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Issues in Performing Retrospective Exposure Assessment

Patricia A. Stewart[A] **and Robert F. Herrick**[B]
[A]Environmental Epidemiology Branch, National Cancer Institute, Rockville, Maryland 20852; [B]Division of Surveillance, Hazard Evaluation and Field Studies, National Institute for Occupational Safety and Health, Cincinnati, Ohio 45226

Historically, investigations of causality of chronic diseases and occupational exposures have relied upon employment within an industry and/or job as a surrogate for exposure. Similarly, for investigations of dose–response relationships, length of employment within these categories has been used. These surrogates, however, may result in large amounts of misclassification of subjects by exposure categories, which may severely affect risk estimates, particularly if the risks are low. Examples from the literature are provided to demonstrate that these surrogates for exposures may lower estimates of disease risks, obscure etiologic agents, create large confidence intervals (thereby reducing the likelihood of finding a statistical association), and affect dose–response relationships. Recently, more investigators have developed semiquantitative assessments, i.e., assigning jobs to low, medium, and high exposure categories. Although this approach is more satisfactory than the historical approach, it is less than satisfactory because the quantitative relationships among the categories are not known. Incorrect weighing of exposure categories can also result in misclassification of subjects when calculating measures such as cumulative exposure. Quantitative assessment, i.e., assigning a value in units used in industrial hygiene monitoring, is ideally the best approach. However, such an approach may be difficult, if not impossible, because monitoring data are rarely sufficient to allow calculation of measured exposure levels. Thus, assessments often require judgment in assigning exposure level, which can also lead to misclassification. Nevertheless, investigators should use the most quantitative procedure possible so as to develop exposure estimates that are reflective of dose. This approach will enhance the power of epidemiologic studies to detect and evaluate exposure–response associations. **Stewart, P.A.; Herrick, R.F.: Issues in Performing Retrospective Exposure Assessment. Appl. Occup. Environ. Hyg. 6:421–427; 1991.**

Introduction

A fundamental question facing researchers considering retrospective occupational studies is: why should quantitative exposure assessments of exposure levels be done? The goal of epidemiologic research of occupational risks is to identify causal associations between occupational risk factors and adverse health effects. A major criterion for causality is the establishment of a dose–response relationship, and some estimate of dose, even a crude surrogate, is essential to evaluate this relationship. Because dose measurements of chemicals on individuals are, for all practical purposes, nonexistent in the workplace, one is forced to rely upon exposure assessment as a way of estimating the dose received by the study population.

Several approaches to exposure assessment have been used in occupational studies, including ever/never employed or exposed, duration of employment or exposure, estimation of semiquantitative levels, i.e., low, medium, and high, and quantitative levels, e.g., in parts per million (ppm). Traditionally, ever/never employed in an industry and duration of employment have been used as surrogates for exposure, but recently, more attempts have been made to quantitatively assess exposures. There are substantial difficulties in estimating levels of exposure when measurements are scanty or missing, which is the usual situation in studies concerned with exposures occurring many years ago (e.g., studies investigating associations with cancer). Thus, although quantitative assessments of exposure levels are desirable, the uncertainty associated with these estimates indicates a need for careful consideration of the strengths and weaknesses of all methods of exposure assessment used in epidemiologic studies. This paper describes some of the limitations of the more traditional measures of exposure and presents what the authors believe are the benefits of quantitative assessments of exposure levels.

Ever/Never Analyses

In many studies, the study subjects are classified by whether they worked in a particular industry. Although the classification by industry may be highly accurate, employees within an industry are likely to be exposed to a variety of chemicals at various levels. Inclusion of workers with heterogeneous exposures may group individuals who have a low risk for the disease of interest (because they have

TABLE I. Relative Risks (RR) and 95% Confidence Intervals (CI) by Ever/Never Employed in an Industry[A]

Industry	Cases	Controls	RR	95% CI	Potential Exposures[B]
Agriculture	24	42	0.8	0.5–1.6	Arsenic
Construction	62	62	1.5	0.9–2.2	Asbestos, paint, wood dust
Oil/gas extraction	18	31	0.8	0.5–1.7	Oils/greases
Petroleum refining/chemical mfg.	47	70	0.9	0.6–1.5	Oils/greases, vinyl chloride, chromium, sulfuric acid
Shipbuilding/repairing	23	30	1.0	0.6–1.9	Asbestos, paint, wood dust, diesel/gas, oils/greases

