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Mortality among 24,865 workers exposed to polychlorinated biphenyls (PCBs) in three electrical capacitor manufacturing plants: a ten-year update

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Abstract

The objective of this analysis was to evaluate mortality among a cohort of 24,865 capacitor-manufacturing workers exposed to polychlorinated biphenyls (PCBs) at plants in Indiana, Massachusetts, and New York and followed for mortality through 2008. Cumulative PCB exposure was estimated using plant-specific job-exposure matrices. External comparisons to US and state-specific populations used standardized mortality ratios, adjusted for gender, race, age and calendar year. Among long-term workers employed 3 months or longer, within-cohort comparisons used standardized rate ratios and multivariable Poisson regression modeling. Through 2008, more than one million person-years at risk and 8749 deaths were accrued. Among long-term employees, all-cause and all-cancer mortality were not elevated; of the *a priori* outcomes assessed only melanoma mortality was elevated. Mortality was elevated for some outcomes of *a priori* interest among subgroups of long-term workers: all cancer, intestinal cancer and amyotrophic lateral sclerosis (women); melanoma (men); melanoma and brain and nervous system cancer (Indiana plant); and melanoma and multiple myeloma (New York plant). Standardized rates of stomach and uterine cancer and multiple myeloma mortality increased with estimated cumulative PCB exposure. Poisson regression modeling showed significant associations with estimated cumulative PCB exposure for prostate and stomach cancer mortality. For other outcomes of *a priori* interest – rectal, liver, ovarian, breast, and thyroid cancer, non-Hodgkin lymphoma, Alzheimer disease, and Parkinson disease – neither elevated mortality nor positive associations with PCB exposure were observed. Associations between estimated cumulative PCB exposure and stomach, uterine, and prostate cancer and myeloma mortality confirmed our previous positive findings.

Key words: polychlorinated biphenyls, cohort study, occupational exposure, cancer, exposure

assessment

Introduction

From 1929 to 1977, 209 polychlorinated biphenyl (PCB) congeners were produced commercially in the United States. Mixtures of PCBs were used widely in industry [Robertson and Ludewig 2011; Robertson and Ruder 2010] and persist in humans and in the environment [Hopf, et al. 2009a]. Increasing concern about potential health and environmental risks led to a 1977 ban on PCB production and distribution in the United States and a 2004 ban on PCB production in 151 signatory countries [United Nations Environment Programme 2004]. In 2013 the International Agency for Research on Cancer (IARC) classified PCBs as definite human carcinogens[Lauby-Secretan, et al. 2013].

Thirty-five years after their use was banned in the United States PCBs are still a potential occupational and environmental exposure for those who repair, maintain, or remove capacitors and transformers containing PCBs and for the general public, as well as for the former workers whose decades of internal exposure to PCBs continue [Beyer and Biziuk 2009]. The National Institute for Occupational Safety and Health (NIOSH) has assembled a cohort of workers who manufactured capacitors using PCBs as a dielectric fluid at plants in Indiana (1957-1977) [Ruder, et al. 2006], and Massachusetts (1939-1976) and New York (1946-1977) [Prince, et al. 2006]. Dielectric fluid formulations (i.e., different commercial products containing some of the 209 PCB congeners) varied across time and across the plants (see Table 1).

Previous reports utilized different requirements for eligibility (one day vs. 90 days) and considered the Indiana plant separately from the Massachusetts and New York plants for most causes of death [Brown 1987; Brown and Jones 1981; Prince, et al. 2006; Ruder, et al. 2006; Sinks, et al. 1992], but jointly for breast cancer incidence [Silver, et al. 2009] and neurodegenerative disease mortality [Steenland, et al. 2006].

The rationale for this study was that by combining the three largest US capacitor manufacturing cohorts and incorporating ten additional years of mortality experience, previous findings and hypothesized relationships could be re-evaluated with greater statistical power due to more workers, longer follow-up, and the integration of the three cohort exposure assessments. The current study extends vital status follow-up an additional ten years through 2008 and includes all workers from the three plants with one day or more of employment during the period when PCBs were in use, but focuses on workers employed 3 months or more. Job-exposure matrixes developed for the three plants were used to estimate cumulative PCB exposure for each worker. The primary purpose was to investigate further the relationship between estimated cumulative PCB exposure and mortality outcomes, particularly among long-term workers employed for three months or longer. Outcomes of *a priori* interest included causes of death with increased risks originally observed in the subcohorts followed through 1998, including hormone-related cancers (i.e., prostate, breast, uterine, and ovarian), multiple myeloma, melanoma, brain and nervous system cancer, stomach cancer, intestinal cancer, and neurodegenerative diseases. Other *a priori* hypotheses were that PCB exposure would affect all-cause mortality, all-cancer mortality, and, specifically, rectal cancer, biliary passages, liver, and gall bladder cancer, and non-Hodgkin lymphoma, outcomes for which other studies indicated increased risks [Brown 1987; Brown and Jones 1981; Rothman, et al. 1997]. More recent results have motivated the addition of thyroid cancer to the *a priori* list [Mallin, et al. 2004; Yard, et al. 2011]. Including all the workers in one analysis and adding ten years of vital status follow-up increases the power of the study.

Materials and methods

Cohort

The cohort included all workers employed at least one day at any of the plants. Records were maintained for 26,588 workers; however, those not employed during the years PCBs were used or employed less than one day were excluded from the final PCB cohort of 25,062 workers. Demographic data sources included work histories and plant records. Records for the New York and Massachusetts workers were originally microfilmed in 1977, although only the 2588 workers considered highly exposed were included in the first analyses [Brown 1987; Brown and Jones 1981]. The cohort was expanded to include all exposed workers at the New York and Massachusetts plants using these microfilmed records, which were verified against Internal Revenue Service (IRS) Employer's Quarterly Earnings Reports for the New York plant [Prince, et al. 2006]. Records for the Indiana workers were microfilmed and data-entered in 1989 [Sinks, et al. 1992].

Exposure assessment

Exposure data sources included company and NIOSH surveys of the plants and plant records. The exposure assessment used previously created plant-specific semi-quantitative job-exposure matrices (JEMs) that are described in detail in [Hopf, et al. 2013; Hopf, et al. 2009b; Hopf, et al. 2010] and briefly here. All jobs were categorized based on PCB exposure intensity and frequency, and qualitatively ranked for inhalation and dermal exposure. For inhalation exposure intensity, air concentration data permitted assignment of exposure units (ppm), but the lack of historical dermal exposure measurements resulted in a unitless measure of dermal exposure intensity. For each job category the product of intensity and frequency (fraction of day exposed) was calculated. Inhalation and dermal JEMs were modified for earlier and later eras

(the former with estimated 20% higher exposure). Since dermal exposures account for a significant proportion of total PCB exposure [Fishbein 1982], a combination JEM averaging inhalation and dermal (1:1) scores was used to estimate PCB exposure for each job by era. Detailed work histories available for each worker were used to estimate cumulative PCB exposure, based on plant, department, job title, and the era-specific combination JEM, and expressed in unit-days or unit-years of exposure (but the "unit" was undefined).

Vital status follow-up

Vital status was originally determined through 1982 for the New York and Massachusetts cohorts using records from the Social Security Administration (SSA) Death Master File, state motor vehicle registration and vital statistics offices, the US Postal Service, and, after 1979, the National Death Index (NDI) [National Center for Health Statistics 2007] [Brown 1987; Brown and Jones 1981]. Vital status was determined through 1984 for the Indiana cohort using records from the SSA and the IRS [Sinks, et al. 1992]. For previous analyses [Brown 1987; Brown and Jones 1981; Sinks, et al. 1992], death certificates had been obtained for pre-1979 deaths and causes of death coded by a trained nosologist. Subsequent vital status updates for all three subcohorts used the NDI [Prince, et al. 2006; Ruder, et al. 2006].

For the present update, cohort member data were submitted to the NDI for determination of vital status through 2008, and NDI-Plus causes of death were obtained. Any worker lost to follow-up before 1979 was classified 'vital status unknown' and considered alive until the date last observed (usually the date last employed). All causes of death (NDI and death certificate-based) were coded to the revision of the International Classification of Diseases (ICD) in effect at the time of death, and mapped to specific cause of death categories (described below). This

study (HSRB 08-DSHEFS-02) has been approved by the NIOSH Human Subjects Review Board. As a records study, it was exempted from informed consent requirements.

