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Use of Multiple-Cause Mortality Data in Epidemiologic Analyses: US Rate and Proportion Files Developed by the National Institute for Occupational Safety and Health and the National Cancer Institute

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The authors have created US mortality rates (age, sex, race, and calendar-time specific) and proportions, using multiple cause-of-death data, for the years 1960–1989. Multiple cause-of-death data include the usual underlying cause of death from the death certificate as well as contributory causes and other significant conditions. US multiple-cause rates and proportions enable the user to calculate the expected occurrences of disease on the death certificates of a cohort under study. There is an average of 2.66 causes and/or contributory conditions listed on US death certificates, increasing over time from 2.54 in the 1960s to 2.76 in the 1980s. The ratio of multiple-cause listings to underlying cause listings varies by disease, from low ratios for cancers to high ratios for diseases such as diabetes, arthritis, prostate disease, hypertension, pneumoconiosis, and renal disease. Use of these data is illustrated with two cohorts. Multiple-cause analysis (but not underlying cause analysis) revealed twofold significant excesses of renal disease and arthritis among granite cutters. For workers exposed to dioxin, neither multiple-cause nor underlying cause analysis indicated any excess of diabetes, an outcome of a priori interest. Good candidates for multiple-cause analysis are diseases that are of long duration, not necessarily fatal, yet serious enough to be listed on the death certificate. *Am J Epidemiol* 1992;136:855–62.

arthritis; causality; diabetes mellitus; dioxins; kidney diseases; silica

Epidemiologists studying mortality have usually confined themselves to analysis by underlying cause of death. However, a typical death certificate also lists contributory causes and may list other diseases (not related to the underlying cause) as "other significant conditions." The underlying cause is chosen by nosologists according to standard guidelines provided by the World Health Organization. These guidelines are based on the order of all diseases listed on the death certificate and on their causal relation. The information on contributory causes and other significant conditions is usually ignored but can provide useful epidemiologic information.

The National Center for Health Statistics makes available multiple cause-of-death data tapes, beginning in 1968 and continually updated. These tapes have a record for each US death, which includes age, race, sex, date of death, underlying cause of death, contributory causes of death, and other significant conditions. Up to 14 separate entries (20 after 1978) may be coded for causes

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Abbreviation: ICD, *International Classification of Diseases.*

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of death and significant conditions. Causes of death and significant conditions are coded according to the *International Classification of Diseases* (ICD) coding system that was in effect at the time of death. These tapes have been described by Israel et al. (1).

To date, there have been few analyses conducted using the National Center for Health Statistics multiple-cause data, although some authors (2, 3) have conducted multiple-cause analyses internal to their cohorts. Wing and Manton (4) used these data to study the presence of hypertension at death in North Carolina and to note a decrease in hypertension over calendar time. These authors calculated rates of hypertension at death by dividing multiple-cause numerator data by population denominators. More recently, Milham (5) used multiple-cause data for the state of Washington to conduct a proportionate mortality analysis by occupation. He determined that farmers suffered an excess of arthritis, while plumbers, pipe fitters, and steam fitters suffered an excess of asbestosis.

We have created a set of rates and proportions for the entire US population using multiple-cause data. These rates and proportions are divided into 5-year age and calendar-time periods from 1960 to 1989, as well as by sex and race (white and nonwhite). Rates and proportions have been created for the 92 categories of death used by the National Institute for Occupational Safety and Health (6). We are in the process of creating additional rates and proportions files for 62 categories of death that are used in another life-table analysis program (OCMAP, see reference 7). These files of rates and proportions are available without charge upon request to the authors. In this paper, we will present two examples of the use of the data with occupational cohorts.

