FROM EYEBALLING TO STATISTICAL MODELLING

METHODS FOR ASSESSMENT OF OCCUPATIONAL EXPOSURE

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Het gieten van een messing legering bij een scheepsschroevenbedrijf. Foto Paul Rocchi

Rubberwerkers tijdens de produktie van "Wellington boots". Foto van The Scotsman, Edinburgh; met toestemming.

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STELLINGEN

1. Homogeen blootgestelde beroepsgroepen bestaan. Alleen minder vaak dan algemeen wordt aangenomen.

   (Dit proefschrift)

2. De bewering van McMichael *et al.* (1976) over beroepsmatige blootstellingen in de rubber industrie: "Environmental differences are much greater between, than within, these 21 work areas" is een prachtig voorbeeld van de volkswijsheid "de wens is de vader van de gedachte".
   (McMichael, 1976. Chronic respiratory symptoms and job type within the rubber industry. J Occup Med 18: 611-617)

   (Dit proefschrift)

3. Het besluit van het IARC om de rubberindustrie op de lijst van bewezen carcinogenen te zetten is een voorbeeld van slecht beleid gebaseerd op zwak epidemiologisch onderzoek ten gevolge van zeer matige blootstellingskarakterisering.
   (IARC, 1987. Overall evaluations of carcinogenicity: An updating of IARC Monographs Volumes 1 to 42. Supplement 7. Lyon, Frankrijk)

   (Dit proefschrift)

4. Als de geopperde twijfel omtrent de vaardigheden van de gemiddelde arbeidshygienist om de blootstelling van werknemers te schatten terecht zou zijn, zou dit zeer welkom zijn voor de arbeidsepidemiologie, omdat zonder problemen gebruik zou kunnen worden gemaakt van de in het kader van controle op normoverschrijding verzamelde blootstellingsgegevens.

5. Voor de toekomst van de arbeidsepidemiologie is het te hopen dat de frequentie van workshops en symposia over historische blootstellingskarakterisering drastisch zal dalen.

6. De historische uitdrukking van een Wageningse dammer: "Ik ken liever geen zetjes, anders ga ik er op spe(u)len", doet onwillekeurig denken aan epidemiologen die arbeidshygiënisten inhuren om beroepsmatige blootstellingen te laten schatten.

7. Gegeven de complexiteit van beroepsmatige blootstelling zou het te prefereren zijn de huidige arbeidsepidemiologische praktijk van het vragen naar mogelijke blootstelling en het kwantitatief vaststellen van het gezondheidseffect om te draaien en voortaan de blootstelling kwantitatief vast te stellen en de werknemer te vragen naar zijn of haar gezondheidstoestand. De kans op zogenaamde negatieve studies zou hiermee drastisch worden verlaagd.

8. Het variabele karakter van de beroepsmatige blootstelling zal er voor zorgen dat het karakteriseren ervan een kunst zal blijven en geen wetenschap in de strikte zin van het woord.

9. De superioriteit van biomarkers ten opzichte van uitwendige blootstellingsmaten die door vele toxicologen wordt gepredikt door te wijzen op individuele biologische variabiliteit, zal slechts aannemelijk worden als ze succesvol kunnen worden toegepast in epidemiologisch onderzoek. Het aantonen van sterke correlaties tussen biomarkers en uitwendige blootstellingsmaten zal het toepassen van biomarkers op grote schaal in epidemiologisch onderzoek vanwege het vaak invasieve karakter eerder ontmoedigen.

10. Het advies van de gezondheidsraad om niet in detail de blootstelling van de Nederlandse bevolking aan electromagnetische velden te bepalen lijkt gericht te zijn op het voorkomen van paniek, want de mogelijkheden voor onderzoek in Nederland zijn legio.
(Gezondheidsraad, 1992. Extreem laagfrequente elektromagnetische velden en gezondheid)

11. Het vervangen van het ontvettingsmiddel 1,1,1,-trichloorethaan, dat als ozonafbrekend product en broeikasgas op de zogenaamde lijst van Montreal staat, door meer toxische stoffen als 1,1,1,-trichloorethyleen en methyleenchloride maakt duidelijk dat de gezondheid van de werkende mens geen enkele rol speelt in het algemene milieubeleid.

12. Het verontrustende feit dat de levensverwachting van linkshandigen negen jaar korter zou zijn wordt ruimschoots gecompenseerd door het feit dat ze creatiever, muzikaler, genialer en beroemder zouden zijn.

13. De opkomst van de Islam en de televisie in West-Afrika zal binnen afzienbare tijd leiden tot het uitsterven van het fenomeen "wonderdammer uit Afrika"

14. Zij die beweren dat Nederland vol is, zijn nog nooit in Hong Kong geweest.

Stellingen behorende bij het proefschrift: From eyeballing to statistical modelling. Methods for Assessment of Occupational Exposure. Hans Kromhout, Wageningen, 4 maart 1994.

In the north of the sad city stood mighty factories in which (so I'm told) sadness was actually manufactured, packaged and sent all over the world, which never seemed to get enough of it.

Salman Rushdie, Haroun and the Sea of Stories

The analysis of variance is (not a mathematical theorem but) a simple method of arranging arithmetical facts so as to isolate and display the essential features of a body of data with the utmost simplicity.

Sir Ronald Fisher in a letter to George Snedecor dated 6 January 1934

Voor mijn ouders

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Chapter 1

Introduction

BACKGROUND

A general problem in epidemiologic studies of the possible health effect of occupational exposure is that in most studies occupational exposure has to be assessed in an indirect manner. Lack of quantitative exposure data has been rather the rule than the exception. However, as early as in the 1950's exposure assessment strategies were elaborated to quantify exposure in an unbiased way (Oldham and Roach, 1952; Ashford, 1958).

In 1952, Oldham and Roach described a long term sampling procedure for measuring coal dust exposure among colliers as part of a longitudinal study of pneumoconiosis. Given the limitations of dust sampling at that time, e.g. only ambient air measurements could be performed since personal measurement devices had not been developed yet, the strategic aspects of their "random colliers" method was thought provoking at that time and even now. Ashford (1958) extended the "random colliers" method to the "man-shift" method, with which the cumulative coal dust exposure of the 35,000 colliers from 25 collieries under consideration over a period of at least ten years was estimated. The "man-shift" method subdivided the population at any particular colliery into homogeneous strata or occupational groups on the basis of occupation, place of work, and shift. To obtain a sample of the environment of any particular stratum, a random selection was made from the population of all man-shifts worked by the members of the stratum. The number of measurements allocated to a stratum was proportional to the product of the duration of the stratum, the standard deviation of the shift exposure indices for the stratum, the square root of the average number of men belonging to the stratum, and a stratum labour turnover and attendance factor. It was believed that the average of the shift exposure indices for any individual belonging to a given stratum, would be virtually indistinguishable from the average of the shift exposure indices for all members of the stratum (Ashford, 1958). In other words, each stratum was assumed to be consisting of uniformly exposed workers (Rappaport, 1991), implying the absence of between-worker exposure variability.

