Exposure to Beryllium and Occurrence of Lung Cancer: Findings From a Cox Proportional Hazards Analysis of Data From a Retrospective Cohort Mortality Study

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Objective: *The objective was to assess highly confounded patterns in a standardized mortality ratio (SMR) analysis of lung cancer in beryllium worker cohorts.* ***Methods:*** *We used Cox proportional hazards single- and multi-variate models to assess confounding and the SMR patterns.* ***Results:*** *We confirmed the lack of association of lung cancer with time worked. We could not confirm the original study's finding of lung cancer highly associated with earlier plants and or with workers hired in the 1940s compared to the 1950s. The pattern of higher rates of lung cancer with increasing latency was attenuated when covariates were added to the model. We could not exclude that the lower SMR and hazard ratios for workers hired in the 1960s might be related to assumed lower beryllium exposures.* ***Conclusion:*** *The patterns observed provide little support for an association of lung cancer with beryllium work factors. This result is likely due to the absence in the original study of a significant overall excess of lung cancer after smoking adjustment.* (J Occup Environ Med. *2009;51:480–486*)

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Beryllium has been labeled a carcinogen in humans by the International Agency for Research in Cancer (IARC)[1] and the National Toxicology Program of the National Institute of Environmental Health Sciences.[2] Prominent among the epidemiological evidence used by IARC was a 1992 report (herein referred to as the 1992 study) discussing findings of a retrospective occupational cohort mortality study conducted by the National Institute on Occupational Safety and Health (NIOSH)[3] on 9225 workers in eight cohorts involved in the extraction of beryllium from ore and other operations involving beryllium. These workers were employed at some time between 1940 and 1969 and followed through 1988 for mortality. The 1992 study reported primarily on the results of a standardized mortality ratio (SMR) analysis, although non-SMR analyses were performed and reported sparingly.

In considering the 1992 study, IARC did not place emphasis on the relative lack of significantly elevated smoking-adjusted SMRs; the overall study smoking-adjusted SMR was 1.12, the confidence limits including 1.00, a finding which has been confirmed and extended by analysis using alternate ways of adjustment for smoking.[4] Similarly, with smoking adjustment to the SMR confidence limits in seven of the eight cohorts the SMR included 1.00. Instead, as did the 1992 study, IARC largely ignored the smoking-adjusted information in the study and focused on statistically significant smoking-unadjusted SMRs in the cohort as a whole (1.26) and in two of the eight cohorts. Most notably IARC inferred a beryllium exposure—lung cancer response from patterns observed among nonsmoking-adjusted SMRs in sub fractions of the data. For example, it was noted that nonsmoking-adjusted SMRs were greater than 1.00 in the three locations with workers hired before 1950, when exposures were believed higher than subsequently. Also SMRs were greater than 1.00 in 4 or 5 locations with workers hired between 1950 and 1959. The observation that SMRs decreased progressively in workers hired before 1950, from 1950 to 1959, and after 1959 was combined with the assumption of a progressive decrease in exposure levels to infer a beryllium exposure – lung cancer response. These observations were used to override other patterns in the data that argued against an exposure-disease relationship. For instance, categories of workers with increasing duration of employment did not have higher SMRs.

There are difficulties inferring patterns among SMRs derived from different cohorts and from sub-analyses of cohorts. As products of indirect standardization, SMRs on different populations are, strictly speaking, not comparable, and are ecologic in nature. Lung cancer SMRs are particularly problematic, because of the instability of lung cancer rates relative to birth cohorts, particularly for persons born between 1870 and 1910, a period in which lung cancer rates across the US rose rapidly with time due to changes in smoking habits. In addition to time, smoking habits have differed by locality, gender, race, social class, and urban-rural status, with consequent implications for lung cancer mortality. Most critical, however, is that the observations reported in the 1992 study and relied on by IARC were highly interrelated and hence highly mutually confounded. SMRs were found to differ by plant, by date of hire, and by length of follow-up. The two earlier plants with the smoking-unadjusted SMRs with confidence limits that did not include 1.0 had larger fractions of workers hired before 1950 and with longer length of follow-up.

The purpose of this study was to analyze the same data used in the Ward 1992 study with a Cox proportional hazards analysis, comparing workers to each other, and comparing hazard ratio (HR) patterns in this analysis with SMR patterns observed in the 1992 study. The objective of this analysis is to address whether the SMR and HR patterns support the hypothesis that there is an association between work with beryllium and the development of lung cancer. A second objective was to utilize the capabilities of the proportional hazard model to examine confounding, and thereby refine the analysis.

