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Loss of Statistical Power Associated with the Use of a Job-Exposure Matrix in Occupational Case-Control Studies

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Case-control studies are important sources of information on the possible associations between occupational exposures and disease. One of the main methodologic difficulties is the retrospective assessment of occupational exposures among study subjects. The job-exposure matrix, or JEM, has been proposed as a means of assigning exposure to study subjects, given only information on their job titles. The purpose of the present analysis was to compare the performance of a JEM with a presumably more valid approach, namely, the assessment of exposure by a team of expert hygienists and chemists. The comparison was based on a data set generated by experts in the course of a large cancer case-control study, from which was created a simple JEM. For each of 160 substances, the statistical power of the original ("gold standard") rating was compared with that of the JEM. For most substances, there was considerable exposure misclassification and consequent loss of power using the JEM. Data are presented to show how this misclassification varies among substances; this information can guide others in the choice of substances for inclusion in a JEM. Dewar, R.; Siemiatycki, J.; Gérin, M.: Loss of Statistical Power Associated with the Use of a Job-Exposure Matrix in Occupational Case-Control Studies. *Appl. Occup. Environ. Hyg.* 6:508-515; 1991.

Introduction

Discovering occupational hazards requires the juxtaposition of two sets of data: information on illness or death among workers and information on their occupations, industries, and/or occupational conditions. The more detailed and valid the information, the greater the chance of finding true associations. Insofar as occupational carcinogens are concerned, it is information on chemical and physical exposures which is desirable, especially concerning exposure incurred many years before the onset of cancer.

In a population-based study that spans a wide range of occupations and industries, it is difficult to obtain infor-

mation on the substances to which study subjects had been exposed many years in the past. Carrying out measurements is impossible. Even for the subset of past workplaces which still exist, it is unlikely that environmental conditions have remained unchanged. Relatively few workplaces have current hygiene records; very few, indeed, have historic hygiene records. In the face of this dearth of hard data, several approaches have been used to infer exposure. Many studies have been based on the collection and analysis of job titles as proxies for exposures. Job titles, for such a purpose, can be collected by interviewing study subjects or by abstracting them from routine records, such as death certificates, tumor registry reports, or hospital records. Some investigators have requested that study subjects provide information about the substances to which they had been exposed, usually by means of a checklist. Recently, there has been some discussion of the use of a job-exposure matrix (JEM) in conjunction with job titles as a means of inferring substance exposures.^(1,2) Perhaps the best that can be done in the context of a population-based, case-control study is to combine an in-depth interview of the subject with an evaluation of the subject's reported job history by a trained team of chemists and/or hygienists for the purpose of inferring exposures.^(3,4) Such experts can synthesize available information about the subject's occupation or industry with the idiosyncrasies of each subject's work habits and work environment. The investigator confronted with a choice among the various alternative approaches has to consider their costs and benefits. However, there is virtually no published evidence on these issues to provide guidance.

For several years, our research group has been carrying out a large population-based, case-control study in Montreal, focusing on occupational exposures as potential risk factors. A relatively costly approach consisting of interviews and evaluation of job histories by a specially trained team

of chemists and hygienists was used. In this paper, this will be referred to as the INT + CHEM design.

In the hope of providing guidance as to the relative merits of alternative approaches to exposure data collection in case-control studies of occupation and cancer, a special series of analyses was carried out within the data set. By configuring aspects of the database appropriately, it was possible to describe costs and statistical benefits not only of the approach actually used but also of a hypothetical approach based on an interview to obtain job titles supplemented by a JEM applied to the job titles to obtain substance exposures (INT + JEM design).

Siemiatycki and co-workers⁽⁵⁾ have shown previously that the costs of the INT + JEM design could be significantly less than the INT + CHEM design for equal-sized studies. However, the present study also showed that for most of the 160 substances which were evaluated, there was significant loss in statistical power in moving from the INT + CHEM design to the INT + JEM design. While this finding held in general across the 160 substances that were analyzed, there were some substances for which the loss in power was less and some for which the loss in power was greater. In practical terms, this means that some substances can be included more effectively in a JEM and some less effectively. The purpose of the present analysis is to describe loss in power and consequent suitability for inclusion in a JEM on a substance-by-substance basis.

Data Sources

A population-based, case-control study was initiated in Montreal in 1979. Ascertainment of incident cases and interviewing were carried out until 1986, and exposure assessment has recently been completed. Several sites of cancer were included in the study; the main ones were esophagus, stomach, colon, rectum, liver, pancreas, lung, prostate, bladder, kidney, melanoma of the skin, and lymphoid tissue. Eligible subjects were those incident cases of any of these cancer sites among males aged 35–70 years and resident in the Montreal area. Between 1979 and 1985, interviews were carried out for 4263 subjects, of whom 3730 were cancer patients and 533 were population controls.

