Applied Occupational and Environmental Hygiene

ISSN: 1047-322X (Print) 1521-0898 (Online) Journal homepage: https://www.tandfonline.com/loi/uaoh20

# Retrospective Evaluation of Occupational Exposures in Cancer Epidemiology: A European Concerted Action of Research

Denis Hémon , Jean Bouyer , F. Berrino , P. Brochard , D. C. Glass , M. Goldberg , H. Kromhout , E. Lynge , B. Pannett , N. Segnan & H. A. Smit

**To cite this article:** Denis Hémon , Jean Bouyer , F. Berrino , P. Brochard , D. C. Glass , M. Goldberg , H. Kromhout , E. Lynge , B. Pannett , N. Segnan & H. A. Smit (1991) Retrospective Evaluation of Occupational Exposures in Cancer Epidemiology: A European Concerted Action of Research, Applied Occupational and Environmental Hygiene, 6:6, 541-546, DOI: 10.1080/1047322X.1991.10387925

**To link to this article:** https://doi.org/10.1080/1047322X.1991.10387925

# Retrospective Evaluation of Occupational Exposures in Cancer Epidemiology: A European Concerted Action of Research

**Denis Hémon,[A] Jean Bouyer,[A] F. Berrino,[B] P. Brochard,[C] D.C. Glass,[D] M. Goldberg,[E] H. Kromhout,[F] E. Lynge,[G] B. Pannett,[H] N. Segnan,[I] and H.A. Smit[J]**

[A]INSERM Unité 170, Villejuif, France; [B]Institute Nazional Dei Tumori, Milano, Italy; [C]INSERM Unité 139, Créteil, France; [D]Institute of Occupational Health, Birmingham, United Kingdom; [E]INSERM Unité 88, Paris, France; [F]Agricultural University, Department of Air Pollution, Wageningen, The Netherlands; [G]Danish Cancer Registry, Copenhagen, Denmark; [H]Medical Research Council, Environmental Epidemiology Unit, Southampton, United Kingdom; [I]Area Di Epidemiologia, Torino, Italy; [J]TNO Institute of Preventive Health Care, Leiden, The Netherlands

Assessing exposures in the investigation of occupational cancer is difficult because of the historical nature of exposures. Yet, misclassification of exposures can have a profound effect on the interpretation of risk. It is therefore important to reduce misclassification as much as possible. In an effort to improve our ability to assess exposures, the European Concerted Action of Research has identified three areas which will be given the attention of researchers: elaboration of job-exposure matrices (JEMs), methods to build ad hoc and general questionnaires, and statistical issues. JEMs should be developed for specific industries after evaluation of individual worksites; improved by using standardized coding systems and by identifying level, probability, calendar time, etc.; and evaluated by comparing their performance with other methods of assessment. Questionnaires for specific exposures, methods to code information obtained from questionnaires to allow better evaluation of exposures, and quality control procedures should be developed. In addition, evaluations of exposures using questionnaires should be compared to evaluations using JEMs. Statistical measures should be developed that evaluate exposure assessment methods, including evaluations of accuracy, i.e., how well a method compares to the real exposure; evaluations with other methods; and determinations of whether a method is able to reproduce well-known relationships. Ways of analyzing epidemiologic data should also be developed including indices of cumulative exposure and the use of probability of exposure. **Hémon, D.; Bouyer, J.; Berrino, F.; Brochard, P.; Glass, D.C.; Goldberg, M.; Kromhout, H.; Lynge, E.; Pannett, B.; Segnan, N.; Smit, H.A.: Retrospective Evaluation of Occupational Exposures in Cancer Epidemiology: A European Concerted Action of Research. Appl. Occup. Environ. Hyg. 6:541–546; 1991.**

## Rationale and General Objectives

Different estimates of the proportion of human cancers that can be attributed to occupational risk factors in industrial countries have been calculated in the past 15 years.[1,2] It is generally recognized that identified occupational carcinogenic exposures can be considered responsible for no less than 4 percent of all human cancers in these countries, with proposed estimates ranging from 4 to 25 percent. This figure applies to the total population, both sexes, and all cancer sites. Occupational risks factors may, therefore, play a still more important role if one considers specific cancer sites and the exposed individuals only.[3]

In the past, identification of occupational carcinogens generally resulted from the observation of clusters of cases arising in highly exposed groups of workers, followed by analytical studies. The great importance of occupational risk factors in the etiology of human cancers has led health authorities, occupational physicians, industrial hygienists, and scientists to look for more systematic approaches that could help to identify occupational cancer risks.