Statistical analysis

Mortality was evaluated using the NIOSH life table analysis system [Schubauer-Berigan, et al. 2011]. Analyses used US mortality rates for 92 (1940-2007) or 119 (1960-2007) cause of death categories [Robinson, et al. 2006] and three neurodegenerative causes of death: Alzheimer disease, amyotrophic lateral sclerosis (ALS), and Parkinson disease [Steenland, et al. 2006]. Race- and gender-specific person years at risk (PYAR) were accumulated for each eligible worker across five-year age and calendar year intervals, beginning on the qualified date of first exposure, or the rate file begin date (January 1, 1940 or January 1, 1960), whichever was later, and ending with the date of death, the date last known alive, or the study end date (December 31, 2008), whichever was earliest. Cohort members with valid social security numbers known to be alive after January 1, 1979, when the NDI began, and not identified as deceased were assumed to be alive on December 31, 2008, as the sensitivity of the NDI is over 95% when social security numbers are available [Cowper, et al. 2002]. For each cause of death, PYAR were multiplied by the gender-race-age-calendar period referent rates and summed to yield an expected number of deaths. The standardized mortality ratio (SMR) is the ratio of observed to expected deaths. The statistical significance of the SMR was determined by a two-tailed test based on the Poisson distribution and a 95% confidence interval (CI) was calculated based on exact (10 or fewer deaths) or approximate (more than 10 deaths) methods.

Plant-specific analyses used state mortality rates (1960-2007) for the 119 cause of death categories. State rates account for local conditions that can influence disease rates (e.g., the gradient of disease with latitude seen for some cancers [Foster, et al. 2008]). A multiple-cause-

of-death analysis considering all causes listed on the death certificates investigated possible excesses in nonmalignant diseases using US multiple cause referent rates (1960-2007) [Steenland, et al. 1992]. Because of the large number of short-term workers, and for comparability to previous updates, we conducted separate analyses of short-term (employment duration less than 3 months) and long-term (employment duration of 3 months or longer) workers.

Within-cohort comparisons

The distribution of estimated cumulative PCB exposure was highly right-skewed (range 10 to 9.6×10^6 unit-days; median 3.2×10^4 unit-days); cutpoints at 40,000, 150,000, and 600,000 unit-days defined quartiles with approximately equal numbers of deaths among long-term workers. Among long-term workers, standardized rates were calculated for each quartile using the sum of all PYAR for each gender-race-age-calendar period stratum as the stratum weight. Directly standardized rate ratios (SRRs) were calculated for each exposure quartile relative to the lowest quartile and 95% CIs were calculated based on a Taylor series approximation of the variance [Rothman and Greenland 1998]. A test for a linear trend was performed based on a weighted regression of the standardized rates [Rothman, et al. 2008]. To account for potential latency, exposure lag periods of 10 and 20 years were evaluated for cancer outcomes. Analyses that considered cumulative exposure excluded 515 workers with periods of unknown exposure who were included in the overall results.

Relations between estimated cumulative PCB exposure and mortality were examined using Poisson regression modeling [Frome 1983] available in the GENMOD procedure in SAS (version 9.2, SAS Institute Inc., Cary, NC). Regression models were performed among long-term workers for prostate, uterine, ovarian, and stomach cancers and multiple myeloma because

a previous analysis of the Massachusetts and New York subcohorts found an exposure-response effect for these outcomes [Prince, et al. 2006]. Effect modification was evaluated for gender, race, and plant using the likelihood ratio test for interaction and confounding by gender, race, age, birth year, and plant, was evaluated using a change-in-estimate criterion of 10%. In these models, estimated cumulative exposure was treated as either a categorical variable (5 categories based on quintiles of the exposure distribution among cases) or a continuous variable. Several exposure transformations (identity, natural logarithm, and square root) were evaluated and the best-fitting model (based on Akaike's information criterion (AIC) [Akaike 1979]) was reported. Exposure lag periods of 0, 5, 10, 15, and 20 years were evaluated and results of the best-fitting lag period (also based on AIC) were reported. Collinearity among model predictors, evaluated for best fitting models using methods for generalized linear models, was not observed [Lesaffre and Marx 1993].

In the Poisson regression models, age and birth year were centered at the median age at death and birth year among cases, so the model intercept estimates the logarithm of the background rate for an unexposed worker at the median age at death and birth year. For some outcomes, variability in the estimated intercepts was observed with some models estimating implausibly low background rates. For this reason, all model forms were re-evaluated using constrained models in which the intercept was specified to fix the background rate across models.

In supplemental analyses, best fitting models were re-evaluated excluding workers with any time in a job category with potential for trichloroethylene (TCE) exposure (time in "setup and/or operate wet machines" or "setup and/or operate dry machines" at Indiana; in "degreaser" at Massachusetts; or in "degreasers and painters" at New York). Analyses were conducted

excluding these solvent-exposed workers because they did not comprise a large enough group to be analysed separately. Two-sided p<0.05 was considered statistically significant.

Results

After exclusions (n=197) for missing data, the final cohort of 24,865 workers contributed 1,019,128 PYAR (Table 2). Through 2008, 8749 cohort members (35%) had died.

In the overall cohort, all-cause mortality was similar to the US population (8749 deaths, SMR 0.97, 95% CI 0.95-1.00), but all-cancer mortality was elevated (2602 cancer deaths, SMR 1.05, 95% CI 1.01-1.09). These results, based on the 1940-2008 time period, were similar to results based on the 1960-2008 time period (presented in Table 3). As only 61 deaths occurred before 1960 and 119 category US and state rates are only available from 1960, we present here only results from 1960 on (8688 deaths). For ease of comparison with previous results we present all categories for which 3 or more deaths occurred.

Compared to the US population, mortality was not significantly elevated in the overall cohort for any individual outcome of *a priori* interest, although statistically significant increases were observed for all cancers combined, all cancers of the digestive organs and peritoneum combined, all respiratory cancers combined, and HIV-related disease (Table 3). Furthermore, significant deficits were observed among all workers for alcoholism, heart diseases, digestive system diseases, symptoms and ill-defined conditions, injuries, suicide and homicide. Similar results were observed (results not shown) when all causes listed on the death certificate were considered.

The median duration of employment in the cohort was less than one year and short-term workers (less than 3 months of employment) comprised nearly one-third of the cohort. Among

these short-term workers, all-cause and all-cancer mortality were elevated with excesses for pharyngeal, pancreatic, lung, and bladder cancers, HIV-related disease, dementia and Alzheimer disease, heart disease, and chronic obstructive pulmonary disease (Table 3). Among long-term workers there was a significant increase in melanoma mortality (41 deaths, SMR 1.41, 95% CI 1.01-1.91); elevations were not observed for other outcomes of *a priori* interest. Mortality among long-term workers was significantly reduced for all causes combined, tuberculosis and HIV-related disease, mental, psychoneurotic, and personality disorders, and respiratory diseases, in addition to those categories with significant decreases in the cohort overall. Additional analyses focused exclusively on the long-term workers.

Table 4 shows mortality for *a priori* outcomes among long-term workers stratified by plant. Using state rates, mortality was significantly elevated among long-term workers for two outcomes of *a priori* interest previously observed at the Indiana plant: melanoma (SMR 2.58, 95% CI 1.38-4.42) and cancers of the brain and other parts of the nervous system (SMR 2.06, 95% CI 1.20-3.29); two outcomes of *a priori* interest previously observed at the New York plant: melanoma (SMR 1.71, 95% CI 1.04-2.64) and multiple myeloma (SMR 1.74, 95% CI 1.08-2.66); but for no outcomes at the Massachusetts plant.

 All-cause and all-cancer mortality was significantly reduced among long-term workers at the Indiana plant, but not among long-term workers at the Massachusetts and New York plants.

Table 5 shows mortality for *a priori* outcomes among long-term workers stratified by sex. Compared to the US population, mortality was significantly elevated for long-term female workers for all cancers (SMR 1.06, 95% CI 1.00-1.13), intestinal cancer (SMR 1.23, 95% CI 1.00-1.49), and ALS (SMR 1.90, 95% CI 1.09-3.09). Among long-term male workers, all-cause mortality was significantly reduced (SMR 0.91, 95% CI 0.88-0.94) but melanoma mortality was

significantly elevated (SMR 1.59, 95% CI 1.06-2.28). In both sexes, multiple myeloma

mortality was elevated, but neither elevation was statistically significant. While long-term male

and female workers had comparable mean and median cumulative exposures in the

Massachusetts subcohort, long-term female workers in the Indiana and New York subcohorts

had lower mean and median cumulative exposures compared to male workers (results not

shown).