The in-depth interview elicited a detailed job history and information on potentially confounding covariables. A specially trained team of chemists and hygienists examined each completed questionnaire and translated each job into a list of potential exposures. They did this on a checklist that explicitly listed 302 substances, selected because they were thought to be relatively common occupational exposures in Montreal. Among the sources of information used by the chemists were: the worker's description of his job environment; documentation from the fields of engineering, chemistry, hygiene, toxicology, and epidemiology; consultation with local experts from selected industries; and the chemists' own experience and technical skills. As this information was tailored to the idiosyncrasies of each worker's job history, it was clearly more valid than any approach that entails lumping together

all workers who share the same job title. Details of the study design, fieldwork methods, and chemical coding method have been described previously^(6,7) as have some methodologic validations^(8,9) and some substantive results.^(10–13)

Most of the data used in this methodologic investigation were derived from the interviews and exposure assessments of the 4263 subjects in the occupational cancer study. With an average of 3.5 jobs per person, there were 14,760 distinct jobs among these study subjects. Our team of chemists and hygienists considered each one of these and rated the corresponding exposures on a checklist of 302 substances. In addition, the job title of each job was coded as per the Canadian Classification and Dictionary of Occupational Titles.⁽¹⁴⁾ These data were all that was needed for the evaluation of the two designs.

Statistical Methods

In the context of the case-control design, there is a well-known formula for estimating statistical power as a function of the following study parameters: sample size, relative risk, prevalence of exposure, and statistical alpha level.⁽¹⁵⁾ If there is nondifferential misclassification in exposure assessment, then the estimated prevalence of the exposure factor may be modified, the estimated relative risk or odds ratio will be displaced toward the null value, and as a result, the power to detect an excess risk will be decreased. The degree of misclassification of the INT + JEM design as compared with the INT + CHEM design can be measured by means of two parameters: sensitivity and specificity. Sensitivity equals the proportion of true positive values (taking INT + CHEM as the "gold standard") that the INT + JEM design also rates as positive. Specificity equals the proportion of true negatives that the INT + JEM design correctly rates as negative. In the context of this study, a positive is an indication that the person was exposed and a negative that he was not exposed.

If p is the true exposure prevalence among controls, R is the true odds ratio, and U and V are, respectively, the sensitivity and specificity of the alternate exposure classification, then the modified relative risk and modified prevalence can be derived by the following equations:

$$R^* = \frac{URp + (1 - V)(1 - p)[(1 - U)p + V(1 - p)]}{[Up + (1 - V)(1 - p)][(1 - U)Rp + V(1 - p)]} \quad (1)$$

$$p^* = pU + (1 - p)(1 - V) \quad (2)$$

The purpose of this study was to compare the statistical power of the INT + JEM design with that available in the benchmark INT + CHEM design. If sensitivity and specificity can be estimated for an alternative data collection design, then the power to detect an association can be calculated using Schlesselman's equation,⁽¹⁵⁾ substituting p^* and R^* for p and R .

For the INT + CHEM design, a relative risk of 2.0, with no misclassification, was assumed. This is not tantamount to assuming that the exposure assessment in the INT + CHEM design was without error. The hypothesized twofold risk

in the INT+CHEM design could be the result of a true twofold risk where the exposure is measured without error, or more plausibly, it could be the result of a much higher true risk that is attenuated down to a twofold risk because of measurement error. When referring to sensitivity and specificity of the INT+JEM design, one has a reference point that is not the absolute truth but rather the exposure assessment obtained from the INT+CHEM design. For the INT+JEM design, the relative risk and prevalence differed from that of the INT+CHEM design because of misclassification; the degree of difference was specific to each substance.

The power to detect a twofold risk, with $n = 2 \times 500$, $\alpha = 0.05$, and a given prevalence, was computed using Schlesselman's equation.⁽¹⁵⁾ This is the power of the INT+CHEM design and serves as the benchmark against which the power of the INT+JEM design can be compared. To derive the corresponding set of 160 statistical power values for the INT+JEM design, it was necessary to create a JEM. The simplest JEM has job codes on one axis, the 160 substances on the other axis, and entries consisting of 0 or 1 indicators, stating whether men in job i are to be considered unexposed or exposed to substance j . From our own data bank, it was possible to derive an empiric matrix with entries indicating the proportion of men in job i who were considered exposed to substance j . To transform this empiric matrix into a simple 0 or 1 JEM, a procedure was used that maximized the power of the JEM relative to the chemists' coding.⁽⁵⁾

The example of polycyclic aromatic hydrocarbons ("PAHs from any source") will illustrate the procedure. First, an estimate was made of the proportion of men in each four-digit job code who had been exposed to PAHs. To transform this array of proportions into an array of 0 or 1 indicators, the optimal cutpoint had to be found for the proportions, above which every subject with the job code would be considered "exposed to PAHs" and below which every subject with the job code would be considered "unexposed to PAHs." The 0 or 1 indicators were generated for each possible cutpoint. For each cutpoint, the vector of 0 or 1 values was applied to the 14,760 job codes in our data bank, and an exposure variable was thereby generated for each job. This was compared with the chemists' coding of exposure to PAH to compute sensitivity and specificity and the corresponding statistical power. The cutpoint that maximized power was taken as the optimal cutpoint. In the case of PAHs, the optimal cutpoint turned out to be 46 percent. The corresponding column in the matrix, therefore, had a 1 for any occupation that had more than 46 percent of workers exposed to PAHs according to our empiric data and a 0 for any occupation which had less. With the optimal cutpoint for PAHs applied to the data bank of 14,760 job codes, and comparing the resulting INT+JEM exposure assessments with the INT+CHEM assessments, the sensitivity was 0.83 and the specificity was 0.97.