Surveillance of cancer incidence and/or mortality rates in large groups of workers has been set up by industries in several countries.[4–6] Record linkage has been constructed in the hope that studies correlating job information with death certificate and/or register data will give clues for etiological hypotheses.[7–9] Finally, case–control studies involving various cancer sites and detailed occupational interviews have been performed to screen for unknown occupational carcinogenic hazards.[10]

In these different contexts, epidemiologists face difficulties. Among the most common is the fact that workers are frequently exposed to several potentially carcinogenic occupational agents, simultaneously and/or sequentially, during their professional careers; moreover, these exposures were likely to have happened a long time ago (recall of 20 or 30 years is often needed) and frequently are not known by the workers themselves. Another problem is

 1047-322X/91/0606-541$2.00/6  

that epidemiologists are now looking mainly for carcinogens that do not have very strong effects, may be not specific, and are widely dispersed among the workforce with a downward trend in levels of exposure.

Under these circumstances, the discovery of new carcinogens implies large-scale studies (often multicentric and performed at an international level) where the problem of exposure assessment has become very crucial. Indeed, misclassification of an individual's exposure status through lack of precision in qualitative and quantitative assessment can have dramatic effects on the power of epidemiologic studies.

Efforts should be made to improve methods of measuring occupational exposures in epidemiologic investigation of cancer. The European Concerted Action of Research that is discussed here attempts to address three main topics:

- **Elaboration of job-exposure matrices (JEMs).** Designed either for population-based, case–control studies or for industry-based cohorts or case–control studies within cohorts, JEMs are often the only way to perform very large-scale studies (based on record linkage using mortality or register data on large cohorts or involving large case–control studies). Improvements are needed to elaborate more specific JEMs, with a more precise estimation of exposure levels.[6,11–13]
- **Methods to build ad hoc and general questionnaires.** An ad hoc questionnaire is the "classical" method for assessing specific exposures when a precise hypothesis exists; general questionnaires are more suited to detect new associations. Improvements could be made in the standardization and reproducibility of questionnaires[14] and in the ways that experts in industrial hygiene translate job histories into exposure histories.[15,16]
- **Statistical issues.** While elaborating on measurement tools, comparison of methods used to assess exposures is an absolute necessity to improve these tools.[17–19] Checking the validity of questionnaires or JEMs against objective measurements[20] should be done whenever possible. Finally, methods of analyzing complex exposure data and evaluating the performances of epidemiologic studies need to be improved.

## Job-Exposure Matrices

The JEM concept was initially proposed by Hoar in 1983.[12] Since then, it has been the subject of many scientific debates. Recently, Kauppinen[6] reviewed some aspects of the JEM concept and its uses.

A JEM may be defined as a cross-classification of a list of job titles with a list of agents to which persons carrying out the jobs may be exposed.[21] The elements of the matrix indicate the presence or absence of exposure within each job title, but additional elements may be incorporated, e.g., indicators of the proportion of exposed persons and the level of exposure. The number and definition of the exposures and job titles vary across different JEMs. A general JEM covers all job titles in a nationwide classification of occupations. A specific matrix is restricted to a selected subset of job titles.

The main function of a JEM is to provide information about the connections between exposures and diseases through the linkage of the job titles with the exposures in a systematic, unbiased way. From the work already performed by different teams, some methodological conclusions already emerge concerning the use of a JEM in epidemiology:

- The quality of the occupational histories is of crucial importance.[22] Exposure/odds ratio (OR) relationships are clearly dampened when the job held at a point in time is considered instead of the complete occupational history.[23]
- Consideration of the total duration and level of exposure is also of importance.[7,23] For instance, Kjuus observed that an exposure/OR relationship based on a score incorporating both duration and level of exposure was clearly steeper than when an "all or none" exposure status was used.[23]
- The probability of exposure for a given job should be considered rather than simple dichotomic information.[24]
- When using JEMs, as with other methods of evaluation of occupational exposures in the context of cohort studies, particular attention should be given to latency periods.[6,23]
- The job classification should be as precise as possible within the framework of the existing classification (3 digits instead of only 2 in the frame of the International Labour Office code, for instance); however, the benefit gained from this extra precision has yet to be evaluated.[23]
- The elaboration of JEMs in specific industries should allow a very precise analysis of job situation and should be encouraged.[6]
- For the purpose of comparing results obtained in different studies, the use of standard classifications for jobs, for industrial activities, and for exposures is necessary.[12]

Only a very small number of studies have been performed that permit a rigorous evaluation of the performances of JEMs. Although the ones available are very informative, they only define a general framework in which further studies could be designed. Those studies should optimally:

- Compare the performances of a JEM and other methods (including other JEMs) on the same sets of data.
- Take into account detailed and complete job history (including job, industrial activities, calendar period).
- Take into account the level and probability of exposure, the duration of exposure, and latency periods.
- Propose improved matrices for the general population and specific industries using large sets of data where case-by-case evaluations by experts have been performed.
- Use standardized codes for jobs, industrial activities, and exposures.

## Questionnaires and Experts

In occupational cancer, the latency periods may vary from 5 to 20 years or more. Because of these long latency periods, it is necessary to have detailed occupational histories of persons enrolled in studies performed to detect occupational cancer risks. Information about the occupational history of study subjects can sometimes be abstracted from existing documentary sources such as clinical records, census records, death certificates, and company records. Most often, however, these data are not available or only available for one company or for a small subset of persons. There is a need for methods that can elicit information on occupational history retrospectively.

A useful method could be the application of questionnaires. Although this method requires the active participation of study subjects (or their surrogates), questionnaires are considered "powerful epidemiological tools because they permit collection from the individual of both relevant exposure information and confounding factors. This applies especially to their use in case–control studies."[25]

Some questionnaires are especially designed to evaluate job titles and/or type of industry. Data from these general questionnaires can either be used as such, or more specific information can be obtained subsequently by experts (case-by-case evaluation) or by application of JEMs.

Other questionnaires are designed to evaluate (specific) exposures directly, either in broad categories or in detail for specific industries. These detailed questionnaires can be administered in conjunction with general questionnaires; or the detailed questionnaires may be administered after basic information on occupational histories has been collected by general questionnaires.

The method of eliciting retrospective information on occupational history by means of questionnaires can be of crucial importance for the detection of occupational cancer risks. However, little is known of their performance in different fields of research, and it is only recently that a number of articles on this subject have been published.[15,16,22,26–36]

In this context, the work performed in the framework of the European Concerted Action of Research endeavors to address some specific points:

- Elaboration of ad hoc questionnaires for some specific exposures.
- Elaboration of standardized coding procedures for the expert evaluation of information available on ad hoc and/or open questionnaires.
- Comparison of the performances of JEMs and questionnaires on the same data sets.
- Elaboration of quality control methods that can be used operationally in the frame of case–control studies in the general population.

## Theoretical and Statistical Aspects

It is now well known that errors in the evaluation of exposures may have important negative effects in epidemiology, particularly concerning statistical inference on OR and other measures of relative risk (RR).[37,38] Greenland[39] has shown that the possibility of compensating misclassification of exposure by increase in sample size is, in fact, limited.

It is therefore of importance that good methods of evaluating occupational exposures should be available. It is also important to improve the indices which can be used to evaluate methods on the one hand and statistical methods of analyzing data on the other.

### Performance Indices

Several techniques for estimating occupational exposures are used in epidemiological studies: questionnaires to workers or to plant supervisors, judgments of experts (chemists, occupational hygienists), and JEMs.

An evaluation of the performances of these approaches can be carried out in several ways.[40] The first one is to evaluate the intrinsic quality of the measurement method, the second one is to compare various methods on the same data set, and the last one is to evaluate the capacity of a method to detect known relationships.