Among long-term workers, directly standardized mortality rates increased with quartiles

of estimated cumulative PCB exposure for stomach and uterine cancer and multiple myeloma;

but not for other *a priori* outcomes evaluated (Table 6). Prostate cancer mortality was elevated

in the highest quartile compared to the lowest quartile (SRR 2.11, 95% CI 1.08-4.13). Similar

results were observed for cancer outcomes when a 10- or 20-year lag period was applied (results

not shown).

Poisson regression models are summarized in Table 7. For the outcomes evaluated

(prostate, uterine, ovarian, and stomach cancers and multiple myeloma), the model with the best-

fitting lag period was reported although model fit did not vary much across lag periods (results

not shown); plant was neither an effect modifier nor a confounder; age and birth year were

positive confounders; and all but two cases were among Caucasians so confounding from race

was not evaluated. Prostate cancer mortality was significantly associated with estimated 20-year

lagged (and log transformed) cumulative PCB exposure among long-term male workers

(adjusted rate ratio (RR) 2.22 at 1000 unit-years, 95% CI 1.06-4.80); however, the RR was

slightly reduced in the constrained intercept model (RR 1.73 at 1000 unit-years, 95% CI 1.08-

2.74). Furthermore, prostate cancer mortality was significantly elevated in the highest exposure

quintile relative to the lowest quintile.

Shorter lag periods provided the best fit for Poisson regression models of uterine (10-year lag period) and ovarian (5-year lag period) cancer mortality among long-term female workers; however, no significant associations were observed with estimated cumulative PCB exposure in any Poisson model evaluated for uterine or ovarian cancer. Stomach cancer mortality among long-term workers was significantly associated with estimated 15-year lagged (and log transformed) cumulative PCB exposure (RR 4.79 at 1000 unit-years, 95% CI 1.83-13.3); however, the rate ratio was diminished, but remained statistically significant in the constrained intercept model. A 10-year exposure lag period was best fitting for Poisson models of multiple myeloma mortality; however, multiple myeloma mortality was not significantly associated with estimated cumulative PCB exposure in any model evaluated. Estimated rate ratios are graphically displayed in Figure 1 along with other model forms evaluated.

Similar results were obtained for best-fitting models for prostate, uterine, and ovarian cancer and multiple myeloma (data not shown) when workers with any time in jobs with potential TCE exposure were excluded; however, for stomach cancer, the RR associated with a 1000 unit-year increase (based on the natural log transformation) decreased to 3.49 (95% CI 1.21-10.8) when workers potentially exposed to TCE were excluded.

Discussion

This update of our capacitor-manufacturing worker study, combining three subcohorts previously analyzed separately, adding ten years of vital status data, and focusing on long-term workers, confirmed and strengthened previous findings. Mortality was elevated for some outcomes of *a priori* interest among subgroups of long-term workers: all cancer, intestinal cancer and amyotrophic lateral sclerosis (women); melanoma (men); melanoma and brain and nervous

system cancer (Indiana plant); and melanoma and multiple myeloma (New York plant). Internal comparisons showed increasing rates of stomach and uterine cancer and multiple myeloma mortality with increasing estimated cumulative PCB exposure. Poisson regression modeling showed significant associations with estimated cumulative PCB exposure for prostate and stomach cancer mortality.

For other outcomes of *a priori* interest – rectal, liver, ovarian, breast, and thyroid cancer, non-Hodgkin lymphoma, Alzheimer disease, and Parkinson disease – neither elevated mortality nor positive associations with PCB exposure were observed. Studies of mortality in cohorts occupationally exposed to PCBs have presented inconsistent findings. Nine cohorts of electrical capacitor and transformer manufacturers have been studied to date (see supplemental table to [Ruder, et al. 2006]). In some cases SMRs were elevated for one sex but not the other. Excess deaths from particular cancers or other diseases have been reported, but there has not been consistency from cohort to cohort, or even within cohort across studies. These inconsistencies might be related to differences in the exposure assessments, to differing procedures at different plants and in different eras, to differing properties and modes of action of the PCB congeners, and to these manufacturing facilities having used varying commercial mixtures of PCB congeners [AccuStandard Inc. 2012].

In our study, the excess melanoma mortality among Indiana and New York workers, but lack of excess among Massachusetts workers, could be due to lifestyle factors, differences in the PCB mixtures used, occupational exposures other than to PCBs, or interplant differences in work practices (see Table 1 comparing the three plants). The original study of the Indiana plant noted that PCB-exposed workers were at greater risk of skin effects, including chloracne and hyperpigmentation [Sinks, et al. 1992]. Several recent papers support an association of

melanoma and PCB exposure: Behrens and colleagues observed an increased risk of uveal melanoma among men with occupational exposure to transformer or capacitor oils (odds ratio 2.74, 95% CI 1.07-7.02) [Behrens, et al. 2010]; Gallagher et al. saw a dose-response effect for melanoma risk and plasma levels of PCBs (p for trend <0.001), comparing melanoma patients and controls [Gallagher, et al. 2011]; and Loomis and colleagues reported increased melanoma risk among electrical utility workers exposed to PCBs [Loomis, et al. 1997]. A review (which included the original study of the Indiana cohort [Sinks, et al. 1992]) of non-solar occupational risk factors for melanoma found increased risks for workers in the electric and electronic industry [Fortes and de Vries 2008]. In 2013 an International Agency for Research on Cancer Working Group concluded that there was sufficient evidence for human cancinogenity of PCBs, based on the analyses of melanoma and PCB exposure [Lauby-Secretan, et al. 2013]. The deficit of melanoma in the Massachusetts subcohort might be related to its ethnic composition; an estimated 30% are of Portuguese or Cape Verdean ethnicity with darker skin pigmentation, which is a protective factor for melanoma [Fortes and de Vries 2008].

Breast, ovarian, uterine and prostate cancer are among those cancers associated with hormonal factors, and endocrine disruptors such as polychlorinated biphenyls [National Research Council 2000] may modify risk. For each of these categories of disease there are additional demographic risk factors which can affect the results, such as shift work, family history, ethnicity, parity and reproductive history [Poole, et al. 2011; Silver, et al. 2009]. In this analysis, which did not include demographic risk factors, we did not see increased risk of breast cancer. However, our nested case-control study of breast cancer, which adjusted for those risk factors, did find increased risk among women of races other than Caucasian [Silver, et al. 2009]. Compared to the lowest exposure quartile, ovarian cancer mortality was elevated in categories of

higher estimated cumulative PCB exposure, but there was no trend of increasing risk with increasing exposure, while we observed increasing standardized rates of uterine cancer mortality across quartiles of estimated cumulative PCB exposure (Table 6). There are recognized reproductive and hormonal risk factors for these cancers but few strong occupational associations [Slack, et al. 2012].

The significantly increased risk of prostate cancer in the highest quartile of estimated cumulative PCB exposure (Table 6) and in the Poisson regression analysis (Table 7) support the association of PCB exposure and increased prostate cancer mortality observed in other cohorts [Charles, et al. 2003; Pesatori, et al. 2013]. Our previous analyses showed this association among the more highly exposed Massachusetts and New York workers [Prince, et al. 2006], but not the Indiana workers [Ruder, et al. 2006].

Stomach cancer mortality was not elevated in the cohort although we observed significant trends with increasing estimated cumulative PCB exposure in SRR and Poisson regression analyses. Poisson regression models of stomach cancer, however, were influenced by widely varying background rates. When the model intercept was constrained to avoid implausibly low background rates, both of these rate ratios were diminished, but remained statistically significant. Park and colleagues [Park, et al. 2012] similarly observed implausibly low model intercepts in some Poisson regression models of the lung cancer SMR in a cohort of workers exposed to cadmium and arsenic; to account for this, they additionally reported rate ratios adjusted to a common unexposed SMR of 0.8. In our study, when workers potentially exposed to TCE were excluded from the analysis, the stomach cancer rate ratio was attenuated (but remained statistically significant), indicating that some of the increased risk was due to confounding by TCE exposure. TCE exposure was associated with stomach cancer in one cohort study of TCE-

exposed workers [Anttila, et al. 1995] but not in others [Blair, et al. 1998; Boice, et al. 2006].

Our Poisson models would have been more robust if the numbers of deaths had been larger; this

limitation could be alleviated for outcomes with long survival using a cancer incidence study.

There were some major differences between male and female workers in our cohort.