The first example involves the use of multiple-cause proportions in a proportionate mortality study (8) of the deaths of 991 granite cutters that occurred after 1960 (the 1960 cutoff was used because of the lack of multiple-cause data for earlier years). The outcomes of interest were arthritis/spondylitis and renal disease. Rheumatoid arthritis has been shown to be increased among granite workers in Finland (9), presumably because of silica-induced autoimmune mechanisms (a high titer of antinuclear antibodies has been observed in granite workers). Osteoarthritis, on the contrary, was not excessive among these workers. Renal disease may be associated with silica, presumably also because of autoimmune mechanisms. Silica has been shown to induce renal disease in animals and has been associated with renal disease in case reports and in a case-control study (10, 11).

The second example involves the use of multiple cause-of-death rates in a cohort study of workers exposed to dioxin during the manufacture of herbicides and other chemicals (12). A recent cross-sectional finding from the Air Force Ranch Hand Study of men who sprayed Agent Orange found that men with higher levels of serum dioxin had significantly more diabetes (13). The same relation was observed in a comparison group of Air Force personnel who did not spray Agent Orange. The median level of serum dioxin among the Ranch Hand men in the 1980s was 13 parts per trillion in the exposed group and 4 parts per trillion in the nonexposed group. To investigate this relation further, we used multiple-cause rates with the manufacturing workers studied by Fingerhut et al. (12). These workers were first exposed to dioxin many years ago (61 percent were exposed 20 or more years before the end of the study). Most diabetes is of the adult-onset type that develops at later ages. The presence of diabetes on death certificates might be expected to reflect disease that developed after dioxin exposure, assuming that dioxin exposure took place relatively early in adult life and that adult-onset diabetes was diagnosed relatively late in life (although certainly there would be exceptions to this general rule). These men had very high serum dioxin levels in the mid-1980s, more than 15 years after the last exposure (mean, 233 parts per trillion in a sample of 253 workers). If dioxin led to diabetes, one might expect to observe more diabetes on the death certificates of these men than expected.

MATERIALS AND METHODS

Multiple-cause data tapes from 1968 to 1984 were obtained from the National Center for Health Statistics. Multiple-cause listings exist in two formats: entity axis and record axis. Both formats include the underlying cause, contributory causes, and other significant conditions. The entity axis format provides a separate code for each disease listed on the death certificate (whether it is an underlying cause, contributory cause, or significant condition). The record axis format uses linkage rules to combine some listings; e.g., "hypertension" and "heart disease" might be combined into a single code for "hypertensive heart disease." In practice, there is only a slight difference in the two formats as far as the total number of listings per certificate. We have used the entity axis listings for our analyses. The observed deaths for the two cohorts studied in our examples were also coded in this manner, using the ICD revision current at the time of death. Files using the record axis were also created, and results were virtually identical.

For each death, each unique ICD code listed in the entity axis contributed one count to one of 92 death categories used by the National Institute for Occupational Safety and Health (6) for each sex, age, and calendar-time category. These death categories group together those causes of death that are similar based on ICD codes (see table 2), and they recognize the appropriate ICD revision codes in effect at the time of death. If two (or more) ICD codes for the same death fell into the same death category, two (or more) counts were given to that death category. Any duplicate ICD codes were reduced to a single one. For ICD codes 800 and above (accidents and injuries), nature-of-injury codes (N codes) sometimes accompany external cause codes (E codes). In these instances, N codes were ignored.

Five-year age categories began at age 15 and continued until a category of all ages above age 85. Five-year calendar-time periods began in 1960 and continued until 1989. The National Center for Health Statistics multiple-cause data were available only for 1968–1988. We duplicated the 1968 data for the years 1965–1967 to create rates and proportions for the 5-year period 1965–1969. The 1965–1969 data were then duplicated for the period 1960–1964. For diseases that were rapidly increasing or decreasing in the 1960s, the 1960–1964 data are somewhat inaccurate, but we wanted to have some data for that period. Similarly, we duplicated the 1988 data for 1989, in order to create data for the 1985–1989 period.