#### *Intrinsic Quality of the Measurement Method*

The intrinsic quality of the measurement method is its ability to correctly quantify the real exposure. For dichotomous exposure, the intrinsic quality of a measurement method is summarized by its sensitivity and specificity. If the prevalence of exposure is also known in the population considered, it is possible to determine the loss in power and the bias of the OR[39,41,42] which are more relevant indices of performance from an operational epidemiologic point of view.

For exposure with several levels or continuous exposure, there is no unique index of intrinsic quality of a measure. Very little work has been performed in this area.[43] Frequently, a good correlation between exact and proxy measures is observed;[40] however, errors in measurement still exist, and magnitude and frequency are generally not quantified.

Finally, the consequences of measurement errors on the ability to control for confounders and/or estimate interaction between several risk factors have not been totally investigated.[18]

In order to evaluate the intrinsic performances of methods, it is necessary to know the "exact" exposure measurement, or at least the one considered the best at a given time. This is possible only in a very limited number of situations when one considers the problem of evaluating exposure integrated over long periods of time, e.g., in cancer epidemiology. For this reason, comparison between methods will often be performed between proxy methods, while the search for objective markers of exposure over long periods of time continues.

#### *Comparison Between Methods*

If one of the two methods is considered as a reference, then indices evoked above can be used. Otherwise, measures of agreement such as "kappa" are generally used.[44,45]

This measure, however, is not the most relevant one in the frame of an epidemiological investigation. For such an investigation, it is relevant to compare OR and power corresponding to the two methods (assuming that these methods are combined with the appropriate statistical inference methods).

Whatever the situation, it is of prime importance to compare methods on the same set of data. Several authors have evaluated the performance of methods in populations that were very different from the one for which they were elaborated, or basic information has been used that was much poorer.[46] For instance, it is clear that good results cannot be expected from a JEM if the information available on jobs is poor in terms of precision or completeness. It is also clear that no method will be able to reproduce well-known relationships between exposure and cancer risk in a population where this exposure is too rare.

This is the reason why some authors compared methods on the same set of data.[40,42,47] This effort should be indeed encouraged and will be developed in the context of the present program of research. This will allow evaluation of the respective merits of the two methods, definition of conditions under which they may be used, and identification of disagreements in order to improve both of them; e.g., comparison of expert evaluation and questionnaire may lead to improvement in the questionnaire and to optimization of the expert work.[47]

#### *Reproduction of Well-Known Relationships*

It is a minimal requirement that a method be able to reproduce well-known relationships, e.g., dose–response[23] or dichotomous[48] relationships between exposures and cancer risks.

Again, it is well known that the reproducibility of a known relationship is highly dependent on population, sampling scheme, information gathered, and the methods by which it was obtained. Reproduction of known relationships should therefore be considered as a very debatable way of comparing methods.

### Elaboration of Statistical Tools

The epidemiologic investigation of cancer risk related to occupational exposure also involves statistical problems in the treatment of data. A number of exposure variables may be used to characterize exposure to a given risk factor in the context of an epidemiological survey of cancer risk. Total duration of exposure, average level of exposure, and cumulative exposure are often considered. Also, age at first exposure and time elapsed since then can modulate the risk associated with a given exposure.

As underlined by several authors,[49–51] it is particularly important to consider the totality of the job history. Also, the different exposure parameters are tightly correlated together, and it is very difficult to separate their influence on risk from epidemiological data.[1] The use of classical multivariate methods is of little help in this context. This is why some authors have proposed the adoption of an *a priori* model for risks[48] which can be combined with classical multivariate methods.[52] It is clear, however, that much remains to be done in this field.

Usually, a JEM associates dichotomous exposure to a given job. As underlined by Olsen,[53] this may lead to the obviously poor situation where all the subjects with a given job are classified as exposed whereas only 10 percent of them were indeed exposed. More extensive information is available in a JEM if the frequency of exposure to specific occupational risk factors in a given job can be estimated from a set of case-by-case expert evaluations of job situations (*a posteriori* matrices).

In addition to the imprecision which is intrinsic to JEMs, poor statistical treatment of the data may contribute to an even greater loss of power and/or bias in OR.[41,54]

We propose to improve the statistical treatment of JEM data by taking into consideration explicitly the probabilistic nature of each cell in the matrix. This research effort, together with the improvement in the elaboration of matrices themselves, will lead to a better knowledge of the advantages or disadvantages of the JEM approach.