Contrary to what one would have expected, the appearance of portable monitoring devices and passive monitoring badges did not lead to more quantitative exposure assessment strategies applied in the framework of epidemiologic studies and it seems that the basic concepts for exposure assessment published by Oldham and Roach (1952) and Ashford (1958) had fallen on stony ground due to lack of development in exposure assessment strategies. Both the apparent high health risks associated with specific exposures and lack of funding led to retrospective studies and will consequently have contributed to stronger emphasis on less quantitative exposure assessment methods. On top of this, some health hazards related to occupational exposure (e.g., asbestos) were detectable without elaborate exposure assessment methods, because the relative risks were so great. The use of non-quantitative occupational exposure proxies like, job titles, occupational title groups, zones, uniform task categories, and subjective estimates resulting from general job-exposure matrices and expert judgements became normal practice in those studies. Also, relatively cheap case-control designs applied in the general population left epidemiologists with study subjects from different industries and workplaces, which in most cases were not accessible or for which quantitative exposure assessment was simply too costly.

Moreover, most occupational exposure data were and still are collected for compliance reasons. The focus of attention in compliance measurement strategies is the exposure of the worst case; in other words the worker or workers with the potential to be the highest exposed and therefore with the highest health risk. In most sampling schemes, low exposed groups of workers within the same premises have hardly been measured at all. Thus, the use of even those data which are available, is of questionable value to epidemiological studies.

In some cases quantitative exposure data have been used to create ordinal exposure estimates or to document exposure levels at which health effects were observed. An illustrative example is formed by the relatively large exposure studies done in the rubber industry in the USA, that were carried out in the course of large epidemiologic studies (van Ert *et al.* 1980; Williams *et al.* 1980) . Although these studies yielded abundant information on plant and occupational title specific exposures to particulates and solvents, it was never used to create quantitative exposure estimates in the epidemiologic studies. Here, once again without any validation or statistical analyses, it was concluded that the developed occupational exposure classification scheme based on occupational titles yielded useful enough surrogates of occupational exposure.

In more recent years, a renewed interest in more precise and valid (quantitative) exposure estimates has emerged. This development can be attributed to the facts that occupational hazards with a strong and specific health risk, like asbestos and mesothelioma, have been studied extensively and that, throughout industry and agriculture, levels of occupational exposure have been reduced, due to application of control measures. Thus, more detailed, precise and valid exposure assessment methods are needed in order to study the small health risks associated with present occupational exposures. Sofar, this renewed interest has resulted in several papers, seminars, workshops, and an European concerted action (Checkoway, 1986; Smith, 1987; Checkoway *et al.*, 1987; Rappaport and Smith, 1991; Stewart and Herrick, 1991; Hemon, *et al.*, 1991; Engström, 1992; Heederik and Hurley, 1993).

Three major developments can currently be recognized in the field of occupational exposure assessment. The first is the measurement of internal dose by biomonitoring and measurement of biomarkers. A second development comprises the development of pharmacokinetic models that estimate internal dose based on quantified external exposure and estimates of biological transport and distribution factors. These models will only be effective when the input variable (external dose or exposure) is accurately measured. The third development can be described as the optimization of existing methods for assessing external exposure. This thesis will focus on this last item of evaluation and optimization of existing methods of occupational exposure assessment.

EXPOSURE AND DOSE

The concepts of dose and exposure are of crucial importance for epidemiology, toxicology and occupational hygiene and therefore a general framework is needed before exposure assessment methods can be dealt with.

A general framework can be found in a recent textbook on principles of exposure measurement in epidemiology by Armstrong *et al.* (1992). They describe dose in accordance with its relationship to the exposed subject and make a distinction between available, administered, absorbed, and active dose.

In an occupational context it is more common practice to make a distinction between external exposure and dose. Exposure in this context comprises the available and administered dose. The available dose is assessed in the worker's environment and can be expressed either as a cumulative exposure or an exposure rate. The administered dose or intake will be dependent on time-behaviour patterns of the worker and can reach the worker by different routes. In occupational hygiene a distinction between available and administered dose is no longer very relevant since the time that personal exposure measurement became possible and fashionable. Therefore, both elements will be replaced by external exposure. More important is the distinction between external exposure and absorbed dose or uptake. Host factors at the portals of entry, such as airway autonomy, will influence the actual uptake and therefore a different uptake might result from a similar administered dose. For instance, a worker with a damaged skin will have a higher uptake of solvents than a colleague with an intact skin. Although more biologically relevant than external exposure, absorbed dose is still not the active or biologically effective dose at the specific targets of the agent inside the body. This measure of dose, the active dose, will be highly influenced by host specific factors, like transport of the agent in the body, distribution among different body compartments, metabolism and excretion from the body. The active dose will eventually give rise to a health effect or disease, which again will depend on host factors like genetic constitution, age, or simultaneous exposure to other agents (e.g., cigarette smoke).

Measurement of external exposure as such might not lead to a correct estimate of the biologically effective dose and therefore might not identify a relationship between an exposure and a health effect, let alone to the assessment of a dose-response relationship. This predicament will of course be absent when a clear-cut relationship between external and internal or biologically effective dose is existent. However, this will hardly ever be the case, because multiple exposure routes, non linear kinetics, interindividual differences and large measurement errors are more the rule than the exception. Absorbed dose and active dose can be measured by biological measurements in body fluids like urine and blood, or exhaled air (*biomonitoring and measurement of biomarkers*). These measurements quite often suffer from analytical errors, that can be very large when compared to measurements of workers' external exposure.

EXPOSURE ASSESSMENT TOOLS AND METHODS

Several methods for occupational exposure assessment have been elaborated and proposed in the (recent) past. The exposure estimates resulting from these methods can be divided into subjective and objective methods. Subjective methods are those in which a worker estimates his or her own exposure and those in which experts estimate exposure based on information supplied by a worker or his or her employer. Objective methods, on the other hand, employ quantitative measurements to define workers' exposures. Given the problems mentioned earlier regarding exposure measurements done for compliance reasons, one could

perhaps argue that these methods are not truly "objective" but are "less subjective" instead.
Another distinction can be made based on the level of assessment relative to the worker. If each worker's exposure is assessed on a personal basis one can speak of a case-by-case assessment. On the contrary, when a worker's exposure is assessed based on, for instance, the mean exposure of a group of workers with whom a common environment or job is shared, one can speak of a group-based assessment.