Generally, multiple-cause data from the National Center for Health Statistics reflect all deaths in the United States. However, in 1972 only a 50 percent sample of deaths in the United States were coded; hence, each 1972 record was counted twice (or duplicated) for our creation of death rates and proportions. Similarly, in 1981–1982 only a 50 percent sample of deaths were coded for multiple cause in 19 of 50 states but, in this case, the National Center for Health Statistics had already duplicated the records for those states for those years on the public use tapes, to adjust the number of deaths to the appropriate level.

To create rates, we divided the total counts described above by the respective age, sex, race, and calendar-time US population (based on census data). For 5-year calendar-time periods, the population at the midpoint of the period was estimated by interpolation from the known populations at the beginning and end of each decade (Bureau of Census midpoint estimates were used for the 1980s).

Other alternative approaches to creating rates were possible. Although we have not done so, rates could be created for all causes that are not underlying (i.e., contributory causes and other significant conditions), for contributory causes alone, or for other significant conditions alone. We felt that the most useful alternative was to create rates and proportions for all causes on the death certificate combined ("any mention"). Another unexplored possibility would be the creation of rates for the occurrence of specific clusters of disease on the death certificate, such as diabetes and renal disease.

In our analysis of a specific exposed pop-

ulation (the dioxin-exposed workers), US multiple cause-of-death rates were multiplied by the appropriate age, sex, race, and calendar-time-specific person-years at risk in the exposed population to determine the expected number of occurrences of disease on the death certificates. These were then summed across age-sex-race-calendar-time categories and compared with the observed number of occurrences of disease on the death certificates of the exposed population. The observed numbers were treated as Poisson variates, and tests of hypotheses and confidence intervals were calculated using standard procedures typical of analyses of standardized mortality ratios.

US proportions were created by defining the denominator as the total number of death certificate listings for all deaths in a given age, sex, race, and calendar-time category. Then the number of listings (counts) for each of the 92 death groups for that age, sex, race, and calendar-time category were used to create 92 numerators. Dividing by the denominators resulted in 92 proportions for each age, sex, race, and calendar-time period. In the analyses of an exposed population (the granite cutters), these proportions were multiplied by the appropriate age, sex, race, and calendar-time-specific total number of occurrences of all diseases on death certificates among the granite cutters (for all 92 National Institute for Occupational Safety and Health death groups) to determine 92 expected numbers of occurrences on death certificates. Expecteds were then summed across age, sex, race, and calendar-time periods. A proportionate mortality ratio, the ratio of observed to expected, was calculated for each National Institute for Occupational Safety and Health death category. Observeds were again treated as Poisson variates.

RESULTS

Table 1 lists the average number of causes and conditions on the death certificate by sex, race, and calendar time. It is apparent that more causes and conditions are being listed on the death certificates over time. Females generally have more causes listed than males, and whites have more causes listed than nonwhites.

Table 2 lists the ratio of multiple causes to underlying cause by the 92 National Institute for Occupational Safety and Health death categories (1965–1989). This ratio represents the number of times a cause appeared anywhere on all US death certificates compared with the number of times that cause appeared as the underlying cause. The ratio is very low for causes that are usually the underlying cause (e.g., cancers) and high for conditions that are rarely the underlying cause (e.g., diabetes, alcoholism, prostate disease). From the standpoint of occupational studies, of particular interest are the high ratios for the categories for pneumoconioses (category 65), renal disease (categories 70 and 71), and arthritis (category 81).

Table 3 gives the proportionate mortality ratio results of both underlying and multiple-cause analyses of the granite cutters for renal disease and arthritis, as well as a few other outcomes of interest. Statistically significant elevations of renal disease and arthritis were observed using multiple cause, but not using underlying cause. Among the

TABLE 1. Number of causes and conditions listed per death certificate by sex, race, and calendar time for the US population, 1965-1989*

	White males	White females	Nonwhite males	Nonwhite females	Total
1965–1969	2.50	2.65	2.25	2.44	2.54
1970–1974	2.56	2.70	2.32	2.54	2.60
1975–1979	2.60	2.74	2.40	2.63	2.64
1980–1984	2.66	2.80	2.48	2.73	2.71
1985–1989	2.71	2.83	2.58	2.83	2.76
Total	2.62	2.76	2.43	2.66	2.66

* Multiple-cause data for 1965–1967 were duplicates of 1968, while data for 1989 were duplicates of 1988.