[A]From Brown *et al.*[1]
[B]Only exposures from the 12 chemical agents evaluated by the industrial hygienist are identified.

little or no exposure to a chemical) with individuals at higher risk (due to their high exposure levels). If this exposure misclassification is random or nondifferential, it may result in a decrease in the estimate of relative risk, and a causal association could be entirely missed. Even if an excess of some disease is identified, it is usually impossible to determine the workplace exposure that may be responsible without a more detailed assessment of exposures.

The limitations in comparisons of relative risks based on employment within an industry relative to those based on specific exposures can be seen in a case–control study of laryngeal cancer.[1] In this study, complete work histories were obtained from the subjects by interview. The job/industry combinations identified by the subjects were evaluated by an industrial hygienist for potential exposure to 12 chemical agents which had previously been associated with laryngeal cancer. Relative risks and confidence intervals (CI) were calculated for employment in specific industries and for potential chemical exposures. These are presented in Tables I and II. In addition, Table I identifies those exposures which may be found in the industry and which had been evaluated by the industrial hygienist. In almost every case, the relative risks for potential contact with the specific chemical were equal to or greater than the relative risks based on employment in a single industry where the substance was used. Moreover, there were no industries in which the excess mortality risk was significant. Even if the association with the construction industry had been statistically significant, it would not have been possible to determine the causative agent. In contrast, when looking at mortality by specific agent, exposure to asbestos, to paint, and to diesel and gasoline fumes and vapors were significantly associated with laryngeal cancer. Thus, by grouping subjects from different jobs by common exposures, not only were possible etiologic agents identified, but the estimates of risk were also increased.

TABLE II. Relative Risks (RR) and 95% Confidence Intervals (CI) by Potential Chemical Exposure*

Chemical	Cases	Controls	RR	95% CI
Arsenic	28	41	0.9	0.7–2.0
Asbestos	88	99	1.5	1.0–2.2
Paint	32	25	2.0	1.0–3.2
Wood dust	33	28	1.8	0.9–2.7
Diesel/gas	79	85	1.5	1.0–2.3
Vinyl chloride	4	4	1.4	0.4–7.3
Chromium	62	66	1.5	0.9–2.2
Oils/greases	119	165	1.0	0.7–1.6
Sulfuric acid	22	42	0.7	0.4–1.4
Glues, lacquers, varnishes, dyes	34	31	1.7	0.8–2.4

*From Brown *et al.*[1]

The misclassification that can result from using "employed in an industry" as the surrogate for exposure may be reduced by estimating the risk of disease by ever/never held a job title. Many jobs, however, have been held by only small numbers of workers; therefore, the relative risks are likely to be associated with large CI. Combining jobs with similar exposures into one group diminishes this problem. Table III, taken from the same study of laryngeal cancer,[1] presents the relative risks for specific job titles. As in Table I, potential chemical exposures from Table II are identified with the job title. Jobs with potential exposure to carcinogens had larger relative risks than when the same workers were classified based on industry. The relative risks by job title were higher than those based on classification by chemical for eight comparisons, were the same in three cases, and were lower in seven cases. The CI for the relative risks based on chemicals, however, were generally narrowed (14 versus 2 which widened), probably reflecting the increase in the number of subjects. For the analyses based on individual jobs, only employment as a woodworker/furniture maker was statistically associated with laryngeal cancer, although there were other jobs associated with high relative risks. Therefore, it appears that, even though the use of job titles as the basis for calculating disease risks provides estimates which are roughly the same level as calculations based on exposures, the small numbers and wider CI make this approach less valuable.