The general frame in which statistical inference problems related to JEM methodology are embedded is the correction of misclassification using information obtained in extraneous surveys or in limited subsamples.[39] This category of problem has only been touched upon at the present time; for instance, few approaches have included adjustments for confounders.

## Conclusions

Research in occupational epidemiology has developed considerably in the past 15 years. It has benefited from the large experience accumulated in this field in a very limited number of countries and research centers over the past century. However, it has also met methodological problems which may be considered new in the sense that the very spread of occupational epidemiology has underlined the necessity of designing robust, standardized methods.

## References


1. Doll, R.; Peto, R.: The Cause of Cancer. Oxford University Press, Oxford, U.K. (1981).
2. Dubrow, R.; Wegman, D.H.: Setting Priorities for Occupational Cancer Research and Control: Synthesis of the Results of Occupational Disease Surveillance Studies. J. Natl. Cancer Inst. 71(6):1123–1142 (1983).
3. Simonato, L.; Vineis, P.; Fletcher, A.C.: Estimates of the Proportion of Lung Cancer Attributable to Occupational Exposure. Carcinogenesis 9(7):1159–1165 (1988).
4. Alho, J.; Kauppinen, T.; Sundquist, E.: Use of Exposure Registration in the Prevention of Occupational Cancer in Finland. Am. J. Ind. Med. 13:581–592 (1988).
5. Blair, A.; Stewart, P.; O'Berg, M.; et al.: Mortality Among Industrial Workers Exposed to Formaldehyde. J. Natl. Cancer Inst. 76(6):1071–1084 (1986).
6. Kauppinen, T.; Partanen, T.: Use of Plant- and Period-Specific Job-Exposure Matrices in Studies on Occupational Cancer. Scand. J. Work Environ. Health 14(3):161–167 (1988).
7. Hsieh, C.C.; Walker, A.M.; Hoar, S.K.: Grouping Occupations According to Carcinogenic Potential: Occupation Clusters from an Exposure Linkage System. Am. J. Epidemiol. 117(5):575–589 (1983).
8. Magnani, C.; Coggon, D.; Osmond, C.; Acheson, E.D.: Occupation and Five Cancers: A Case–Control Study Using Death Certificates. Br. J.