Common classifications of exposure measures can be found in the literature (Vihma 1981; Checkoway, 1986; Stewart and Herrick, 1991; Kauppinen, 1991; Blair and Stewart, 1992). Quite a few authors imply with such classifications that as the measure of exposure becomes more detailed and quantitative the estimate of exposure measure becomes more relevant, valid and precise. However, this does not have to be true. For instance, a non-causative agent or chemical can have been measured very precisely in a cohort of workers but will show no relationship with the health effect of interest. The exposure measure in this case will have been assessed very well, but will not be relevant to the health outcome. At the same time an elevated risk can be inferred for a subjective ordinal exposure measure based merely on job title. Therefore, a precise exposure measure will not necessarily lead to an exposure-response relationship and a subjective measure might well do so. Indeed, a subjective semiquantitative estimate of exposure for a certain job might be more valuable and less misleading than one or a few non-representative measurements performed during an extraordinary situation (Kromhout, 1992).

CONTENTS

Several exposure assessment methods ranging from subjective semiquantitative methods to quantitative monitoring and to modelling will be discussed. In particular, attention will be given to important aspects like misclassification, validity, precision, and grouping procedures.

In chapter 2 the performance of two general job-exposure matrices is discussed within the context of a study of lung cancer incidence in the Zutphen cohort, the Dutch contribution to the Seven-Countries study. The performance of the two general job-exposure matrices is set against an exposure assessment method based on self-reported exposure measures. An alternative, population-specific job-exposure matrix, based on self-reported data, is proposed.

In chapter 3 the ability of different "experts" like occupational hygienists, supervisors and workers to semiquantitatively estimate occupational exposure is studied. A second study on subjective estimation by occupational hygienists is described in chapter 4. This study focused on underlying mechanisms of the subjective estimation process.

The results of a survey of occupational exposures in the rubber manufacturing industry in the Netherlands form the basis of chapters 5 and 6. In chapter 5 the current levels of exposures throughout the industry are discussed as well as statistical linear models describing the factors affecting exposure in this industry. In chapter 6 the consequences of the observed exposure variability in the rubber industry for epidemiologic studies are discussed. Different grouping schemes which can be applied in epidemiologic studies in this industry are compared based on new statistical parameters related to differences in exposure level between groups (resolution), homogeneity of exposures within a group, and the precision of the exposure estimate.

In chapter 7 the results are reported of an analysis of exposure variability within a longitudinal database of approximately 20,000 measurements collected throughout industry. The effect of measurement strategy, environmental and production factors on both the within- and between-worker components of occupational exposure are studied. Consequences of this variability for the design of future exposure assessment methods are discussed.

The results of a large survey of occupational exposures to 60 Hz magnetic fields among randomly selected workers in 28 job categories in five electric utility companies are discussed in chapter 8. The measurement strategy was developed to facilitate the analysis of exposure variability within and between occupational groups and workers, and to elaborate an efficient population-specific job-exposure matrix. This matrix will be used for linking health outcomes like leukaemia and brain cancer to occupational magnetic field exposures among electric utility workers in epidemiological studies.

In the final chapter the findings of all previous presented studies are extensively discussed and a general direction is outlined for more powerful occupational epidemiologic studies in the future.

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Chapter 2

Performance of two general job-exposure matrices in a study of lung cancer morbidity in the Zutphen cohort[1]

[1] H. Kromhout, D. Heederik, L. M. Dalderup, and D. Kromhout, *American Journal Epidemiology* **136** (1992) 698-711. Part of this chapter has been presented at the seventh international symposium "Epidemiology in Occupational Health" Tokyo October 1989 and was published in Sakurai, H., Okazaki, I, and Omae, K. Eds. (1990) *Occupational Epidemiology*. Elsevier Science Publishers B.V. Amsterdam ICS No. 889, pp. 43-46.

ABSTRACT

Data from a general population cohort of 878 men from the town of Zutphen, the Netherlands, were used to evaluate the performance of two general job-exposure matrices. Exposures, generated by the job-exposure matrices on the basis of job histories, were compared. The validity of those exposures was measured against exposures reported by the participants in 1977/1978. The performance of the different exposure measures was assessed in proportional hazards analyses of lung cancer morbidity incidence. The two general job-exposure matrices generally disagreed with regard to exposure classification because of differences in exposure assessment and the level of detail of the job axis. When compared with self-reported exposures, the sensitivity of both job-exposure matrices was low (on average, below 0.51), while the specificity was generally high (on average, above 0.90). Self-reported exposures to asbestos, pesticides, and welding fumes showed elevated risk ratios for lung cancer, which were absent for exposures generated by the two job-exposure matrices. Thus, a population-specific job-exposure matrix is proposed as an alternative to general job-exposure matrices developed elsewhere. Such a matrix can be constructed from the results of in-depth interviews of a job-stratified sample of cohort members. Sound validation and documentation of exposure assessment methods used in job-exposure matrices are recommended.

INTRODUCTION

A job-exposure matrix (JEM) is a cross-classification of occupations, industries, and exposures within a given job (Olsen, 1988). Since the notion was introduced in the early 1980s, there has been considerable expectation attached to its potential role in occupational epidemiology. Hoar *et al.* (1980) claimed that their JEM (hereafter referred to as the Harvard JEM) enhanced the value of information on occupation by placing subjects from different industries and with different occupations in the same exposure category based on similar chemical and physical exposures. They indirectly validated their JEM by reanalysing a case-control study on bladder cancer. The relative risk estimated for persons with a heavy exposure to aromatic amines was higher than the relative risk found for any industrial category. Pannett *et al.* (1985) concluded that for occupational data elicited by means of a postal questionnaire, self-reported exposure estimates offer little advantage over those provided at lower cost by their JEM (hereafter referred to as Medical Research Council (MRC) JEM). However, using various general JEMs in case-control studies of lung cancer, others were not able to demonstrate the ability of a JEM to detect exposure to well-known carcinogens such as asbestos, arsenic, and chromium (Hinds *et al.*, 1985; Coggon *et al.*, 1984; Magnani *et al.*, 1987).

