The Estimation of Expected Rates in Occupational Disease Epidemiology

PHILIP E. ENTERLINE, Ph.D.

PROBABLY no environment impinging on the health of man has so much effect and is so malleable as the environment in which he works. No doubt, because of this, there has been great interest in relating working conditions to health, an interest that predates more general epidemiologic studies of disease and which has occupied many outstanding epidemiologists and medical statisticians.

For some diseases evidence of an unfavorable effect of the working environment has been strong, and control measures have been sufficiently obvious so that these diseases have ceased to be important occupational hazards. Such conditions as lead intoxication, mercury poisoning, and benzol poisoning have largely disappeared because they were easily identified as associated with the occupational environment, and industrial hygiene measures were relatively simple and easily applied. In some instances, as in bladder cancer in the dye industry and phossy jaw in the match industry, the use of certain substances was discontinued to protect the health of workers.

It is certain that many important occupational exposures remain which affect health and elevate morbidity and mortality rates. These exposures may either be primary in the etiology of disease or may merely serve to aggravate existing conditions. Hatch feels that the aggravation factor is an important area for future work in occupational health and that the great majority of health problems of industrial workers probably are not caused directly by conditions of work but may be increased in severity and progression by insults at the work place (*1*).

The first step in the identification of many of the harmful occupational exposures which remain or which are likely to occur in the future is to identify the separate effects of the occupational environment on disease and disability. One method of doing this will be to compare the rate at which disease and disability develop in a population exposed to fairly well-defined working environments with an expected rate derived from a population not so exposed. In many instances this will call for considerably more sophistication in the application of epidemiologic methods than has been required in the past. Any population is unique, and this seems particularly true of persons pursuing a given occupation at a particular place and time. No other experience of any other population is precisely applicable for the estimation of an expected rate. Nevertheless, estimates will be needed. This is a brief discussion of some problems encountered in deriving such estimates.

Infrequent Diseases

At the outset it should be noted that some diseases occur so infrequently that only a few cases can produce information of epidemiologic sig-

Dr. Enterline is chief, Biometrics and Social Studies Branch, Division of Occupational Health, Public Health Service.

nificance, and elaborate attempts to estimate expected rates are unnecessary. For example, the early discovery by Sir Percival Potts that scrotal cancer occurred with unusual frequency among chimney sweeps, and the conclusion that some agent in their working environment was responsible, was made relatively easy by the fact that scrotal cancer is extremely rare, and only a few cases with a common occupational exposure are strong evidence of cause and effect. In a more recent example, Wagner and co-workers reported on the occurrence of mesothelioma in South Africa (*2*). They accumulated a series of 47 cases, a remarkably large number in view of the total reported in the world's literature at the time of their report, and related nearly all of these cases to asbestos exposure.

Overwhelming Effects of Job Exposures

Some environmental exposures produce such an overwhelming response that elaborate attempts to estimate expected rates are unnecessary. The effects of working in the production of chromates on lung cancer rates provide an excellent example. Machle and Gregorius studied insurance records for seven chromate producing plants and compared the percentage of total deaths among chromate workers attributed to lung cancer with the percentage in a group of industrial policyholders in the Metropolitan Life Insurance Company (*3*). Among chromate workers, 42 of a total 193 deaths were caused by lung cancer; among the industrial policyholders only 10 of a total 733 were attributed to lung cancer. Annual mortality rates per 100,000 for cancer of the lungs and bronchi were also compared with rates for male employees of an oil refining company.

Occupation	*50 years of age or less*	*Over 50 years of age*
Chromate workers	197	480
Oil refining company workers	5	22

Deriving Expected Rates

For relatively frequent conditions with a variety of likely etiological agents and for which there are no overwhelming occupational effects, explicit comparisons with an expected rate are necessary. Frequently, the theoretical question to be answered is whether illness occurs at the same rate in a cohort entering a particular occupation as it would have occurred if this cohort had chosen another occupation similar in all respects to the occupation under study except that the "extra" hazard did not exist.

This type of question can probably best be answered by dividing the subjects randomly into groups, with some groups exposed to the agent or agents under investigation, some not so exposed, and all groups followed to determine the incidence of disease and death. Although this experimental method is clearly preferable, most investigations of the etiology of disease in human populations, for ethical or other reasons, usually must be based on the observation of naturally occurring events. However, the results of observational investigations can approach the results of experimental studies if reasonable care is exercised in the derivation of an expected rate.

The advantage of the experimental investigation in studies of disease is that it permits control of all variables which might affect observable disease so that the separate effects of the agent under investigation can be measured. Since many of these variables can be readily identified, such as age, sex, diagnostic criteria, economic level, and general living conditions, reasonable care in the selection of a control group can greatly improve the usefulness of observational studies. As Hill puts it, in conducting such studies, "one must have the experimental approach firmly in mind" (*4*). That is, in conducting observational studies one must attempt to "hold constant" all relevant variables other than the variable under investigation.