The comparison of designs was carried out for each of the 160 most prevalent substances on the exposure checklist. For each substance, the power of each design to detect

the same hypothetical relative risk of 2.0, in hypothetical studies having the same sample size of 2×500 , and the same alpha level of 0.05 was estimated. For the prevalence of exposure, another crucial parameter in determining power, two different approaches were used, each giving rise to a distinct set of results. In the first approach, it was assumed that the lifetime prevalence of exposure was the same for all substances, namely, 4 percent; in the second, it was assumed that the lifetime prevalence of exposure was that observed in our study for each substance.

For a given level of misclassification, the degree of loss of power depends on other parameters including the prevalence of exposure. If two substances entail the same level of classification but one is more prevalent than the other, the more prevalent one will appear to retain power better than the other. Thus, the substances with high prevalence, such as PAHs, appear to be at some advantage. To "level the playing field" among substances, a set of analyses were carried out using the same prevalence for all 160 substances, namely, 4 percent. The power to detect a twofold risk, with $n = 2 \times 500$, $\alpha = 0.05$, and a prevalence of exposure of 4 percent, would be 0.801. This then was the power of the INT+CHEM design for all 160 substances. The JEM used was the same one as in the preceding approach. For the PAH example, the sensitivity and specificity were 0.83 and 0.97. Assuming a relative risk of 2.0, prevalence of 4 percent, and applying Equations 1 and 2 to these data gives $R^* = 1.61$ and $p^* = 0.07$. The resulting power of the INT+JEM design for PAH is 0.67. In this way, the power was derived for all 160 substances.

The second approach was based on the observed prevalence of exposure. For the PAHs example, the lifetime prevalence of exposure in our study population was 68 percent. The power to detect a twofold risk, with $n = 2 \times 500$, $\alpha = 0.05$, and a prevalence of exposure of 68 percent, would be 1.00 (rounded to two decimal points). The misclassification of the INT+JEM design would change the relative risk to 1.65 and the prevalence of exposure to 58 percent; the resulting power would be 0.98. This entire procedure was repeated for each of the 160 substances evaluated, thus deriving the power for the design INT+JEM for each substance.

Results

Table I presents the sensitivity and specificity of the INT+JEM design as compared with the INT+CHEM design for each of the 160 substances. The table then presents a comparison of power to detect a hypothetical twofold risk by the INT+JEM design with that by the INT+CHEM design for each substance, under two different strategies for defining prevalence. Under strategy 1, the prevalence of exposure in the INT+CHEM design is 4 percent for all substances, and the corresponding power to detect the hypothetical twofold risk is 0.801. The prevalence, odds ratio, and resulting power that correspond to the level of misclassification are also shown. The substances in this table are listed in descending order of the power under INT+JEM for strategy 1.

TABLE I. Power of the INT + JEM Design Compared with the Power of the INT + CHEM Design under Two Different Strategies for Estimating the Lifetime Prevalence of Exposure for each of 160 substances

