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Update of the mortality study of workers exposed to polychlorinated biphenyls (PCBs) in two Italian capacitor manufacturing plants

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PCB; cohort study; mortality; cancer

Parole chiave
PCB; studio coorte; mortalità; tumori

Summary
Background: *PCB carcinogenicity to humans is still controversial. Cohort mortality studies in PCB-exposed workers reported elevated risks for the following causes of death: liver, stomach, digestive, brain, prostate cancers and non-Hodgkin lymphoma.* **Objectives:** *The purpose of this study was to update as of December 2006 the mortality experience of two Italian cohorts of workers employed in the manufacture of capacitors impregnated with PCBs.* **Methods:** *Age-gender-and calendar period adjusted Standardized Mortality Ratios (SMRs) and 95% Confidence Intervals (CI) were calculated using regional rates. Analyses by duration of employment and time since first employment were performed.* **Results:** *Vital status was ascertained for 98.9% of the study subjects. Mortality from biliary tract cancer among males (SMR 3.91; 95%CI 1.47-10.41), digestive cancer "not otherwise specified" in the whole cohort (SMR 2.54; 95%CI 1.21-5.34), and brain cancer in Plant 1 (SMR 2.13; 95%CI 1.02-4.48), were significantly increased. Increased risks were also observed for Hodgkin's and non-Hodgkin lymphoma. No linear associations between mortality and duration of employment or latency were observed for these cancers. Mortality from stomach cancer did not differ from expectation in the whole cohort, however an increasing risk with increasing duration of employment was detected (p for trend=0.02).* **Conclusions:** *The current update suggests possibly increased cancer risks in PCB-exposed workers, affecting in particular the digestive system, brain, and lymphohemopoietic tissue. However the limited sample size, the lack of clear trends with duration of employment or with latency period, preclude to derive definite conclusions about PCB exposure and the increased cancer risks.*

Riassunto
«Aggiornamento dello studio di mortalità in lavoratori esposti a policlorobifenili (PCB) in due aziende italiane produttrici di trasformatori». **Introduzione:** *La cancerogenicità dei policlorobifenili (PCB) nell'uomo è tuttora controversa. Gli studi in coorti lavorative hanno riportato rischi aumentati per tumori del fegato, dello stomaco,*

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dell'apparato digerente, dell'encefalo, della prostata e linfomi non-Hodgkin. **Obiettivi:** *Scopo del presente studio è l'estensione del follow-up al Dicembre 2006 di una coorte di lavoratori in due aziende produttrici di trasformatori impregnati con PCB in Lombardia.* **Metodi:** *Sono stati calcolati i Rapporti Standardizzati di Mortalità (SMR) e gli Intervalli di confidenza al 95% (IC) utilizzando come riferimento i tassi della regione Lombardia.* **Risultati:** *Lo stato in vita è stato accertato per il 98,9% della coorte. Sono stati osservati incrementi significativi della mortalità per tumori del tratto biliare nei maschi (4 casi, SMR 3,91; IC 95% 1,47-10,41), del digerente "non altrimenti specificati" nell'intera coorte (7 casi, SMR 2,54; IC 95% 1,21-5,34), e dell'encefalo nella Ditta 1 (7 casi, SMR 2,13; IC 95% 1,02-4,48). Anche la mortalità per malattia di Hodgkin (4 casi) e linfomi non-Hodgkin (8 casi) è risultata aumentata. Non sono emersi chiari andamenti della mortalità per durata dell'attività lavorativa o per latenza. Solo il tumore dello stomaco ha mostrato un incremento della mortalità all'aumentare della durata della attività lavorativa (p per il trend=0,02).* **Conclusioni:** *Lo studio ha evidenziato incrementi di rischio a carico dei tumori dell'apparato digerente, dell'encefalo e del tessuto linfoemopioietico. L'associazione tra esposizione a PCB e tali rischi rimane incerta per l'assenza di andamenti rilevanti con la durata dell'attività lavorativa e la latenza e il piccolo numero di casi.*

