Use of a Job-Exposure Matrix to Assess Occupational Exposures in Relation to Birth Defects

Carol Louik, ScD
Howard Frumkin, MD, DrPH
Michael J. Ellenbecker, ScD
Rose H. Goldman, MD, MPH
Martha M. Werler, ScD
Allen A. Mitchell, MD

Accurate exposure assessment remains a challenge in occupational epidemiology. We evaluated one approach, use of a job-exposure matrix (JEM), by applying the National Institute for Occupational Safety and Health (NIOSH) JEM to a large case-control birth defects study that included parental occupation information. We investigated the JEM exposure predictions in several ways and found that for a substantial proportion of the parents in the birth defects study, the JEM yielded either no exposure data or nonsense predictions. Among exposure predictions that were plausible, most were of low probability. The high probability exposure predictions were statistically unstable, and neither low nor high probability exposure predictions were reliable. There was considerable discrepancy between the JEM predictions and expert assessments for five exposures of interest. Application of the NIOSH JEM to the birth defects study database (and probably other databases as well) does not provide a useful means of assessing occupational exposures.

A major challenge in case-control studies of occupational exposures is the assessment of past exposures. Detailed interviews with subjects or proxies are sometimes used, but these are expensive, time-consuming, logistically difficult, and limited by low validity when administered either to study subjects[1,2] or, as is often necessary, to spouses.[3,4] Expert assessment based on occupational histories is an expensive and time-consuming alternative, and it is further limited by the scarcity of qualified experts.[5,6]

A third approach is the job-exposure matrix (JEM).[7–9] A JEM is a cross-classification of job titles and exposures that allows exposure to be inferred on the basis of the job title[10] (or, in more complex JEMs, on the basis of a job title, industry, and/or calendar times of employment). A large number of JEMs have been described, some designed for population-based studies[7,11–14] and others designed for use in specific industries such as electric utilities,[15] paint manufacturing,[16] or welding.[17]

The advantages and disadvantages of JEMs have been discussed extensively in recent years.[5,8,18–20] Exposure assessment derived from JEMs may entail considerable misclassification and lead to biased risk estimates. Validity is thought to improve if a JEM is based on empirical data; if it uses probabilities and/or scales of exposures rather than dichotomous designations; if it is confined to specific exposures, plants, industries, or worker populations rather

From the Slone Epidemiology Unit, School of Public Health, Boston University School of Medicine, Brookline, Mass. (Dr Louik, Dr Werler, Dr Mitchell); the Department of Environmental and Occupational Health, Rollins School of Public Health, Emory University, Atlanta, Ga. (Dr Frumkin); the Department of Work Environment, University of Massachusetts, Lowell, Mass. (Dr Ellenbecker); and the Occupational and Environmental Health Center, The Cambridge Hospital, Cambridge, Mass. (Dr Goldman).

Address correspondence to: Carol Louik, ScD, Slone Epidemiology Unit, 1371 Beacon Street, Brookline, MA 02446; e-mail clouik@slone.bu.edu.

than being broadly inclusive; and if appropriate statistical analytical techniques are used.

The National Institute for Occupational Safety and Health (NIOSH) JEM, developed in the 1980s and described in the literature in 1991,[13] is one of the largest job-exposure matrices, and it has been made widely available to investigators by NIOSH. Several epidemiological studies have used the NIOSH JEM, either to estimate the extent of certain exposures[21–23] or to test etiological hypotheses regarding workplace exposures.[24] It is therefore important to evaluate the validity of the NIOSH JEM.

Several approaches to such an evaluation are available.[25] First, one might use a definitive accepted standard, comparing JEM predictions with objective measurements of exposure. Second, one might compare the exposure predictions generated by two different JEMs. Third, one might compare JEM predictions with expert assessments. Fourth, one might test known associations using JEM-derived exposure predictions; if such studies replicate known associations (and do not identify unlikely associations), then the validity of the JEM is supported. Several studies have critically evaluated JEMs in one or more of these ways.[5,20,26–31]

This report describes an evaluation of the utility and validity of the NIOSH JEM. We applied the JEM to an existing database, the Slone Epidemiology Unit Birth Defects Study (BDS), to test its performance as a tool for evaluating risks of occupational exposures. We used four approaches: (1) describing the distributions of exposures predicted by the JEM among the BDS parents; (2) assessing the JEM's performance in demonstrating a reported association; (3) comparing JEM predictions with expert assessments for three specific exposures; and (4) examining expert agreement with the JEM as a function of probability of exposure.

Methods

The methods of the BDS have been described previously.[32] The study includes infants with a wide variety of birth defects drawn from participating hospitals in the metropolitan areas of Boston (initiated in 1976), Philadelphia (1977), and southeastern Ontario (1979) and from one-third of the state of Iowa (1983 to 1985). Mothers are interviewed by trained nurses, typically in the subject's home, within 6 months of the infant's birth. The interview elicits information on a wide variety of medical and demographic factors as well as environmental exposures, especially medications. Industry and occupation of both mother and father at the time of conception are ascertained. Occupations are coded by using an industry/occupation dictionary derived from the system developed by Hoar et al.[7] This approach uses a two-digit industry code based on the Standard Industrial Classification and a three-digit occupation code based on the *US Dictionary of Occupational Titles*. We expanded the industry codes to three digits and the occupation codes to five digits to allow greater specificity in coding.

