Effects of Three Features of a Job-Exposure Matrix on Risk Estimates

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We tested the impact of three features of a job-exposure matrix on risk estimates in a case-control study that evaluated the association of methylene chloride and astrocytic brain cancer. These features were probability of use of the agent; the consideration of decade of predominant use of methylene chloride within each occupation; and the use of a more specific industrial-occupational coding system. We compared the risk estimates obtained with and without these features. The introduction of each feature had a striking effect on the estimate of relative risk. The odds ratio ranged from 1.47 with none of these features, to 2.47 with high probability of exposure within industry and occupation, to 4.15 with high probability of exposure and specific industrial-occupational coding, to 6.08 with the three features together. These results indicate that the degree of exposure misclassification can be reduced by the introduction of these features into the job-exposure matrix. (Epidemiology 1994;5:124–127)

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Job-exposure matrices (JEM) are cross-classifications of job titles and/or industries by chemical exposures that allow estimation of relative risks by exposures rather than by job title and/or industry categories.[1,2] The advantages and disadvantages of using job-exposure matrices in estimating exposure for epidemiologic studies have been discussed in detail elsewhere.[1–8] In this methodologic exercise, we describe three features that we used in a job-exposure matrix [Gómez M, Cocco PL, Dosemeci M, Stewart PA, Blair A. Occupational exposure to chlorinated aliphatic hydrocarbons: a job-exposure matrix. Am J Ind Med (in press)] and discuss their effects on the risk estimates of the association between astrocytic brain cancer and methylene chloride.[9] Our objective is to evaluate the individual and combined effects of these features of exposure on risk estimates.

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Methods

A job-exposure matrix for methylene chloride was developed to investigate the risk of astrocytic brain cancer from exposure to this substance in a case-control study.[9] We identified three important difficulties in retrospective exposure assessment in constructing an effective matrix [Gómez *et al*, Am J Ind Med (in press)]. These difficulties were the heterogeneity of probability of exposure across industries, over time, and within 4-digit occupational codes. We detail here how we expanded the concept of the job-exposure matrix to take advantage of this heterogeneity.

Methylene chloride is a solvent used in a wide range of industries, with different frequencies of use and intensities of exposure. A probabilistic approach to assess exposure to a solvent may be helpful because, although it may be quite clear that some solvent was used, it is often difficult to know which solvent was used solely on the basis of job and/or industry title. For example, although most painters may have exposure to methylene chloride, the likelihood of occurrence (probability) of exposure is higher in an automotive body repair shop than in painting houses in the building construction industry. We therefore assigned three levels of probability (low, medium, high) to industries and occupations deemed to have exposure to methylene chloride.

In addition to variation of use across industries, the patterns of use of methylene chloride and other sol-

vents have changed over time. For example, methylene chloride has been used as a fumigant since the 1960s, but not before. On the other hand, methylene chloride was used by anesthetists in the first half of the century, but generally not after the 1950s. Although these shifts in usage patterns are not always clearly demarcated, general trends by decade usually can be described. Consequently, after reviewing the literature, we assigned a qualitative (yes or no) evaluation of exposure to methylene chloride by decade. For example, the qualitative exposure assignment to anesthetists would be "yes" for the decades between 1900 and 1950 and "no" for the subsequent decades.

Finally, to reduce the total number of assessments in a case-control study, the jobs and industries held by the study subjects are typically translated into codes, using standard occupational and industrial classification systems. These coding systems were designed for purposes other than occupational exposure classification, and each individual code may include several industries or occupations with substantially different exposures. Thus, classification by exposure may be considerably diluted when a general code is used to group several subindustries or occupations. For example, the industry code for paint remover production in the Standard Industrial Classification (SIC) system[10] is under code 2851 (paints, varnishes, lacquers, enamels, and allied products). This 4-digit SIC code covers manufacturing of 49 paint-related substances, including coating enamels, plastic lacquers, paint driers, paint removers, waterproof paints, plastic paints, varnishes, wood stains, etc. Except for the paint remover manufacturing industry, almost all subindustries under code 2851 are unlikely to have exposure to methylene chloride. Thus, the codes assigned to industry and job titles should be as specific as possible to differentiate exposure-related industries and occupations from unexposed ones. To accomplish this, we created an additional digit to the SIC and the Standard Occupational Classification[11] (SOC) code systems to differentiate critical industries and occupations exposed to methylene chloride from those not exposed.

Assignments of probability weights and decade indicators were carried out for each industrial and occupational code at every level of specificity (2-, 3-, 4-, and 5-digit). When we collapsed the more specific codes into less specific ones (for example, from 5-digit to 4-digit), we used the levels of probability and decade indicators assigned for the less specific codes. We used 21-year duration of exposure as a cutpoint in the analysis, because preliminary analyses showed a stronger dose-response relation among subjects with 21 or more years of exposure.

To evaluate the impact of these three matrix features on risk estimates, we compared the relative risks for astrocytic brain tumor obtained by assessment of exposure to methylene chloride with and without each feature. Maximum likelihood estimates of the odds ratios (ORs) and corresponding 95% confidence intervals[12] were calculated (with adjustment for age and state), comparing subjects having 21 or more years of exposure to methylene chloride with those considered unexposed.