Introduction

Polychlorinated biphenyls (PCBs) were introduced in the industrial production at the beginning of the 1930s and were widely used as dielectric fluids in capacitor and transformer manufacturing plants. In 1980 their use and production were banned in Italy. Some properties of PCBs, such as high environmental persistence, and tendency to accumulate in lipids contribute to their ubiquity in environmental media and have induced concern for their toxic effects after prolonged exposure (6). Whether exposure to PCBs may increase cancer risk in humans is still controversial. In 1987 the International Agency for Research on Cancer (IARC) (8) declared that there was sufficient evidence of PCB carcinogenicity in animals and limited in humans. Recently, the dioxin-like PCB 126 has been classified as a human carcinogen (9) based on sufficient evidence in experimental animals and strong mechanistic arguments that support receptor-mediated effects related to activation of cell replication, alterations in apoptosis and increases in oxidative stress. Studies of PCB-exposed workers have shown increased risks for several cancer sites such as liver and biliary tract (13, 16, 17), prostate (4, 17), brain (19), stomach (13, 17), intestinal cancers (13, 21) and non-Hodgkin lymphoma (10), but study limitations (e.g. small sample size, co-exposures, lack of adjustment for confounders) and the absence of clear exposure-response trend prevented any firm conclusion (2, 7). The most recent update of mortality studies in subjects exposed to PCBs through the ingestion of contaminated oils, showed increased risks for all-type, lung and liver cancers in Yusho patients (15) and stomach and lympho-hematopoietic neoplasms in Yu-Cheng patients (11).

The purpose of this study was to combine the experience of two Italian cohorts of workers employed in the manufacture of capacitors impregnated with PCBs and to update their mortality follow-up to December 2006 in order to examine the possible carcinogenic effects of their PCB exposure allowing for a longer observation period and a larger sample size. The mortality of workers in Plant 1 had been examined for the period 1946-1982 (1) and subsequently up to 1991 (20); whereas workers in Plant 2 had been followed up to 2002 (3). The interpretation of the results was limited by the small number of events, however suggestive increased risks for lymphatic and hemopoietic neoplasms (Plant 1) and for gastrointestinal cancers (both Plants) emerged.

Material and methods

The study population included all workers who had worked for at least 1 week between 1946 and

1978 in Plant 1 (544 males and 1,551 females) and all workers employed between 1950 and 1982 in Plant 2 (373 males and 97 females).

In both plants the use of PCBs was banned in 1980 and replaced with other dielectric fluids.

In Plant 1, mixtures containing 54% chlorine (Aroclor 1254 and Pyralene 1476) were used until 1965 and were later progressively replaced by mixtures containing 42% chlorine (Pyralene 3010, 3011) until 1970 when only the latter were used. A few environmental measurements were done in 1954 when 3 cases of chloracne were reported among autoclave operators and in 1977 when 4 cases of chloracne were diagnosed in workers engaged in impregnating capacitors with PCBs. In 1954 three environmental measures reported values of Aroclor 1254 of 5200, 6400 and 6800 $\mu g/m^3$ (18), whereas the airborne concentrations of Pyralene 3010 in 1977 ranged between 48 and 275 $\mu g/m^3$ (14). PCBs on the workplace surfaces and on the workers' hands were also measured in 1977 and 1982 (before and after PCB banning) and showed a significant decrease (maximum values on workplace surfaces: 159 $\mu g/m^3$ in 1977 and 6.3 $\mu g/m^3$ in 1982; workers' hand values in the corresponding years: 9.2 and 1.5 $\mu g/m^3$ respectively). PCBs were also measured in the blood of 37 workers: the mean concentration of 54% chlorine PCBs were 282.8 ppb (SD=163.4) in 1977 and 202.8 ppb (SD=111.7) in 1982; the mean concentration of 42% chlorine PCBs showed a greater decline (142.8 ppb in 1977 and 42.9 ppb in 1982).

Plant 2 has been producing electrical capacitors since 1950. In 1988 the production was replaced by maintenance and repair activities. Until 1980, they used as dielectric fluid a mixture of PCBs (Apirolio) which later was replaced by mineral oils containing small quantities of PCBs (< 100 ppm). No environmental measurements were available.

Vital status of all workers was updated through December, 2006 and was ascertained through the vital statistic offices of the towns of subjects' last residence. Death certificates were obtained and coded according to the International Classification of Disease (IX version).