The job-exposure matrix developed by NIOSH is based on data gathered as part of the National Occupational Hazard Survey, a national survey of businesses representative of US industry, conducted from 1972 to 1974, with data from a stratified sample of 4636 US workplaces. It was designed to describe health and safety conditions in the workplace and to determine the extent of exposures to chemical, physical, and biological agents. The NIOSH JEM offers several advantages over other matrices. It is based on empirical data from a representative sample of all major sectors of US industry. In addition to providing a simple yes/no exposure indicator for each pairing of a job/industry combination and a chemical, the NIOSH JEM also provides a probability of exposure. (For each job/industry combination, the database includes the number of persons observed, the denominator, and the number exposed to a given chemical, the numerator.) As a nationally based matrix, the NIOSH JEM was intended to have broad applicability in occupational health research. Details of the data collection process and the development of the matrix have been described.[13]

To evaluate the utility of the NIOSH JEM in occupational teratogen research, we first assigned exposures and exposure probabilities to each of the 12,188 mothers and 12,017 fathers for whom data on occupation existed in our files in the following manner: (1) all existing industry/occupation codes in the BDS were first converted to Census codes to be compatible with the NIOSH JEM; and (2) information contained in the JEM was then used to assign to each BDS parent (a) exposures to specific agents, and (b) probabilities for those exposures.

Describing the Distributions of Exposures

We next reviewed the exposure predictions that emerged. First, we observed the extent to which BDS parents could be assigned exposure probabilities by the JEM, and we noted the categories of BDS parent occupations for which the JEM did not provide information. Then we created distributions of probabilities of exposure to specific chemicals for a wide variety of industry/occupation pairs, and we reviewed these distributions.

Evaluating JEM's Performance in Assessing a Previously Reported Association

For this component of our evaluation, we selected an association previously reported in the literature: maternal exposure to organic solvents and malformations of the genitourinary tract.[33] We reviewed the numbers of mothers who were predicted by JEM to be exposed to various solvents, and we selected a solvent,

benzene, with a high number of exposed mothers for analysis. Preliminary examination of the data showed an elevated odds ratio for benzene in relation to kidney malformation and sufficient power, so we elected to explore this hypothesis in further detail.

Cases included mothers of infants with a diagnosed kidney malformation who were either stillborn or liveborn. Controls were mothers of infants with a malformation other than kidney. Both cases and controls were restricted to women who reported an industry/occupation combination for which the JEM could provide exposure information. We calculated the odds of exposure to benzene among infants with kidney malformations, treating exposure as a dichotomous variable, with "exposed" defined as any non-zero probability of exposure.

Comparing JEM Predictions With Expert Assessments

We selected three chemical exposures for expert review on the basis of the following criteria: (1) they must include at least some industry/occupation combinations in the JEM with high probabilities of exposure, (2) our reviewers must consider themselves sufficiently knowledgeable about them to make valid assessments, and (3) they are of potential interest in birth defects epidemiology. The three chemical exposures selected were dichlorodifluoromethane (218 combinations), propylene glycol (231 combinations), and amorphous fused silica (234 combinations). For each of these exposures, the reviewers independently rated each job held by BDS parents according to four levels of exposure: none, low (probability greater than 0 but less than one-third), moderate (probability between one-third and two-thirds), and high (probability greater than two-thirds). We evaluated the concordance between these expert assessments and the JEM predictions by calculating the proportion of industry/occupation combinations that were assigned the same exposure level by the JEM and by both (or neither) expert.

Assessing Expert Agreement With JEM as a Function of Probability of Exposure

As an extension of our benzene analysis, two of the authors, an occupational medicine physician (HF) and an industrial hygienist (MJE), independently reviewed all industry/occupation combinations that had been designated as benzene-exposed or xylene-exposed by the JEM. Each reviewer assigned a dichotomous (yes/no) exposure status to each industry/occupation combination. We then stratified the industry/occupation combinations considered to be exposed by the JEM according to decile of exposure probability assigned by the JEM. Within each decile, we calculated the proportion of industry/occupation pairs that the experts had considered exposed. We also examined the exposure probabilities as a function of the number of observations in the JEM.

Results

Distributions of Exposures

The process of converting BDS occupation codes to JEM-compatible codes revealed some apparent incongruities in the JEM. For example, the industry "insurance" includes the occupation "investigators and adjusters, except insurance." The occupation "groundskeepers and gardeners, except farm" is listed in 39 industries. For 14 of these, "soil" is identified as an exposure, but for the remaining 25, it is not. In addition, the occupation "farmers, except horticultural" is listed *only* in the industry "radio and television broadcasting."

Among the 12,188 mothers and 12,017 fathers with industry and occupation data in the BDS, 3786 (31%) mothers and 5955 (50%) fathers were assigned exposures by the JEM. Among the occupations not included in the JEM (and therefore not assigned exposure designations) were some common ones, such as elementary and secondary schoolteachers (n = 891), computer systems analysts (n = 299), computer operators (n = 301), dental laboratory technicians (n = 103), lawyers (n = 248), and police officers (n = 196).

After identifying the most common JEM-derived exposures among BDS parents, we examined the exposure probabilities assigned by the JEM for these exposures. Three general patterns were apparent, as illustrated in Figs. 1 through 3. Although the majority of exposures occurred at low probability in virtually all cases, for some (Fig. 1), there was a substantial proportion with probability of 0.5 or greater. For others (Fig. 2) there was a decreasing frequency as probability level increased but still a measurable number of exposures above 0.5. However, for most agents (Fig. 3), exposures at a probability of greater than 0.5 were rare.

JEM's Performance in Demonstrating a Reported Association

There were 38 cases and 3748 controls for whom the JEM could assign exposures. Of these, benzene exposure was assigned to 13 cases and 612 controls. When maternal exposure to benzene was defined without regard to probability of exposure (ie, exposure as a dichotomous variable), the odds ratio for kidney malformations was 2.7 (95% confidence interval, 1.4 to 5.1). When adjusted for potential confounding by maternal age, maternal education, parity, religion, calendar time, maternal smoking, paternal smoking, geographic region, and baby's sex, the odds ratio for kidney malformations increased to 3.2 (95% confidence interval, 1.5 to 6.8).