Measuring Nonoccupational Effects

One of the reasons the rate of disease deviates in a given occupational group from some expected rate is the influence of nonoccupational factors. The problem is illustrated by data shown in table 1 (*5, 6*). Tuberculosis is usually associated with work in dusty trades, such as coal mining, and it is generally believed that dust inhalation is probably a potentiating factor in this disease. By comparison with workers

Table 1. Tuberculosis death rates per 100,000 among coal miners and other groups of workers, selected age groups, United States, 1950

Age group (years)	Coal miners	All occupations	Professional workers	Intermediate occupations	Laborers
20–24	23.5	12.3	2.4	7.2	32.8
25–34	35.7	18.8	3.3	13.4	58.5
35–44	75.6	34.0	7.9	28.5	100.2
45–54	156.9	56.8	25.3	49.1	143.3

SOURCES: References 5 and 6.

in all occupational groups, coal miners have a high death rate, but compared with laborers, the death rate among coal miners is relatively low (table 1). Which is the proper comparison for an evaluation of the importance of the work environment? Certainly more data would be needed to answer the question than are available in table 1. In view of the relevance of general living conditions to the development of tuberculosis, it would seem important that the group selected for comparison should have living conditions roughly similar to those of coal miners.

A method for detecting an effect of the nonoccupational environment on variations in disease rates among groups of workers is illustrated by Higgins' data (*7*). He calculated standardized mortality ratios for bronchitis among men in certain occupations in England and Wales and their wives (table 2). Without the similar ratios for wives one might readily conclude that bronchitis is associated with the working environment.

Comparable Diagnostic Criteria

Another problem in developing expected disease rates is illustrated by a study of mortality from lung cancer among asbestos miners in Quebec, Canada (*8*). In this study a cohort of miners, identified in 1950, was followed for the 6-year period 1950–55. Twelve deaths from cancer of the lung were noted. To determine whether this number was excessive, average annual age-specific male death rates were computed for the Province of Quebec for the years 1954 and 1955 and applied to the cohort under study. Table 3 shows the actual number of deaths among miners and in the entire Province for each of the 6 years of the study. For the Province, the number of deaths increased sharply during the period. The years 1954–55 were selected for computing expected rates on the grounds that at least part of the increase from 1950–55 was the result of improved recognition and reporting of lung cancer and the years 1954–55 more nearly represented diagnostic levels as they related to miners. The outcome of the study hinged upon which years were used in computing the expected lung cancer death rate. Using 1954 and 1955 on which to base the expected number provides a contrast of 6 as compared with 12 actually observed, a difference not statistically significant ($P>0.05$). On the other hand, if death rates for the 6-year period had been averaged, as is usually done in this type of study, the contrast would have been 4 expected as compared with 12 actually ob-

Table 2. Standardized mortality ratios for bronchitis among agricultural workers, coal miners, and foundrymen, aged 20–64 years, England and Wales

Occupation	1931		1951	
	Men	Wives	Men	Wives
Farmers	36	49	31	52
Agricultural workers	52	66	53	82
Hewers and getters	170	182	200	190
Others underground	126	162	93	177
Surface workers	172	225	131	139
Iron and steel foundry workers	179	288	177	217

SOURCE: Reference 7.

Table 3. Lung cancer deaths among all males and among asbestos miners, Quebec Province, Canada

Year	All males	Asbestos miners
1950	196	3
1951	220	2
1952	245	0
1953	303	3
1954	303	1
1955	357	3

SOURCE: Reference 8.

served, a statistically significant difference ($P<0.05$).

Since a simple test of statistical significance was decided on as a method for accepting or rejecting an association of asbestos mining and lung cancer, the question of diagnostic comparability was crucial to the study. Unfortunately no data were presented to support the authors' belief that diagnostic criteria differed in the manner specified between the population studied and the population from which expected rates were derived. As a result, doubt is cast on the conclusion that asbestos mining and lung cancer are not associated.

This study illustrates the difficulty in epidemiologic studies of diseases for which diagnostic criteria may be in a state of flux. The sharp rise in the number of lung cancer deaths in Quebec Province is indeed suggestive of some change in diagnostic criteria or nomenclature during a 6-year period. It would be a difficult task, however, to demonstrate that this change did not apply equally to asbestos miners, particularly in view of the small numbers of lung cancer deaths noted in this group. Thus, if comparability of diagnostic criteria can be questioned, studies to detect modest environmental effects may be of limited value.