Workers contributed to person-years from the beginning of employment at the plant until exit from the study (because of death, or loss to follow-up,) or until the end of the study period. We calculated cause-specific Standardized Mortality Ratios (SMR) as the ratio of observed and expected deaths using as reference the mortality rates specific by age, gender, and calendar years of the Lombardy region (where both plants are located). Approximate 95% confidence intervals (CI) were calculated using the formula for Var[ln(SMR)]= 1/O, where O is the number of observed cases. Analyses by plant, gender, duration of employment and time since first employment were performed. Tests for trend were calculated by treating the variable as ordinal (5). All statistical analyses were carried out using Stata 12.

Results

The main characteristics of the cohort are presented in table 1. A greater proportion of subjects in Plant 1 was hired at young ages (84.2% <25 years) and in the outer years (87.8% before 1969). Also the distribution by duration of employment differed between the two plants with a larger number of subjects with duration < 10 years in Plant 1. The mean attained age at the end of the follow-up was 61.8 years (SD=8.0) in Plant 1 and 64.0 years (SD=12.0) in Plant 2.

Vital status ascertainment was almost 99% successful. We found 418 deaths and obtained death certificates for 408 (97.6%). The proportion of lost to follow-up was very low in both plants.

In table 2 SMR and 95% CI are reported for the whole cohort and stratified by plant and gender. In the whole cohort mortality from all causes and all cancers did not differ from expectations. Cancers of the biliary tract showed a 70% increased mortality: all cases occurred among males which showed a four-fold increased risk (4 deaths, SMR 3.91, 95% CI 1.47-10.41). Mortality from digestive cancers not otherwise specified (NOS) was clearly increased (SMR 2.54; 95% CI 1.21-5.34) and the increase was consistent by plant and gender. Other increased risks were found for prostate (7 deaths, SMR 1.66; 95% CI 0.79-3.49) and brain cancer (8 deaths, SMR 1.82; 95% CI 0.91-3.63). Seven out

Table 1 - Vital status and main characteristics of PCB-exposed workers stratified by plant

	Plant 1		Plant 2		Total	
	Nr	%	Nr	%	Nr	%
Males	544	26.0	373	79.4	917	35.8
Females	1,551	74.0	97	20.6	1,648	64.2
Total	2,095	470	2,565			
Age at first employment						
< 25	1,764	84.2	259	55.1	2,023	78.9
25-34	269	12.8	117	24.9	386	15.0
35-44	51	2.4	64	13.6	115	4.5
45 +	11	0.5	34	6.4	41	1.6
Year of first employment						
< 1960	541	25.8	169	23.3	710	25.2
1960-69	1,298	62.0	158	21.8	1,456	51.6
1970-79	256	12.2	375	51.7	631	22.4
1980 +	-		24	3.3	24	0.9
Duration of employment (years)						
< 10	1,628	77.7	201	43.2	1,829	71.5
10-20	397	19.0	137	29.5	534	20.9
20 +	70	3.3	132	28.4	202	7.9
Time since first employment (years)						
< 20	54	2.6	37	8.0	91	3.6
20-40	672	32.1	231	49.7	903	35.3
40 +	1,369	65.4	202	43.4	1,571	61.4
Vital status as of 31/12/2006						
Alive	1,825	87.1	294	62.6	2,119	82.6
Dead (cause of death known)	237	11.3	171	36.4	408	15.9
Dead (cause of death unknwon)	8	0.4	2	0.4	10	0.4
Lost to follow-up	25	1.2	3	0.6	28	1.1
Total person-years	86,407		16,851		103,258	

of 8 brain deaths occurred in Plant 1 yielding a two-fold increased risk (SMR 2.13; 95%CI 1.02-4.48). Mortality from lymphomas was increased in the whole cohort (12 deaths; SMR 1.89; 95%CI 1.07-3.32); 4 deaths from Hodgkin's disease (HD) were observed in Plant 1 yielding a higher than three-fold increased risk that concerned primarily the women. A 65% increased mortality from non-Hodgkin lymphoma (NHL) was observed in the whole cohort, and consistently across cohorts and genders.

For most of the examined non-neoplastic causes (circulatory diseases, respiratory diseases and digestive diseases), mortality was lower than expected. The number of deaths from liver cirrhosis did not differ from the expectation.