17 arthritis deaths, there were five that specifically listed rheumatoid arthritis, four that listed both arthritis and silicosis or tuberculosis, one that listed both arthritis and renal disease, and seven that listed arthritis alone. Results for the category pneumoconioses (largely silicosis) and other chronic obstructive pulmonary disease show that many more listings of these causes are detected using multiple-cause data, but that this actually results in a lower proportionate mortality ratio than was observed using underlying cause. Results for lung cancer and stomach cancer are similar for multiple and underlying cause, as is generally the case for any cancer.

Table 4 gives standardized mortality ratio results for selected causes of death for the dioxin-exposed workers. Results for several cancers and for ischemic heart disease parallel findings from underlying cause data. The multiple-cause data capture many more deaths with diabetes than do the underlying cause data, but observed deaths conform with expected deaths, and the thesis that dioxin exposure leads to diabetes is not supported by these results.

DISCUSSION

The use of multiple cause-of-death data potentially provides a new tool for epidemiologic analysis of mortality data. For many causes of deaths, the ratio of observed to expected deaths using multiple cause will be similar to that ratio using underlying cause (this was the case for our example with dioxin-exposed workers). That is, multiple-cause analysis may not reveal any new association between exposure and disease. However, even if the point estimate of effect (e.g., the standardized mortality ratio or proportionate mortality ratio) remains the same, for many causes of death the sample size of observed deaths and expected deaths is increased using multiple-cause data, and confidence intervals for the ratio of observed to expected are correspondingly narrowed. Furthermore, in some instances the use of multiple-cause data may give different point estimates, revealing an association not seen using underlying cause data. Such is the case for the granite cutter study we have analyzed here. With the use of multiple causes of death, the number of death certificates listing arthritis was double that expected in the cohort, while underlying cause analysis was uninformative (only one death observed). This finding confirms one earlier report (9) and suggests that further research is needed in understanding how silica might induce arthritis. Similarly, the granite cutters had a twofold excess of renal disease as evidenced by multiple-cause data, whereas underlying cause data indicated only a smaller nonsignificant excess. This finding confirms associations of renal disease and silica observed in case reports and one epidemiologic study (11). It is possible that both the arthritis and the renal disease reflect similar reactions of the immune system that are triggered by silica.

One peculiarity of using multiple-cause rates as described here (for standardized mortality ratio analyses) is that the usual assumption of independence of cause-specific rates may not hold. Consider a cohort exposed to a lung carcinogen, showing a large excess of death due to lung cancer as an underlying cause. The excess lung cancer deaths would result in an artificial excess in the cohort compared with the US population for all other specific causes in a multiple-cause analysis, proportional to the increase in lung cancer deaths. For example, if the investigator was interested in arthritis in a multiple-cause analysis, arthritis counts on the death certificates in the observed cohort would be artificially elevated because of the excess lung cancer deaths. The extent of this bias is not likely to be great in most practical situations. One solution, motivated by Manton and Stallard's discussion of "patterns of failure" (14), would be to divide the multiple-cause rates for arthritis into a rate for arthritis occurring with lung cancer and without lung cancer. Separate expected and observed deaths would be generated for both. However, this solution requires the investigator to create his or her own special rates. A more general but crude approach to this kind of bias might be an adjustment of cause-specific observed deaths in the multiple-cause analysis upwards or downwards proportional to the departure of the

TABLE 2. Ratio of the number of occurrences of a cause anywhere on US death certificates versus occurrences as an underlying cause, 1965–1989