Methods

Methods Used in this Analysis

We used a data file supplied by NIOSH containing the data from the 9225 members of the eight cohorts that were used in the 1992 study, including coding of cause of death as lung cancer. By data use agreement, we did not identify any subject. As a consequence, we could not independently ascertain the accuracy of any portion of the data file. We have used it as supplied to ensure comparability of the analyses. We calculated descriptive statistics that summarize demographics and employment patterns of the workers in each facility (Table 1). As in the original article, workers employed in more than one plant or whose plant of employment was unknown were grouped into cohorts labeled multi and unknown, respectively.

We used Cox proportional hazards model analytic methods to examine relationships between demographic and employment patterns in those workers who died of lung cancer compared with other workers. All statistical analyses described below were performed using release 10.0 of the statistical package Stata.[5]

Because there was considerable diversity among the plants with respect to the proportion of person-years of follow-up at the older ages (Table 1, row 11), and since lung cancer mortality increases steeply with age, especially after age 50, we calculated age adjusted rates for each plant using the indirect method[6] with the age specific mortality rate in each of four age groups (under 50, 50 to 59, 60 to 69, and 70+) in the cohort as a whole serving as the standard (Table 1).

HRs were estimated using Cox proportional hazard regression analysis[7] with the time variable being age. The workers entered the cohort on first employment at the plant and exited the cohort at death or at the date of last ascertainment, December 31, 1988. Wald tests[5] were used to examine hypotheses concerning differences among HRs.

Covariates Used in the Cox Proportional Regression Analysis

When we looked at the six covariates of greatest interest, we found many strong pair-wise correlations between these covariates. We decided to conduct each analysis with no covariates, with the two we thought most important and with all the covariates. The covariates thought most important were date of birth, due to the strong variation in rates of lung cancer by birth cohort, and person-years of follow-up, due to person-years being strongly related to lung cancer SMR in the 1992 study and associated with date of hire and plant. These are used in the covariate analyses (Table 2) and were defined as follows.

Date of Birth. We grouped date of birth into four categories: before 1910, 1911–1919, 1920–1929, and 1930 and later.

Person-Years of Follow-Up. We grouped person-years of follow-up, the time from hire to death or censor alive, into three categories: less than

TABLE 1
Characteristics of Workers by Cohort

Variable (Years of Operation)	Lorain (1935–48)	Lucky (1950–58)	Elmore (1958–)	Cleveland (1937–73)	Reading (1935–2000)	Hazleton (1958–78)	Multi	Unknown	Total
Total workers	1,192	405	1,323	1,593	3,569	590	257	296	9,225
Percentage of workers hired									
1940s and before	99.3	19.5	—	19.7	63.4	—	53.3	14.9	43.6
1950s	0.7	80.2	42.3	47.3	22.5	38.1	41.6	43.6	31.5
1960s	—	0.2	57.7	33.0	14.1	61.9	5.1	41.6	24.9
Mean age at hire	29	29	27	32	32	32	30	33	31
Mean year of hire	1944	1951	1962	1956	1949	1962	1949	1958	1953
Employed <1 yr %	84.6	61.5	29	47.2	53.8	19.7	0.8	44.3	49.4
Mean employment tenure (years)	0.65	1.27	8.14	3.84	5.32	9.65	18.87	2.15	5.24
25th percentile	0.04	0.25	0.62	0.31	0.17	1.60	7.51	0.5	0.21
Median	0.15	0.57	4.06	1.13	0.78	8.09	19.93	1.00	1.02
75th percentile	0.51	1.81	15.14	4.41	4.58	17.61	30.26	2.25	5.81
Mean person-yr (called latency in original article[1])	32.5	32.7	25.1	28.5	30.3	25.1	34.0	25.5	29.3
Total person-yr	38,239	13,232	33,252	45,369	108,186	14,837	8,707	7,511	269,333
Proportion of total person-yr at ages above 60 yr	0.19	0.14	0.07	0.17	0.2	0.09	0.17	0.18	0.17
Proportion alive at date of censor (1988)	50.0	68.9	86.5	70.3	55.1	83.9	64.6	73.3	65.9
Percentage of workers followed to age 60 and above	72.0	58.7	21.2	57.4	62.9	31.7	67.3	43.2	54.4
Lung cancer deaths	57	9	15	44	120	13	13	9	280
Crude lung cancer mortality rate* (95% CI)	1.49 (1.15–1.93)	0.69 (0.35–1.31)	0.45 (0.27–0.75)	0.97 (0.72–1.30)	1.11 (0.93–1.33)	0.88 (0.56–1.51)	1.49 (0.68–2.30)	1.20 (0.42–1.98)	1.04 (0.92–1.16)
Lung cancer mortality (95% CI)†	1.34 (1.04–1.74)	0.72 (0.37–1.38)	0.88 (0.53–1.47)	0.96 (0.71–1.29)	0.97 (0.74–1.15)	1.29 (0.93–1.07)	1.45 (0.65–2.25)	1.16 (0.39–1.93)	1.04 (0.92–1.16)