Substance ^c	Se ^d	Sp ^e	Strategy 1 ^a			Strategy 2 ^a					
			INT + JEM			INT + CHEM		INT + JEM			Power ^h
			Prev ^f	OR ^g	Power ^h	Prev ⁱ	Power ^j	Prev ^f	OR ^g	Power ^k	
Fertilizers	0.94	1.00	0.04	1.96	0.77	0.06	0.90	0.05	1.97	0.88	
Pesticides	0.86	1.00	0.04	1.92	0.72	0.07	0.93	0.06	1.94	0.89	
Calcium oxide	0.84	1.00	0.04	1.94	0.72	0.13	0.99	0.11	1.95	0.98	
Arsenic compounds	0.84	1.00	0.04	1.92	0.72	0.04	0.78	0.03	1.92	0.69	
Grain dust	0.84	1.00	0.03	1.96	0.72	0.08	0.96	0.07	1.96	0.92	
Cooking fumes	0.82	1.00	0.03	1.95	0.71	0.07	0.93	0.05	1.95	0.87	
Calcium oxide fumes	0.90	0.98	0.06	1.71	0.70	0.07	0.94	0.08	1.78	0.87	
Cellulose nitrate	0.85	0.99	0.04	1.83	0.69	0.03	0.70	0.03	1.80	0.59	
Mineral spirits + BTX ^k	0.86	0.97	0.07	1.63	0.69	0.17	1.00	0.17	1.79	0.98	
Calcium sulfate	0.86	0.99	0.04	1.79	0.69	0.11	0.99	0.10	1.88	0.96	
Wood varnishes, stain	0.82	0.99	0.04	1.83	0.68	0.06	0.90	0.05	1.86	0.80	
Mineral wool fibers	0.86	0.99	0.05	1.76	0.68	0.05	0.88	0.06	1.79	0.78	
Mild steel dust	0.84	0.99	0.04	1.78	0.68	0.18	1.00	0.16	1.89	0.99	
Alumina	0.87	0.98	0.05	1.70	0.68	0.17	1.00	0.16	1.85	0.99	
Formaldehyde	0.83	0.95	0.08	1.58	0.68	0.23	1.00	0.22	1.75	0.99	
Linseed oil	0.86	0.99	0.04	1.78	0.68	0.05	0.88	0.06	1.81	0.78	
Silicon carbide	0.86	0.98	0.05	1.72	0.68	0.06	0.93	0.07	1.78	0.84	
Aluminum compounds	0.86	0.98	0.06	1.67	0.68	0.21	1.00	0.20	1.84	0.99	
Stainless steel dust	0.87	0.98	0.05	1.72	0.68	0.05	0.86	0.06	1.75	0.75	
Wood comb. products	0.81	0.99	0.04	1.84	0.67	0.04	0.83	0.04	1.85	0.71	
Solvents	0.84	0.97	0.06	1.65	0.67	0.41	1.00	0.36	1.80	1.00	
Metal oxide fumes	0.86	0.98	0.05	1.70	0.67	0.20	1.00	0.18	1.85	0.99	
Iron compounds	0.82	0.99	0.04	1.81	0.67	0.26	1.00	0.22	1.88	1.00	
PAH ^l from any source	0.83	0.97	0.07	1.61	0.67	0.68	1.00	0.58	1.65	0.98	
Other pyrolysis fumes	0.85	0.98	0.05	1.70	0.67	0.18	1.00	0.17	1.85	0.99	
Abbrasives dust	0.84	0.99	0.05	1.76	0.67	0.25	1.00	0.22	1.87	1.00	
Ethylene glycol	0.77	1.00	0.03	1.89	0.67	0.04	0.83	0.04	1.89	0.71	
Fiberglass	0.85	0.98	0.05	1.71	0.67	0.05	0.88	0.06	1.75	0.77	
PAH from wood	0.81	0.99	0.04	1.83	0.67	0.04	0.84	0.04	1.85	0.71	
Aliphatic ketones	0.86	0.98	0.06	1.67	0.67	0.08	0.96	0.09	1.76	0.88	