Results

The effects of probability of use, decade of use, and more specific coding on relative risk estimates are shown in Table 1. When evaluating the risks of astrocytic brain cancer by probability of exposure (first column) without consideration of decade and without specific coding, a clear exposure-response relation is seen with increasing probability (ORs = 1.31, 1.52, and 2.47 for low, medium, and high levels of probability).

TABLE 1. Odds Ratios and 95% Confidence Intervals (CI) for Astrocytic Brain Tumor by Exposure to Methylene Chloride for Subjects Who Have at Least 21 Years of Exposure Based on Probability, Specific Coding, and Decade Features

	Without Decade Feature						With Decade Feature					
	Without Code Feature			With Code Feature			Without Code Feature			With Code Feature		
Probability Feature	Cases	OR	95% CI	Cases	OR	95% CI	Cases	OR	95% CI	Cases	OR	95% CI
Without probability feature	121	1.47	0.95–2.27	64	1.68	1.04–2.71	68	1.12	0.71–1.78	24	1.74	0.86–3.58
Low probability	46	1.31	0.74–2.31	32	1.23	0.68–2.21	21	0.81	0.41–1.58	12	1.18	0.47–2.96
Medium probability	58	1.52	0.89–2.62	21	2.09	0.94–4.73	35	1.28	0.69–2.38	4	1.53	0.28–8.98
High probability	17	2.47	0.96–6.46	11	4.15	1.11–16.9	12	1.85	0.64–5.42	8	6.08	1.11–43.8

The second column identifies the risk estimates with the more specific coding but without evaluating use by decade. The last two columns show the relative risks obtained including the decade feature, also presented without and with the specific codes. Introducing specific codes increased the relative risk estimate for astrocytic brain cancer at every probability level, irrespective of whether evaluation by decade was made, except at the lowest probability, where the decade was not evaluated. The estimate increased considerably (OR = 6.08) when all three features were used. In fact, the introduction of each feature had a striking effect on the estimate of relative risk, from OR = 1.47 with none of the features, to 2.47 for people with high probability of exposure, to 4.15 with high probability and more specific coding of industries and job titles, and to 6.08 when accounting for the high probability of use, specific codes, and the decade of exposure.

Discussion

The increase in the estimated relative risk of astrocytic brain cancer from methylene chloride exposure associated with the use of probability of exposure, assignment of exposure by decade, and use of more specific occupational codes indicates that these features improved the accuracy of the job-exposure matrix.

The strength of an exposure-disease association was our measure of refinement in exposure assessment. The use of an exposure-disease relation as a measure of accuracy of exposure assessment is based on the assumptions that: (a) there is a true positive association between exposure to methylene chloride and risk of astrocytic brain cancer; (b) the study population reflects this association observed in the general population; (c) work histories collected from the study subjects are accurate enough to observe the true association; (d) the diagnosis of astrocytic brain cancer was reasonably correct; (e) the exposure misclassification that occurred after accounting for the three features described in this report is nondifferential; and (f) misclassification patterns occurring in this study reduced the true effect toward the null value.

One might question whether the strength of an exposure-disease relation should be used as a measure of accuracy of the exposure assessment in this study. The argument for such an approach is based on the fact that nondifferential misclassification cannot create an artificial trend when there is no true association between the exposure and disease.[13] It may, however, reverse the direction of the trend when there is a *bona fide* association. We think it is unlikely that methylene chloride has a protective effect against astrocytic brain cancer. Thus, the magnitude of the observed risk can be used as a measure of the improved accuracy of these features in a job-exposure matrix.

Other investigators have used "probability" either as a unique matrix feature[14,15] or as one of the factors included in an algorithm for calculating cumulative dose.[4] Exposure assignment by decades was introduced because the use patterns of solvents, including methylene chloride, have changed over time. Inclusion of this feature in matrices was suggested by Hoar *et al*[1] and has been employed by Blair *et al*[14] and Kjuus *et al*.[15] The relative risk of astrocytic brain cancer from exposure to methylene chloride increased from 4.15 to 6.08 when decade of exposure was considered.

The risk of astrocytic brain cancer in the highest probability category of exposure to methylene chloride was increased from 1.85 to 6.08 by the introduction of more specific codes for jobs and industries when exposures were assessed by decade. A smaller but still substantial effect was observed without consideration of decade (from 2.47 to 4.15). Thus, assigning more specific codes appeared to increase the accuracy of the exposure assessments substantially. Industrial hygienists encounter difficulties when assigning exposures to standard classification codes for occupations and industries. We are aware of the fact that assignment of more specific occupational codes would be an increase in workload for a coder. Nevertheless, we still recommend assigning more specific codes because of this substantial effect on risk estimates.

The three features of the job-exposure matrix improved the accuracy of exposure assessments. Accuracy of exposure assessment could probably be further improved by assigning semiquantitative values (low, medium, and high) rather than yes/no to the decade feature. In this methodologic study, these relatively simple modifications in traditional assessment procedures resulted in higher observed risks, indicating that they may have notable effects in reducing exposure misclassification when using a job-exposure matrix.

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