The different experiences with general JEMs demonstrate the need for assessment of the reliability and validity of the exposure information generated by those JEMs. To our knowledge, the validity of exposure estimates generated by general JEMs has hardly been studied. From data published by Ferrario *et al.* (1988), it was possible to calculate the validity of their JEM in terms of sensitivity and specificity compared with questionnaire exposure classification. The sensitivity of their JEM was higher than the specificity (1.00 vs 0.73). The authors showed that their JEM underestimated the level of exposure of those exposed. Linet *et al.* (1987) examined the concordance between the Harvard JEM and an occupation-exposure linkage method based on data collected in the National Occupational Hazard Survey of the National Institute for Occupational Safety and Health (1978). They also studied the agreement of the Harvard JEM and the National Occupational Hazard Survey JEM with self-reported exposure information by respondents in a case-control interview study of chronic lymphatic leukemia. Concordance on exposure for the two occupation-exposure linkage methods was fairly poor although it was better for some specific exposures studied. A higher proportion of the study population self-reported exposure to benzene and asbestos than was assessed by the two JEMs. With the self-reported exposure information as the "gold standard" the sensitivity was in general very low (0.10 to 0.47) and the specificity quite high (0.87 to 0.91), which is in contrast with the results for the JEM of Ferrario *et al.* (1988).

The influence of the validity of JEMs on risk estimates depends highly on the proportion exposed within the study population (Kauppinen and Partanen, 1988). With only a low proportion of subjects exposed (less than 5 percent), even a minor deviance from perfect specificity will result in a marked underestimation of the degree of association. The higher the proportion exposed, the greater will be the influence of a decrease in sensitivity. Flegal *et al.* (1986) offered a theoretical background for the relation between misclassification of exposure and bias in the relative risk estimate. They derived a formula for the relation between the observed relative risk under nondifferential misclassification and the sensitivity and specificity of the exposure estimate, the true relative risk and the true prevalence of exposure in the population. They concluded that the potential degree of bias should be evaluated for each situation separately, because the possible effects of misclassification of exposure on relative risks are complex and not easily generalized.

The objective of the present study was to evaluate the performance of the Harvard and MRC JEMs using data from a general population cohort in the Netherlands in which the MRC JEM was previously used to study the relation between chronic nonspecific lung disease and occupational exposures (Heederik *et al.*, 1989; Heederik *et al.* 1990). First, the concordance between exposures generated by the two general JEMs was examined. Second, the self-reported exposure information was used as a "gold standard" to evaluate the validity of both JEMs. Consequently, self-reported and JEM-generated exposures were used in a survival analysis with 7-year incidence of lung cancer as the outcome variable. Finally, a population-specific JEM was built from the self-reported exposures and individual job histories in order to include all of the original cohort members and 25 years of follow-up in another survival analysis.

MATERIALS AND METHODS

Subjects

Information from the Zutphen Study, the Dutch contribution to the Seven Countries Study (Keys *et al.*, 1967) was used as a basis for the present study. This longitudinal study of the relationship between diet, other risk factors, and chronic diseases followed men from the town of Zutphen from 1960 to 1985. Zutphen is an old industrial town in the eastern part of the Netherlands that had approximately 25,000 inhabitants in 1960. From all men born between 1900 and 1919 who had lived in Zutphen for at least five years, a random sample of 1,088 men was selected to participate in a longitudinal study. Of the 1,088 invited men, 878 took part in the medical examination. Data on risk factors like smoking were recorded according to the Seven Countries Study protocol (Keys *et al.*, 1967).

Questionnaire, interview, and JEMs

In 1977 and first months of 1978, the surviving members of the original cohort were medically examined. As part of this examination, information about job history was collected with a self-administered questionnaire. The cohort members could also indicate to which of 27 chemicals or groups of chemical agents they had been exposed during their (different) jobs and leisure time activities. The cohort members were interviewed by one of the authors (L.M.D.) about their jobs and exposure histories before the actual medical examinations were conducted and additional information was added to the questionnaires. Of the original cohort, 611 men attended (92 percent of the survivors). The information on occupational exposures in the questionnaires was coded only recently. Ninety-nine percent (n=603) of the questionnaires were available.

The occupational data were coded in 1990 according to the British Registrar General's 1968 classification of industries (Central Statistical Office, 1968) and the 1966 classification of occupations (General Register office, 1966) for the JEM of Pannett *et al.* (1985) by one of the authors (H.K.). Coding was repeated for the

JEM of Hoar *et al.* (1980) using five-digit occupation codes. The first two digits comprise an industry code based on the *Standard Industrial Classification Manual* of the US Bureau of the Budget (1970). The final three digits designate task or process and are based on the occupational title number of the US *Dictionary of Occupational Titles* (US Department of Labor, 1965). If the name of a specific factory or company was mentioned, additional information was gathered to confirm the classification of this industry from occupational health services in the region, the Chambers of Commerce of Zutphen and Arnhem, and other local authorities. By this procedure, more than 90 percent of the factories and companies mentioned were traced. The other 10 percent had to be coded with less information. On the basis of these codes, exposures were generated with the two general JEMs, the main characteristics of which are presented in table 1.

Table 1. Main characteristics of the MRC and Harvard JEMs

	Harvard JEM	MRC JEM
Job axis	Five digits (two digits industry code; three digits task or process code); 500 different code combinations	669 job groups
Exposure axis	376 different (groups of) agents	50 different (groups of) agents
Exposure degree	5 categories: 0 None 1 Light 2 Moderate 3 Heavy 9 Unknown	4 categories: 0 None 1 Low 2 High 9 Unknown
Exposure evaluation	Job content Hazard classification of jobs by Hueper and Conway (1964)	Other JEMs Textbooks of industrial hygiene, occupational medicine, toxicology, and chemistry Published papers Direct enquiry of trade federations
Job/exposure combinations	15,000	33,450

Medical information

Between 1960 and 1973, all subjects were medically examined annually and thereafter in 1977-1978 and 1985. In 1980 and 1982, a questionnaire was administered concerning their health status. Information on self-reported morbidity was verified by contacting the participant's general practitioner. The vital status of the 878 men was verified after 25 years of follow-up. Each person had a complete follow-up. During the 25 years of follow-up, 430 men died. Information on the cause of death was obtained from the death certificate, and from the hospital and/or the general practitioner. The underlying cause of death was coded according to the Eighth Revision of the *International Classification of Diseases* (ICD-8) (WHO, 1969).

In 1986, all morbidity data collected between 1960 and 1985 were checked and were uniformly coded by one physician. Lung cancer incidence (ICD-8 code 162) was defined as the first year in which the diagnosis of lung cancer was clinically established. More detailed information about the medical examination and coding of the mortality and morbidity data can be found in Heederik *et al.* (1992).

