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An Investigation into an Excess of Cancer of Other and Unspecified Sites Among Chemical Workers

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ABSTRACT

Earlier, we reported an excess of mortality from cancer of other and unspecified sites among 37,682 male employees of Dow Chemical facilities in Midland and Bay City, Michigan. A follow-up study was conducted and has found the excess to be principally attributable to three factors: 1) the occurrence of eleven deaths in the cohort from malignant mesothelioma, site unspecified; 2) the unavailability to our nosologist of additional diagnostic information obtained by the states for twelve of the deaths, which would have allowed coding them to specific cancer sites; and 3) the residence of a substantial share of employees within neighboring Bay County, an area known to have a death rate from ill-defined cancer which is twice the national average. Although it should be confirmed through additional studies based on a larger sample of records, we found the certification practices of a samll group of physicians were the major contributor to Bay County's high rate of ill-defined cancer. The findings are illustrative of some of the limitations associated with using vital records for occupational health research, but some constructive action steps are proposed.

INTRODUCTION

In 1987, we reported the cause-specific mortality experience of 37,682 male employees from the Midland or Bay City, Michigan facilities of The Dow Chemical Company (Bond et al, 1987). Although the number of deaths from total cancer was less than expected, there was a statistically significant excess of mortality from cancer of other and unspecified sites (169 observed vs. 125.3 expected; SMR = 135; 95% CI = 115-157). The excess appeared unrelated to each of the various factors that were examined, including: age at and year of death, duration of employment, latency, age at or year of hire, and pay status (hourly or salaried). Several alternative explanations were considered, but none could be addressed directly without undertaking further study.

One possible explanation was the excess was due to a greater than expected occurrence of deaths from one or more of the individual cancer types that are pooled together into the category "cancer of other and unspecified sites". As used in the the Monson (1974) analysis program, the category is a wastebasket for: uncommon cancers of miscellaneous sites (e.g., male breast); cancers specified as secondary (e.g., liver) or, in some instances, not specified as primary; as well as cancers with no specification of the site.

Another explanation we considered was the possibility that our nosologist was coding the death certificates without the benefit of the additional diagnostic information obtained by the State Offices of Vital Statistics through querying of the certifying physician. Not every certificate prompts a query, but unspecified cancers are among the diagnoses routinely queried by most states. Lacking the additional diagnostic information, our nosologist would arrive at a less-specific underlying cause of death code than nosologists at the state or at the National Center for Health Statistics (NCHS, 1980).

That the certification practices of one or several local physicians could be responsible was considered yet another possibility. Subsequent to conducting the original investigation, we discovered that neighboring Bay County had twice the national death rate for ill-defined cancer in the period 1970-79 (Riggan et al, 1983). Although we incorporated a comparison with seven East-Central Michigan counties in our original study, Bay County was not included among them because of differing population characteristics. Nevertheless, approximately 16% of employees from these facilities reside there.

In the present paper, we systematically investigate the degree to which each of those three possibilities contributed to the excess cancer of other and unspecified sites in the cohort.

METHODS AND MATERIALS

Certificates for the 169 deaths coded to cancer of other and unspecified sites were reviewed to distinguish the 128 which were truly unspecified from the 41 coded to miscellaneous other sites.

To determine if the cohort had experienced excess mortality from one or more of the miscellaneous cancer sites, we calculated expected numbers of deaths in the cohort using the NIOSH lifetable program (Waxweiler et al, 1983), which includes rates for several of the individual cancer sites that are pooled together in the Monson (1974) analysis program.

To evaluate the role of querying, we attempted to obtain the underlying cause of death codes which had been assigned by the states' nosologists (and presumably accepted by NCHS), either directly from the death certificate itself (the codes were often handwritten on the copy) or by arrangement with the State Offices of Vital Statistics. Of the 169 deaths in the study, we obtained the codes for 157 (92.9%). If the state code was more specific than our nosologist's code, then we concluded that the state must have had access to additional diagnostic information that was unavailable to us.

Finally, to determine whether Bay County residents were over-represented among the employee deaths from unspecified cancers, we undertook a nested case-control study. Two control groups were chosen from among other members of the cohort. The first was comprised of the 7,635 deaths from other causes. The second was a subset of the first, and was comprised of the 1,549 deaths from specified cancer sites. County of residence was abstracted from the death certificate. We then calculated the exposure odds ratio for having been a resident of Bay County. This was done both adjusted and unadjusted for age at and year of death (Mantel and Haenszel, 1959).

RESULTS

Table 1 presents observed and expected deaths, SMRs and 95% confidence intervals for the miscellaneous cancers. Small excesses were noted for connective tissue cancer and male breast cancer, and a slight deficit for liver cancer, unspecified as primary or secondary. Rates were not available from the NIOSH program (Waxweiler et al, 1983) to permit calculation of expected numbers of deaths from cancer of other endocrine glands or mesothelioma; however, the eleven deaths from mesothelioma undoubtedly represent an excess.