Generally the men exhibited the "healthy worker effect", while the women did not (Table 5). It

has been noted that working and general populations of women differ in risk factors [Bond, et al.

1987] and female and male employees in the same industry may have different tasks even if they

have the same job title [Stellman 1999]. The observed mortality differences between male and

female workers may be due to differences in work assignments, differences in physiology, and

differences in how their bodies reacted to PCBs [Eng, et al. 2011; Messing and Mager Stellman

2006; Silvaggio and Mattison 1994]. Since various PCB congeners have estrogenic, anti-

estrogenic, androgenic or anti-androgenic properties [Diamanti-Kandarakis, et al. 2009], it

follows that female-male hormonal differences might be associated with the activity of PCBs in

the body [Meeker and Hauser 2010; Salehi, et al. 2008].

Our *a priori* causes of interest, based on several case-control studies, included non-

Hodgkin lympohoma [Engel, et al. 2007; Rothman, et al. 1997]. However, we did not find an

increase in NHL mortality nor an association between NHL and estimated cumulative exposure.

The findings of our cohort mortality study differed from those of the case-control studies of NHL

incidence. This discrepancy may be due to differences in the study populations and the outcome

variable (death vs diagnosis).

We did not find excesses for other *a priori* outcomes (rectal cancer, biliary passages,

liver, and gall bladder cancer, or thyroid cancer). The cancer incidence study we are conducting

on this combined cohort may provide some additional insight, particularly for cancers with high

survival rates such as thyroid cancer [National Cancer Institute 2011].

A strength of this combined cohort mortality update study is the detailed exposure assessment. The data available to construct the job-exposure matrices included individual work histories, detailed job descriptions for hourly jobs, and exp sets of exposure measurements collected at the plants [Hopf, et al. 2013; Hopf, et al. 2009b; Hopf, et al. 2010]. However, as in most records-based retrospective occupational cohort studies, we had no information on risk factors explored in case-control studies, such as family history or genetic susceptibility; lifestyle choices, such as smoking or sun exposure, that could affect mortality; or on previous or subsequent employment.

This last limitation is significant because a majority of cohort members worked a year or less at one of the plants (Table 2). Increased mortality among short-term workers has been reported, particularly for causes of death associated with disorders that might affect employment or with an unhealthy lifestyle. Those who are only briefly in a workplace might leave because of sensitization to work materials, and possibly the beginning of work-related chronic conditions [Langseth and Kjaerheim 2006], or shorter durations of employment might be associated with more pre-employment hospitalizations for alcohol use, accidents, and the effects of violence [Kolstad and Olsen 1999]. We have no lifestyle or hospitalization information for our cohort. However, our analyses showed different mortality profiles for short-term and long-term workers, as have been found in other studies [Boffetta, et al. 1998; Kolstad and Olsen 1999]. Significant excess mortality from all cancers, digestive and respiratory cancers, and HIV-related diseases were seen among the third of the cohort that worked fewer than three months. Among long-term workers only the excess of melanoma deaths was statistically significant. These differences could be due to lifestyle differences as well as differences in occupational exposure or

physiological reactions to that exposure.

In conclusion, we found evidence of associations between employment in capacitor manufacturing and increased total cancer and intestinal cancer mortality among female long-term workers and excess melanoma mortality for male long-term workers. The associations in our life table analyses convey moderate increased risk. We did not observe increased risk for several *a priori* causes of death for which case-control studies observed increased risk. The internal comparisons show increasing risk with estimated cumulative exposure for uterine, prostate and stomach cancer, and multiple myeloma.

Thirty-five years after PCB use was banned, the former workers in our cohort continue to be exposed internally to PCBs. Occupational and environmental exposure also continues for those who repair, maintain, or remove capacitors and transformers containing PCBs and for the general public, emphasizing the continued importance of understanding health risks associated with PCB exposures.

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Table 1

Differences among the three capacitor manufacturing plants in the NIOSH capacitor cohort

Determinant		Indiana	New York	Massachusetts
Chemicals[a]	Aroclor 1254 use	--	1946-1955 [b]	1939-1958 [c]
	Aroclor 1242 use	~1958-1971	1955-1971	1958-1976
	Aroclor 1016 use	1971-1977	1971-1977	1976-~1977
	Other Aroclors	Yes – (detected by EPA around the plant where used oil was dumped): Aroclors 1248, 1254, and 1260	Yes – occasional use of Aroclor 1221 (50% mono-Cl + 35% di-Cl + 5% tri and tetra Cl) 1971-1975	No
	Dielectric fluids other than PCBs	No	Yes after 1977: Bis(2-ethylhexyl) phthalate (**DEHP)**, castor oil, and mineral oil	Yes – castor oil and mineral oils used in large capacitors
	Degreasing solvent	TCE	TCE, detergent from 1977	TCE, degreasing station often leaked
Process description	Method of filling capacitors with PCBs	Manual	Manual 1946-1960; some automation after 1960 Flood filling temperatures >100°C	Manual
	Process changes over time	Yes, but timing and nature of change unknown	Few changes	Very few changes made from 1947-1977
Plant-specific information	Years of operation using Aroclors	1958-1977	1946-1977	1939-1977
	Ventilation	Leakage of oil mist from impregnation chambers because the oil seal was broken Local exhaust ventilation provided but often not used Insufficient duct size in chamber filling area Degreaser leaked TCE, open tanks Exhaust vapors re-entered work area Painting booths not equipped with ventilation	General dilution ventilation iInstalled in 1965; upgrade in 1976 reduced exposures 75% from 1976 to 1977	No local ventilation for oven opening – PCBs were exhausted from the impregnation ovens by opening the doors
	Personal protective equipment	Respirators provided but no training or change out schedule – mostly not used by the workers	Not documented	Not documented
	Plant lay-out	1968 expansion of plant with new non-PCB production areas Very small area of the plant dedicated to manufacturing with PCBs	Two different facilities Frequent changes Large spills at both facilities frequent due to the set-up of the manufacturing process.	Impregnation on 1st and 2nd floors Capacitors were moved from department to department and from floor to floor PCB areas not physically separated
	Manufacture of items other than PCB-filled capacitors	Yes – manufactured shunt capacitors, series capacitors, lighting arresters, reclosers and breakers, switches, potential devices, and line traps	No	Yes – produced mica and tubular capacitors
	Exposure category values used in job-exposure matrix	[Hopf, et al. 2009b]	[Hopf, et al. 2013]	[Hopf, et al. 2010]
	High	230	750	770
	Medium	140	300	550
	Low	50	50	180
	Baseline	5	10	50

Abbreviations: PCB, polychlorinated biphenyl; TCE, trichloroethylene

[a]   When plants changed from one Aroclor product to another, the substitution process was gradual over several months during which more

than one product would be in use.

[b]   Different periods of use of various Aroclors have been reported: Aroclor 1254 from 1946-1954 and Aroclor 1242 from 1954-1971 [Taylor, et al. 1991]; Aroclor 1016 from 1971-1976 [Jones, et al. 1978; Taylor, et al. 1991]; occasional use of Aroclor 1221 [Jones, et al. 1978].

[c]   Date of switch from Aroclor 1254 to Aroclor 1242 is uncertain.

Table 2
Cohort demographics and vital status as of December 31, 2008, NIOSH Capacitor Cohort

Characteristic	Entire cohort	Plant Indiana (1957-1977)	Massachusetts (1938-1976)	New York (1946-1977)
Total workers	25,062	3,601	12,616	8,845
Excluded from analysis [a]	197	21	58	118
Total analyzed	24,865	3,580	12,558	8,727
Vital status [b]				
Dead	8,749 (35%)	1,021 (29%)	4,489 (36%)	3,239 (37%)
Alive	15,356 (62%)	2,479 (69%)	7,591 (60%)	5,286 (61%)
Lost to follow-up	760 (3%)	80 (2%)	478 (4%)	202 (2%)
Race, gender				
Caucasian females	6,719 (27%)	555 (16%)	3,832 (31%)	2,332 (27%)
Females of other races	275 (1%)	19 (<1%)	220 (2%)	36 (<1%)
Race-unknown females [c]	6,083 (24%)	282 (8%)	4,377 (35%)	1,424 (16%)
Caucasian males	2,171 (9%)	517 (14%)	787 (6%)	867 (10%)
Males of other races	42 (<1%)	11 (<1%)	25 (<1%)	6 (<1%)
Race-unknown males [c]	9,575 (39%)	2,196 (61%)	3,317 (26%)	4,062 (47%)
Age at first employment (years)				
Median (interquartile range)	22.4 (18.7-29.7)	24.2 (20.9-31.4)	19.7 (17.4-27.5)	24.4 (21.0-31.1)
Mean ± standard deviation	25.6 ± 9.1	27.0 ± 8.2	24.1 ± 9.7	27.1 ± 8.3
Duration of employment (years)				
Median (interquartile range)	0.77 (0.18-4.0)	1.26 (0.29-5.6)	0.45 (0.11-2.5)	1.20 (0.32-5.8)
Mean ± standard deviation	3.75 ± 6.33	3.93 ± 5.25	3.12 ± 6.18	4.57 ± 6.83
Estimated cumulative exposure (unit-days) [d]				
Unknown	515	22	476	17
Lowest quartile (0-<10,000)	7423 (30%)	1444 (40%)	3593 (29%)	2386 (27%)
Second quartile (10,000-<60,000)	7243 (29%)	1116 (31%)	3657 (29%)	2470 (28%)
Third quartile (60,000-< 400,000)	6091 (24%)	878 (25%)	2850 (23%)	2363 (27%)
Highest quartile (≥400,000)	3593 (14%)	120 (3%)	1982 (16%)	1491 (17%)
Person-years at risk				
Sum	1,019,128	138,219	528,572	352,337