Analyses by jobs or industries, in addition to affecting the size of the relative risks and the width of the CI, do not directly provide information regarding the agent(s) in the environment causing the disease. Investigators oftentimes make the assumption that it is the most obvious exposure, or the exposure of the highest concentration or of the greatest toxicity, that is causing the disease. This assumption, however, may not be correct. In a mortality study of workers in steel pickling operations, the predominant exposure was to sulfuric acid mist.[2] Some workers in the study, however, were found to have mixed exposures to sulfuric and other acids. When standard mortality ratios (SMR) for lung cancer were determined, workers exposed only to sulfuric acid had a lower risk of lung

TABLE III. Relative Risks (RR) and 95% Confidence Intervals (CI) by Ever/Never Held a Job[A]

Job	Cases	Controls	RR	95% CI	Potential Exposures[B]
Welder/cutter	18	18	1.2	0.7–3.0	Asbestos, chromium
Boilermaker	5	1	7.0	0.8–66.9	Asbestos, chromium
Mechanic	33	46	1.0	0.6–1.8	Asbestos, oils/greases
Plumber/pipefitter	15	14	1.5	0.9–4.2	Asbestos
Painter	11	7	2.2	0.8–6.3	Paint
Excavating	6	6	1.4	0.4–4.0	Diesel/gas
Driver	15	12	1.8	0.8–3.8	Diesel/gas
Carpenter	19	15	1.8	0.8–3.5	Glues, lacquers, varnishes, dyes, wood dust
Woodworker/furniture maker	7	1	9.9	1.0–68.8	Glues, lacquers, varnishes, dyes, wood dust
Machinist	5	13	0.5	0.2–1.6	Oils/greases
Farmer	23	45	0.7	0.5–1.4	Arsenic, diesel/gas, oils/greases

[A]From Brown *et al.*[1]
[B]Only exposures from the 12 chemical agents evaluated by the industrial hygienist are identified.

cancer (SMR = 139) than workers with mixed acid exposures (SMR = 192) or those exposed to other acids (SMR = 224). If analyses had been based only on industry or job title rather than on exposure, and if one assumed that the predominant exposure accounted for the excess risk, one might have concluded that the excess was entirely due to sulfuric acid exposures.

This lack of information about specific exposures in analyses by industry or by job title makes corrective and preventative action difficult. Associating an industry or a job, in which there may be multiple exposures, with an excess disease risk is not particularly useful to the public health practitioner, especially when resources are limited. Reducing exposure to a single chemical is often more feasible than reducing all exposures associated with a workplace. Moreover, regulatory agencies are more likely to regulate specific chemical exposures than general workplace conditions.

Duration of Employment or Exposure

Traditionally, duration of employment in an industry or a job, or duration of exposure, has been used to investigate the existence of a dose–response relationship. Duration may be a reasonable surrogate for exposures only under certain conditions.[3,4] These are:

1. The intensity of exposure is the same for all workers holding the job (or industry) being analyzed.
2. Exposure levels have remained the same over time.
3. The intensity of exposure is related to tenure of employment.

A study by Dement *et al.*[5] illustrates a case in which these conditions were not met. Exposure monitoring data from a chrysotile asbestos plant were available back to 1930, and the estimated mean exposures for jobs in the nine departments presented in Table IV are derived from that report. The range of means for all the jobs within each department and the minimum and maximum exposure measurements for those jobs are presented. Exposure levels varied widely both within and across the different departments. For example, jobs in the fiber preparation and waste recovery operation had mean exposure levels that ranged from 26 to 78 fibers/cc. These levels can be contrasted with the jobs in the light weaving operation where the mean exposure levels ranged from 3 to 7 fibers/cc, a much narrower and much lower level of exposure. Grouping subjects who worked in the fiber preparation operation

TABLE IV. Mean Chrysotile Asbestos Levels (fibers/cc) and Range in an Asbestos Plant by Department and Time Period[A]

Department	1930	1936–1939	1945–1946	1965–1966	1971–1975
Fiber preparation and waste recovery	26–78[B] (11–118)	—[C]	8–24 (5–30)	6–17 (4–21)	—
Carding	11–23 (7–32)	5–11 (4–14)	2–5 (2–6)	4–9 (4–11)	—
Ring spinning	7–8 (6–9)	—	—	7–9 (6–10)	5–6 (5–7)
Mule spinning	5–7 (4–9)	—	—	—	—
Foster winding	10–21 (1–41)	4–8 (3–13)	—	—	—
Twisting	25–36 (13–53)	5–8 (4–10)	—	—	—
Universal winding	4–8 (3–13)	—	—	—	—
Heavy weaving	5–31 (2–39)	1–8 (1–12)	—	—	—
Light weaving	3–7 (2–10)	—	—	—	—

[A]Reported by Dement *et al.*[5]
[B]In the original report, means of specific jobs were provided. The first range indicates the range of the means, whereas the range in the parentheses represents the range of all the samples for all the jobs in that department.
[C]Denotes no change.

with subjects working in light weaving with the same duration of employment or duration of exposure would result in severe misclassification of actual exposures.

