USE OF MULTIPLE-CAUSE MORTALITY DATA IN EPIDEMIOLOGIC ANALYSES

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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 standard guidelines provided by the World Health Organization, which 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 U.S. 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 U.S. 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 of death and significant conditions. Causes of death and significant conditions are coded according to the International Classification of Diseases (ICD) coding system which was in effect at the time of death. To date there have been few etiologic analyses conducted using the National Center for Health Statistics multiple cause data.

We have created U.S. mortality rates (age, sex, race, and calendar-time specific) and proportions using multiple cause-of-death data, for the years 1960-1989 (data from 1960-1967 were imputed). U.S. multiple cause rates and proportions enable the user to calculate expected occurrences of disease on the death certificates of a cohort under study. There are an average of 2.66 causes/contributory conditions listed on U.S. death certificates, increasing over time from 2.54 in the 1960's to 2.76 in the 1980's. 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 two-fold 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.

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 associations not seen using underlying cause data.

Multiple cause data reflects the prevalence of specific diseases at death. Diseases which have a high ratio of multiple cause listings versus underlying cause listings on the death certificate are candidates for multiple cause analysis. Diseases which 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.

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