Statistical analysis

The agreement between the two matrices in exposure classification for 25 agents, the subset of agents common to both JEMs, was assessed by calculating Cohen's kappas and 95 percent confidence intervals (Fleiss, 1981) as a measure of agreement, after the five exposure categories of the Harvard JEM and the four categories of the MRC JEM were merged into two categories (table 2). The exposure estimates were merged in two different ways, resulting in a dichotomy of exposed versus nonexposed (A) and high exposure versus low exposure and nonexposed (B) (table 2). This resulted in both a lenient (A) and a stringent (B) classification of exposure. Next, validity in terms of sensitivity and specificity, using the self-reported exposures as the "gold standard" was calculated for 14 exposures of the MRC JEM and eight exposures of the Harvard JEM. Confidence intervals for the sensitivity and specificity were calculated using the formula: $p \pm z_{0.95} \sqrt{p(1-p)/n}$, where p represents the estimated sensitivity or specificity and n represents the

Table 2. Merging of exposure levels of the Medical Research Council (MRC) and Harvard job-exposure matrices (JEMs) in a lenient (A) and strict (B) manner

Exposed vs non-exposed (A)			High exposed vs low exposure and non-exposed (B)		
Exposure category	Harvard JEM	MRC JEM	Exposure category	Harvard JEM	MRC JEM
Exposed	1 Light 2 Moderate 3 Heavy 9 Unknown	1 Low 2 High 9 Unknown	High exposure	3 Heavy 9 Unknown*	2 High
Non-exposed	0 Nonexposed	0 Nonexposed	Low exposure and non-exposed	1 Light 2 Moderate 0 Nonexposed	1 Low 9 Unknown 0 Nonexposed

* The authors have been notified of the fact that the "9s" in the Harvard JEM exposure codings, although specified as "exposed but level unknown," should have been treated as "3s," meaning "exposed at a high level" (S. Hoar-Zahm, personal communication, 1992). Readers should therefore be aware that this JEM was applied in a different way than in several other published studies which have used the Harvard JEM.

number of observations.

The self-reported exposure information and the information generated by both matrices was subsequently used in a 7-year (1978-1985) follow-up analysis of the cohort. The relation between occupational exposure and 7-year incidence of lung cancer was analyzed in a proportional hazards analysis (Cox, 1972), adjusting for smoking habits (pack-years up to 1960) and age. To use the total follow-up data, we created a population-specific JEM for 10 self-reported exposures. This JEM had the same job axis as the British JEM, and exposure was arbitrarily assigned to a job when at least 10 percent of the performers of a job reported an exposure in 1977/1978. Jobs for which less then 10 percent or none of the performers reported the exposure were considered nonexposed. Exposure information generated by this JEM and the two other JEMs was used in a second survival analysis covering the total follow-up period (1960-1985). In this analysis, all lung cancer cases were taken into account, but only information about each cohort member's job held in 1960 could be used.

Table 3. Self-reported occupational exposures in 1,002 jobs for 603 men in the Zutphen Study, 1977/1978

Agent	No. of jobs	% of jobs	No. of men	% of men
1. Chemists' raw materials	0	0	0	0
2. Asphalt	12	1.2	10	1.7
3. Pesticides	12	1.2	12	2.0
4. Bleach	9	0.9	8	1.3
5. Raw materials, processing aids, finished articles used in the chemical industry	14	1.4	12	2.0
6. Printing materials: printing inks copying paper, carbon paper, etc.	45	4.5	41	6.8
7. Wood finishing and conservation products	9	0.9	7	1.2
8. Hairdresser's materials: hair dye, cold wave fluid, etc.	4	0.4	4	0.7
9. Dyes for textile and utensils	3	0.3	3	0.5
10. Fertilizers	17	1.7	17	2.8
11. Synthetic fibre raw materials and processing aids	6	0.6	5	0.8
12. Laboratory chemicals	8	0.8	7	1.2
13. Welding materials, welding fume	53	5.3	36	5.9
14. Glues	58	5.8	52	8.6
15. Oil (drilling oil, cooling oil, lubricants)	91	9.1	72	11.9
16. Solvents for metal	40	4.0	31	5.1
17. Solvents for textile	3	0.3	3	0.5
18. Pharmaceutical raw materials and processing aids	0	0	0	0
19. Plastics raw materials and processing aids	8	0.8	6	1.0
20. Passive smoking	35	3.5	27	4.5
21. Painting materials (paint, varnish, lacquers, pigments)	63	6.3	54	9.0
22. Soldering fumes	46	4.6	31	5.1
23. Dust (asbestos, cement, wood, chalk, quartz)	108	10.8	95	15.8
24. Upholstering glues and preservatives	14	1.4	11	1.8
25. Tar, pitch, bitumen	20	2.0	17	2.8
26. Foods and allied products industry processing aids, preservatives, bleach, colorants	3	0.3	3	0.5
27. Other hazardous substances	4	0.4	3	0.5
At least one exposure	378	37.7	303	50.2

The survival analyses were performed using the PHGLM procedure of SAS (1986) on a VAX computer (Digital Equipment Corporation, Concord, Massachusetts). The hazard ratios were calculated from the regression coefficients by taking the antilog of the regression coefficients. Ninety-five percent confidence intervals were calculated using the standard error of the regression coefficient. Details can be found in Heederik *et al.* (1992).

RESULTS

Job history and self-reported exposure of the 1977/1978 population

The 603 subjects for which self-reported information on job history and occupational exposure was available reported a total of 1,002 jobs. Fifty-five percent reported one job, 29 percent two jobs, and 16 percent reported three or more jobs. Thirty percent of the 603 cohort members had changed industry during their working career. The mean duration of a job was 26.6 year (based on information on 95 percent of the jobs). The self-reported exposures are shown in table 3. Only exposure to oil and dust was reported by more than 10 percent of the men. Fifty percent of the interviewed men reported an exposure to at least one of the 27 exposures.

Agreement between JEMs

The Harvard matrix systematically generated a larger number of exposed subjects than the MRC matrix for the majority of the agents. The MRC matrix appeared to be more conservative in attributing high exposures to acrylonitrile, aromatic amines, arsenic, asbestos, benzene, cadmium, carbon tetrachloride, chlorophenols, chromium, cold, ethylene oxide, formaldehyde, lead, mercury, polychlorinated biphenyls, pesticides, styrene, ultraviolet light, and waxes than the Harvard matrix. On the other hand high exposures to coal tar, epoxy resins, organic solvents, and paints were more frequently assigned by the MRC matrix. The concordance between the JEMs is shown in table 4. Except for chromium, cold, pesticides, styrene, and wood dust, the agreement was poor (Cohen's kappa <0.40). Classifying only high exposure cases as exposed (B) made the agreement even worse, with the exception of exposure to wood dust (Cohen's kappa=0.87, 95 percent confidence interval 0.81-0.93).