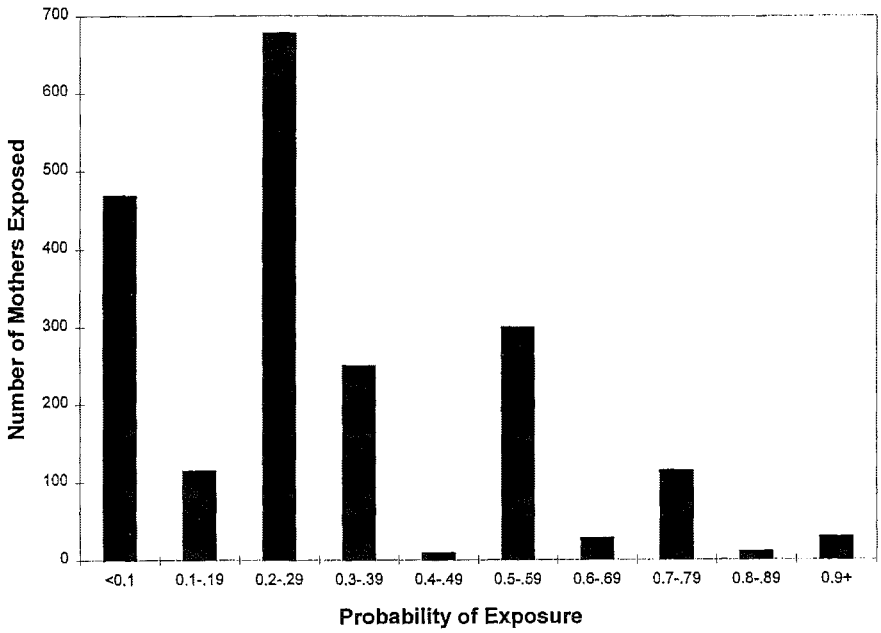

Fig. 1. Distribution of exposure probabilities for dichlorodifluoromethane in mothers.

JEM Predictions Compared With Expert Assessments

Among the mothers in the BDS database, the JEM designated a total of 67 industry/occupation combinations as benzene-exposed. Examples included "registered nurse" in "hospitals" and various occupations in the printing industry. In 46 (69%) industry/occupation combinations, both reviewers agreed that the job would likely include benzene exposure; an additional 19 (28%) were classified as benzene-exposed by only one of the reviewers. Both reviewers agreed that two jobs (3%) were *not* likely to be benzene-exposed; one of these ("registered nurse" in "hospitals") accounted for 85% of the benzene-exposed mothers in this analysis.

For dichlorodifluoromethane, propylene glycol, and silica, the reviewers assigned exposure ratings of none, low, moderate, and high. Reviewers were considered to have agreed if their categorical ratings matched exactly. With this definition, the reviewers agreed in 67% of industry/occupation combinations for dichlorodifluoromethane, 72% of combinations for propylene glycol, and 79% of combinations for silica. Agreement was 20%, 3%, and 2%, respectively, between at least one reviewer and the JEM. Much of the agreement between reviewers was attributable to jobs that, although considered exposed by the JEM, were rated as "no exposure" by both reviewers. Even among the 20 industry/occupation combinations to which the JEM assigned a probability level of 1.0, 14 (60%) were considered as unexposed by both reviewers. Examples included dichlorodifluoromethane exposure among "cashiers" at "gasoline service stations," and "managers and administrators" in "banking," and silica exposure among "supervisors and proprietors" in the "retail florist" industry.

Assessing Expert Agreement With JEM as a Function of Probability of Exposure

The agreement between expert assessment and JEM assignment, stratified by the JEM-assigned probability of exposure, is shown in Table 1, for the case of benzene. The proportion of industry/occupation combinations for which both reviewers agreed with the JEM exposure assignment increased as the probability level increased, but there were only six industry/occupation combinations with probabilities greater than 0.5. Because this result was unexpected, we repeated the analysis using a different exposure, xylene; the results are shown in Table 2. For xylene, agreement with JEM exposure assignment also increased with probability of exposure. However, lack of agreement also increased with high probability of exposure. In fact, of five jobs with a JEM-assigned probability of 1.0, our experts assigned a probability of 0 to three of them. Thus, even among industry/occupation combinations with high probability of exposure, there was considerable disagreement with expert assessment.

Because the relationship between probability level and degree of agreement was not as strong as anticipated, we investigated the manner in which the probabilities were derived within the JEM itself. For each industry-occupation pair, the JEM provides (A) the number of workers surveyed by the National Occupational Hazard Survey, and (B) for each exposure, the number of workers in that industry/occupation who were observed to have been exposed. A measure of probability can then be calculated by dividing B by A. For dichlorodifluoromethane, propylene glycol, and silica, we grouped industry-occupation pairs according to deciles of JEM-assigned probability level and examined the numbers of observations on which these probabilities were based. Further, for each decile of probability, we calculated the mean and median number of observations for each industry-occupation pair within that decile.

This analysis revealed an inverse relation between the probability level and the number of observations on which that probability was based (Figs. 4 through 6). In particular, in all cases in which high probabilities of exposure were assigned, the number of observations on which they