National Institute of Occupational Safety and Health death category and code	Ratio	Deaths*	%
1. Respiratory tuberculosis (ICD† 010–012)	2 79	67.0	0.14
2. Other tuberculosis (ICD 013–018)	2.12	17 0	0.04
3. MN† lip (ICD 140)	1 50	3.8	0.01
4. MN tongue (ICD 141)	1.26	46.2	0.10
5. MN other buccal cavity (ICD 142–145)	1 29	60 1	0.13
6. MN pharynx (ICD 146–149)	1.23	89 9	0.19
7. MN esophagus (ICD 150)	1.12	184.0	0.39
8. MN stomach (ICD 151)	1.11	375.0	0.79
9. MN intestine (ICD 152–153)	1.18	1,054 7	2.21
10. MN rectum (ICD 154)	1.20	232.2	0.49
11. MN liver, biliary tract (ICD 155 0, 155.1, 156)	1.11	181.2	0.38
12. MN liver not specified (ICD 155.2)	1.31	71.0	0 15
13. MN pancreas (ICD 157)	1.07	508.8	1.07
14 MN peritoneum, other digestive (ICD 158, 159)	1.24	49.2	0 10
15. MN larynx (ICD 161)	1.37	82.4	0 17
16 MN trachea, bronchus, and lung (ICD 162)	1 09	2,311.8	4.85
17. MN other respiratory (ICD 160, 163–165)	1.32	32.4	0 07
18. MN breast (ICD 174–175)	1.17	867.0	1.82
19 MN cervix uteri (ICD 180)	1.14	139.6	0 29
20. MN other uterus (ICD 179, 181–182)	1.22	144.7	0.30
21. MN ovary (ICD 183)	1.08	267.4	0.56
22. MN other female organs (ICD 186, 187)	1.29	23.9	0.05
23. MN prostate (ICD 185)	1 42	539.5	1.13
24. MN other male organs (ICD 186, 187)	1 21	21.0	0.04
25. MN kidney (ICD 189.0–189.2)	1 18	185.6	0.39
26. MN other urinary organs (ICD 188, 189.3–189.9)	1.32	238.4	0 50
27. MN skin (ICD 172–173)	1 30	148.0	0 31
28. MN eye (ICD 190)	1.35	7.2	0.02
29. MN brain, nervous system (ICD 191, 192)	1.08	209.3	0.44
30 MN thyroid (ICD 193)	1.24	24.8	0.05
31. MN bone (ICD 170)	1.36	34.1	0.07
32. MN connective tissue (ICD 171)	1.15	48.7	0 10
33. MN other sites (ICD 194–199)	8 10	657.9	1 38
34. Lymphosarcoma/reticulosarcoma (ICD 200)	1 15	131.9	0.28
35. Hodgkin's disease (ICD 201)	1 21	61.2	0 13
36. Leukemia (ICD 204–208)	1 30	362.8	0 76
37. Other hematopoietic neoplasms (ICD 202–203)	1 24	316.9	0.67
38. Benign neoplasms of eye, brain (ICD 224, 225)	1.58	20 5	0.04
39. Unspecified neoplasms of eye, brain (ICD 237.5–237.9, 239.6, 239.7)	1 37	53 6	0.11
40. Other benign neoplasms (ICD 210–223, 226–237 4, 238.0–239.5, 239.8, 239 9)	2 61	67 5	0.14
41. Diabetes (ICD 250)	3 82	920.3	1.93
42. Pernicious anemias (ICD 281.0, 281 9)	7 87	6.9	0 01
43. Other anemias (ICD 280, 281.1–281 8, 282–285)	8 83	73 3	0.15
44. Coagulation defects (ICD 286, 287)	5 46	33.5	0.07
45 All other blood-forming organs (ICD 288, 289)	3.37	41.7	0.09
46. Alcoholism (ICD 303)	4.36	108.9	0.23
47. Other mental disorders (ICD 290–302, 204–319)	7 91	200.1	0.42
48. Multiple sclerosis (ICD 340)	1 68	38 2	0.08
49. Other nervous system (ICD 320–337, 341–389)	4.64	456.9	0.96
50. Rheumatic heart disease (ICD 390–398)	2.14	278.5	0.58
51. Ischemic heart disease (ICD 410–414)	1 50	15,214.7	31.90
52. Chronic endocardial disease (ICD 424)	2.41	116 6	0.24
53. Other myocardial degeneration (ICD 429 0, 429 1)	4.50	86.3	0.18
54. Hypertension with heart disease (ICD 402, 404)	1.58	462 8	0.97
55. Other heart disease (ICD 420–423, 425–428)	7.04	2,378.1	4.99
56. Hypertension without heart disease (ICD 401, 403, 405)	12.10	188.2	0 39
57. Cerebrovascular disease (ICD 430–438)	1.92	4,557.2	9.56
58. Diseases of arteries and veins (ICD 415–417, 440–459)	4.91	1,677.6	3.52
59. Acute respiratory infections (ICD 460–466)	4.61	21.1	0.04
60. Influenza (ICD 487)	1.45	84.9	0.18
61. Pneumonia (ICD 480–486)	3.32	1,381.1	2.90
62. Chronic bronchitis (ICD 490, 491)	2.39	113 4	0.24
63. Emphysema (ICD 492)	2.72	452.1	0.95
64. Asthma (ICD 493)	3.17	68.8	0.14
65. Pneumoconioses, other respiratory (ICD 470–478, 494–519)	4.17	1,054 1	2.21
66 Diseases of the stomach (ICD 531–537)	2.90	221 9	0.47
67 Hernia (ICD 550–553, 560)	3.69	144 6	0 30