We compared the underlying cause of death codes assigned by state nosologists to those assigned by our nosologist and found 12 instances in which the state had coded the death to a specified cancer site.

The case-control analysis of the 116 remaining unspecified cancers revealed statistically significant elevated odds ratios for having been a resident of Bay County (Table 2). The strength of the association was unaltered by the choice of control group, or by adjustment for age at and year of death.

We further subset our cases and controls to include only those who were residents of Bay County to investigate whether the high rate of unspecified cancer could be attributed to one or several certifiers or institutions. Although one physician was listed as the certifier for six of the unspecified cancer deaths, no other individual physician was named on more than two certificates. However, when we grouped physicians by their medical degree (M.D. or D.O.), we observed a striking five-fold risk associated with the physician having been a Doctor of Osteopathy (Table 3).

DISCUSSION

Through additional investigation we were able to determine that an excess of mortality from cancer of other and unspecified sites was attributable to three independent factors.

1. The cohort experienced an excess of malignant mesothelioma, presumably as a consequence of exposure to asbestos during employment at Dow or elsewhere.

2. Because the additional diagnostic data obtained via querying by the states was not available to our nosologist for coding the underlying cause of death, a differential misclassification bias was introduced. Deaths which were coded to specific cancer sites in the national database, which formed the basis for our comparison, were coded to unspecified cancers in our data set.

3. A sizeable share of the cohort resides within Bay County, an area known to have a death rate from unspecified cancer which is twice the national average.

The cohort experienced an excess of 44 deaths from cancer of other and unspecified sites. Our best estimate is that the mesotheliomas account for 25% of that, querying by the states accounts for another 25%, and the remainder can be attributed to the high mortality rate for ill-defined cancer in neighboring Bay County.

These problems will be repeated in future investigations unless specific action is taken to prevent them. With regard to the differential misclassification bias introduced by the unavailability of queried information to our nosologist, we have been aware of the potential for this problem for several years (Bond et al, 1982). Although we always ask for any queried information from the states whenever we request death certificates, we seldom receive it. The problem could be avoided altogether, if cause of death codes were made available from the National Death Index. Unfortunately, the contracts with State Vital Statistics offices (by which NCHS obtains the NDI records) currently permit only the release of date of death, state where the death occurred, and certificate number (Patterson and Bilgrad, 1986). Any arrangement for the NDI's release of cause of death codes must, of course, provide for appropriate remuneration to the states and protect the confidential nature of the records.

It is somewhat ironic that a higher death rate from ill-defined cancer in neighboring Bay County was partially responsible for our finding, because we attempted to control for regional differences in

mortality rates in our analysis of this cohort. Unfortunately, Bay County was not among the seven east-central counties we pooled together to provide a comparison. Future analyses of employees from these facilities should either directly or indirectly incorporate a comparison with Bay County.

Our finding that the certification practices of some osteopathic physicians may be responsible for the higher rate of ill-defined cancer in Bay County is an interesting one, but should be confirmed through additional study employing a larger sample of records. Toward that end, we alerted the Michigan Department of Public Health, Center for Health Statistics, and it is our understanding that they have confirmed this (personal communication with George Van Amburg). This problem can be remediated via targeted educational programs, to the benefit of the vital statistics system upon which many investigators depend.

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TABLE 1

Observed and Expected Deaths,

SMRs and 95% Confidence Intervals for Miscellaneous

Other Cancer Sites

Site (ICDA-8)	Observed	Expected*	SMR	95% CI
Connective and other soft-tissue (171)	11	7.3	151	75-270
Male breast (174)	5	2.7	185	60-432
Other endocrine glands (194)	4	NA	-	-
Liver, unspecified as primary or secondary (197.8)	10	14.2	70	34-130
Mesothelioma (199.1)	11	NA	-	-

NA = Not Available

*Expected numbers of deaths were calculated based on age- and calendar-year specific mortality rates of U.S. white males (Waxweiler, et al, 1983).

TABLE 2

Crude and Adjusted Odds Ratios by Control Group

for the Association with Residence in Bay County

	Resident of Bay County					
	Yes	No	cOR	95% CI	aOR	95%CI
Cases	33	83				
All Other Decedents	1,272	6,228	1.9	1.3-2.9	1.9	1.3-2.8
Specified Cancers	261	1,288	2.0	1.3-3.0	1.9	1.2-2.9

cOR = unadjusted odds ratio

aOR = odds ratio adjusted for age and year of death

TABLE 3

Crude and Adjusted Odds Ratios for the Association with the Certifying Physician Having Been a Doctor of Osteopathy

	Certifier a D.O.					
	Yes	No	cOR	95% CI	aOR	95%CI
Cases	14	19				
Specified Cancers	32	227	5.2	2.5-10.8	5.0	2.3-10.8

cOR = unadjusted odds ratio

aOR = odds ratio adjusted for age and year of death