Ind. Med. 44(11):769–776 (1987).
9. Swanson, G.M.; Schwartz, A.G.; Burrows, R.W.: An Assessment of Occupational and Industry Data from Death Certificates and Hospital Medical Records for Population-Based Cancer Surveillance. Am. J. Pub. Health 74(5):464–467 (1986).
10. Siemiatycki, J.; Richardson, L.; Gerin, M.; et al.: Associations Between Several Sites of Cancer and Nine Organic Dusts: Results from an Hypothesis-Generating Case–Control Study in Montreal. Am. J. Epidemiol. 123(2):235–249 (1986).
11. Ferrario, F.; Continenza, D.; Pisani, P.; et al.: Description of a Job-Exposure Matrix for Sixteen Agents Which are or May be Related to Respiratory Cancer. In: Progress in Occupational Epidemiology. Excerpta Medica (1988).
12. Hoar, S.: Job Exposure Matrix Methodology. J. Toxicol.–Clin. Toxicol. 21(1&2):9–26 (1983–84).
13. Magnani, C.; Pannett, B.; Winter, P.D.; Coggon, D.: Application of a Job-Exposure Matrix to National Mortality Statistics for Lung Cancer. Br. J. Ind. Med. 45(1):70–72 (1988).
14. Fidler, A.T.; Baker, E.L.; Letz, R.E.: Estimation of Long Term Exposure to Mixed Solvents from Questionnaire Data: A Tool for Epidemiological Investigations. Br. J. Ind. Med. 44:133–141 (1987).
15. Gerin, M.; Siemiatycki, J.; Kemper, H.; Begin, D.: Obtaining Occupational Exposures Histories in Epidemiologic Case–Control Studies. J. Occup. Med. 27(6):420–426 (1985).
16. Goldberg, M.S.; Siemiatycki, J.; Gerin, M.: Inter-rater Agreement in Assessing Occupational Exposure in a Case–Control Study. Br. J. Ind. Med. 43(10):667–676 (1986).
17. Heederik, D.; Kromhout, H.; Boleij, J.: Variability of Exposure Measurements—Consequences in Occupational Epidemiology. Fifth International Symposium Epidemiology in Occupational Health. Los Angeles (September 1986).
18. Kupper, L.L.: Effects of the Use of Unreliable Surrogate Variables on the Validity of Epidemiologic Research Studies. Am. J. Epidemiol. 120(4):643–648 (1984).
19. Linet, M.S.; Stewart, W.F.; Van Natta, M.L.; et al.: Comparison of Methods for Determining Occupational Exposure in a Case–Control Interview Study of Chronic Lymphocytic Leukemia. J. Occup. Med. 29(2):136–141 (1987).
20. Lauwerys, R.; Bernard, A.: Biological Monitoring of Exposure to Industrial Toxic Substances. Present-Day Situation and Prospects for Development. Scand. J. Work Environ. Health 11(3 Spec No):155–164 (1985).
21. Steineck, G.; Plato, N.; Alfredson, L.; Norell, S.E.: Application of a Job-Exposure Matrix on Census Data, Some Methodological Considerations. In: Progress in Occupational Epidemiology. Excerpta Medica (1988).
22. Acheson, E.D.: What are Job Exposures Matrices? In: Job Exposure Matrices. MRC Environmental Epidemiology Unit, University of Southampton, Southampton, U.K. (1983).
23. Baumgarten, M.; Siemiatycki, J.; Gibbs, G.W.: Validity of Work Histories Obtained by Interview for Epidemiologic Purposes. Am. J. Epidemiol. 118(4):583–591 (1983).
24. Kjuus, H.: Strategies for Coding Data on Total Occupational History. Experiences from a Case-Referent Study on Lung Cancer. In: Use of Job Exposure Matrices in the Nordic Countries. Kraeftens Bekaempelse, Cancerregisteret, Kobenhavn, Denmark (1988).
25. EEC Workshop: Methodology of Assessment of Occupational Exposures in the Context of Epidemiological Detection of Cancer Risks. EEC Report EUR 11810 EN. European Economic Community, Luxembourg (1989).
26. Bond, G.G.; Bodner, K.M.; Sobel, W.; et al.: Validation of Work Histories Obtained from Interviews. Am. J. Epidemiol. 128(2):343–351 (1988).
27. Bourbonnais, R.; Meyer, F.; Theriault, G.: Validity of Self Reported Work History. Br. J. Ind. Med. 45(1):29–32 (1988).
28. Eskenasi, B.; Pearson, K.: Validation of a Self-Administered Questionnaire for Assessing Occupational and Environmental Exposures of Pregnant Women. Am. J. Epidemiol. 128(5):1117–1129 (1988).
29. Goldberg, J.D.; Siemiatycki, J.; Gerin, M.: Correspondence. Br. J. Ind. Med. 44:426–428 (1987).
30. Holmberg, C.; Hernberg, S.: Congenital Defects and Occupational Factors: A Comparison of Different Methodological Approaches. Scand. J. Work Environ. Health 5:328–332 (1979).