Cutting fluids	0.71	1.00	0.03	1.95	0.66	0.09	0.98	0.07	1.95	0.92	
Cutting fluids >1955	0.72	1.00	0.03	1.94	0.66	0.06	0.92	0.05	1.95	0.81	
Sulfuric acid	0.79	1.00	0.04	1.84	0.66	0.15	1.00	0.13	1.90	0.98	
Hydraulic fluid	0.74	1.00	0.03	1.89	0.66	0.04	0.82	0.03	1.90	0.68	
Metallic dust	0.84	0.98	0.05	1.72	0.66	0.29	1.00	0.26	1.85	1.00	
Mineral spirits	0.83	0.97	0.06	1.63	0.66	0.12	0.99	0.12	1.75	0.94	
Inorg. insul. dust	0.80	0.99	0.04	1.79	0.65	0.11	0.99	0.09	1.88	0.95	
Concrete dust	0.81	0.99	0.04	1.77	0.65	0.10	0.98	0.09	1.85	0.93	
Urea-formaldehyde	0.71	1.00	0.03	1.93	0.65	0.05	0.86	0.04	1.94	0.72	
Aromatic alcohols	0.72	1.00	0.03	1.91	0.65	0.06	0.92	0.05	1.93	0.81	
Cutting fluids <1955	0.73	1.00	0.03	1.90	0.65	0.07	0.94	0.05	1.92	0.85	
Alkyds	0.64	1.00	0.03	1.98	0.64	0.04	0.83	0.03	1.98	0.66	
Copper compounds	0.79	0.99	0.04	1.77	0.64	0.13	0.99	0.11	1.87	0.97	
Soldering fumes	0.72	1.00	0.03	1.89	0.64	0.07	0.94	0.05	1.92	0.84	
Iron fumes	0.79	0.99	0.04	1.77	0.64	0.10	0.98	0.08	1.85	0.92	
PAH from petroleum	0.81	0.98	0.05	1.65	0.64	0.64	1.00	0.52	1.68	0.99	
PAH from other source	0.82	0.98	0.05	1.68	0.64	0.21	1.00	0.19	1.83	0.99	
Hypochlorites	0.70	1.00	0.03	1.90	0.64	0.06	0.91	0.04	1.92	0.78	
Acetic acid	0.78	0.99	0.04	1.79	0.64	0.04	0.82	0.04	1.80	0.66	
Aromatic amines	0.77	0.99	0.04	1.81	0.64	0.08	0.95	0.06	1.86	0.86	
Lub. oils and grease	0.80	0.98	0.05	1.70	0.64	0.32	1.00	0.27	1.82	1.00	
Javel water	0.71	1.00	0.03	1.90	0.64	0.06	0.90	0.04	1.92	0.76	
Nickel compounds	0.80	0.99	0.04	1.75	0.64	0.08	0.95	0.07	1.82	0.86	
Isopropanol	0.72	1.00	0.03	1.86	0.63	0.04	0.82	0.03	1.87	0.65	
Calcium carbonate	0.65	1.00	0.03	1.95	0.63	0.07	0.94	0.05	1.95	0.82	
Alkanes (C ₁₈ +)	0.79	0.98	0.05	1.70	0.63	0.36	1.00	0.30	1.81	1.00	
Brick dust	0.68	1.00	0.03	1.91	0.63	0.04	0.77	0.03	1.91	0.59	
Propane comb. product	0.75	0.99	0.04	1.82	0.63	0.04	0.78	0.03	1.81	0.61	
Engine emissions	0.79	0.99	0.04	1.73	0.63	0.43	1.00	0.34	1.79	1.00	
Carbon monoxide	0.80	0.97	0.06	1.63	0.63	0.52	1.00	0.42	1.73	1.00	
Diesel engine emissions	0.79	0.99	0.04	1.74	0.63	0.17	1.00	0.14	1.86	0.98	
Rayon fibers	0.74	0.99	0.04	1.80	0.62	0.03	0.71	0.03	1.76	0.52	
Methane	0.77	0.99	0.04	1.73	0.62	0.05	0.87	0.05	1.76	0.71	