Table IV also demonstrates that exposure levels may not remain static over time, and if they change, they do not always drop. In some departments, exposure levels remained essentially constant, e.g., mule spinning, universal winding, and light weaving. In the carding operation, an unusual situation occurred: the mean levels dropped from 11–23 to 2–5 fibers/cc until 1965–66 when they rose to 4–9 fibers/cc. In the fiber preparation and waste recovery operation, however, the mean exposure levels dropped from 26–78 fibers/cc in 1930 to 6–17 fibers/cc in 1965. Subjects who worked from 1930 to 1945 in the fiber preparation operation had much higher asbestos levels than subjects who worked their 15 years during 1960–1975 in that same department. Grouping subjects by duration, however, would put such subjects in the same analytical category, thereby lowering the estimated risk of disease for the 1930–1945 group and raising the risk of the 1960–1975 group.

The third condition, i.e., that the measure of exposure (whether it is level of exposure at a point in time or cumulative exposure over a lifetime) is related to duration of employment, may also not be fulfilled. This condition contradicts the popular notion that newly hired workers are assigned to the most highly exposed jobs. Although there may be circumstances when either situation may occur, the sweeping generalization that duration of employment is predictive of any measure of exposure for all jobs or all workplaces may be erroneous. This issue was evaluated from exposure estimates developed for a retrospective study of formaldehyde workers.[6,7] Subjects were classified into duration of employment categories by the number of years they had accumulated on a designated day in the study (December 31, 1965).[8] The median estimated formaldehyde exposure level on that day was calculated for all subjects who fell into each duration category. This analysis provides a cross-sectional analysis of the estimated 8-hour time-weighted average (TWA) exposures and the durations of employment experienced by the study subjects on that day (Table V). When seven of the plants in this study were combined, the median TWA level for workers across the different duration categories was about the same on that day (0.2–0.3 ppm). For most plants, the estimated level of exposure was not associated with duration of employment. In one plant (plant 1), however, the median TWA exposure level appeared to drop with increasing duration, particularly for workers employed 15 years or more. In two plants (plants 8 and 10), the TWA rose and then fell again as duration increased. When the jobs held by the newly hired and long-term workers were analyzed, there was also no strong evidence that newly hired or long-term workers had substantially different exposure levels;[8] this indicated that, in this investigation, duration of employment was not related to the level of exposure.

Another way to evaluate the usefulness of the duration measure as a surrogate for exposure is to compare classification of workers by duration with other measures of exposure. From the study of formaldehyde workers cited above,[6] duration of employment and duration of formaldehyde exposure were analyzed for correlation with measures of cumulative, average, highest TWA, and peak formaldehyde exposures for the total cohort and for the ten individual plants in the study (Table VI).[9] For the total

TABLE VI. Correlation Coefficients (r) of Duration and Measure of Exposure[A]