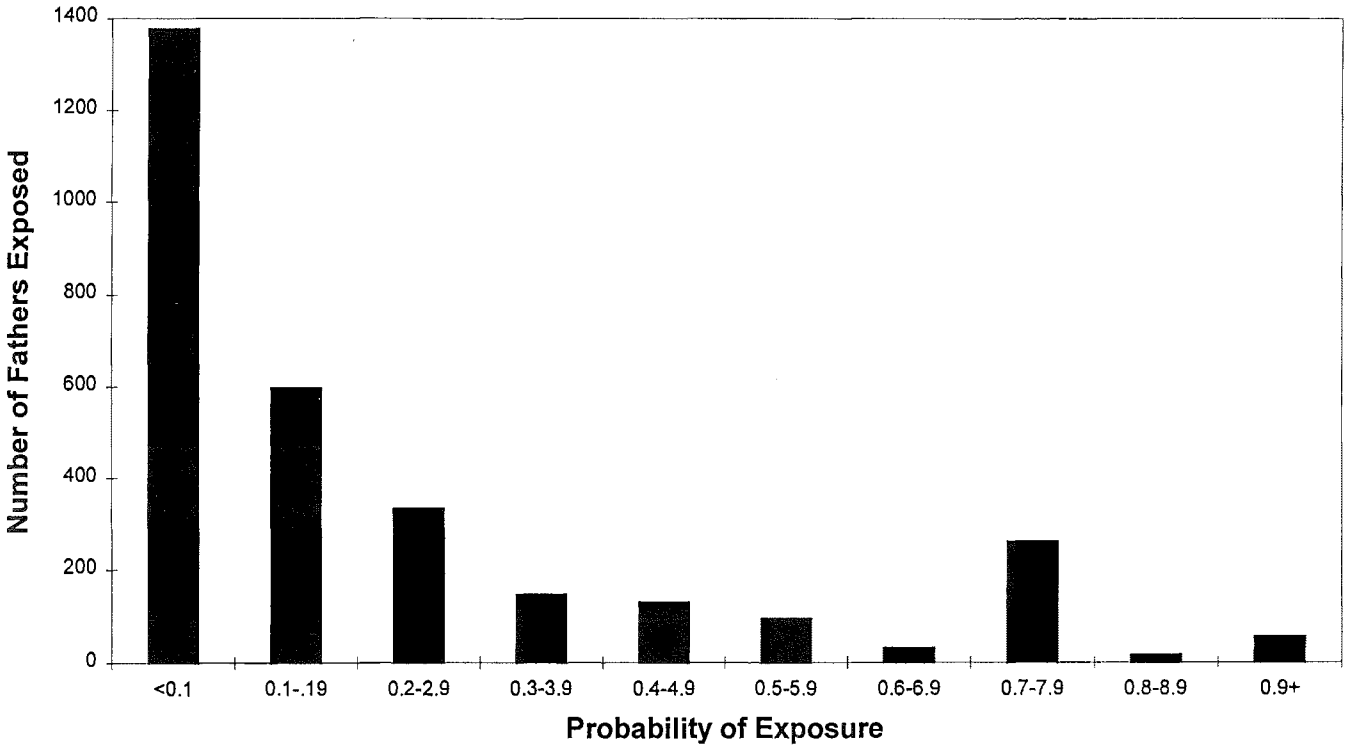

Fig. 2. Distribution of exposure probabilities for dichlorodifluoromethane in fathers.

were based was small—in many cases, fewer than five. Although small sample sizes alone need not imply inaccuracy, expert review of benzene and xylene probabilities concluded that these high probabilities did not accurately reflect the likelihood of exposure.

Discussion

In theory, the concept of a matrix such as the JEM offers an efficient tool for the investigation of potential associations between workplace exposures and adverse health outcomes. By providing a mechanism that systematically links an industry/occupation combination with workplace exposures, a matrix would allow researchers to infer exposures that were not directly measured. The NIOSH JEM has particular potential because it is based on direct observation of a large number of workplaces and is thus built on a large body of empirical exposure data; it also provides the probability of exposure to a given substance for each industry-occupation pairing.

We found that a substantial number of industry/occupation combinations could not be coded to the JEM, that the majority of industry/occupation combinations in the JEM show very low probabilities of most exposures, and that higher probabilities of exposure are based on very few observations. We also found a number of exposure assignments with both high and low probabilities that seemed to be anomalous. For example, the JEM considered banking managers to have a 100% probability of exposure to xylene but a 0% probability of exposure to paper. Laborers in the bus and urban transit industry were assigned a 100% probability of exposure to soap, janitors in eating and drinking places were assigned a 10% probability, and cooks in eating and drinking places had only a 0.7% probability of soap exposure. Overall, when comparing expert reviews with JEM exposure predictions, we found low concordance. However, the JEM did demonstrate an association for which prior evidence had established some basis, maternal benzene exposure and kidney malformations.

Several published studies have evaluated the NIOSH JEM, two by comparing it with another matrix and two by comparing JEM findings with expert assessment. Cicioni et al[34] compared JEM predictions with expert assessments for one exposure, asbestos, by using cases and controls from the Los Angeles County Cancer Surveillance Program. Their findings were similar in key respects to ours. Many of the jobs in the Program database did not have information in the JEM, and there was considerable disagreement between JEM predictions and expert assessments. Of 4116 cases classified as "exposed" by the JEM, 1851 (45%) were considered to be unexposed by the experts. Of 288 cases classified as "high exposure" by the experts, 180 (62.5%) were classified as unexposed by the JEM. These authors noted the importance of timing, especially in a study of long-latency diseases; although the JEM observations dated from 1972 to 1974, the