Results of analysis by duration of employment and latency for selected outcomes are reported in table 3 and 4 respectively. Stomach cancer showed an increasing risk with increasing duration of employment (p for trend=0.02). Mortality from "NOS digestive cancer" was steadily increased across all

Table 2 - Mortality (1946-2006) from selected cancer causes stratified by plant and gender

Cause of death (ICD-9 code)	Total			Plant 1			Plant 2			Males			Females		
	OBS	SMR	95% CI	OBS	SMR	95% CI	OBS	SMR	95% CI	OBS	SMR	95% CI	OBS	SMR	95% CI
All causes (001-999)	418	0.98	0.89-1.08	245	0.93	0.82-1.05	173	1.06	0.91-1.23	285	1.00	0.89-1.13	133	0.93	0.79-1.10
All cancers (140-208)	183	0.98	0.85-1.13	112	0.91	0.75-1.09	71	1.13	0.89-1.42	122	1.09	0.91-1.30	61	0.82	0.63-1.05
Digestive (150-159)	62	0.99	0.77-1.27	37	0.93	0.67-1.28	25	1.10	0.74-1.63	47	1.16	0.87-1.54	15	0.68	0.41-1.13
Esophage (150)	3	0.79	0.25-2.45	2	0.93	0.23-3.73	1	0.60	0.08-4.28	2	0.62	0.16-2.48	1	1.72	0.24-12.21
Stomach (151)	16	1.03	0.63-1.67	8	0.87	0.43-1.73	8	1.26	0.62-2.51	11	1.01	0.56-1.83	5	1.06	0.44-2.54
Colon (153)	13	1.17	0.68-2.02	7	0.93	0.44-1.95	6	1.69	0.76-3.76	11	1.78	0.99-3.22	2	0.41	0.10-1.62
Rectum (154)	3	0.64	0.21-1.98	1	0.32	0.05-2.30	2	1.25	0.31-5.00	2	0.72	0.18-2.89	1	0.52	0.07-3.70
Liver (155)	7	0.57	0.27-1.20	5	0.67	0.28-1.62	2	0.41	0.10-1.65	5	0.54	0.22-1.30	2	0.67	0.17-2.66
Biliary tract (156)	4	1.70	0.64-4.54	2	1.16	0.29-4.66	2	3.16	0.79-12.64	4	3.91	1.47-10.41			
Pancreas (157)	9	1.09	0.57-2.10	8	1.43	0.72-2.86	1	0.38	0.05-2.67	8	1.63	0.82-3.27	1	0.30	0.04-2.12
Digestive NOS (159)	7	2.54	1.21-5.34	4	2.18	0.82-5.80	3	3.28	1.06-10.17	4	2.60	0.98-6.92	3	2.47	0.80-7.67
Respiratory (160-165)	43	0.89	0.66-1.21	21	0.78	0.51-1.20	22	1.04	0.68-1.57	39	0.97	0.71-1.32	4	0.52	0.19-1.38
Larynx (161)	4	1.06	0.40-2.84				4	2.03	0.76-5.42	4	1.11	0.42-2.96			
Lung (162)	39	0.92	0.67-1.26	21	0.89	0.58-1.36	18	0.97	0.61-1.54	35	0.99	0.71-1.37	4	0.59	0.22-1.57
Melanoma (172)	1	0.50	0.07-3.53				1	2.08	0.29-14.74	1	0.99	0.14-7.02			
Skin (173)	2	0.86	0.21-3.42				2	3.24	0.81-12.96	2	1.61	0.40-6.45			