Type of Operation	Cumulative	Average	Highest TWA	Peak
Employment Duration				
Total Cohort	0.4	− 0.1	0.1	0.2
Resins, MC (#1)[B]	0.8	− 0.4	0.1	0.1
F, MC (#2)	0.8	− 0.1	0.2	0.2
Plywood (#3)	0.8	− 0.2	0.1	0.4
Film (#4)	0.6	< − 0.1	0.2	0.2
Film (#5)	0.3	0.1	0.1	0.1
Resins, DL (#6)	0.7	< − 0.1	0.3	0.3
F, Resins, MC (#7)	0.7	0.1	0.4	0.3
Resins, MC, MP (#8)	0.7	− 0.3	< − 0.1	0.2
Resins, MC, MP (#9)	0.6	− 0.1	0.1	0.1
F, Resins, MC (#10)	0.6	− 0.3	0.1	< 0.1
Exposure Duration				
Total Cohort	0.6	0.0	0.2	0.3
Resins, MC (#1)	0.9	− 0.2	0.2	0.2
F, MC (#2)	0.9	− 0.1	0.3	0.2
Plywood (#3)	0.9	− 0.2	0.1	0.4
Film (#4)	0.8	0.3	0.4	0.4
Film (#5)	0.6	0.5	0.5	0.1
Resins, DL (#6)	0.7	0.1	0.4	0.3
F, Resins, MC (#7)	0.8	0.2	0.4	0.4
Resins, MC, MP (#8)	0.7	− 0.3	0.0	0.2
Resins, MC, MP (#9)	0.8	0.0	0.2	0.2
F, Resins, MC (#10)	0.8	0.1	0.1	0.2

[A]From Blair *et al.*[9]
[B]MC = molding compounds, F = formaldehyde, DL = decorative laminates, MP = molded products

TABLE V. Median Level of Formaldehyde Exposure (Number of People) by Duration of Employment, as of December 31, 1965*

Duration of Employment, yrs	Plant 1	2	3	6	7	8	10	Total
< 1	1.0 (17)	3.1 (8)	0.1 (23)	0.1 (67)	0.1 (31)	0.3 (65)	0.5 (14)	0.2 (225)
1–4	0.8 (117)	3.2 (72)	0.1 (98)	0.2 (296)	0.1 (78)	0.7 (89)	− (0)	0.2 (750)
5–9	0.9 (102)	3.2 (53)	0.1 (58)	0.1 (169)	0.1 (104)	0.3 (59)	1.1 (14)	0.2 (559)
10–14	0.8 (139)	3.1 (86)	0.1 (7)	0.2 (272)	0.1 (148)	0.2 (60)	0.5 (73)	0.3 (785)
> 15	0.3 (139)	3.1 (122)	0.1 (16)	0.3 (367)	0.1 (151)	0.3 (71)	0.3 (297)	0.3 (1163)

*From Stewart *et al.*[8]

cohort, duration of employment correlated moderately with cumulative exposure (r = 0.4), whereas duration of exposure correlated somewhat better (r = 0.6). In the individual plants, however, the correlation coefficients between duration of employment and cumulative exposure ranged from 0.3 to 0.8 and for duration of exposure, 0.6 to 0.9. For average, highest TWA, and peak exposures, the correlations with the duration measures were much lower, and in some plants, they were negative (r = −0.4 to +0.4 with employment duration and r = −0.3 to +0.5 with exposure duration).

There are some studies in which analyses of mortality have been conducted using more than one exposure classification strategy. A recent report compared disease risks by duration and any other measure of exposure as demonstrated in 25 studies.[(10)] A monotonic exposure–response relationship, i.e., a trend which rose with each increasing analytical category, was seen more often with cumulative exposure and intensity of exposure than with duration of exposure. Moreover, when comparing the risk of disease in the highest exposure category, 68 percent of the studies found the highest relative risk using level of exposure, compared to 19 percent of the studies using duration as the measure of exposure. These data indicate that analyses by duration are less likely to uncover exposure–response gradients than analyses based on level of exposure and that relative risks are likely to be smaller.

This is shown quite nicely in the asbestos study by Dement *et al.*,[(5,11)] in which the authors presented mortality of lung cancer risk by both duration of employment and cumulative exposure. The SMR by years employed at the company rose as duration of employment increased up to 20–29 years; however, at 30 or more years, the SMR dropped and was no longer significant (Table VII).[(11)] SMRs using cumulative exposure, however, rose consistently and stayed significantly elevated. Similarly, in a nested case–control study examining the risk of mortality from leukemia, duration of employment in benzene-exposed jobs and cumulative exposure to benzene were analyzed in a conditional logistic regression.[(12)] The strongest single predictor of death from leukemia was cumulative exposure (χ^2 = 6.4, p = 0.01) compared to duration of exposure and average exposure rate.