Table 4. Agreement (Cohen's kappa) between two job-exposure matrices for exposure to 25 agents, classified both in a lenient (A) and strict (B) manner: 1,002 jobs for 603 men in the Zutphen Study, 1977/1978

Agent	A* (95% CI)†	B‡ (95% CI)
Acrylonitrile	0.25 (0.19 0.31)	0.17 (0.13 0.20)
Aromatic amines	0.08 (0.04 0.13)	0.07 (0.03 0.10)
Arsenic	0.16 (0.12 0.20)	.§
Asbestos	0.24 (0.18 0.30)	0.04 (-0.02 0.10)
Benzene	0.30 (0.25 0.35)	0.11 (0.06 0.16)
Beryllium	0.01 (-0.00 0.02)	.‖
Cadmium	0.10 (0.04 0.16)	.§
Carbon tetrachloride	0.29 (0.24 0.35)	-0.01 (-0.03 0.01)
Chlorophenol	-0.01 (-0.05 0.03)	-0.00 (-0.05 0.05)
Chromium	0.44 (0.38 0.50)	-0.04 (-0.08 0.01)
Coal tar	0.20 (0.14 0.27)	0.01 (-0.05 0.07)
Cold	0.55 (0.49 0.61)	0.33 (0.28 0.38)
Ethylene oxide	0.02 (-0.04 0.07)	-0.01 (-0.04 0.03)
Epoxy resins	0.07 (0.02 0.12)	.§
Formaldehyde	0.01 (-0.04 0.07)	0.07 (0.01 0.13)
Lead	0.17 (0.12 0.23)	0.03 (-0.00 0.07)
Mercury	0.00 (-0.06 0.07)	.§
Organic solvents	0.11 (0.07 0.15)	0.02 (-0.03 0.07)
Paints	0.03 (0.01 0.06)	-0.01 (-0.05 0.03)
PCBs¶	0.26 (0.20 0.31)	.§
Pesticides	0.44 (0.38 0.50)	.§
Styrene	0.52 (0.46 0.58)	0.16 (0.13 0.20)
UV-light	-0.01 (-0.06 0.03)	0.10 (0.07 0.13)
Waxes	-0.07 (-0.13 0.00)	-0.00 (-0.02 0.01)
Wood dust	0.69 (0.63 0.75)	0.87 (0.81 0.93)

* Both high and low exposed classified as exposed
† CI, confidence interval
‡ Only high exposed classified as exposed
§ No exposed subjects were generated by one of the matrices
‖ *Neither matrix generated exposed subjects*
¶ PCBs, polychlorinated biphenyls

Validity of exposures generated by the matrices

Figures 1-4 show the sensitivity and specificity of the matrices compared to the self-reported exposures for both classifications (A and B) of exposure levels of the JEMs. In general, sensitivity appeared to be much lower than specificity. The sensitivity of the MRC JEM ranged from 0 to 0.72 when only high exposed jobs were considered as exposed (B). The sensitivity increased and ranged from 0 to 0.91 when all exposed jobs were classified as exposed (A). The sensitivity was highest for exposure to coal dust, organic solvents, pesticides, printing materials,

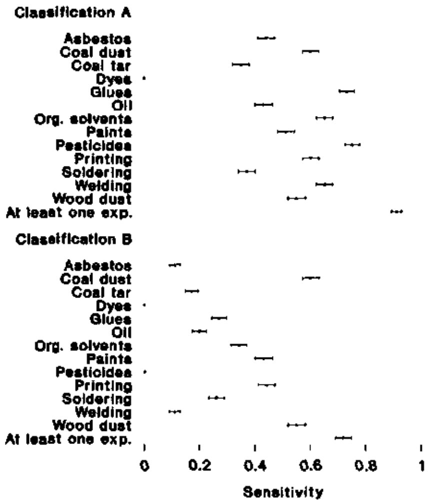

Figure 1. Sensitivity of the Medical Research Council matrix, considering both low and high exposure subjects exposed (A classification) and considering only high exposure subjects as exposed (B classification): The Zutphen Study, 1977/1978. Org., organic; exp., exposure

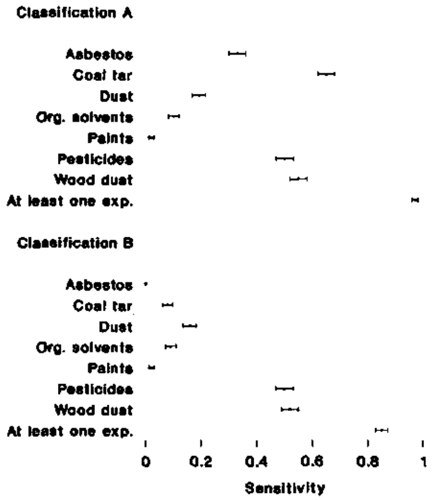

Figure 3. Sensitivity of the Harvard matrix, considering both low and high exposure subjects as exposed (A classification) and considering only high exposure subjects as exposed (B classification): The Zutphen Study, 1977/1978. Org., organic; exp., exposure

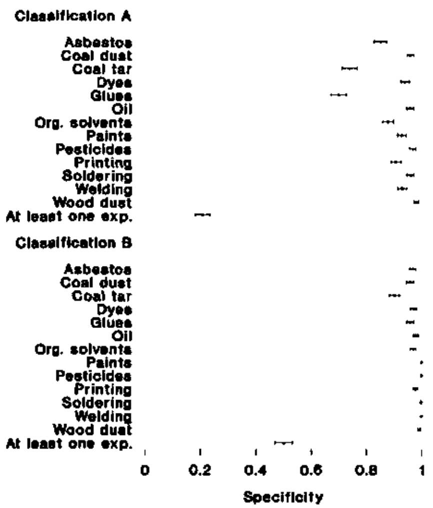

Figure 2. Specificity of Medical Research Council matrix, considering both low and high exposure subjects exposed (A classification) and considering only high exposed subjects exposed (B classification): The Zutphen Study, 1977/1978. Org., Organic; exp., exposure.

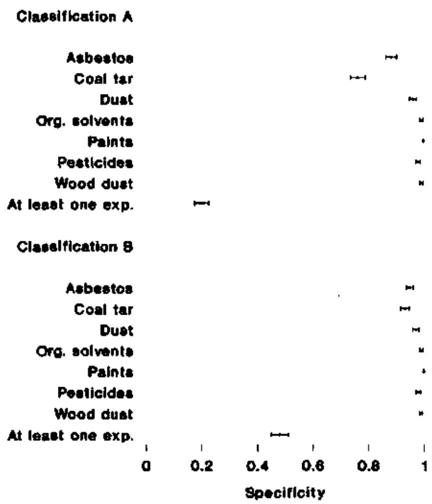

Figure 4. Specificity of the Harvard matrix, considering both low and high exposure subjects as exposed (A classification) and considering only high exposure subjects as exposed (B classification): The Zutphen Study, 1977/1978. Org., organic; exp., exposure.

welding fumes, and glues. The Harvard JEM showed somewhat different results. The sensitivity of the Harvard JEM was very low when the more stringent (B) classification of exposure levels was used (on average, 0.20). Only for wood dust exposure and exposure to pesticides the sensitivity was above 0.50. Using the less stringent classification (A) increased the sensitivity for most exposures, but it stayed below the level of the MRC JEM. The specificity of the MRC JEM was generally very high (on average, 0.98) when the B classification of exposure levels was used. The specificity of the Harvard JEM was comparable. The less stringent classification (A) resulted in a decrease of specificity to 0.90 for the MRC JEM. The specificity of the Harvard JEM decreased only four percent, on average.