*Per 1,000 person-yr.
†Per 1,000 person-yr adjusted for total person-yr at ages <50, 50–59, 60–69, and 70+.

15 years, 15 to 29 years, and above 30 years.

The other four variables, cohort, employment tenure, date of hire, and age at hire, were included in the comprehensive analysis in which all six variables were present. These four variables are defined below.

Cohorts. There were eights cohort categories consisting of five individual facilities, Reading, Lorain, Hazleton, Luckey, and Elmore, one composite facility, Cleveland, comprised of the Perkins and St. Clair plants populations, and the categories of beryllium workers who either worked at more than one plant (multi) or whose site of work was unknown (unknown).

Employment Tenure. Employment tenure, the length of time from first hire to final termination, was grouped in four quartile categories, as follows: 2 days to under 0.21 years, 0.22 to 1.02 years, 1.03 to 5.81 years, and 5.82 years and over.

Date of Hire. We formed three categories of date of hire, 1935–1949, 1950–1959, and 1960–1969.

Age at Hire. We formed four quartile categories of age at hire as follows: under 22 years, 22 to 27.5, 27.5 to 27.6 to 37.2, and over 37.2 years.

Results

Overview

In the 1992 study, three patterns of SMRs were considered highly important to the interpretation of the data. Much of the analysis was conditioned on the statistically significant SMRs in the Lorain (1.69) and Reading (1.24) cohorts. Ignored were the lower SMR in the contemporaneous Cleveland cohort (1.08) and the intermediate SMR (1.39) in the later Hazleton cohort, because the confidence intervals of the SMRs for these cohorts included 1.0. In the HR analysis, in which none of the cohorts differ significantly from the reference cohort, the patterns do not support the hypothesis that the earlier date of originations of the cohort

TABLE 2

Lung Cancer SMRs From the 1992 Study Compared With Univariate and Multivariate Lung Cancer Hazard Ratios