Breast (174)	16	0.79	0.48-1.28	13	0.69	0.40-1.19	3	1.93	0.62-6.00				16	0.79	0.48-1.29
Genito-urinary tract (179-189)	23	1.10	0.73-1.66	13	0.92	0.54-1.59	10	1.48	0.80-2.75	14	1.32	0.78-2.23	9	0.88	0.46-1.69
Prostate (185)	7	1.66	0.79-3.49	3	1.77	0.57-5.50	4	1.59	0.60-4.24	7	1.66	0.79-3.49			
Bladder (188)	6	1.57	0.70-3.49	3	1.63	0.53-5.06	3	1.51	0.49-4.67	6	1.77	0.80-3.94			
Kidney (189)	2	0.53	0.13-2.12				2	1.46	0.36-5.83	1	0.38	0.05-2.71	1	0.87	0.12-6.21
Brain (191)	8	1.82	0.91-3.63	7	2.13	1.02-4.48	1	0.89	0.13-6.31	4	1.82	0.68-4.84	4	1.82	0.68-4.84
Lympho-hemopoietic tissue (200-208)	18	1.28	0.80-2.02	14	1.40	0.83-2.36	4	0.98	0.37-2.60	9	1.22	0.63-2.34	9	1.34	0.70-2.57
Lymphomas (200-202)	12	1.89	1.07-3.32	9	1.97	1.02-3.79	3	1.66	0.54-5.16	5	1.49	0.62-3.58	7	2.32	1.11-4.88
Hodgkin's disease (201)	4	2.64	0.99-7.03	4	3.58	1.34-9.54				1	1.32	0.19-9.37	3	3.96	1.28-12.27
non-Hodgkin lymphoma (200, 202)	8	1.65	0.83-3.30	5	1.45	0.60-3.49	3	2.13	0.69-6.62	4	1.54	0.58-4.10	4	1.78	0.67-4.74
Multiple myeloma (203)	1	0.47	0.07-3.35	1	0.68	0.09-4.83				1	0.92	0.13-6.50			
Leukemia (204-208)	5	0.89	0.37-2.13	4	1.01	0.37-2.67	1	0.61	0.09-4.32	3	1.02	0.33-3.16	2	0.74	0.19-2.97
Diabetes mellitus (250)	5	0.73	0.30-1.74	2	0.49	0.12-1.96	3	1.07	0.34-3.31	5	1.11	0.46-2.67			
All circulatory diseases (390-459)	96	0.80	0.65-0.97	46	0.70	0.52-0.93	50	0.91	0.69-1.20	77	0.85	0.68-1.06	19	0.64	0.41-1.01
Ischemic heart disease (410-414)	43	0.82	0.61-1.11	21	0.77	0.50-1.18	22	0.88	0.58-1.34	38	0.88	0.64-1.20	5	0.56	0.23-1.35
Cerebrovascular disease (430-438)	19	0.64	0.41-1.00	10	0.61	0.33-1.14	9	0.67	0.34-1.29	15	0.73	0.44-1.21	4	0.44	0.17-1.18
Respiratory disease (460-519)	15	0.85	0.52-1.42	6	0.70	0.32-1.55	9	1.00	0.52-1.93	10	0.72	0.39-1.33	5	1.38	0.57-3.32
Digestive disease (520-579)	26	0.86	0.58-1.26	15	0.84	0.50-1.39	11	0.88	0.49-1.60	19	0.88	0.56-1.37	7	0.81	0.39-1.70
Cirrhosis of the liver (571)	22	1.02	0.67-1.54	13	1.01	0.59-1.75	9	1.01	0.53-1.95	17	1.07	0.67-1.73	5	0.86	0.36-2.06
Unknown (799.9)	10			8			2			5			5		
Accidents (800-999)	38	1.16	0.84-1.60	26	1.16	0.79-1.70	12	1.17	0.66-2.06	21	0.94	0.62-1.45	17	1.62	1.01-2.61