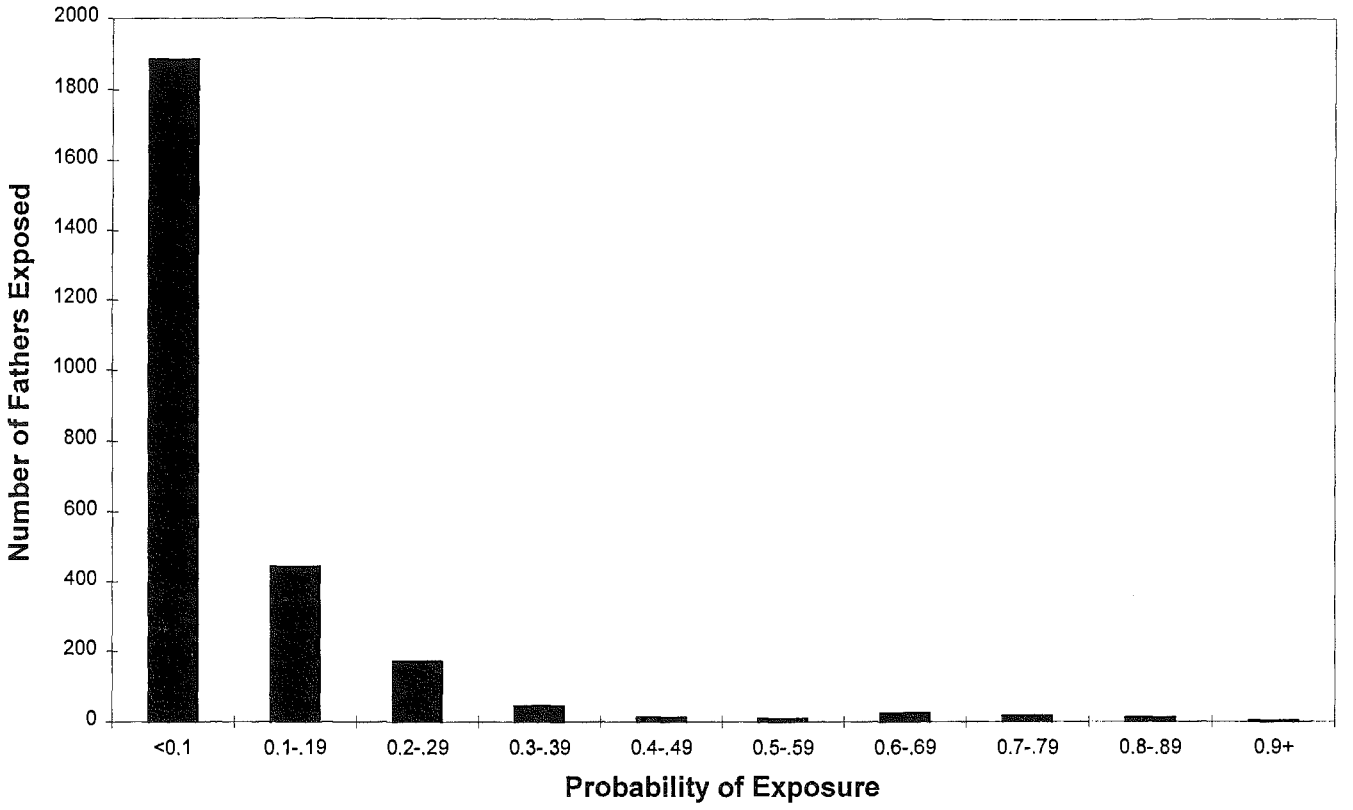

Fig. 3. Distribution of exposure probabilities for propylene glycol in fathers.

TABLE 1
Rates of Agreement* Between Experts Regarding Exposure Status According to Probability Level: Benzene

JEM-Assigned *P* Level	No. of Jobs	Both Experts Agree With JEM		Neither Expert Agrees With JEM	
		n	%	*n*	%
<0.1	44	30	57	2	5
0.1–0.19	11	7	64	0	–
0.2–0.29	3	2	67	0	–
0.3–0.39	3	2	67	0	–
0.4–0.49	0	–	–	–	–
0.5–0.59	3	2	67	–	–
0.6–0.69	1	1	100	0	–
0.7–0.79	0	–	–	–	–
0.8–0.89	1	1	100	–	–
0.9–0.99	1	1	100	–	–
1.0	0	–	–	–	–
Total	67	46	69	2	3

* Experts defined exposure only as dichotomous ("yes/no") variable.

exposures relevant to their cases may have occurred years earlier, limiting the applicability of the JEM. A further limitation they noted was that the JEM provides probabilities of exposure—but not exposure intensity, which facilitates exposure misclassification. Rybicki et al[30] compared three approaches to exposure assessment: self-report, expert review by an industrial hygienist, and the NIOSH JEM. The exposures of interest were three metals: copper, lead, and iron, and the subjects were 188 workers in manufacturing industries in the Detroit area. Agreement between the industrial hygienist and the JEM ranged from 69.2% to 86.0%. With industrial hygiene review considered as the definitive standard, the JEM sensitivity ranged from 0% (for lead) to 21.2% (for copper), and the JEM specificity ranged from 86.4% (for iron) to 92.6% (for lead).

Linet et al[35] compared an early version of the JEM with a job-exposure matrix previously published by Hoar et al[7]. Their subjects were 342 cases and 342 controls in a case-control study of chronic lymphocytic leukemia in Baltimore. The two matrices yielded divergent odds ratios for most exposures, with the Hoar matrix generally yielding estimates twice as high as those of the NIOSH JEM. Kappa statistics for concordance of the two matrices were reported for 14 exposures (sev-

en each in the cases and controls). Of these, only five were greater than 0.25, reflecting a low level of agreement between the two matrices. Hawkes and Wilkins[31] used a similar approach, comparing the predictions of the NIOSH JEM with those of the Hoar matrix. They studied 214 exposures, using occupations in the metal; paper and wood; and chemical, drug, and paint industries. Kappa and G statistics, reflecting agreement between the two matrices, were derived for each industry/occupation combination. The kappa statistics ranged from 0.02 to 0.27 in the metal industry, from −0.07 to 0.24 in the paper and wood industries, and from −0.12 to 0.14 in the chemical, drug, and paint industries, indicating poor agreement. Additional analyses supported the same conclusion. Although comparisons of two job-exposure matrices do not permit conclusions about the validity of either, the low levels of agreement between them raise doubts about both.