Both JEMs had a very high sensitivity for the exposure category "at least one exposure" when the A classification was used. On the other hand, the specificity for this category was very low.

Risk estimates with different exposure estimates

Of the 603 participating men who participated in the medical examination of 1977/1978, 18 had not participated in the 1960 examination and were excluded. For six men, information on smoking habits was insufficient, leaving a group of 579 men. Persons who had a diagnosis of lung cancer before 1978 were excluded from the analyses (15 persons). The remaining population of 564 men had, on average, smoked for 27.8 years (standard deviation (SD) = 10.9) until 1960, and the average number of pack-years was 14.4 (SD = 10.9). During the follow-up period (1978-1985), 31 men developed lung cancer.

The results of the multivariate proportional hazards analyses for 7-year lung cancer incidence are shown in table 5. The difference between risk estimates for JEM-generated and self-reported exposures were substantial. The MRC JEM underestimated the hazard ratios for exposure to asbestos, pesticides, and welding fumes, compared with self-reported exposures. For most other exposures, the hazard ratios were overestimated. The gain in sensitivity by using the A classification did

Table 5. Hazard ratios for different exposures classified in both a lenient and strict manner: 7-year incidence of lung cancer (adjusted for age and smoking habits) in a multivariate proportional hazards analysis of 564 men in the Zutphen Study 1978-1985*

Agent	$HR_{MRC}A$	No.	$HR_{MRC}B$	No.	HR_{SELF}	No.
At least one exposure	1.82 (0.43-7.66)†	495	1.40 (0.60-3.27)	388	1.38 (0.67-2.81)	284
Asbestos	1.36 (0.61-3.03)	115	1.37 (0.33-5.77)	25	2.14 (0.29-15.70)	8
Coal tar	2.59 (1.27-5.30)	170	2.16 (1.01-4.58)	90	0.95 (0.13-6.95)	20
Organic solvents	1.12 (0.50-2.51)	132	0.71 (0.17-2.99)	49	0.49 (0.12-2.07)	69
Paints	1.17 (0.45-3.06)	84	.‡	26	0.38 (0.05-2.80)	47
Pesticides	1.24 (0.29-5.29)	33	.	0	4.44 (1.05-18.74)	10
Wood dust	1.05 (0.25-4.41)	36	1.68 (0.40-7.04)	25	0.67 (0.09-4.65)	26
Coal dust	1.17 (0.28-4.92)	31	1.17 (0.28-4.92)	31	1.33 (0.10-5.65)	10
Dyes	0.65 (0.15-2.73)	49	0.56 (0.08-4.11)	29	.‡	3
Glues	0.89 (0.44-1.82)	250	1.14 (0.34-3.77)	45	1.30 (0.23-2.55)	50
Oils	1.68 (0.69-4.12)	62	2.00 (0.69-5.76)	31	1.34 (0.51-3.51)	65
Printing inks	1.03 (0.39-2.68)	91	1.20 (0.29-5.07)	29	0.43 (0.02-7.35)	39
Soldering fumes	2.05 (0.78-5.36)	46	1.38 (0.19-10.14)	12	1.79 (0.54-5.88)	30
Welding fumes	1.56 (0.64-3.81)	74	.‡	6	2.37 (0.83-6.78)	35
Agent	$HR_{HARVARD}A$	**No.**	$HR_{HARVARD}B$	**No.**	HR_{SELF}	**No.**
At least one exposure	3.36 (0.46-24.71)	501	1.72 (0.70-4.19)	398	1.38 (0.67-2.81)	284
Asbestos	1.21 (0.49-2.96)	92	1.00 (0.24-4.20)	35	2.14 (0.29-15.70)	8
Coal tar	0.96 (0.45-2.03)	186	0.99 (0.30-3.29)	51	0.95 (0.13-6.95)	20
Organic solvents	0.96 (0.13-7.05)	20	0.96 (0.13-7.05)	20	0.49 (0.12-2.07)	69
Paints	.‡	4	.‡	4	0.38 (0.05-2.80)	47
Pesticides	1.71 (0.41-7.21)	21	1.71 (0.41-7.21)	21	4.44 (1.05-18.74)	10
Wood dust	1.30 (0.31-5.44)	30	1.51 (0.36-6.35)	27	0.67 (0.09-4.95)	26
Dust	1.20 (0.36-3.94)	46	0.50 (0.07-3.68)	34	2.13 (0.98-4.65)	89

* $HR_{MRC}A$, hazard ratio of exposures generated by the MRC matrix and classified the lenient way; No., number of men exposed; $HR_{MRC}B$, hazard ratio of exposures generated by the MRC matrix and classified the strict way; HR_{self} hazard ratio of self-reported exposures; $HR_{HARVARD}A$, hazard ratio of exposures generated by the Harvard matrix and classified the lenient way; $HR_{HARVARD}B$, hazard ratio of exposures generated by the Harvard matrix and classified the strict way

† Numbers in parentheses, 95% confidence interval

‡ No lung cancer cases among those exposed

not result in more comparable hazard ratios, probably because of a simultaneous loss in specificity, which has a great influence when only a small proportion of the population is exposed. The Harvard JEM also underestimated the elevated hazard ratios for asbestos, pesticides, and dust exposure. Using the A classification or the more stringent B classification led to comparable hazard ratios. The gain in sensitivity presumably counterbalanced the loss in specificity. Considering the exposure category "at least one exposure" with a self-reported prevalence of over

50 percent, it is evident that both matrices gave more comparable results when the stringent B classification was used. The almost perfect sensitivity reached with the A classification for this exposure did not outweigh the very low specificity.