Abbreviations: ICD-9: International Classification of Diseases; OBS: observed number of deaths; SMR: standardized mortality ratio; CI: confidence interval; NOS: not otherwise specified

Table 3 - Mortality from selected cancer causes by duration of employment (years)

Cause of death (ICD-9 code)	< 10			10-20			20+		
	OBS	SMR	95%CI	OBS	SMR	95%CI	OBS	SMR	95%CI
All cancers (140-208)	108	1.01	(0.84 - 1.22)	38	1.02	(0.74 - 1.40)	37	0.87	(0.63 - 1.21)
Digestive (150-159)	34	0.98	(0.70 - 1.38)	8	0.64	(0.32 - 1.27)	20	1.30	(0.84 - 2.02)
Stomach (151)	4	0.49	(0.18 - 1.31)	4	1.25	(0.47 - 3.33)	8	1.88	(0.94 - 3.75)
Colon (153)	8	1.25	(0.62 - 2.49)				5	2.04	(0.85 - 4.90)
Liver (155)	6	0.92	(0.41 - 2.04)				1	3.30	(0.04 - 2.15)
Biliary tract (156)	3	2.13	(0.68 - 6.60)				1	2.19	(0.31 - 15.56)
Pancreas (157)	6	1.25	(0.56 - 2.78)	1	0.60	(0.08 - 4.29)	2	1.13	(0.28 - 4.50)
Digestive NOS (159)	3	1.95	(0.63 - 6.04)	2	3.63	(0.91 - 14.52)	2	3.01	(0.75 - 12.05)
Prostate (185)	2	1.39	(0.35 - 5.54)	3	3.78	(1.22 - 11.73)	2	1.01	(0.25 - 4.05)
Bladder (188)	1	0.62	(0.09 - 4.38)	2	2.68	(0.67 - 10.72)	3	2.05	(0.66 - 6.36)
Brain (191)	5	1.74	(0.72 - 4.17)	3	3.40	(1.10 - 10.55)			
Lympho-hemopoietic neoplasms (200-208)	12	1.36	(0.77 - 2.39)	5	1.84	(0.76 - 4.42)	1	0.39	(0.05 - 2.76)
Hodgkin's lymphoma (201)	3	2.82	(0.91 - 8.74)	1	3.75	(0.53 - 26.62)			
non-Hodgkin lymphoma (200,202)	6	2.00	(0.90 - 4.46)	2	2.11	(0.53 - 8.44)			
Leukemia (204-208)	3	0.85	(0.27 - 2.62)	1	0.93	(0.13 - 6.62)	1	0.98	(0.14 - 6.98)

Abbreviations: ICD-9: International Classification of Diseases; OBS: observed number of deaths; SMR: standardized mortality ratio; CI: confidence interval; NOS: not otherwise specified

categories. A more than three-fold increased risk for prostate cancer was found among workers with duration of employment 10-19 years. NHL and HD were increased in workers employed for less than 20 years.

The analysis by time since first employment (table 4) did not show any distinct pattern for any of the examined causes. Statistically increased risks were found for NOS digestive cancers and bladder cancer after 40 years; NHL showed the highest risks for time since first employment less than 30 years.

Discussion

The mortality experience of two Italian cohorts of PCB-exposed-workers was examined within a 60 year span and showed increased risks for causes of "a priori" interest that had been previously reported in excess in other cohort studies.

Mortality from biliary tract cancer was significantly elevated among males. Our finding is corroborated by experimental data and is consistent with previous epidemiological studies in PCB-exposed workers (13, 16, 17). The observed excess, nonetheless, was based on a small number of deaths (no 4), and was not related to duration of employment and latency. All cases had latency longer than 10 years but duration of employment was below 10 years in three of them and very short (1 years) in both workers at Plant 1.

Mortality from all digestive cancers did not differ from expectations, however we found a higher than two-fold increased risk for "NOS digestive cancers" concerning both plants and both genders. The risk was steadily increased across different categories of duration of employment and the excess became statistically significant, based on 4 cases, after 40 years of latency. Noteworthy is the increasing risk with increasing duration of employment for stomach cancer. A positive association between stomach cancer and cumulative PCB exposure was shown in a previous mortality study (17).

Other findings that warrant discussion are the increased mortality from brain cancer and lymphomas.

The brain cancer excess emerged mainly in Plant 1 and the highest risk was seen for workers employed for 10-19 years, with no cases in the highest duration category. Results in other cohort studies are inconsistent. The more recent follow-up

Table 4 - Mortality from selected cancer causes by time since first employment (years)