Selective Factors

Observable disease rates among employed persons are no doubt affected by nonoccupational environmental factors and by diagnostic criteria. In addition, selective factors act to modify observable disease. In general, working populations tend to be healthier than the total population from which they are drawn. Unhealthy persons frequently do not attempt to enter the labor market. Also, many companies have a preplacement examination which further tends to insure a healthy work force. Mortality rates for a working population in nonhazardous employments should vary, therefore, from rates for a general population because of selective factors. For example, for conditions which have a sudden onset and are rapidly fatal, rates should be similar for both groups, but the workers should have a lower rate than the general population for conditions with predisposing illness and long periods of incapacity, such as rheumatic heart disease.

Table 4. Lung cancer deaths and rates among du Pont males, 1956–60, and United States white males, 1958

Age	du Pont deaths	Rates per 100,000		Ratio: U.S. to du Pont
		du Pont rates	U.S. rates	
All ages	88	23.2	[1] 30.3	1.3
25–44	10	4.0	5.3	1.3
45–54	34	38.0	50.1	1.3
55–64	44	114.0	141.8	1.2

[1] Adjusted to the age distribution of the du Pont Co.

SOURCE: Reference 9.

Table 5. Observed and expected number of deaths from specified causes among employees of the cigarette division, American Tobacco Co., October 1946–December 1952

Cause	Expected number	Observed number	Ratio: expected to observed
All causes	500	338	1.48
Cancer, all forms	60	44	1.36
Cancer of respiratory system	7	6	1.17
Cardiovascular diseases	239	161	1.48
Coronary disease	81	65	1.25

SOURCE: Reference 10.

The influence of selective factors may be reflected in a study by Pell and Fleming (*9*). They compared the death rate for cancer of the lung among male employees of E. I. du Pont de Nemours and Company during the period 1956–60 with the U.S. white male death rate for 1958 (table 4). At all ages the U.S. rate was 30 percent higher than the rate among du Pont employees. One cannot help being impressed with the possible influence of selective factors in this instance since lung cancer is of sufficiently short duration to be only rarely cause for exclusion on the basis of a pre-employment examination, and, since it usually occurs at older ages, is an unlikely reason for persons not entering the labor force. Alternative explanations for the low rate among du Pont employees would, of course, include more favorable environmental factors or a difference in diagnostic criteria.

A study by Dorn and Baum of mortality among workers in cigarette factories in Virginia, North Carolina, and Kentucky extends these observations to causes of death in addition to lung cancer (*10*). Mortality for selected causes of death was compared with expected mortality based on the experience of the general population of North Carolina and Virginia, the two States where most employees worked (table 5). Death rates for cardiovascular disease were a third lower among employees of these cigarette companies when compared with the general population, and for all forms of cancer, were roughly 25 percent lower.

Both studies illustrate the possible influence of selective factors. Moreover, they suggest that occupational hazards could be easily overlooked when a rate for employees in a particular industry is compared with an expected rate based on a more broadly defined population. In a population with a lung cancer death rate 30 percent below that for the U.S. population, for example, some agent could be introduced which would double the lung cancer death rate without causing an alarming deviation above an expected rate based on the total U.S. experience.

Discussion

In planning epidemiologic investigations of the contributions of occupational environments to relatively frequent diseases with a variety of likely etiological agents, and without overwhelming occupational effects, expected rates should be derived wherever possible as part of the original study design. Some of the work currently in progress at the Division of Occupational Health, Public Health Service, illustrates the kinds of measures which will probably be increasingly important in the future if etiological agents in the occupational environment are to be identified.

A long-term study of the development of lung cancer among uranium miners fortunately contains sufficient detail regarding the work environment of these men to permit grouping by extent of their occupational exposure to radon, the likely etiological factor being studied. Thus, lung cancer mortality is being compared between uranium miners with high radon exposures and miners with low exposures. A large-scale study of pulmonary diseases among bituminous coal miners includes examinations of other manual workers living in or near coal mining communities and of the wives of both groups. A study of the mortality experience of men working in the asbestos textile industry includes for comparison a large cohort of men working in about the same geographic area in the cotton textile industry. The question to be answered is whether asbestos is carcinogenic, particularly to the lungs. The similarity between the industrial processing of raw material which produces asbestos textiles and the industrial process which produces cotton textiles provides an opportunity for a comparison which is likely to produce meaningful information.

It is apparent that in these studies the comparisons proposed will be imperfect. Nevertheless, they represent attempts to refine expected rates and may ultimately point the way toward improvements in occupational disease epidemiology. If a suitable provision for estimating expected rates cannot be incorporated in future epidemiologic studies of occupational environments, the desirability of elaborate data collection will be, in many instances, questionable. The credibility of epidemiologic associations for many important diseases will hinge on the extent to which the characteristics of the population used for comparison approach the characteristics of the population under study.

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