(Table continued on next page)

TABLE 2. Continued

National Institute of Occupational Safety and Health death category and code	Ratio	Deaths*	%
68. Cirrhosis of the liver (ICD 571)	1.52	734.6	1.54
69. Other digestive diseases (ICD 520–530, 540–543, 555–558, 562–570, 572–579)	4.57	760.1	1.60
70. Acute renal failure (ICD 580, 581, 584)	5.70	56.3	0.12
71. Chronic renal disease (ICD 582, 583, 585–587)	4.75	277.8	0.58
72. Kidney infection (ICD 590)	3.01	118.4	0.25
73. Urinary calculi (ICD 592, 594)	2.85	15.7	0.03
74. Hyperplasia of prostate (ICD 600)	4 22	32.5	0.07
75. Other diseases of male organs (ICD 601–608)	3.75	13.0	0.03
76 Diseases of the breast (ICD 610, 611)	8.94	0.7	0.00
77. Diseases of the female organs (ICD 614–629)	4.31	11.9	0.03
78. Other genitourinary disease (ICD 588, 589, 591, 593, 595–599)	5.36	235.0	0.49
79. Infections of the skin (ICD 680–686)	6.04	13.9	0.03
80. Other diseases of the skin (ICD 690–709)	6.73	50.7	0.11
81. Arthritis/spondylitis (ICD 711–716, 720, 721)	10.70	51.7	0.11
82. Osteomyelitis/periostitis (ICD 730)	3.67	61.	0.01
83. Other musculoskeletal (ICD 710, 717–719, 722–729, 731–739)	4.55	76 8	0.16
84. Symptoms, ill-defined conditions (ICD 780–796, 798, 799)	17.10	548.5	1.15
85. Transportation accidents (ICD E800–848, E929.0, 929.1)	1.02	1,245.0	2.61
86. Accidental poisoning (ICD E850–869, E929.2)	1.23	119.9	0.25
87. Accidental falls (ICD E880–888, E929.3)	1.64	362.6	0.76
88. Other accidents (ICD E890–928, E929.4–929.9)	1.47	535.2	1.12
89. Medical complications (ICD E870–879, E930–949)	10.30	70.2	0.15
90. Suicide (ICD E950–995)	1.01	655.9	1.38
91. Homicide (ICD E960–978)	1.03	468.9	0.98
92. Other causes (all others)	5.29	865.3	1.82

* *Deaths in 1,000s. Total deaths are slightly inaccurate (less than 1%) because 1965–1967 data duplicate those of 1968, and* 1989 data duplicate those of 1988.