TABLE I. (Con't.)

Substance ^c	Se ^d	Sp ^e	Strategy 1 ^a			Strategy 2 ^b				
			INT + JEM			INT + CHEM		INT + JEM		
			Prev ^f	OR ^g	Power ^h	Prev ⁱ	Power ^j	Prev ^f	OR ^g	Power ^h
Copper fumes	0.78	0.99	0.05	1.70	0.62	0.04	0.77	0.04	1.68	0.59
Phenol-formaldehyde	0.68	1.00	0.03	1.89	0.62	0.05	0.84	0.03	1.90	0.67
Lead compounds	0.78	0.98	0.05	1.65	0.62	0.49	1.00	0.39	1.74	1.00
Cleaning agents	0.73	1.00	0.03	1.82	0.62	0.17	1.00	0.13	1.88	0.98
Arc welding fumes	0.79	0.98	0.05	1.68	0.62	0.12	0.99	0.11	1.80	0.95
Alkanes (C ₅ -C ₁₇)	0.78	0.98	0.06	1.62	0.62	0.37	1.00	0.31	1.77	1.00
Polyester fibers	0.69	1.00	0.03	1.88	0.62	0.04	0.81	0.03	1.88	0.63
Crystalline silica	0.71	1.00	0.03	1.84	0.62	0.25	1.00	0.18	1.86	0.99
Industrial talc	0.68	1.00	0.03	1.90	0.62	0.06	0.92	0.04	1.92	0.79
Waxes, polishes	0.71	1.00	0.03	1.85	0.62	0.06	0.90	0.04	1.88	0.76
Extenders	0.65	1.00	0.03	1.93	0.62	0.06	0.90	0.04	1.94	0.75
Carbon black	0.67	1.00	0.03	1.88	0.61	0.05	0.88	0.04	1.90	0.72
Polychloroprene	0.68	1.00	0.03	1.88	0.61	0.03	0.71	0.02	1.86	0.52
Styrene-butadiene rubber	0.73	0.99	0.04	1.77	0.61	0.04	0.83	0.04	1.79	0.64
Zinc compounds	0.77	0.99	0.04	1.69	0.61	0.11	0.99	0.10	1.80	0.93
Animal, vegetable glue	0.75	0.99	0.04	1.75	0.61	0.04	0.79	0.04	1.74	0.60
Natural gas	0.70	0.99	0.03	1.79	0.60	0.03	0.69	0.03	1.74	0.48
Ammonia	0.73	0.99	0.04	1.76	0.60	0.11	0.99	0.09	1.85	0.93
Gas welding fumes	0.75	0.99	0.04	1.71	0.60	0.12	0.99	0.10	1.82	0.94
Biocides	0.72	0.99	0.03	1.79	0.60	0.11	0.99	0.08	1.86	0.92
Zinc fumes	0.75	0.99	0.04	1.69	0.60	0.04	0.77	0.04	1.67	0.56
Wood dust	0.71	0.99	0.03	1.80	0.60	0.24	1.00	0.17	1.86	0.99
Nitrogen oxides	0.72	0.99	0.04	1.76	0.59	0.22	1.00	0.16	1.85	0.99
Organic dyes	0.70	0.99	0.03	1.77	0.59	0.09	0.97	0.07	1.84	0.86
Portland cement	0.63	1.00	0.03	1.89	0.59	0.08	0.96	0.05	1.91	0.83
Iron oxides	0.72	0.99	0.04	1.76	0.59	0.11	0.99	0.09	1.85	0.92
Excavation dust	0.65	1.00	0.03	1.87	0.59	0.11	0.99	0.07	1.90	0.91
Synthetic fibers	0.62	1.00	0.03	1.91	0.59	0.07	0.93	0.04	1.92	0.78
Rubber dust	0.67	1.00	0.03	1.81	0.58	0.04	0.78	0.03	1.80	0.56
Propane	0.69	0.99	0.03	1.79	0.58	0.04	0.84	0.04	1.80	0.63
Unsat. aliph. hydrocarbons	0.72	0.99	0.04	1.70	0.58	0.06	0.90	0.05	1.75	0.72
Wool fibers	0.66	1.00	0.03	1.83	0.58	0.06	0.92	0.04	1.87	0.74
Aluminum alloy dust	0.70	0.99	0.04	1.75	0.58	0.07	0.94	0.06	1.81	0.79
Toluene	0.73	0.98	0.05	1.65	0.58	0.15	1.00	0.12	1.79	0.96
Soot	0.61	1.00	0.03	1.89	0.58	0.09	0.97	0.06	1.92	0.85
MAHM ^m	0.74	0.98	0.04	1.67	0.58	0.36	1.00	0.27	1.78	1.00
Chromium compounds	0.72	0.99	0.04	1.72	0.58	0.14	1.00	0.11	1.83	0.95
Chrysotile asbestos	0.70	0.99	0.04	1.73	0.57	0.19	1.00	0.14	1.84	0.98
Other paints, varnishes	0.72	0.98	0.05	1.63	0.57	0.14	0.99	0.11	1.77	0.94
Iron dust	0.67	0.99	0.03	1.78	0.57	0.04	0.83	0.03	1.79	0.61
Titanium dioxide	0.58	1.00	0.02	1.93	0.57	0.04	0.82	0.02	1.93	0.59
Acetylene	0.71	0.99	0.04	1.71	0.57	0.05	0.86	0.04	1.73	0.64
Inorg. pigments	0.60	1.00	0.03	1.89	0.57	0.09	0.98	0.06	1.91	0.86
Chromium fumes	0.64	1.00	0.03	1.80	0.56	0.04	0.77	0.03	1.79	0.53
Chlorinated alkanes	0.71	0.98	0.05	1.61	0.56	0.11	0.99	0.09	1.73	0.88
Nylon fibers	0.67	0.99	0.03	1.73	0.56	0.03	0.71	0.03	1.70	0.47
Fabric dust	0.54	1.00	0.02	1.94	0.56	0.10	0.98	0.05	1.93	0.86
Chlorinated alkenes	0.71	0.98	0.05	1.63	0.56	0.06	0.91	0.06	1.68	0.69
Copper dust	0.60	1.00	0.03	1.84	0.55	0.05	0.86	0.03	1.86	0.63
Natural rubber	0.65	0.99	0.03	1.77	0.55	0.05	0.84	0.03	1.78	0.60
Other mineral oils	0.55	1.00	0.02	1.91	0.55	0.04	0.80	0.02	1.91	0.55
Diesel oil	0.65	0.99	0.03	1.75	0.55	0.04	0.81	0.03	1.76	0.56
Cotton dust	0.60	1.00	0.03	1.83	0.55	0.09	0.97	0.06	1.88	0.84
Carbon tetrachloride	0.70	0.99	0.04	1.65	0.55	0.05	0.84	0.05	1.67	0.60
Manganese fumes	0.52	1.00	0.02	1.96	0.55	0.06	0.90	0.03	1.96	0.67
Methanol	0.63	0.99	0.03	1.76	0.54	0.05	0.88	0.04	1.79	0.65
Ozone	0.57	1.00	0.02	1.86	0.54	0.07	0.93	0.04	1.89	0.73
Tin compounds	0.62	1.00	0.03	1.78	0.54	0.10	0.98	0.06	1.85	0.86
Aliphatic aldehydes	0.69	0.98	0.05	1.57	0.54	0.27	1.00	0.20	1.74	0.98
Fluorides	0.62	1.00	0.03	1.79	0.54	0.04	0.77	0.03	1.78	0.51
Inks	0.52	1.00	0.02	1.90	0.53	0.04	0.78	0.02	1.90	0.51
Chromium (VI) compounds	0.63	0.99	0.03	1.73	0.53	0.10	0.98	0.07	1.82	0.85
Polyacrylates	0.59	1.00	0.03	1.80	0.53	0.03	0.73	0.02	1.78	0.46
Kerosene	0.56	1.00	0.02	1.84	0.53	0.06	0.92	0.04	1.87	0.69

TABLE I. (Con't.)