An argument for the use of duration is that it can be measured more accurately than estimates of exposure. The question at this point, however, is whether an accurate measurement of a poor surrogate of dose is better than a less precise measurement of a more relevant surrogate? Several lines of evidence presented here indicate that duration is not necessarily a good measure of level of exposure. Analyses based on estimated levels tend to reveal exposure–response gradients which are not always apparent when duration is used as a surrogate measure. Quantitative estimates of exposure should be considered for other reasons. Investigators often continue to follow cohorts after the initial results have been published. Over time, the importance of the more recent, and probably more accurate, exposure estimates will increase because the effects of current exposures will be more relevant to disease developing in the future. Finally, it is only by making exposure estimates, by trying new approaches, and by attempting to evaluate accuracy and reliability in today's studies that better exposure estimates will be made in future studies.

TABLE VII. Lung Cancer Mortality Risk Estimates by Duration of Employment and Cumulative Exposure to Asbestos[A]

Years Employed	SMR	Cumulative Exposure (fibers/cc × days)	SMR
< 10	185[B]	< 1000	140
10–19	476[B]	1000 – 10,000	279[B]
20–29	976[B]	10,000 – 40,000	352[B]
> 30	410	> 40,000–100,000	1166[B]

[A]From Dement *et al.*[(11)]
[B]$p < 0.05$

The arguments presented here are not to suggest that ever/never or duration of employment or exposure should not be performed. These measures can be useful in hypothesis-generating studies, particularly when using readily available records. In addition, if the environmental conditions specified by Checkoway[(3)] are met, duration can be a good measure of cumulative exposure in analytic studies. Moreover, exposure assessment may not be possible or may require more financial or time resources than are available to the investigator. Investigators should recognize, however, that relying upon ever/never or duration of employment as the sole measures of exposure will probably result in misclassification which will enhance the probability of missing associations.

Semiquantitative Estimates

The limitations of ever/never or duration as a method for evaluating exposure–response relationships have led some investigators to use a semiquantitative approach in which they create relative exposure categories, e.g., high, medium, and low. This type of analysis has been successful in finding associations, particularly in case–control studies. Unfortunately, few investigators have described in detail the procedures followed for the estimation of exposures, although one approach has been suggested.[(13)]

There may be several drawbacks to using semiquantitative assessment. The practice of ranking jobs into semiquantitative categories requires that weights be assigned to each of the categories to allow analysis by cumulative exposure. These weights are typically arbitrary, usually 1, 2, and 3, designating low, medium, and high exposure levels. Such an assignment assumes that a job in the medium category has twice the exposure level as a job in the low category and two-thirds the exposure level as a job in the high category. It is not known how well these weights reflect reality. In one study,[(14)] air monitoring was conducted on various job tasks in five industries, and the sampling results were used to calculate an arithmetic mean for each task. These means were used to place each of the

TABLE VIII. Relative Exposure Levels of Two Occupational Hygienists' Semiquantitative Exposure Categories[A]

Industry	Occupational Hygienist	Exposure Category			
		None	Minor	Medium	High
1	OH1	—[B]	1.00	5.87	9.41
2	OH2	1.00	4.92	17.32	3.96
3	OH1	1.00	3.00	12.50	8.33
3	OH2	1.00	2.80	3.40	5.40
4	OH1	1.00	1.40	1.60	3.20
4	OH2	1.00	1.40	2.00	3.80
5	OH1	—	1.00	2.00	3.88
5	OH2	1.00	0.59	1.94	3.00
Average	OH1	1.00	1.60	5.49	6.21
	OH2	1.00	2.43	6.17	4.04
Average		1.00	2.01	5.83	5.12

[A]From Kromhout *et al.*[14]
[B]Not provided.

tasks into one of four exposure categories and to derive an overall mean for the exposure category. Independent of the monitoring, two occupational hygienists classified the tasks into four exposure categories ranging from no exposure (1) to high exposure (4). Using the authors' data, the relative differences in the means of the exposure categories were calculated by dividing the mean measured exposure value of the lowest exposure category into each of the higher exposure categories (Table VIII). Thus, for occupational hygienist 2 (OH2), the means of the exposure categories in industry 2 were 2.5, 12.3, 43.3, and 9.9 mg/m^3. Dividing the lowest mean in this series (2.5) into the means of each category results in relative values of 1.00, 4.92, 17.32, and 3.96. As can be seen in Table VIII, the overall average relative increases were not 1, 2, 3, and 4, but rather 1.00, 2.01, 5.83, and 5.12. This study suggests that using arbitrary weights provide less accurate weights than estimates of exposure levels. More investigation, however, is needed in this area.