Our evaluation suggests two major practical limitations to the JEM. First, many common occupations in the BDS were not included in the JEM, leading to substantial loss of information. Because the distribution of job titles among BDS mothers is similar to that observed in a repre-

TABLE 2
Rates of Agreement* Between Experts Regarding Exposure Status According to Probability Level: Xylene

JEM-Assigned *P* Level	No. of Jobs	Both Experts Agree With JEM		Neither Expert Agrees With JEM	
		n	%	*n*	%
<0.1	141	83	59	4	3
0.1–0.19	32	17	53	3	9
0.2–0.29	17	9	53	0	–
0.3–0.39	7	4	57	2	29
0.4–0.49	9	7	78	1	11
0.5–0.59	7	5	71	1	14
0.6–0.69	2	1	50	0	–
0.7–0.79	4	4	100	0	–
0.8–0.89	2	2	100	0	–
0.9–0.99	1	1	100	0	–
1.0	5	2	40	3	60
Total	227	135	59	14	6

* Experts defined exposure only as dichotomous ("yes/no") variable.

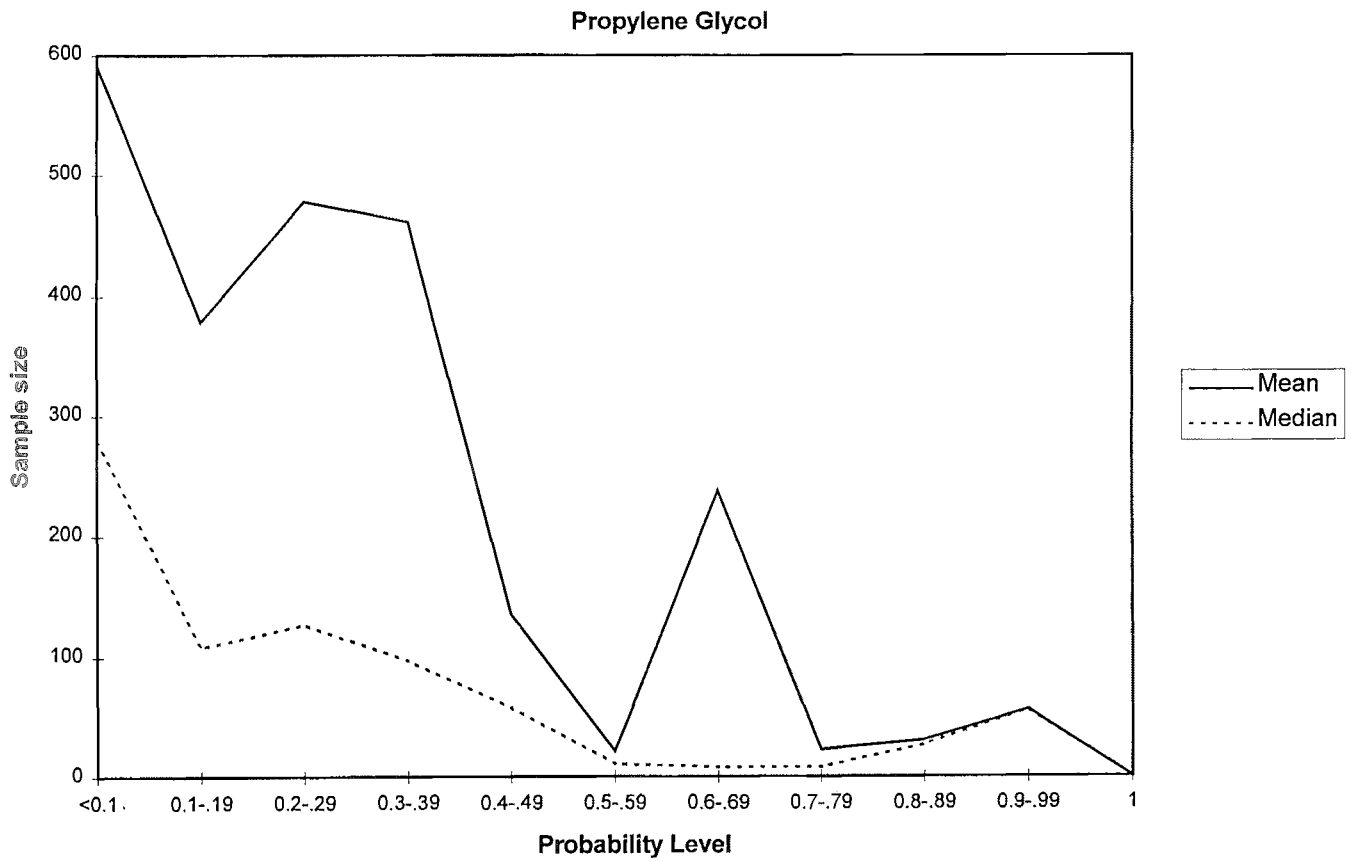

Fig. 4. Mean and median sample sizes of occupations according to exposure probability for propylene glycol.