Substance ^c	Se ^d	Sp ^e	Strategy 1 ^a			Strategy 2 ^a				
			INT + JEM			INT + CHEM		INT + JEM		
			Prev ^f	OR ^g	Power ^h	Prev ⁱ	Power ^j	Prev ^f	OR ^g	Power ^h
Aliphatic alcohols	0.62	0.99	0.03	1.76	0.53	0.10	0.98	0.07	1.84	0.85
Metal coatings	0.61	0.99	0.03	1.75	0.53	0.08	0.96	0.05	1.82	0.79
Ultraviolet radiation	0.55	1.00	0.02	1.84	0.52	0.04	0.81	0.02	1.84	0.53
Hydrogen sulfide	0.60	1.00	0.03	1.78	0.52	0.04	0.81	0.03	1.78	0.53
Nickel fumes	0.59	1.00	0.03	1.78	0.52	0.04	0.77	0.03	1.77	0.49
Sulfur dioxide	0.66	0.99	0.04	1.65	0.52	0.15	1.00	0.11	1.79	0.94
Leaded gasoline	0.58	1.00	0.03	1.80	0.52	0.13	0.99	0.08	1.87	0.91
Alkanes (C ₁ -C ₄)	0.60	0.99	0.03	1.74	0.51	0.10	0.98	0.06	1.83	0.83
Amphibole asbestos	0.59	1.00	0.03	1.76	0.51	0.08	0.96	0.05	1.83	0.77
Inorg. acid solutions	0.62	0.99	0.03	1.70	0.51	0.15	1.00	0.10	1.82	0.93
Coal comb. products	0.54	1.00	0.02	1.82	0.50	0.05	0.86	0.03	1.84	0.58
Titanium compounds	0.47	1.00	0.02	1.91	0.50	0.05	0.88	0.03	1.92	0.58
Manganese compounds	0.44	1.00	0.02	1.95	0.49	0.07	0.94	0.03	1.95	0.67
Flour dust	0.42	1.00	0.02	1.98	0.49	0.04	0.77	0.02	1.98	0.46
PAH from coal	0.51	1.00	0.02	1.83	0.49	0.09	0.97	0.05	1.88	0.79
Benzo(a)pyrene	0.60	0.99	0.03	1.69	0.49	0.24	1.00	0.15	1.81	0.98
Liquid fuel comb. products	0.54	1.00	0.03	1.74	0.48	0.07	0.93	0.04	1.80	0.67
Coal dust	0.48	1.00	0.02	1.87	0.48	0.06	0.91	0.03	1.89	0.62
Tin fumes	0.49	1.00	0.02	1.84	0.48	0.05	0.84	0.02	1.85	0.52
Xylene	0.53	1.00	0.03	1.72	0.46	0.12	0.99	0.07	1.83	0.86
Plastic dust	0.55	0.99	0.03	1.66	0.45	0.06	0.91	0.04	1.71	0.59
Hydrogen chloride	0.48	1.00	0.02	1.79	0.45	0.09	0.97	0.05	1.85	0.75
Clay dust	0.37	1.00	0.01	1.98	0.45	0.03	0.68	0.01	1.99	0.36
Benzene	0.51	1.00	0.02	1.72	0.44	0.18	1.00	0.10	1.83	0.93
Synthetic adhesives	0.53	0.99	0.03	1.68	0.44	0.16	1.00	0.09	1.81	0.91
Cellulose	0.46	1.00	0.02	1.78	0.44	0.07	0.93	0.03	1.83	0.63
Lead fumes	0.40	1.00	0.02	1.86	0.42	0.04	0.82	0.02	1.86	0.44
Aliphatic esters	0.41	1.00	0.02	1.84	0.42	0.04	0.79	0.02	1.83	0.41
Turpentine	0.33	1.00	0.01	1.98	0.42	0.06	0.91	0.02	1.97	0.54
Asphalt	0.32	1.00	0.01	1.98	0.41	0.04	0.77	0.01	1.98	0.38
Alkali, caustic solution	0.46	0.99	0.03	1.61	0.37	0.08	0.96	0.04	1.71	0.61
Coal tar and pitch	0.30	1.00	0.01	1.87	0.35	0.03	0.67	0.01	1.83	0.27
Heating oil	0.29	1.00	0.01	1.86	0.34	0.05	0.84	0.01	1.87	0.38

^aIt is assumed that in the INT + CHEM design the true lifetime prevalence is 0.04 and the true odds ratio is 2.0. Given an alpha of 0.05 and number of cases = number of controls = 500, the resulting power to detect the risk would be 0.801 for all substances.

^bIt is assumed that in the INT + CHEM design the true lifetime prevalence equals that which was observed in the Montreal study and the true odds ratio is 2.0.

^cSubstances are ranked by power under the INT + JEM design for strategy 1.

^dSensitivity of the INT + JEM design compared with INT + CHEM.

^eSpecificity of the INT + JEM design compared with INT + CHEM.

^fPrevalence of exposure under INT + JEM, computed by Equation 2 in text.

^gOdds ratio under INT + JEM, computed by Equation 1 in text.

^hPower to detect the OR in the preceding column, with alpha = 0.05 and number of cases = number of controls = 500.

ⁱPrevalence as observed.

^jPower to detect an OR of 2.0, with alpha = 0.05 and number of cases = number of controls = 500.

^kBTX = benzene, toluene, or xylene.

^lPAH = polycyclic aromatic hydrocarbons.

^mMAH = monocyclic aromatic hydrocarbons.