Cause of death (ICD-9 code)	< 20			20-29			30-39			40 +		
	OBS	SMR	95% CI	OBS	SMR	95% CI	OBS	SMR	95% CI	OBS	SMR	95% CI
All cancers (140-208)	35	1.46	(1.05 - 2.04)	38	0.99	(0.72 - 1.36)	49	0.81	(0.61 - 1.07)	61	0.95	(0.74 - 1.22)
Digestive (150-159)	9	1.28	(0.67 - 2.46)	12	1.00	(0.57 - 1.76)	16	0.80	(0.49 - 1.31)	25	1.06	(0.72 - 1.57)
Stomach (151)	1	0.42	(0.06 - 2.96)	6	1.76	(0.79 - 3.92)	3	0.64	(0.21 - 1.98)	6	1.18	(0.53 - 2.61)
Colon (153)	1	0.83	(0.12 - 5.92)	1	0.50	(0.07 - 3.51)	5	1.40	(0.58 - 3.37)	6	1.39	(0.63 - 3.10)
Liver (155)	2	1.75	(0.44 - 7.01)				2	0.52	(0.13 - 2.07)	3	0.59	(0.19 - 1.83)
Biliary tract (156)	1	7.69	(1.08 - 54.61)	1	2.70	(0.38 - 19.20)	1	1.25	(0.18 - 8.87)	1	0.96	(0.14 - 6.82)
Pancreas (157)	1	1.43	(0.20 - 10.14)	3	2.07	(0.67 - 6.41)	2	0.73	(0.18 - 2.90)	3	0.90	(0.29 - 2.79)
Digestive NOS (159)	1	5.88	(0.83 - 41.76)				2	2.16	(0.54 - 8.62)	4	3.58	(1.34 - 9.54)
Prostate (185)	1	4.00	(0.56 - 28.40)	1	1.75	(0.25 - 12.40)	1	0.95	(0.13 - 6.74)	4	1.71	(0.64 - 4.56)
Bladder (188)				1	1.56	(0.22 - 11.10)				5	2.87	(1.20 - 6.90)
Brain (191)	2	2.70	(0.68 - 10.81)	1	0.98	(0.14 - 6.96)	3	2.02	(0.65 - 6.27)	2	1.72	(0.43 - 6.87)
Lympho-hemopoietic (200-208)	6	1.93	(0.87 - 4.29)	5	1.82	(0.76 - 4.38)	4	1.03	(0.39 - 2.75)	3	0.68	(0.22 - 2.12)
Hodgkin's lymphoma (201)	2	2.41	(0.60 - 9.63)	1	3.13	(0.44 - 22.20)	1	4.51	(0.63 - 32.02)			
Non-Hodgkin lymphoma (200,202)	2	2.90	(0.72 - 11.59)	3	3.23	(1.04 – 10.0)	2	1.36	(0.34 - 5.43)	1	0.57	(0.08 - 4.05)
Leukemia (204-208)	2	1.40	(0.35 - 5.59)	1	0.87	(0.12 - 6.17)				2	1.27	(0.32 - 5.08)

Abbreviations: ICD-9: International Classification of Diseases; OBS: observed number of deaths; SMR: standardized mortality ratio; CI: confidence interval; NOS: not otherwise specified

of an Indiana capacitor manufacturing cohort (19) showed an increased mortality for brain cancer without however a clear dose-response relationship with estimated cumulative PCB exposure. Excess mortality from brain cancer was found for workers with intermediate, but not high, cumulative exposure in a large cohort of workers at five electrical power companies in the United States (12). No other studies of capacitor manufacturing workers confirmed these findings.

Four deaths from HD yielded a threefold significant increase in Plant 1 only and mainly among females, whereas mortality from NHL was modestly increased in both plants. No clear relationship with duration of employment and latency emerged. The epidemiological evidence of a possible association between PCB exposure and NHL has been recently reviewed by Kramer et al (10) which stated that " although findings from occupational cohort studies are quite inconsistent, results from case-control studies conducted in the general population and toxicological data demonstrating immunosuppressive and inflammatory effects of PCBs support a possible role of PCBs in lymphomagenesis".

In summary, although the mortality patterns of our cohorts highlighted increased risks for cancers of a priori interest in PCB-exposed workers, our findings cannot confirm if the observed excesses are related to PCB exposure due to limited sample size, lack of exposure-response relationship with duration of employment and absence of trend with latency.

Smoking, alcohol and diet are potential risk factors for liver and intestinal cancers, however their possible role as confounders is expected to be small in this cohort since mortality from other conditions associated to these lifestyle factors, such as ischemic heart diseases, respiratory diseases and liver cirrhosis was lower or similar to the expected. Other differences in environmental and socioeconomic factors between the cohort and the reference population are unlikely to have played a strong role due to the use of the regional population as comparison. Selection bias was improbable, given the high percentage of traced workers.

In conclusion, the current update of the mortality of these cohorts suggests possible increased risks

for PCB-exposed workers that need, however, to be further explored in larger studies with well characterized exposure.

NO POTENTIAL CONFLICT OF INTEREST RELEVANT TO THIS ARTICLE WAS REPORTED

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