[a] Missing employment dates ($n = 124$), missing date of birth ($n = 72$), missing date of death ($n = 1$).

[b] For the analysis, workers lost to follow-up were considered alive until the date lost to follow-up.

[c] Race/ethnicity was not available for the majority of cohort members. For the analysis, race was assumed to be Caucasian, based on racial demographics in the geographic areas.

[d] Estimated cumulative exposure could not be calculated for 515 workers with periods of unknown exposure level. Cut-points based on quartiles of estimated cumulative exposure for all decedents.

Table 3
Standardized mortality ratios overall and by duration of employment, NIOSH Capacitor Cohort, 1960-2008 [a]

Underlying cause of death [b]	Entire cohort (n = 24,865)			Short-term workers [c] (n = 7,647)			Long-term workers [c] (n = 17,218)		
	OBS	SMR [d]	95% CI	OBS	SMR	95% CI	OBS	SMR	95% CI
All causes	8688	0.99	0.97-1.01	2255	1.17	1.12-1.22	6433	0.94	0.91-0.96
All cancers	2593	1.06	1.02-1.10	686	1.20	1.11-1.30	1907	1.01	0.97-1.06
MN of buccal cavity and pharynx	45	1.12	0.82-1.50	17	1.89	1.10-3.03	28	0.90	0.60-1.29
MN of tongue	12	1.25	0.65-2.18	3	1.38	0.28-4.02	9	1.21	0.55-2.30
MN of other parts of buccal cavity	15	1.36	0.76-2.24	4	1.67	0.46-4.28	11	1.27	0.64-2.28
MN of pharynx	18	0.94	0.56-1.48	10	2.31	1.11-4.25	8	0.54	0.23-1.06
MN of digestive organs and peritoneum	603	1.09	1.00-1.18	151	1.23	1.04-1.44	452	1.05	0.95-1.15
MN of esophagus	60	1.21	0.92-1.55	10	0.90	0.43-1.66	50	1.29	0.96-1.71
MN of stomach	58	1.04	0.79-1.35	12	1.01	0.52-1.77	46	1.05	0.77-1.40
MN of intestine except rectum	231	1.11	0.97-1.27	56	1.23	0.93-1.60	175	1.08	0.92-1.25
MN of rectum	50	1.21	0.90-1.59	9	0.98	0.45-1.85	41	1.27	0.91-1.73
MN of biliary passages, liver and gall bladder	63	0.98	0.76-1.26	19	1.29	0.78-2.01	44	0.89	0.65-1.20
MN of pancreas	136	1.08	0.90-1.28	42	1.47	1.06-1.98	94	0.96	0.78-1.18
MN of peritoneum and other and unspecified of digestive organs	5	0.53	0.17-1.24	3	1.40	0.29-4.10	2	0.27	0.03-0.99
MN of respiratory system	797	1.08	1.00-1.15	230	1.35	1.19-1.54	567	0.99	0.91-1.08
MN of larynx	24	1.32	0.85-1.97	8	2.04	0.88-4.02	16	1.13	0.64-1.83
MN of trachea, bronchus, and lung	766	1.07	0.99-1.15	221	1.34	1.17-1.53	545	0.99	0.91-1.07
MN other parts of respiratory system	7	1.52	0.61-3.14	1	0.91	0.02-5.09	6	1.71	0.63-3.72
MN of breast	239	1.01	0.89-1.15	74	1.15	0.90-1.44	165	0.96	0.82-1.12
MN of female genital organs	143	1.00	0.84-1.18	39	1.03	0.73-1.41	104	0.99	0.81-1.20
MN of cervix uteri	31	1.12	0.76-1.60	10	1.29	0.62-2.37	21	1.06	0.66-1.62
MN of other and unspecified parts of uterus	34	1.07	0.74-1.50	6	0.75	0.28-1.63	28	1.18	0.78-1.70
MN of ovary, fallopian tube, and broad ligament	69	0.88	0.68-1.11	20	0.96	0.59-1.48	49	0.85	0.63-1.13
MN of other female genital organs	9	1.75	0.80-3.32	3	2.38	0.49-6.95	6	1.54	0.57-3.36
MN of male genital organs	87	0.96	0.77-1.18	9	0.57	0.26-1.09	78	1.04	0.82-1.30
MN of prostate	87	0.99	0.80-1.23	9	0.61	0.28-1.16	78	1.07	0.85-1.34
MN of urinary organs	109	1.08	0.89-1.31	31	1.43	0.97-2.02	78	0.99	0.78-1.24
MN of kidney	56	1.03	0.78-1.34	14	1.12	0.61-1.88	42	1.01	0.73-1.36
MN of bladder and other urinary organs	53	1.15	0.86-1.50	17	1.84	1.07-2.95	36	0.97	0.68-1.35
MN of other and unspecified sites	335	1.06	0.95-1.18	80	1.06	0.84-1.32	255	1.06	0.94-1.20
MN of bone	6	1.12	0.41-2.44	3	2.25	0.46-6.59	3	0.75	0.15-2.18
Melanoma	47	1.20	0.88-1.60	6	0.60	0.22-1.30	41	1.41	1.01-1.91
Other MN of skin	9	0.93	0.42-1.76	4	1.87	0.51-4.78	5	0.66	0.21-1.54
Mesothelioma	7	1.53	0.61-3.15	1	0.94	0.02-5.26	6	1.70	0.62-3.71
MN of connective tissue	14	0.94	0.51-1.57	3	0.78	0.16-2.27	11	0.99	0.50-1.77
MN of brain and other parts of nervous system	67	1.01	0.78-1.28	14	0.83	0.45-1.39	53	1.07	0.80-1.40
MN of thyroid gland	3	0.52	0.11-1.53	0	0.00	0.00-2.76	3	0.68	0.14-2.00
MN of other and unspecified sites	181	1.07	0.92-1.24	49	1.27	0.94-1.68	132	1.02	0.85-1.21
Neoplasms of lymphatic and hematopoietic tissue	235	1.01	0.88-1.15	55	1.02	0.77-1.33	180	1.01	0.86-1.16
Hodgkin disease	9	0.76	0.35-1.45	4	1.28	0.35-3.27	5	0.58	0.19-1.35
Non-Hodgkin lymphoma	93	0.99	0.80-1.21	24	1.11	0.71-1.65	69	0.95	0.74-1.20
Multiple myeloma	45	1.12	0.82-1.50	4	0.45	0.12-1.14	41	1.31	0.94-1.78
Leukemia and aleukemia	88	1.02	0.82-1.25	23	1.15	0.73-1.73	65	0.98	0.75-1.24
Benign and unspecified neoplasms	30	0.90	0.61-1.29	9	1.19	0.54-2.25	21	0.82	0.51-1.26
Tuberculosis and HIV-related disease	47	1.23	0.91-1.64	32	2.80	1.91-3.95	15	0.56	0.32-0.93
Respiratory tuberculosis	3	0.47	0.10-1.36	1	0.81	0.02-4.50	2	0.38	0.05-1.39
HIV-related	44	1.45	1.06-1.95	31	3.13	2.13-4.44	13	0.64	0.34-1.09