TABLE II. Distribution of Statistical Power Over the 160 Substances, for the INT + CHEM Method and the INT + JEM Method, for Each of the Two Strategies of Assigning Prevalence of Exposure

Power ^a	Strategy 1		Strategy 2	
	INT + CHEM	INT + JEM	INT + CHEM	INT + JEM
< 0.20	0	0	0	0
0.20-0.40	0	3	0	4
0.40-0.60	0	78	0	30
0.60-0.80	0	79	23	47
0.80-0.90	160	0	40	25
0.90-1.00	0	0	97	54

^aPower to detect an OR of 2.0, with alpha = 0.05 and number of cases = number of controls = 500.

Strategy 2 uses a more realistic estimate of prevalence in the INT + CHEM design, namely, that observed in our study. The panel for strategy 2 shows the prevalence and resulting power of the INT + CHEM design as well as the corresponding parameters for INT + JEM. It is more difficult to appreciate the loss in power under strategy 2, where the baseline differs from substance to substance, than under strategy 1. Since power is not on a linear scale, the power loss under strategy 2 tends to be greatest for those substances with relatively low prevalence.

Table II summarizes the distribution of statistical power for the two exposure assessment methods, for each of the two strategies for assigning prevalence of exposure. For strategy 1, the power for the INT + CHEM design is 0.801 for all 160 substances, and the distribution in the corresponding INT + JEM design is a result of varying rates of misclassification. For strategy 2, the distribution of power under the INT + JEM design is a result of variation in true prevalence of exposure, as well as in rates of misclassification. It can be seen from both strategies that while there was loss of power in going from INT + CHEM to INT + JEM, the loss of power was not very great for many substances. Misclassification in this context is a job-specific notion. That is, in computing sensitivity and specificity, the units of observation were the 14,760 jobs, not the 4263 men. A different approach, and one which was implemented elsewhere,⁽⁵⁾ is to aggregate over the study subjects' complete occupational histories and to carry out the estimation of sensitivity and specificity with the subjects as the units of observation. The ability of the JEM to predict lifetime job exposures will typically be less than the ability to predict it for job-specific exposures; this explains the relatively more favorable appearance of the INT + JEM results in the current analysis as compared with the results presented in the earlier analysis.⁽⁵⁾

Discussion

In the context of a population-based, case-control study aimed at a wide range of historic occupational exposures, it is doubtful if other approaches could elicit more valid exposure data than a combination of interview with cases and controls to obtain lifetime job histories and evaluation of each job history by a team of experts.^(3,4) There can, of course, be variation in the quality of interviewing and in the nature and quality of exposure attribution. There is not much experience in the world with such an intensive approach; the authors may have the greatest cumulative experience. However, this approach does involve a substantial financial investment as well as the presence of experts. Perhaps because of the difficulties of establishing and financing such a methodology, there has been growing interest in the use of JEMs to facilitate the task of retrospective exposure assessment in population-based, case-control studies.

While there are a few JEMs that have been produced by other investigators,^(1,17) none of these has proven to be versatile and valid.^(18,19) Linet *et al.*⁽¹⁸⁾ showed that there

was poor to moderate agreement between the JEM of Hoar *et al.*⁽¹⁾ and data collected in the National Occupational Hazard Survey.⁽²⁰⁾ At present, the main drawback of any design based on a JEM is the unavailability of a JEM that is well suited to the purpose of a population-based, case-control study.

Taken as a whole, the results show that there is quite a loss of statistical power in going from the INT + CHEM design to the INT + JEM design. Power in the INT + JEM design is less than that attainable in the INT + CHEM design because the twofold risk assumed in the latter design is diluted by misclassification; the INT + JEM design is, therefore, required to detect relative risks lower than 2. As the relative risk to be detected decreases, for fixed sample size and alpha, the power decreases. The performance of the INT + JEM design in our study represents the upper limit of the quality that might be expected since the JEM was designed to optimize power vis-à-vis the INT + CHEM design and it was developed and tested on the same data set. A JEM transplanted from one locale to another would entail greater misclassification and greater loss of power. The JEM which this study produced was the best simple JEM that could be produced from the available data set. It would be possible to produce a more complex JEM incorporating probabilities of exposure, dimensions for calendar time and industry, and notions of degree of exposure.

A substance will be highly suitable for inclusion in a JEM if there are some job titles in which everyone is exposed to the substance, while no one in all other job titles is exposed. The further the pattern of exposure strays from this ideal, the less suitable the substance is for inclusion. If the same proportion is exposed to the substance in every job title, the substance cannot be included in a JEM. Departures from the ideal can occur because of the reality of the distribution of the substance in different job titles or because of random error in assessing exposure by the experts who create the database. Table I indicates which substances among the 160 evaluated are, in fact, amenable to inclusion in a JEM. This should guide investigators in deciding whether to build a matrix for a given substance and whether to place faith in certain parts of existing JEMs. For some substances, the loss in power was small, whereas for others, it was considerable. This variation in effect was a result of the different degrees of misclassification associated with different substances. The degree of loss of power is also a function of the prevalence of exposure. An investigator looking to Table I for guidance should assess whether the prevalence of exposure in his/her locale is likely to be closer to the prevalence observed in Montreal (in which case, the last panel of Table I is applicable) or closer to 4 percent (in which case, the first panel of Table I is applicable).

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