in the incidence of asbestosis seen between studies.

When a disease is well defined and the case fatality rate is high, such as occurs with lung cancer, the mortality rate will be similar to the incidence of the disease. In contrast, when the disease is not well defined or is difficult to diagnose and the case fatality rate is not high, the mortality rate will be less than the incidence. Unlike lung cancer, the onset of asbestosis is not always life threatening. As the disease progresses and health deteriorates, a subject may seek medical care. In the interim, however, the victim may die from other more easily recognizable causes and the existence of the asbestosis and its associated morbidity will not have been ascertained, even though asbestosis may have been the underlying or contributing cause of death. This is a special problem with diseases like asbestosis which are virtually absent in populations that are not exposed to asbestos.

Hammond, Selikoff, and Seidman (Ex. 84-47, p. 475) note that "what is recorded on the death certificate is not always [based on] the best available information on the cause of death. For example, in the absence of the patient's physician, the certificate may be signed by a doctor who knows less about the case; or an autopsy may indicate that the tentative diagnosis of cause of death was incorrect." In addition, a review of available evidence, such as from the medical record, may indicate that the patient died of another cause of death. Hammond et al. (84-47) reviewed all available medical information, including the death certificates for all deaths in a cohort of insulators. Two causes of death were established: one based on the death certificate (DC) only; and a second cause based on the best evidence available. Seventy-six cases of asbestosis were identified from the death certificate. On the other hand, 160 cases were identified on the basis of the best evidence. In contrast, 638 deaths due to cardiovascular disease were ascertained from DC, while only 566 were identified from the best evidence. These data are consistent with the work of Dement et al. (84-37) who found a statistically significant excess risk of cardiovascular disease among asbestos textile workers. This is unusual because the SMR for cardiovascular disease in working populations is consistently less than 100, reflecting a "healthy worker effect."

Unlike diseases such as lung cancer and mesothelioma, which have a relatively short interval between diagnosis and death, individuals with asbestosis experience a relatively long and debilitating period of morbidity. Dr. Holstein, a pulmonary physician, described a typical case:

> The main symptom of asbestosis is progressive shortness of breath. When this has its onset in its typically insidious and gradual manner, the individual thinks that he is just getting older or getting a little overweight, can't run as fast as he used to, or gets out of breath more easily than he used to; and attributes it to factors such as the ones I mentioned. A little later on, the person begins to notice that in fact, he or she can't do the things that many other people the same age can do. . . . As time goes on, the dependence on younger workers becomes greater and greater, until pretty soon, the individual is experiencing the fact that he or she really can't carry out the job without such dependence. . . . Eventually, in the very severe cases, a person's life consists of sitting in an armchair on the ground floor with an oxygen tank, and disconnecting it just long enough to get up and go to the bathroom.

Hence, there are limitations to using death certificates to determine the extent of mortality attributable to asbestosis. Cases will be underascertained and the person-years of morbidity, i.e., the period between diagnosis of asbestosis and death, are not considered. For these reasons, risk analyses of mortality caused by asbestosis will understate the true risk of disease.

3. Epidemiologic Studies

A number of studies have shown an excess risk of asbestosis in workers exposed to asbestos. Individual exposure data in units of fibers/cc-years are available from three studies, all of which show substantial excess risks below 100 fibers/cc-years (the cumulative lifetime exposure permitted by the 2-f/cc-standard) (Berry et al., Ex. 84-20; Dement et al., Ex. 84-35; Finkelstein, Ex. 84-44). These studies are critically reviewed below. Individual exposure data were also used in two other studies but were reported in units of mppcf-years (McDonald et al., Ex. 84-065; Enterline et al., Ex. 84-43). Several other studies that show an excess risk of asbestosis are not reviewed here because the exposure measure was expressed only as duration of time exposed (Weiss, Ex. 84-097; Doll, Ex. 84-40; Pearle, Ex. 84-079) rather than as exposure level.

The approach for assigning exposure levels to individuals, the method used for person-years analysis, the case definition, the completeness of case ascertainment, and the length of the followup period are directly related to the estimated risk of asbestosis at a defined exposure level. These factors are particularly relevant to the studies of Berry et al. (Ex. 84-20, Dement et al. (Ex. 84-35), and Finkelstein (Ex. 84-44).

All three of these studies, which assigned individual exposures in units of fibers/cc, used person-years analysis to estimate the risk of asbestosis in groups of workers defined by their cumulative exposure to asbestos. To derive such estimates the number of years that workers are exposed must be summed for all workers exposed at each exposure level. If an individual leaves the workplace, subsequent years of followup are assigned to the final cumulative exposure incurred by the individual. Two methods are typically used to assign person-years of observation to the cumulative exposure levels incurred during employment. The first approach assigns the number of person-years of observation before the disease is diagnosed in each successive cumulative exposure category. For example, four exposure groups are defined in terms of employment: greater than 5 years; 5-9 years; 10-14 years; and 15+ years. An individual with 20 years of employment contributes person-years of exposure to all four exposure groups. The same principle applies if asbestos exposure is defined as cumulative fibers/cc rather than duration of employment. That is, before person-years of exposure can be assigned to any cumulative exposure group, a worker must have first experienced a lower cumulative exposure; the person-years of exposure are then assigned in accordance with the length of time the worker spent at each exposure level. An alternative approach assigns the total number of person-years of observation only to the highest cumulative exposure group, i.e., in our example, to the denominator for the 15- to 20-year cumulative exposure group. Use of the latter method underestimates the disease incidence in the higest exposure groups and overestimates the incidence in the lowest exposure groups. Dement et al. (Ex. 84-35) and Berry et al. (Ex. 84-20) both used the first approach, while Finkelstein (Ex. 84-44) took the second approach.

The completeness of case ascertainment is directly related to the length of the followup period. If a study's followup period is relatively short, then cases will be underascertained and the risk of disease will be underestimated. In addition, if latency is related to cumulative exposure, i.e., if the median latency is short for high-exposure groups and longer for the low-exposure groups, then the rates for each cumulative exposure group will be underestimated