Cause	OBS	SMR	95% CI	OBS	SMR	95% CI	OBS	SMR	95% CI
Diseases of the blood and blood forming organs	32	0.89	0.61-1.25	3	0.38	0.08-1.12	29	1.02	0.69-1.47
Diabetes mellitus	206	0.91	0.79-1.04	54	1.05	0.79-1.36	152	0.87	0.74-1.02
Mental, psychoneurotic, and personality disorders	113	0.84	0.69-1.01	39	1.40	0.99-1.91	74	0.69	0.54-0.87
Alcoholism	19	0.60	0.36-0.94	10	1.20	0.58-2.21	9	0.39	0.18-0.74
Other mental disorders	94	0.91	0.74-1.12	29	1.48	0.99-2.12	65	0.78	0.60-0.99
Dementia and Alzheimer disease [e]	116	1.04	0.86-1.24	32	1.57	1.08-2.22	84	0.92	0.73-1.14
Disorders of the nervous system and sense organs	254	1.09	0.96-1.24	60	1.22	0.93-1.57	194	1.06	0.92-1.22
Multiple sclerosis	14	0.91	0.50-1.53	3	0.68	0.14-1.98	11	1.01	0.50-1.81
Other diseases of the nervous system and sense organs	240	1.11	0.97-1.26	57	1.27	0.96-1.65	183	1.07	0.92-1.23
Amyotrophic lateral sclerosis [e]	31	1.34	0.91-1.90	11	1.95	0.97-3.50	20	1.14	0.70-1.76
Parkinson disease [e]	45	1.14	0.83-1.52	3	0.42	0.09-1.22	42	1.30	0.94-1.76
Diseases of the heart	2520	0.96	0.92-1.00	593	1.14	1.05-1.23	1927	0.92	0.87-0.96
Rheumatic heart disease, including fever	28	0.71	0.47-1.03	6	0.71	0.26-1.55	22	0.71	0.45-1.08
Hypertension with heart disease	60	0.71	0.54-0.92	19	1.07	0.65-1.68	41	0.62	0.44-0.84
Ischemic heart disease	1984	0.96	0.92-1.01	454	1.12	1.02-1.23	1530	0.92	0.88-0.97
Chronic disease of endocardium	44	0.87	0.63-1.17	7	0.69	0.28-1.42	37	0.91	0.64-1.26
Cardiomyopathy	86	1.08	0.86-1.33	27	1.50	0.99-2.18	59	0.96	0.73-1.23
Conduction disorder	148	1.08	0.91-1.27	42	1.46	1.05-1.98	106	0.98	0.80-1.19
Other diseases of the heart	170	0.98	0.84-1.14	38	1.12	0.79-1.54	132	0.95	0.79-1.12
Other diseases of the circulatory system	734	0.96	0.89-1.03	136	0.89	0.74-1.05	598	0.98	0.90-1.06
Cerebrovascular disease	478	0.94	0.85-1.02	89	0.88	0.71-1.09	389	0.95	0.86-1.05
Hypertension without heart disease	43	0.96	0.69-1.29	3	0.32	0.07-0.95	40	1.12	0.80-1.53
Diseases of the arteries, veins and lymphatic vessel	213	1.02	0.88-1.16	44	1.02	0.74-1.37	169	1.02	0.87-1.18
Diseases of the respiratory system	725	0.98	0.91-1.06	196	1.29	1.11-1.48	529	0.91	0.83-0.99
Influenza	3	0.59	0.12-1.73	0	0.00	0.00-3.67	3	0.74	0.15-2.15
Pneumonia (except newborn)	213	1.07	0.93-1.23	51	1.32	0.98-1.74	162	1.01	0.86-1.18
Chronic obstructive pulmonary disease	400	1.00	0.91-1.10	118	1.40	1.16-1.68	282	0.90	0.79-1.01
Asthma	16	0.97	0.55-1.57	6	1.47	0.54-3.21	10	0.80	0.38-1.47
Other respiratory diseases	89	0.81	0.65-1.00	21	0.90	0.56-1.38	68	0.78	0.61-0.99
Diseases of the digestive system	320	0.85	0.76-0.95	96	1.11	0.90-1.36	224	0.78	0.68-0.89
Diseases of the skin and subcutaneous tissue	8	0.75	0.32-1.48	0	0.00	0.00-1.58	8	0.96	0.41-1.89
Diseases of the musculoskeletal system and connective system	33	0.85	0.58-1.19	10	1.09	0.52-2.00	23	0.78	0.49-1.16
Diseases of the genito-urinary system	136	0.89	0.75-1.05	34	1.08	0.74-1.50	102	0.84	0.69-1.02
Chronic and unspecified nephritis and renal failure and other renal sclerosis	90	1.12	0.90-1.38	25	1.46	0.95-2.16	65	1.03	0.80-1.32
Symptoms and ill-defined conditions	45	0.52	0.38-0.70	16	0.79	0.45-1.29	29	0.44	0.29-0.63
Transportation injuries	167	0.78	0.66-0.91	60	0.94	0.72-1.21	107	0.71	0.58-0.86
Falls	39	0.70	0.50-0.96	2	0.17	0.02-0.61	37	0.85	0.60-1.17
Other injury	120	0.79	0.66-0.95	49	1.19	0.88-1.57	71	0.65	0.50-0.81
Intentional self-harm	110	0.73	0.60-0.88	39	0.92	0.66-1.26	71	0.66	0.51-0.83
Assault and homicide	23	0.44	0.28-0.67	13	0.82	0.44-1.40	10	0.28	0.13-0.51
Other causes	207	0.91	0.79-1.04	64	1.17	0.70-1.49	143	0.82	0.69-0.97
Unknown cause	226			64			162		

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; OBS, observed deaths; MN, malignant neoplasm; SMR, standardized mortality ratio.

[a]   All results exclude workers who died ($n = 61$) or were lost to follow-up ($n = 324$) prior to the rate file begin date (1 January 1960).

[b]   International Classification of Disease (ICD) codes were mapped to underlying cause of death categories as described by Robinson et al. (2006) and tabulated on the NIOSH website (http://www.cdc.gov/niosh/ltas/rates.html). All major categories of causes of death are presented. Some minor categories of causes of death are not presented because there were two or fewer deaths in the category or the category was not of *a priori* interest and the SMR was not in statistically significant excess.

[c] Short-term workers worked less than 3 months; long-term workers worked 3 months or longer.

[d] The SMR is the ratio of observed to expected (based on US underlying cause of death rates, 1960-2007) deaths; 95% CI was estimated based on the Poisson distribution.

[e] Neurodegenerative outcomes based on US underlying cause of death rates, 1960-2007. Dementia and Alzheimer disease (excluding arteriosclerotic dementia) includes ICD codes 304-305 (revision 7), 290.0-290.1 (revision 8), 290.0-290.3 and 331.0 (revision 9), and G30 (revision 10); amyotrophic lateral sclerosis includes ICD codes 306 (revision 7), 348.0 (revision 8), 335.2 (revision 9), and F01 (revision 10); and Parkinson disease includes ICD codes 350 (revision 7), 342 (revision 8), 332 (revision 9), and G20-G21 (revision 10).

Table 4

Standardized mortality ratios for outcomes of *a priori* interest among long-term workers (3 months or longer) by plant, NIOSH Capacitor Cohort, 1960-2008 [a]

