9	1.03	0.21–3.01	0	0.9	0.00	0.00–4.05	3	3.8	0.78	0.16–2.28
Xylene:												
All sites (140–204)	**13**	**24.1**	**0.54**	**0.29–0.92**	11	7.4	1.48	0.74–2.64	24	31.5	0.76	0.49–1.13
Gastrointestinal (150–154)	2	3.5	0.58	0.07–2.09	0	1.1	0.00	0.00–3.30	2	4.6	0.44	0.05–1.58
Lung, bronchus (162.0–1)	1	3.3	0.30	0.01–1.67	2	1.1	1.83	0.22–6.59	3	4.4	0.68	0.14–1.98
Nervous system (193)	2	1.5	1.34	0.16–4.85	1	0.4	2.76	0.07–15.4	3	1.9	1.62	0.33–4.72
Lymphohematopoietic tissue (200–204)	1	2.0	0.50	0.01–2.79	2	0.5	3.77	0.46–13.6	3	2.5	1.18	0.24–3.45

[a] Statistically significant results are indicated in boldface type

non-Hodgkin's lymphoma (SIR 0.71), one case of Hodgkin's disease (SIR 1.52), and one case of multiple myeloma (SIR 1.76) for toluene as well as two cases of non-Hodgkin's lymphoma (SIR 2.14), and one case of leukemia (SIR 1.28) for xylene.

Discussion

In general there appeared to be no overall excess in the carcinogenic risk of solvent workers in the present study. For the aromatic hydrocarbons combined, the only statistically significant increase was seen in the risk for nervous system tumors – also including the benign ones – at 10 years after the first personal measurement. Even though there is suggestive support for associations of hydrocarbons with these tumors from some previous studies among solvent workers, no firm conclusions can be drawn. The evidence on brain tumors among solvent workers is also limited because many of the studies have not reported the risk of this primary site in detail.

On the other hand, the decrease in the overall and lung cancer risks for a short follow-up and latency period probably reflects some biases in the comparison design, e.g., due to selection of healthy workers in the monitored work. Any large underestimation due to deficits in the cohort tracing and follow-up in this study is unlikely. The personal identity was traced for 99% of the samples and for practically all of the samples for toluene and xylene.

To check the possibility of errors raising from social-class-related factors such as smoking, alcohol, or nutrition, we computed relative risk estimates of some selected cancers for the styrene-exposed population with reference to a parallel cohort on monitoring of blood lead levels in Finland. The comparison was made with workers who had been monitored for blood lead during 1973–1983 and whose blood lead levels had never clearly exceeded those of the general population (< 0.8 μmol/l, see Anttila et al. [2]). This comparison was done in a case-control design for cancers of the colon, rectum, pancreas, nervous system, and lymphohematopoietic system using conditional logistic regression matched for gender, birth year, and age at diagnosis. The comparison did not reveal any material change in the risk estimates obtained in the present cohort analyses. These additional analyses suggest that social-class-related factors are not an obvious explanation for the increased incidence of certain cancer types among the solvent workers.

In the present study a statistically significant increase was seen in rectal cancer among the styrene-exposed workers. A previous study has reported a similar increase for substantial exposure to styrene (OR 4.1, 90% CI 1.4–12, 5 cases) [30]. The previous cohort studies on styrene [17, 20, 24, 37] have not reported in detail the risk of this primary site. We cannot rule out, however, the possibility that the excess in our data was an artefact related to multiple comparisons or correlations with some unknown occupational factors.

With regard to styrene, there is some consistency in the risk for pancreatic cancer demonstrated by previous studies on comparably heavy exposure, mainly among laminators. The internal comparison within the large European multicentric study suggested a dose-response relationship between heavy exposure to styrene and the risk for pancreatic cancer [17]. The pooled summary RR [13] for a cumulative exposure of ≥ 100 ppm × years was 1.93 (95% CI 1.04–3.59) as based on 21 exposed cases. In the large United States study there were five cases involving a cumulative exposure of ≥100 ppm × years, respectively (SMR 1.06) [37]. The smaller study in the United States did not report the site-specific SMR for the pancreas [24]. The pooled RR, extracted from the two large studies and combined with the present cohort, shows about a 60% excess risk for pancreatic cancer (RR 1.64, 95% CI 1.00–2.67, 29 cases) following heavy exposure to styrene. Additional support for an association has been obtained in a Danish study in the reinforced plastics industry (RR = 3.4, 8 cases, among those with a high probability of exposure to styrene and a duration of employment of ≥ 1 year) [20]. There is some overlap between the IARC multicentric investigation and the extension of the Danish study. No increase in the pancreatic cancer risk has been reported within other industries using styrene, where the exposure levels are lower than in the lamination industry [15].

Concerning etiology, only little is known about the development of malignancies in the pancreas. The observation that pancreatitis may be linked with pancreatic cancer [12] is of potential importance for styrene. However, pancreatitis is a rare disease, and there is no evidence of excess mortality due to pancreatitis among highly-exposed laminators. In the Danish study there was an almost 2-fold excess in mortality due to chronic pancreatitis among reinforced plastics workers; the excess was confined to short-term workers with a low probability of exposure and was thus probably not attributable to styrene [20].

We observed a slightly increased risk of nervous system tumors for styrene. A 2- to 3-fold increase in the incidence of benign tumors of the nervous system, particularly meningiomas, has been reported in an animal experiment [23]. Only one of the previous cohort studies among styrene workers has used incidence records in the follow-up [18, 20] that also recognize benign tumors. There appeared to be no excess within the reinforced plastics industry as a totality.

The present study did not provide much new information on the potential risks for lung cancer or lymphohematopoietic malignancies due to styrene. There was no support for an increased risk for breast cancer, which was similar to the results of previous cohort studies among female workers [8, 17, 18, 24, 37]. An association has been proposed in a study using occupational titles on death certificates as the source of exposure information [6]. Excess cancers of the female genital organs have appeared in some of the previous cohorts following styrene exposure [8, 17, 24, 37]. Because the excess is based on very small numbers, no clear conclusion on the role of occupational factors can be drawn.

Concerning toluene and xylene, there appeared to be no support for carcinogenic effects in our study. Marginal excess found in the risk for lung cancer and for lymphohematopoietic malignancies warrant further follow-up. It is very difficult to estimate reliably the overall evidence for these two solvents because in most studies they have been used in mixtures. In both of the cohorts with considerably heavy exposure to toluene, benzene may also have been used during earlier decades [32, 35]. One cannot completely rule out the potential effects of benzene on the results.

In conclusion, the present study covered three aromatic solvents that are related chemically and toxicologically. Of these, styrene was usually present alone, whereas toluene and xylene often caused a combined exposure with other solvents. The study is not supportive of a large increase in the carcinogenic risks for these solvents. Smaller risks cannot be ruled out for some specific primary sites, however. Exposure to any of these hydrocarbons increased the risk for rectal cancer and for nervous system tumors. There was an excess risk for pancreatic cancer following exposure to styrene, which was consistent with the results of previous studies among highly exposed employees. No evidence of a risk for lung or hematopoietic cancers was seen for any of the solvents, yet the statistical power for the specific solvents is low and the follow-up period is short. A future update will reassess these associations. More studies are warranted on solvents, with detailed information on lifetime exposures and habits being collected whenever possible.

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