Variable	SMR US	Relative SMR	Hazard Ratio Univariate (95% CI)	Hazard Ratio Date of Birth and Year of Follow-Up as Covariates§	Hazard Ratio Full Six Variable Model§
Cohort total	1.26*	—	—	—	—
Plants					
Cleveland	1.08	1	1	1	1
Lorain	1.69*	1.56	1.36 (0.92–2.02)	1.39 (0.92–2.11)	1.26 (0.80–1.99)
Luckey	0.82	0.76	0.76 (0.37–1.56)	0.74 (3.59–1.51)	0.62 (0.30–1.28)
Elmore	0.99	0.92	1.00 (0.56–1.80)	1.04 (0.57–1.89)	1.20 (0.65–2.22)
Reading	1.24†	1.15	0.98 (0.69–1.38)	1.05 (0.74–1.51)	1.00 (0.69–1.48)
Hazleton	1.39	1.29	1.44 (0.77–2.67)	1.48 (0.78–2.77)	1.87 (0.96–3.61)
Multi	1.67	1.55	1.56 (0.84–2.89)	1.50 (0.80–2.80)	1.64 (0.84–3.18)
Unknown	1.33	1.23	1.18 (0.57–2.41)	1.23 (0.60–2.53)	1.19 (0.58–2.46)
Employment tenure					
<1 yr	1.32*	1	1	1	1
1–5 yr	1.19	0.90	0.89 (0.66–1.20)	0.93 (0.69–1.26)	0.99 (0.73–1.34)
5–10 yr	1.26	0.95	0.94 (0.59–1.48)	1.01 (0.64–1.60)	0.95 (0.59–1.54)
>10 yr	1.19	0.90	0.80 (0.578–1.11)	0.83 (0.59–1.16)	0.75 (0.51–1.11)
Date of hire					
1935–50	1.42†	1	1	1	1
1950–59	1.24	0.87	1.08 (0.83–1.41)	0.94 (0.69–1.28)	1.12 (0.77–1.63)
1960–69	0.62	0.44	0.58 (0.35–0.94)	0.48 (0.27–0.85)	0.54 (0.29–1.03)
Date of birth				Person-yr of follow-up only	
Before 1900	1.20‡	1	1	1	1
1900–1910	1.36‡	1.13	2.25 (1.44–3.51)	2.00 (1.26–3.18)	2.19 (1.33–3.60)
1910–1929	1.27‡	1.06	2.76 (1.81–4.20)	2.23 (1.38–3.60)	2.35 (1.26–4.37)
1930+ after	0.63‡	0.53	1.74 (0.75–4.02)	1.34 (0.56–3.23)	1.41 (0.47–4.22)
Age at hire					
Quartile in yr					
Under 22	1.12‡	1	1	1	1
22–27.5	1.49‡	1.33	1.16 (0.75–1.80)	1.16 (0.74–1.81)	1.17 (0.78–1.83)
27.6–37.2	1.20‡	1.07	0.83 (0.55–1.27)	0.79 (0.49–1.27)	0.83 (0.51–1.35)
Over 37.2	1.21‡	1.08	0.55 (0.36–0.84)	0.66 (0.36–1.23)	0.77 (0.40–1.49)
Person-yr of follow-up				Date of birth only	
<15 yrs	0.89	1	1	1	1
15–30 yrs	1.20†	1.35	1.64 (1.08–2.50)	1.33 (0.85–2.08)	1.19 (0.73–1.93)
>30 yrs	1.46*	1.64	2.26 (1.48–3.46)	1.55 (0.95–2.53)	1.08 (0.56–2.10)

*Two-sided *P* value less than 0.01.
†Two-sided *P* value less than 0.05.
‡SMRs calculated in this study.
§Date of birth (before 1910, 1911–1919, 1920–1929, and 1930 and later), Person-yr of follow-up (less than 15 yr, 15 to 30 yr, and above 30 years, Cohort (Reading, Lorain, Hazleton, Luckey and Elmore, Cleveland, Multi, and Unknown), Employment tenure (2 d to under 0.21 yr, 0.22 to 1.02 yr, 1.03 to 5.81 yr, and 5.82 yr and over), Date of hire (1935–1949, 1950–1959, and 1960–1969), Age at hire (under 22.0, 22 to 27.5, 27.5 to 27.6 to 37.2, and over 37.2 yr).

was associated with a higher relative index of lung cancer, with or without adjustment for covariates.

The second was the pattern of SMR by date of hire, the categories being <1950, 1950–1959, and 1960–1969, the assumption being that exposure were very much higher in the earliest period, <1950, and progressively lower thereafter. Although the SMR sequence 1.42, 1.24, 0.62 is very dramatic, the big differential is between the 1950s and 1960s where the reduction is 50%, rather than between the pre-1950s and the 1950s where the reduction is small (13%). This was clear in the HR analysis, where HR did not decrease going from persons hired in the 1940s to those hired in the 1950s and, like the SMR, underwent a major reduction in the 1960s hire subcohort. Because it was assumed in the 1992 study that exposures declined progressively and significantly across these three sub-cohorts, the declining SMRs were interpreted as an exposure-response relationship. The failure to find a 1940s to 1950s effect suggests the need to revise this interpretation.

The third was length of follow-up (latency). Person-years close to hire did not have elevated SMRs but with time from hire the SMR for the subsequent categories of length of follow-up had increasing SMRs (0.89, 1.20, 1.46). This pattern is also evident in the HR analysis with no covariates (1.0, 1.64, 2.26). Addition of date of birth moderates this to a pattern almost identical to that of the SMR, while the full model attenuates it almost entirely (1.0, 1.19, 1.08), and it attenuates further when the cohort variable is removed from the multivariate analysis (1.0, 1.14, 0.98). The latter raises the question of whether the increase in SMR with time from hire is a primary or a secondary effect. If the timing of a relative rise in lung cancer following exposure to beryllium is thought to be due to the exposure, the adding of covariates that are thought to model the degree of beryllium exposure, such as decade of hire and facility where worked, or that better characterize the underlying risk of lung cancer, such as birth cohort and age at hire, should accentuate the relationship rather than attenuate it.