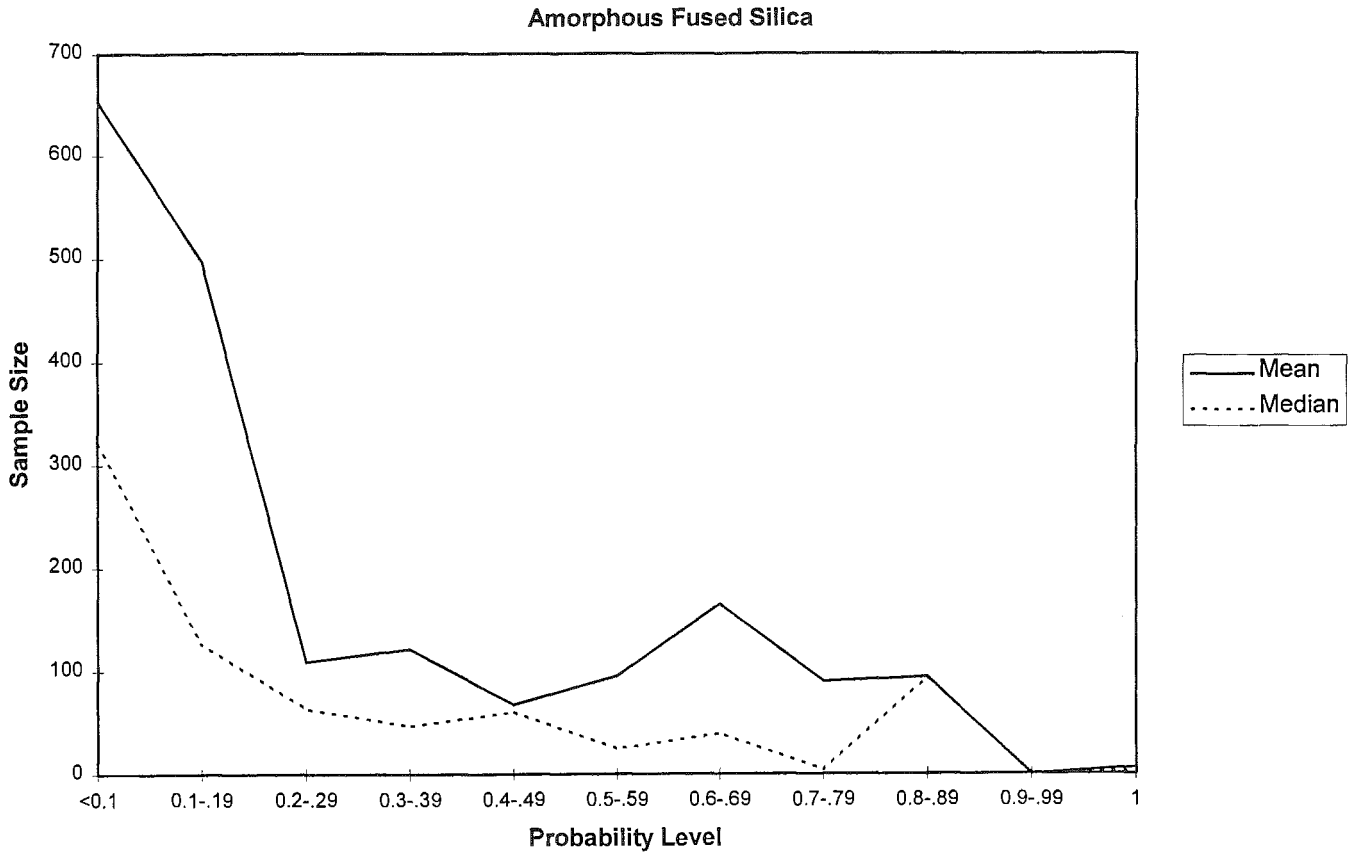

Fig. 5. Mean and median sample sizes of occupations according to exposure probability for amorphous fused silica.

sentative sample of childbearing US women who were surveyed as part of the National Natality and National Fetal Mortality Survey,[36] this problem is likely to affect other data sets as well. Also, because the BDS data were collected years before application of the JEM, some of the job descriptions in the database were not specific enough to allow definitive coding of job titles.

Second, we encountered a tradeoff between validity and statistical power, one in which neither option seems to be satisfactory. One could ignore the levels of probability associated with each exposure and industry-occupation pairing, as we did initially, but because every worker in a job with *any* level of exposure, no matter how low, would be considered exposed, this approach would result in substantial misclassification. For example, in our analysis of benzene and kidney malformations, 85% of "exposed" mothers were registered nurses, which has a JEM exposure probability of 0.02.

Perhaps jobs with low probabilities of exposure (eg, 0.1 or less) provide no information and should be excluded from consideration. Because the vast majority of exposures in the NIOSH JEM have very low probabilities for most jobs, excluding individuals with exposures of low probability would sacrifice large amounts of data, diminishing the power of the JEM. However, there is an even more fundamental problem with this approach. Restricting the JEM to industry/occupation combinations with high probability of exposure requires that these probability estimates be meaningful.

As discussed above, high probabilities assigned by the JEM are unstable. To a large extent, this is to be expected. To obtain a probability of less than 0.01, one must observe more than 100 people in that job. However, one can derive a probability of 1.0 on the basis of only a single observation. Indeed, in virtually all instances when high probabilities were assigned, the samples on which they were based were very small—in many cases, fewer than five observations. Of particular importance, judgments of our occupational medicine and industrial hygiene expert reviewers suggest that these assessments are not only unstable, but also of questionable validity. For example, in our initial benzene analysis, we had ignored the JEM-assigned probabilities and had classified as "exposed" all jobs with non-zero probability of benzene exposure. In fact, the probability of exposure assigned by the JEM to hospital-based registered nurses is 0.015. Such a low probability of exposure could explain why neither expert reviewer considered the job to be benzene-exposed.