31. Pershagen, G.; Axelson, O.: A Validation of Questionnaire Information on Occupational Exposure and Smoking. Scand. J. Work Environ. Health 8(1):24–28 (1982).
32. Rona, R.J.; Mosbech, J.: Validity and Repeatability of Self-Reported Work History in EEC Countries. In: Progress in Occupational Epidemiology. Excerpta Medica (1988).
33. Rosenberg, C.R.; Mulvihill, M.N.; Fischbein, A.; Blum, S.: An Analysis of the Validity of Self Reported Occupational Histories Using a Cohort of Workers Exposed to PCBs. Br. J. Ind. Med. 44:702–710 (1987).
34. Rosenstock, L.; Lofengo, J.; Heyer, N.H.; Carter, W.B.: Development and Validation of a Self-Administered Occupational Health History Questionnaire. J. Occup. Med. 26:50–54 (1984).
35. Stewart, W.F.; Tonascia, J.A.; Matanoski, G.M.: The Validity of Questionnaire-Reported Work History in Live Respondents. J. Occup. Med. 29(10):795–800 (1987).
36. Turner, D.W.; Schumacher, M.C.; West, D.W.: Comparison of Occupational Interview Data to Death Certificate Data in Utah. Am. J. Ind. Med. 12:145–151 (1987).
37. Flegal, K.M.; Brownie, C.; Haas, J.D.: The Effects of Exposure Misclassification on Estimates of Relative Risk. Am. J. Epidemiol. 123:736–751 (1986).
38. Sosenko, J.M.; Gardner, L.B.: Attribute Frequency and Misclassification Bias. J. Chronic Dis. 40:203–207 (1987).
39. Greenland, S.: Statistical Uncertainty Due to Misclassification: Implications for Validation Substudies. J. Clin. Epidemiol. 41(12):1167–1174 (1988).
40. Kromhout, H.; Oostendorp, Y.; Heederik, D.; Boleij, J.S.M.: Agreement Between Qualitative Exposure Estimates and Quantitative Exposure Measurements. Am. J. Ind. Med. 12:551–562 (1987).
41. Ghozlan, A.; Lellouch, J.: L'importance des Erreurs de Classification en Epidémiologie. Rev. Epidemiol. Santé Publique 33:220–227 (1985).
42. Segnan, N.; Ronco, G.; Costa, G.; Ponti, A.: Marginal Benefit in the Assessment of the Occupational Exposure and Validity Implication. EEC Report EUR 11810 EN. European Economic Communities, Luxembourg (1989).
43. Marshall, J.; Priore, R.; Graham, S.; Brasure, J.: On the Distorsion of Risk Estimates in Multiple Exposure Level Case-Control Studies. Am. J. Epidemiol. 113(4):464–473 (1981).
44. Fleiss, J.L.: Statistical Methods for Rates and Proportions. John Wiley & Sons, New York (1981).
45. Thompson, W.D.; Walter, S.D.: A Reappraisal of the Kappa Coefficient. J. Clin. Epidemiol. 10:949–958 (1988).
46. Hémon, D.: Epidémiologie des risque d'origine professionnelle: quelques problemès méthodologiques. Rev. Epidemiol. Santé Publique 34:230–236 (1986).
47. Ferrario, F.; Berrino, F.; Pisani, P.; et al.: Assessing Occupational Exposures from Job Histories to Structures "ad-hoc" Questionnaires. EEC Report EUR 11810 EN. European Economic Communities, Luxembourg (1989).
48. Smith, A.H.: Waxweiler, R.J.; Tyroler, H.A.: Epidemiologic Investigation of Occupational Carcinogenesis Using a Serially Additive Expected Dose Model. Am. J. Epidemiol. 112(6):787–797 (1980).
49. Illis, W.R.; Swanson, G.M.; Satariano, E.R.; Schwartz, A.G.: Summary Measures of Occupational History: A Comparison of Latest Occupation and Industry with Usual Occupation and Industry. Am. J. Pub. Health 77(12):1532–1534 (1987).
50. Smith, A.H.: Looking Backwards from Outcome to Exposure to Assess Cancer Latency. J. Chronic Dis. 40(suppl. 2):113–117 (1987).
51. Spirtas, R.; Fendt, K.: An Algorithm for Linking Job Titles with Individual Exposures in Occupational Epidemiology Studies. In: Job Exposure Matrices, pp. 39–47. Conference Report. Medical Research Council, Southampton, U.K. (1982).
52. Lubin, J.H.: A Reformulation of the Serially Additive Expected Dose Method for Occupational Cohort Data. Am. J. Epidemiol. 118(4):592–598 (1983).

53. Olsen, J.: Use and Misuse of Job-Exposure Matrices. In: Use of Job Exposure Matrices in the Nordic Countries. Kraeftens Bekaempelse, Cancerregisteret, Kobenhavn, Denmark (1988).

54. Copeland, K.T.; Checkoway, H.; McMichael, A.J.; Holbrook, R.H.: Bias due to Misclassification in the Estimation of Relative Risk. Am. J. Epidemiol. 105(5):488–495 (1977).