Underlying cause of death [b]	Indiana plant (*n* = 2,794)			Massachusetts plant (*n* = 7,499)			New York plant (*n* = 6,925)		
	OBS	SMR [c]	95% CI	OBS	SMR	95% CI	OBS	SMR	95% CI
All causes	800	0.79	0.73-0.84	2998	1.02	0.98-1.05	2635	0.92	0.89-0.96
All cancers	246	0.83	0.73-0.94	860	0.99	0.92-1.05	801	1.02	0.95-1.09
MN of stomach	4	0.73	0.20-1.87	28	1.26	0.83-1.81	14	0.59	0.32-0.99
MN of intestine except rectum	21	0.85	0.53-1.30	80	1.01	0.80-1.25	74	0.98	0.77-1.23
MN of rectum	2	0.43	0.05-1.55	15	0.86	0.48-1.41	24	1.52	0.97-2.26
MN of biliary passages, liver and gall bladder	5	0.7	0.23-1.63	22	1.05	0.66-1.59	17	0.77	0.45-1.24
MN of breast	8	0.64	0.28-1.26	99	0.91	0.74-1.11	58	0.86	0.65-1.11
MN of other and unspecified parts of uterus	0	0	0-2.11	18	1.22	0.72-1.93	10	1.09	0.52-2.01
MN of ovary, fallopian tube, and broad ligament	1	0.24	0.01-1.34	34	0.99	0.69-1.39	14	0.65	0.36-1.09
MN of prostate	9	0.62	0.28-1.18	25	1.08	0.70-1.59	44	1.25	0.91-1.68
Melanoma	13	2.58	1.38-4.42	8	0.63	0.27-1.24	20	1.71	1.04-2.64
MN of brain and other parts of nervous system	17	2.06	1.20-3.29	18	0.93	0.55-1.47	18	0.98	0.58-1.55
MN of thyroid	1	1.71	0.04-9.52	1	0.49	0.01-2.72	1	0.49	0.01-2.74
Non-Hodgkin lymphoma	11	0.94	0.47-1.67	39	1.23	0.87-1.68	19	0.6	0.36-0.94
Multiple myeloma	2	0.4	0.05-1.46	18	1.32	0.78-2.09	21	1.74	1.08-2.66
Dementia and Alzheimer disease [d]	2	0.24	0.03-0.85	46	0.99	0.73-1.32	36	0.98	0.69-1.36
Amyotrophic lateral sclerosis [d]	2	0.72	0.09-2.59	8	1.07	0.46-2.11	10	1.37	0.66-2.53
Parkinson disease [d]	5	1.14	0.37-2.67	16	1.17	0.67-1.89	21	1.48	0.91-2.26

Abbreviations: CI, confidence interval; OBS, observed deaths; MN, malignant neoplasm; SMR, standardized mortality ratio.

[a] All results are for long-term workers (employed for 3 months or longer) and exclude workers who died (*n* = 58) or were lost to follow-up (*n* = 155) prior to the rate file begin date (1 January 1960).
[b] For cause of death outcomes of *a priori* interest. Complete results available from the first author.
[c] The SMR is the ratio of observed to expected deaths (based on state-specific underlying cause of death rates, 1960-2007); 95% CI was estimated based on the Poisson distribution.
[d] Neurodegenerative outcomes based on US underlying cause of death rates, 1960-2007.

Table 5

Standardized mortality ratios for outcomes of *a priori* interest among long-term workers (3 months or longer) by sex, NIOSH Capacitor Cohort, 1960-2008 [a]

Underlying cause of death [b]	Women (n = 8,642)			Men (n = 8,576)		
	OBS	SMR [c]	95% CI	OBS	SMR	95% CI
All causes	3155	0.97	0.94-1.01	3278	0.91	0.88-0.94
All cancers	983	1.06	1.00-1.13	924	0.97	0.90-1.03
MN of stomach	13	0.75	0.40-1.28	33	1.25	0.86-1.75
MN of intestine except rectum	102	1.23	1.00-1.49	73	0.92	0.72-1.16
MN of rectum	22	1.52	0.95-2.30	19	1.07	0.65-1.67
MN of biliary passages, liver and gall bladder	25	1.12	0.73-1.65	19	0.70	0.42-1.10
MN of breast	163	0.96	0.82-1.12	2	1.68	0.20-6.07
MN of other and unspecified parts of uterus	28	1.18	0.78-1.70			
MN of ovary, fallopian tube, and broad ligaments	49	0.85	0.63-1.13			
MN of prostate				78	1.07	0.85-1.34
Melanoma	12	1.11	0.57-1.94	29	1.59	1.06-2.28
MN of brain and other parts of nervous system	19	0.85	0.51-1.33	34	1.25	0.87-1.75
MN of thyroid	2	0.79	0.10-2.84	1	0.54	0.01-3.04
Non-Hodgkin lymphoma	37	1.07	0.75-1.48	32	0.84	0.58-1.19
Multiple myeloma	20	1.30	0.80-2.01	21	1.32	0.82-2.01
Dementia and Alzheimer disease [d]	62	0.96	0.73-1.23	22	0.82	0.51-1.24
Amyotrophic lateral sclerosis [d]	16	1.90	1.09-3.09	4	0.44	0.12-1.12
Parkinson disease [d]	16	1.12	0.64-1.81	26	1.45	0.94-2.12

Abbreviations: CI, confidence interval; OBS, observed deaths; MN, malignant neoplasm; SMR, standardized mortality ratio.

[a]   All results are for long-term workers (employed for 3 months or longer) and exclude workers who died (n = 58) or were lost to follow-up (n = 155) prior to the rate file begin date (1 January 1960).
[b]   For cause of death outcomes of *a priori* interest. Complete results available from the first author.
[c]   The SMR is the ratio of observed to expected (using United States underlying cause of death rates, 1960-2007) deaths; 95% CI was estimated based on the Poisson distribution .
[d]   Neurodegenerative outcomes based on US underlying cause of death rates, 1960-2007.

Table 6

Standardized rate ratio analyses among long-term workers (3 months or longer), NIOSH Capacitor Cohort, 1960-2008

Underlying cause of death [a]	Estimated cumulative PCB exposure (unit-days)												P value [c]
	0-<40,000			40,000-<150,000			150,000-<600,000			≥600,000			
	OBS	SRR [b]	95% CI	OBS	SRR	95% CI	OBS	SRR	95% CI	OBS	SRR	95% CI	
All causes	1600	1	[ref]	1467	1.08	1.00-1.17	1531	1.19	1.10-1.28	1547	1.07	0.98-1.17	0.60
All cancers	511	1	[ref]	462	1.14	1.00-1.29	417	1.10	0.96-1.25	427	1.17	0.98-1.39	0.24
MN of stomach	4	1	[ref]	6	2.11	0.58-7.67	15	5.14	1.66-15.9	17	8.37	2.52-27.8	<0.001
MN of intestine except rectum	41	1	[ref]	48	1.42	0.92-2.19	35	1.08	0.68-1.72	43	0.93	0.60-1.45	0.36
MN of rectum	10	1	[ref]	9	1.11	0.43-2.84	6	0.76	0.26-2.18	14	1.56	0.60-4.02	0.50
MN of biliary passages, liver and gall bladder	11	1	[ref]	9	0.98	0.39-2.48	6	0.76	0.27-2.17	15	1.53	0.66-3.58	0.27
MN of breast	41	1	[ref]	43	1.24	0.80-1.94	29	0.87	0.53-1.41	39	0.90	0.57-1.42	0.31
MN of other and unspecified parts of uterus	6	1	[ref]	5	1.06	0.31-3.60	6	1.29	0.40-4.19	9	1.35	0.46-3.98	<0.001
MN of ovary, fallopian tube, and broad ligament	6	1	[ref]	14	3.22	1.19-8.69	9	1.81	0.62-5.26	12	2.31	0.83-6.42	0.40
MN of prostate	17	1	[ref]	21	1.73	0.90-3.32	14	1.28	0.62-2.64	25	2.11	1.08-4.13	0.14
Melanoma	21	1	[ref]	5	0.34	0.13-0.92	10	0.78	0.37-1.68	3	0.20	0.06-0.70	0.21
MN of brain and other parts of nervous system	22	1	[ref]	9	0.53	0.24-1.16	13	0.82	0.41-1.64	7	0.58	0.21-1.56	0.67
Non-Hodgkin lymphoma	17	1	[ref]	23	1.84	0.95-3.55	14	1.23	0.58-2.65	12	1.03	0.44-2.45	0.78
Multiple myeloma	9	1	[ref]	9	1.02	0.39-2.65	9	1.12	0.43-2.92	12	1.31	0.52-3.32	<0.001
Dementia and Alzheimer disease	20	1	[ref]	10	0.54	0.25-1.17	16	0.77	0.39-1.51	35	1.29	0.73-2.29	0.13
Amyotrophic lateral sclerosis	6	1	[ref]	2	0.38	0.08-1.93	5	0.95	0.28-3.18	7	1.44	0.41-5.03	0.22
Parkinson disease	9	1	[ref]	12	1.68	0.68-4.11	7	0.89	0.32-2.47	11	1.19	0.47-2.98	0.97

Abbreviations: CI, confidence interval; MN, malignant neoplasm; OBS, observed deaths; SRR, standardized rate ratio.

[a] For cause of death outcomes of interest *a priori* (thyroid cancer was omitted due to small numbers).
[b] SRR, comparing mortality rates in higher quartiles with rate in the lowest quartile, obtained by direct standardization. Quartiles based on cumulative PCB exposure among decedents with 90 days or more of employment.
[c] P value for test of linear trend in the standardized rates.