† ICD, *International Classification of Diseases*, Ninth Revision; MN, malignant neoplasms.

TABLE 3. Proportionate mortality ratios (PMRs) for granite cutters*

Disease and code	PMR for underlying cause	95% CI†	PMR for multiple causes	95% CI
Acute renal disease (ICD† 580, 581, 587)	1.36 (1)‡	0.01–7.58	1.93 (8)	0.83–3.79
Chronic renal disease (ICD 582, 583, 585Ɛn587)	1.60 (7)	0.64–3.30	2.18 (26)	1.43–3.20
Arthritis (ICD 711–716, 720, 721)	1.29 (1)	0.01–7.21	2.01 (17)	1.17–3.21
Pneumoconiosis and chronic obstructive pulmonary disease (ICD 470–478, 494–519)	5.53 (88)	4.44–6.81	3.61 (336)	3.24–4.02
Lung cancer (ICD 162)	1.26 (69)	0.98–1.60	1.12 (78)	0.89–1.40
Stomach cancer (ICD 151)	1.50 (16)	0.86–2.44	1.47 (17)	0.86–2.35

* Based on 991 deaths after 1960

† CI, confidence interval; ICD, *International Classification of Diseases*, Ninth Revision

‡ Numbers in parentheses, number of deaths.

all-cause mortality rate (based on underlying cause) of the observed cohort from the standard population's all-cause mortality rate.

There are other limitations to the use of multiple-cause data. For example, other investigators have shown that ancillary causes such as diabetes are underreported on the death certificate (15, 16). However, this might be expected to affect both the exposed and the referent populations equally. Physicians in different geographic areas are likely to fill out death certificates differently. Some may be more (or less) thorough than the US average, resulting in more (or less) listings on the death certificate than expected. For this reason, more caution must be exercised

TABLE 4. Standardized mortality ratios (SMRs) for dioxin-exposed workers*

Disease and code	SMR for underlying cause	95% CI†	SMR for multiple causes	95% CI
Diabetes (ICD† 150)	1.07 (16)‡	0.61–1.75	1.05 (58)	0.80–1.36
Ischemic heart disease (ICD 410–414)	0.96 (393)	0.87–1.06	1.03 (479)	0.93–1.12
Connective tissue cancer (ICD 171)	3.38 (4)	0.92–8.65	3.07 (4)	0.84–7.85
Hematopoietic cancer (ICD 200–208)	1.09 (24)	0.70–1.62	1.12 (28)	0.74–1.61
Lung cancer (ICD 162)	1.62 (24)	1.04–2.41	1.13 (96)	0.92–1.38

* Based on 993 deaths after 1960.
† CI, confidence interval; ICD, *International Classification of Diseases*, Ninth Revision.
‡ Numbers in parentheses, number of deaths.

when analyzing multiple-cause data compared with underlying cause data. One might be especially concerned in the situation where only a handful of physicians were responsible for the death certificate data for an entire exposed group. For example, this might occur when the exposed group comprised workers from a single plant in an isolated area (this was not the case for either of the two cohorts studied here, each of which was composed of workers from many separate work sites in different geographic areas). One partial solution to this problem is to use local multiple-cause rates rather than US rates.

Multiple-cause data reflect the prevalence of specific diseases at death. Diseases that have a high ratio of multiple-cause listings versus underlying cause listings on the death certificate are candidates for multiple-cause analysis. Diseases that have a long course and are often not the cause of death, but are serious enough to be noted by the physician on the death certificate, are the best candidates for multiple-cause analysis.

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