To add perspective, we performed additional analyses of SMRs and HRs on date of birth and age at hire, which were not reported in the 1992 study. The quite different date of birth patterns in SMRs and HRs was fully predictable from the standpoint of their respective calculations. However, the SMR and HR patterns are slightly different in that the SMR for date of birth 1930+ is lower than the other three SMRs whereas this not true of the HRs, with and without covariates. Conversely, the SMR analyses by quartiles of age at hire did not show large differences, whereas the HRs decrease in the category of the oldest age at hire.

Discussion

Examination of patterns of disease in this cohort study presents challenges with respect to analysis and interpretation. Both analyses, SMR and HR, present data as ratios, using expected mortality based on US lung cancer rates, and the lung cancer experience of an index plant, Cleveland, respectively, as the denominators. As smoking tobacco in the form of cigarettes is the primary cause of lung cancer during this period, differences between the referents, the US and Cleveland, respectively, could be due to differences in effects of smoking, of beryllium or of both.

The geographical location of the Multi- and Unknown cohorts was not reported in the 1992 study, and of interest would be their distribution in terms of first plant or the company worked and last plant or company worked. For the six cohorts tied to a location, all were located in two adjacent US north-east-central states, Ohio and Pennsylvania. Their location was such that three would draw workers primarily from town-rural environments (Hazleton, Luckey, Elmore), two from small city industrialized environments (Lorain, Reading), and one from a large city heavily industrialized environment (Cleveland). This raises two pertinent questions: to what degree did smoking habits in these areas differ from US rates over time, with associated differences in the rate of lung cancer, and to what degree did other employment, antecedent or consequent to beryllium employment, contribute to risk of lung cancer? This study does not address those questions, but they are relevant to understanding the differences between the SMR and HR analyses. Both the SMRs and the HRs presented here are uncorrected for cigarette smoking or for other lung cancer-causing exposures.

To interpret the study variables in more detail, we start with the three inter-related demographic variables antecedent to beryllium exposure: date of birth, date of hire, and age at hire. In the SMR analysis, there are two straight forward findings, later date of birth (>1929) and later date of hire (>1959) are associated with a lower ratio. Age at hire is not associated with lung cancer at all. In the HR analysis date of birth demonstrates clearly the expected birth cohort differences, and date of hire looks very much like the SMR, lower for those hired after 1959. There is an additional suggestion of lower rates associated with age at hire over 27 and 37. This might be a birth cohort effect, as older age at hire is associated with earlier date of birth, but the effect is attenuated only modestly by the addition of date of birth and the other variables associated with early date of birth, eg, early hire, cohort, and long follow-up. The important observation from the standpoint of beryllium exposure is that the ratios by date of hire are not compatible with a progressive reduction of exposures from the 1940s to the 1950s to the 1960s. There was not a reduction from the 1940s to the 50s in the HR from the population hired in the 1940s to the population hired in the 1950s. From the 1950s to the 1960s there is a very large drop. The HR and SMR patterns are similar. Can the 56% fall in SMR to well below 1.00 and the similar fall in HR be interpreted as a beryllium effect? Because, we doubt that even lowered beryllium exposure or any other industrial exposure would cause the SMR to fall to well below 1.0, there may be an additional explanation, eg, a reduction (compared to the US) in cigarette smoking rates over time among the workers in the plants which were hiring in the 1960s, primarily Elmore. Our ability to interpret beyond this is limited by the gaps in overlap in the dates of hire of the separate cohorts or in the length of follow-up. These gaps may limit the correction of confounding via introduction of covariates into the regression model.

Turning to the three variables that commence with hire into a beryllium exposed cohort, the plant where employed, length of employment, and length of follow-up, we face the same limits in control of the confounding between these variables. Some plants, Lorain and Luckey, have no long tenure workers. Some have a low percentage of persons followed to the age of high incidence of lung cancer, 60 years and up, such as Elmore, and some a large percentage, such as Lorain and Reading. The median time worked varies from 0.15 (Lorain) to 8.09 (Hazleton) years. There is a very small decrease in SMR and HR with longer time worked (SMR: 1.32, 1.19, 1.26, 1.19; HR: 1.0, 0.90, 0.95, 0.90). But the interplant heterogeneity is marked, the two plants with the highest lung cancer age adjusted mortality rates (Table 1) SMRs and HRs, Hazleton and Lorain, having, respectively, the greatest and least mean length of employment.