Table 7

Poisson regression models among long-term workers (3 months or longer) for selected underlying cause of death outcomes, NIOSH Capacitor Cohort

	Rate ratio (95% confidence interval) [a]				
	Continuous models [b]		Categorical models [c]		
Cause of death	Unconstrained [d]	Constrained [d]	Estimated cumulative PCB exposure (unit-years)	Unconstrained [d]	Constrained [d]
Prostate cancer	2.22 (1.06 to 4.80)	1.73 (1.08 to 2.74)	0 to <77	1 [reference]	1 [reference]
			77 to <240	1.21 (0.58 to 2.49)	1.20 (0.61 to 2.22)
			240 to <990	1.27 (0.63 to 2.58)	1.27 (0.67 to 2.27)
			990 to <3200	1.52 (0.73 to 3.14)	1.51 (0.78 to 2.75)
			≥3200	2.30 (1.14 to 4.67)	2.28 (1.24 to 4.00)
Uterine cancer	2.88 (0.62 to 15.2)	1.70 (0.71 to 3.95)	0 to <110	1 [reference]	1 [reference]
			110 to <380	1.05 (0.30 to 3.51)	1.08 (0.34 to 2.93)
			380 to <880	1.68 (0.48 to 5.62)	1.72 (0.55 to 4.59)
			880 to <2500	1.28 (0.36 to 4.44)	1.32 (0.41 to 3.59)
			≥2500	1.30 (0.35 to 4.67)	1.34 (0.40 to 3.80)
Ovarian cancer	1.07 (0.96 to 1.15)	1.08 (0.98 to 1.16)	0 to <120	1 [reference]	1 [reference]
			120 to <250	3.29 (1.26 to 9.08)	3.47 (1.46 to 7.89)
			250 to <870	1.52 (0.54 to 4.36)	1.61 (0.64 to 3.75)
			870 to <3200	1.49 (0.52 to 4.32)	1.57 (0.61 to 3.74)
			≥3200	2.57 (0.89 to 7.60)	2.71 (1.03 to 6.58)
Stomach cancer	4.79 (1.83 to 13.3)	1.99 (1.05 to 3.71)	0 to <110	1 [reference]	1 [reference]
			110 to <650	1.48 (0.54 to 4.03)	0.95 (0.39 to 2.09)
			650 to <1000	7.07 (2.66 to 19.0)	4.43 (1.91 to 9.41)
			1000 to <2100	5.13 (1.98 to 13.6)	3.20 (1.43 to 6.67)
			≥2100	3.04 (1.11 to 8.42)	1.88 (0.80 to 4.07)
Multiple myeloma	1.09 (0.99 to 1.17)	1.09 (0.99 to 1.17)	0 to <54	1 [reference]	1 [reference]
			54 to <170	1.19 (0.42 to 3.45)	1.28 (0.49 to 3.11)
			170 to <980	0.78 (0.28 to 2.26)	0.84 (0.33 to 2.02)
			980 to <3300	1.27 (0.46 to 3.66)	1.37 (0.54 to 3.27)
			≥3300	1.46 (0.48 to 4.47)	1.59 (0.57 to 3.96)

[a]   Rate ratios are adjusted for age and birth year; rate ratios for stomach cancer are additionally adjusted for gender. All models incorporate the best-fitting (based on model AIC) exposure lag period: 20 years for prostate, 10 years for uterine, 5 years for ovarian, 15 years for stomach, and 10 years for multiple myeloma.

[b]   For continuous model, the rate ratio is at 1000 unit-years of lagged exposure and based on the regression model with the best-fitting (based on model AIC) exposure transformation: natural logarithm (prostate, uterine, and stomach cancers) and identity (ovarian cancer and multiple myeloma).

[c]   For categorical models, cutpoints were selected based on quintiles of the lagged exposure distribution among cases.

[d]   The unexposed baseline rate (or low exposed for the categorical model) was either unconstrained or constrained to be 180 deaths per 100,000 for prostate cancer, 17 deaths per 100,000 for uterine cancer, 31 deaths per 100,000 for ovarian cancer, 30 deaths per 100,000 for stomach cancer, and 19 deaths per 100,000 for multiple myeloma, respectively.
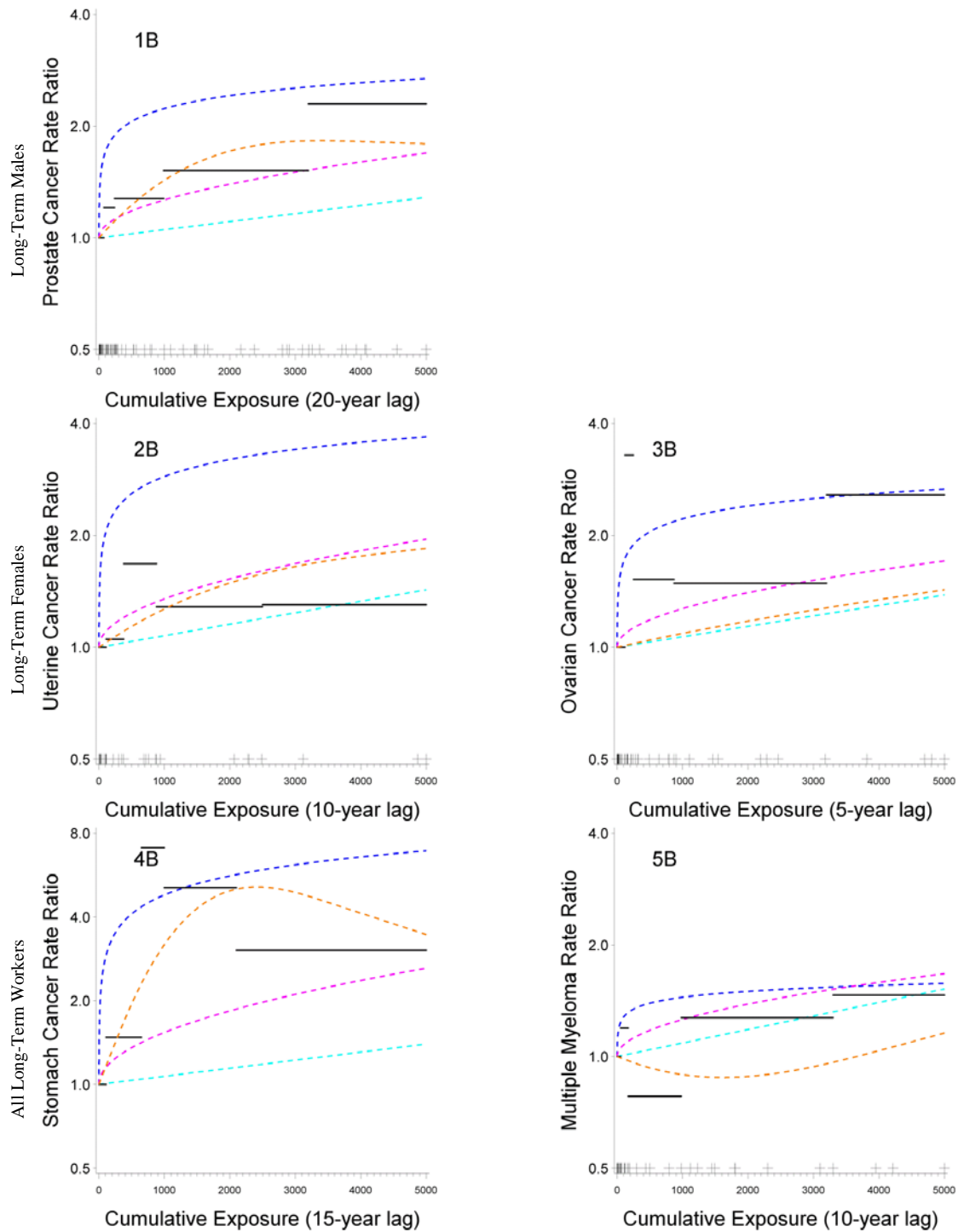
Figure 1

Poisson regression models with lagged cumulative exposure (unit-years) among long-term workers. Rate ratios are adjusted for age and year of birth for prostate, uterine, and ovarian cancer, and for gender, age, and year of birth for stomach cancer and multiple myeloma. Cumulative exposure for the cases, indicated by the cross-hatches on the horizontal axis, was truncated at 5000 unit-years for 7 prostate, 3 uterine, 5 ovarian, 3 stomach, and 3 multiple myeloma cases. Black lines indicate categorical treatment of cumulative exposure and dashed curves indicate identity (cyan), natural log (blue), square root (magenta), and restricted cubic spline (orange) transformations.