When developing estimates of the most likely exposure level for each job based on low, medium, and high exposure categories, there may be a tendency to think less carefully about the relative difference between jobs because the exposure categories may be broad and are nonquantitative. This type of assessment may be somewhat less accurate than methods that require quantitative estimates, but it could be countered by using a more expansive scale with 10 or 20 categories. It would seem, however, that a more quantitative scale would be better based on a more familiar scale, such as ppm. Furthermore, as with ever/never or duration analyses, this approach provides no information on actual levels of exposures, which is desirable from a public health standpoint.

Quantitative Assessment

There are several reasons why developing point estimates of exposure levels, when possible, is a better approach than placing jobs into semiquantitative categories.

1. It forces the person performing the exposure assessment to think carefully about the relative exposure levels experienced by the jobs. The assessor must evaluate the different parameters that affect exposure levels and compare these to the other jobs in the study.
2. The scale, e.g., ppm, is familiar to the assessor.
3. By having actual quantitative estimates, new analyses can easily be performed if the investigators want to change the cutpoints of the exposure categories. Reclassification of subjects into categories with different exposure boundaries between low, medium, and high, however, requires a new assessment effort.
4. Investigators may be more likely to describe how the assessments were made when developing quantitative estimates than when assigning semiquantitative categories.
5. If after developing quantitative estimates, the assessor does not believe that the available exposure information supports their use, the subjects can be grouped into fewer categories on the basis of their quantitative estimates. Such an approach was taken in the study of formaldehyde workers.[6]

In general, assessment of quantitative exposure levels is, ideally, more appropriate than other exposure assessment approaches because it may more closely approximate the true measure of dose. This approach, however, is not without its problems. Exposure data on occupational chemicals are all too few. The authors know of no retrospective studies of long-term diseases, such as cancer, in which sufficient monitoring data for chemical exposures were available for the investigators to use these data for all study subjects, although such data may be available for ionizing radiation exposures. For this reason and for convenience, estimates are usually developed on the basis of job tasks or title; but even then, monitoring data are usually more available for jobs of heavier exposure than for jobs of low exposure. In addition, monitoring data usually are available for the more recent years, which is acceptable for investigations of diseases with relatively short latency periods, but not for diseases with longer latency periods, e.g., cancer.

As a result of this lack of data, investigators often use qualitative information to supplement monitoring data or to estimate exposure levels where monitoring data are missing. Some researchers, however, are uncomfortable with this approach and point out the probability of introducing errors when estimates are not based on actual measurements. This concern is valid, and undoubtedly, some estimates result in misclassification of subjects. It is believed that the critical issue is not whether a quantitative approach results in misclassification, but whether the misclassification is greater than it would have been using some other approach, i.e., ever/never, duration, or semiquantitative exposure. The authors believe that evaluating each job, or job task, for its possible exposure level, taking into account the relative differences between jobs, is likely to ensure a better estimation of exposures and, therefore, less misclassification of subjects than other approaches.

Summary

This paper has described and compared popular approaches to assess retrospective exposure levels. Analyses using ever/never employed in an industry or job can result in misclassification of exposure due to the heterogeneity of exposures and levels within an industry or job and do not promote the opportunity to evaluate exposure–response gradients. Duration of employment or exposure, although allowing for an evaluation of exposure–response relationships, can also result in misclassification unless specific conditions occur. Semiquantitative assessments of jobs into low, medium, and high exposure categories allow evaluation of exposure–response relationships and should result in less exposure misclassification than duration, but this approach requires the development of arbitrary weighting factors. Quantitative assessments are the preferable approach but are subject to much uncertainty when monitoring data are lacking. Investigators can, however, reduce exposure misclassification by developing the quantitative estimates and using them to classify the subjects into a small number of exposure categories. Using the best possible procedure that is most reflective of dose will enhance the power of the epidemiologic study to detect and evaluate etiologic associations.

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