The 1992 study appears to have been interpreted by sorting first on statistical significance in interpreting Lorain and Reading as the plants with a clear beryllium-lung cancer relationship, even though Reading ranked fifth of the eight cohorts in SMR. Looking at the patterns in both the HR and the SMR analyses, Lorain's rank varies from first to third, and so does Hazleton, whereas Reading varies from fifth to seventh among the cohorts. Thus, the patterns from simple ranking of the magnitudes of SMRs and HRs give a different pattern from the ranking after discounting based on the number of subjects or person years (width of confidence intervals). Interpreting the plant SMRs with respect to other factors yields no clear patterns. Early plants (Lorain, Reading, Cleveland) may be high or low, the middle plant (Luckey) is low, and the later plants (Hazelton, Elmore) may be high or low.

Increasing person-years of follow-up, or time from hire, was associated with increases in both SMR and HR., except in the full HR model, which may be highly important. The 1992 study described this relationship between length of follow-up and SMR in the results and several tables but did not refer to it in either the discussion or in the summary. In contrast, the IARC review does refer to this 1992 study finding in their summary of the human carcinogenicity data. If one considers that the mean age of hire in the 1992 study was 31, at 15 years latency the age would be 46 and at 30 years, 61. This indicates that for most subjects the 0 to 15 interval would be at very low risk for lung cancer, the 15 to 29 interval would be a period of rising, higher risk, and the 30+ interval the period of highest risk. This makes the HR results, even corrected for date of birth, highly understandable, as they reflect this rising risk with age. When date of birth is added the trend in HRs attenuates slightly. When cohort, date of hire, age at hire, and length of employment are added the trend in HRs attenuates completely. All of the variables added to the model are potential confounders of the HR for latency and lung cancer as they may be associated with both.

Sources of Error

This analysis concerns lung cancer for two beryllium work factors (plant and employment tenure) and several demographic factors (date of birth, date of hire, age at hire, and length of follow-up). It is not adjusted for smoking, which was the primary cause of lung cancer during this period. Thus, the patterns are interpretable only with the assumption that smoking practices did not confound any pattern of interest. The analysis does not contain any actual data on beryllium exposure, and inferences of exposure-response must include assumptions about connections between the measured factors and beryllium exposure levels. We did not adjust in our thinking for *P* values or confidence intervals when inspecting reviewing patterns. There is doubtless more instability in the SMRs and HRs derived from smaller cohorts, and cohorts with fewer person-years as a result of fewer years of follow-up, but although the true value might be higher or lower, we considered the estimates to be unbiased.

Conclusions

Based on our Cox proportional hazards model analysis of the NIOSH cohort data, and examination of the HR patterns in this analysis along with the SMR patterns, all unadjusted for smoking, we conclude that:

1. Use of statistical significance to separate the importance of the Lorain and Reading plant SMRs from those of the other cohorts produces a different pattern analysis than does one which that considers the magnitude of the SMRs and HRs without editing on confidence intervals or *P* values.
2. There is little evidence that the cohort SMRs and HRs differ from each other. This is not surprising given the relatively narrow range of all the cohort SMR and HR results, 0.62 to 1.87.
3. The date of earliest hire into each cohort is not related to the cohort SMRs and HRs.
4. Neither beryllium employment tenure nor age at hire (age at first exposure to beryllium) are related to lung cancer risk.
5. Interpretation of lower SMRs and HRs in persons first hired in the 1960s and in persons with shorter length of follow-up, is problematic as they are mutually confounded. In the full model, the lower HR in the 1960s hires persists while the length of follow-up effect is attenuated, suggesting the 1960s effect is real and the length of follow-up effect is not. It cannot be excluded that the lower SMR and HRs in the persons hired in the 1960s may be related to lower exposures in the 1960s.

This analysis of smoking-unadjusted SMR and HR patterns in eight cohorts of beryllium workers finds little to suggest that beryllium exposure is influencing the occurrence of lung cancer with the possible exception that if beryllium exposure was significantly reduced in persons hired in the 1960s compared to earlier. The lack of patterns linking lung cancer to beryllium exposure is likely related to the finding in both the original 1992 study[3] and the subsequent reanalysis[4] that with smoking adjustment there was not an overall excess of lung cancer in the eight cohorts of beryllium workers.

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