Thus, the high probability levels in the JEM are very unstable because

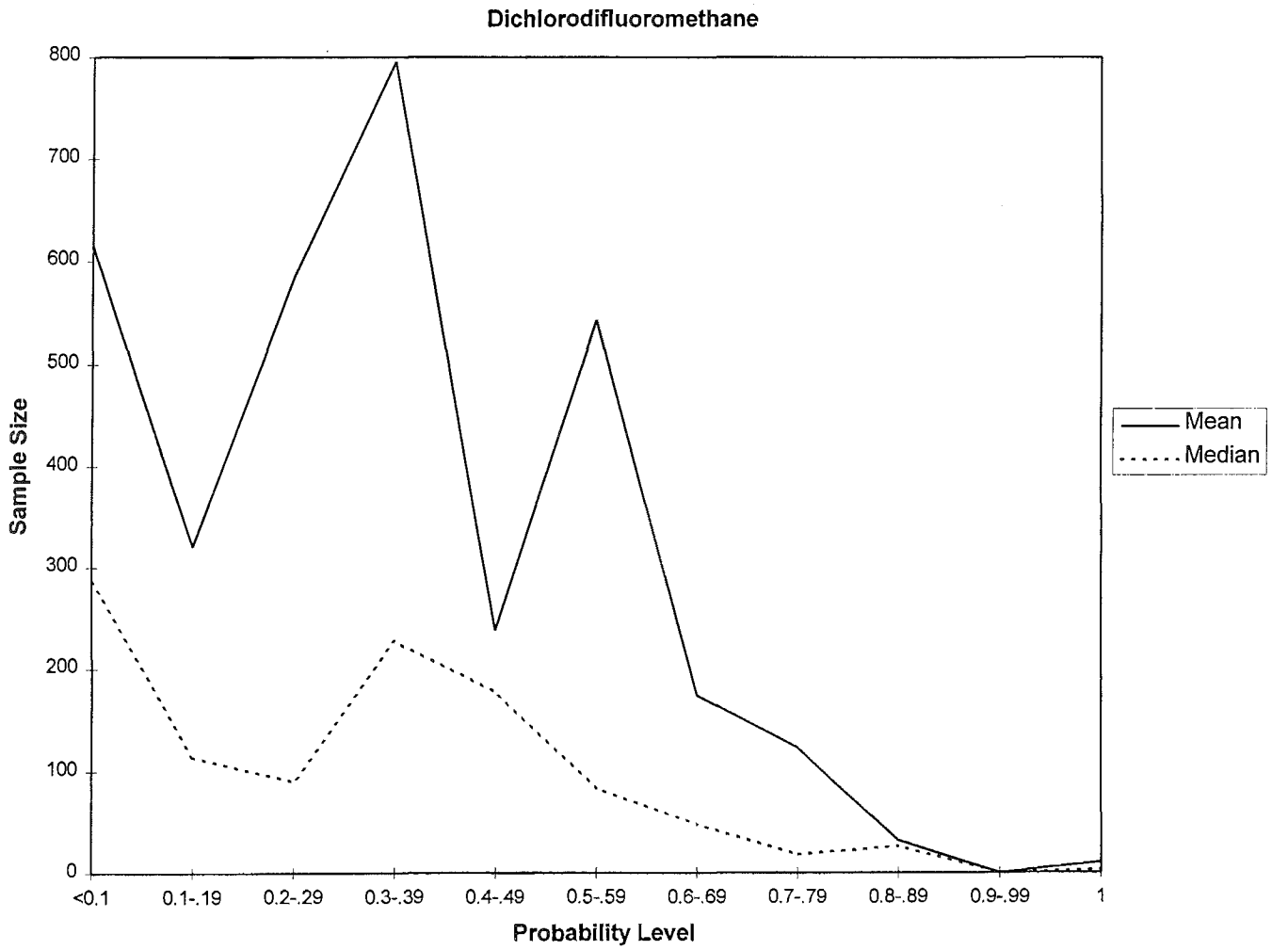

Fig. 6. Mean and median sample sizes of occupations according to exposure probability for dichlorodifluoromethane.

they are based on so few observations and are of questionable validity; the low probability levels, which involve the greatest numbers of people, are of little value because these occupations cannot realistically be considered exposed. We conclude that application of the NIOSH JEM to the BDS or similar epidemiological databases does not provide a reliable means for assessing occupational exposures in relation to health outcomes.

Given the nature of our analysis, we cannot determine whether the problems we identified are unique to the NIOSH JEM or are related to the more global limitations inherent in making job-exposure inferences.[20,25,28,37,38] It may be that the information contained in an industry/occupation combination is simply not sufficient to allow valid inference of chemical and physical exposures, whether by means of a matrix or even by expert review. Almost every industry or occupation listed in the Census codes encompasses a large number of diverse titles, and such heterogeneity would itself create difficulty in assigning exposures. Our experience with the Hoar linkage system also supports this theory. We earlier rejected the Hoar system because of the large number of invalid exposure assignments that we discovered. We had hoped that the inclusion of a measure of probability of exposure (as contained in the JEM) would reduce this problem, but it did not.

The concept of a matrix may be applicable in certain situations; for example, matrices developed for specific industries or for individual studies may be sufficiently detailed to provide a useful mechanism for inferring exposures. As another alternative to automated exposure assignments based on a generalized matrix such as the JEM, one might consider review of job titles by industrial hygienists as a means of identifying exposures. Reviews by our consultants of the job titles of BDS parents resulted in a higher degree of agreement between them than with the JEM for exposures to a limited number of selected substances. However, this approach is limited by the ability of the experts.

An approach we have not investigated that avoids reliance on job titles would be to focus on a relatively small number of exposures that are of potential interest. Experts could then review job *descriptions* rather than job *titles* to determine exposure status. This would enable one to focus on a subset of industries and occupations and ask more directed questions when gathering occupation information in an interview, thus ensuring that relevant information is available to make exposure assessments. It is of interest to note that Siemiatycki et al, in a comparison of several methods of determining exposure status, found that despite its high absolute cost, an approach similar to this was the most cost-effective.[6]

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Women by the Numbers

Percent of highest ranking corporate executives who are female: 3.8.
Percent of top corporate earners who are female: 2.7.
Percent of women in "line" jobs with profit-and-loss responsibility in Fortune 500 companies: 6.2.
Percent of Fortune 500 companies with at least one woman corporate officer: 75.
Average lifetime cumulative earnings for a 50-year old woman versus a 50-year old man: $496,000 versus $1.1 million (US Department of Labor).
Median annual pension income: $3000 for women, $7800 for men (US Department of Labor).
Millions of US working women: 1900 – 5.3, 1950 – 18.4, 1997 – 63 (US Census and Bureau of Labor Statistics).

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