Population-specific JEM

Using the total 25 years of follow-up data extended the analysis to the total cohort population that was originally medically examined in 1960. Of these 878 men, 856 were included in the proportional hazards analyses, because information on smoking habits was lacking for 14 men, information on 1960 occupation was

Table 6. Hazard ratios for different occupational exposures classified in both a lenient and strict manner: 25-year incidence of lung cancer (adjusted for age and smoking habits) in a multivariate proportional hazards analysis of 856 men in the Zutphen Study, 1960-1985*

Agent	$HR_{MRC}A$	No.	$HR_{MRC}B$	No.	$HR_{SELFJEM}$	No.
Asbestos	1.00 (0.51-1.97)†	122	0.47 (0.06-3.41)	21	1.40 (0.44-4.48)	32
Coal tar	1.39 (0.82-2.35)	190	1.61 (0.82-3.18)	74	0.63 (0.20-3.03)	49
Organic solvents	0.90 (0.44-1.82)	127	0.27 (0.04-1.91)	47	1.44 (0.81-2.56)	143
Paints	0.88 (0.35-2.21)	72	0.57 (0.08-4.08)	24	0.98 (0.45-2.16)	96
Pesticides	1.19 (0.43-3.29)	39	.	0	0.62 (0.09-4.46)	19
Wood dust	1.44 (0.52-4.00)	51	1.69 (0.53-5.45)	32	1.57 (0.71-3.44)	69
Oils	1.79 (0.89-3.63)	58	3.52 (1.52-8.15)	21	1.71 (0.99-2.93)	133
Soldering fumes	1.85 (0.74-4.61)	32	.‡	7	2.24 (1.17-4.29)	62
Welding fumes	1.09 (0.50-2.40)	69	1.54 (0.37-6.30)	13	1.93 (1.05-3.55)	84
Agent	$HR_{HARVARD}A$	*n*	$HR_{HARVARD}B$	No.	$HR_{SELFJEM}$	No.
Asbestos	0.75 (0.34-1.64)	118	0.37 (0.05-2.64)	31	1.40 (0.44-4.48)	32
Coal tar	0.97 (0.54-1.75)	183	0.53 (0.13-2.18)	43	0.63 (0.20-3.03)	49
Organic solvents	0.56 (0.08-4.06)	22	0.58 (0.08-4.16)	21	1.44 (0.81-2.56)	143
Paints	.‡	5	.‡	5	0.98 (0.45-2.16)	96
Pesticides	.‡	9	.‡	9	0.62 (0.09-4.46)	19
Wood dust	1.56 (0.48-5.03)	35	1.66 (0.52-5.37)	33	1.57 (0.71-3.44)	69
Dust	1.32 (0.48-3.63)	39	1.32 (0.42-4.22)	30	1.66 (1.00-2.75)	198

* $HR_{MRC}A$, hazard ratio of exposures generated by the MRC matrix and classified the lenient way; No., number of men exposed; $HR_{MRC}B$, hazard ratio of exposures generated by the MRC matrix and classified the strict way; $HR_{SELFJEM}$ hazard ratio of exposures generated by the matrix based on self-reported exposures; $HR_{HARVARD}A$, hazard ratio of exposures generated by the Harvard matrix and classified the lenient way; $HR_{HARVARD}B$, hazard ratio of exposures generated by the Harvard matrix and classified the strict way

† Numbers in parentheses, 95% confidence interval

‡ No lung cancer cases among those exposed

insufficient to code for seven men, and one subject was diagnosed with lung cancer before 1960. The average number of years smoked was 28.7 (SD = 11.2), and the average number of pack years 15.0 (SD = 11.2). During the follow-up period (1960-1985), 67 men developed lung cancer.

The results of the 25-year proportional hazard analysis are given in table 6. The elevated hazard ratios for exposure to asbestos, dust, organic solvents, soldering fumes, and welding fumes as assessed by the population-specific JEM were underestimated by the MRC and Harvard JEMs. Using either the A or B classification did not result in more comparable hazard ratios for the Harvard JEM. However, exposures generated by the MRC JEM A classification showed more comparable hazard ratios than the B classification. The hazard ratio for exposure to coal tar and oils were overestimated by the MRC JEM for both classifications. Exposures generated by the population-specific JEM yielded generally higher hazard ratios than comparable exposures generated by the two other JEMs.

DISCUSSION

This study showed a distinct lack of concordance between two general JEMs applied in a general population study. The reasons for this became evident after we examined the differences in exposure attribution. For example, occupations that were classified as having a high exposure to arsenic, asbestos, and wood dust by at least one of the matrices are shown in table 7. Most differences in exposure classification are due to differences in assigning a specific exposure to a certain occupation. However, it is also evident from table 7 that differences occur because of differences in the level of detail of the job-axis. For instance, while all 16 trench diggers had a high exposure to asbestos according to the MRC JEM, only two trench diggers in gas distribution were assigned a high asbestos exposure by the Harvard JEM. The fact that this JEM divided the 16 trench diggers into different industries made a differentiation in exposure possible. One of the reasons for the

Table 7. Occupations and numbers of men with high exposures to arsenic, asbestos and wood dust generated by the Harvard job-exposure matrix and the Medical Research Council job-exposure matrix: The Zutphen study, 1977/1978*

		Harvard only		MRC only		Both	
Exposure	No.*	Occupation	No.	Occupation	No.	Occupation	No.
Arsenic	42	Farmer	13				
		Plant gardener	14				
		Pest controller	2				
		Miner	3				
		Smelter	1				
		Food processing	4				
		Fuel processing	5				
Asbestos	75	Locomotive operator	21	Trench digger	14	Trench digger in gas distribution	2
		Fireman	10	Construction worker	9	Laborer in engineering trade	1
		Switchman	7	Bricklayers' laborer	3		
		Gas distribution service	6				
		Miner	2				
Wood dust	27			Crating	2	Woodworker	5
				Forester	1	Carpenter	15
						Cabinetmaker	4

* Number of persons.

apparent differences in assigning exposures might be related to the fact that the JEMs originate from two different countries. Existing differences in occupational exposure between the United States and Britain might be reflected in this way, but it is unlikely that this will lead to the observed discordance.

The criteria used for assigning an exposure to a job are of course the essence of the JEM method for determining occupational exposure. Assigning an exposure to a job on lenient criteria will result in a higher sensitivity but, at the same time, a lower specificity. Using very strict criteria (for instance, the requirement that all persons performing a specific job have to be exposed before an exposure will be assigned) will make the specificity perfect but will lower the sensitivity drastically. The validity of exposures generated by the JEMs compared with self-reported exposures confirmed this point. Considering only the highly exposed as exposed, the average sensitivity was 0.27 and 0.20 for the MRC and Harvard JEM, respectively. Considering all exposed subjects as exposed (the more lenient classification) yielded increased average sensitivities of 0.51 and 0.33, respectively, but produced decreased average specificities (0.98 to 0.90 and 0.97 to 0.94). Furthermore, it is obvious that exposure assessment via a JEM will be defined by the level of detail of the job axis, because it is implicitly assumed that all persons performing this job will be exposed. In other words, the jobs on the job axis are considered homogeneous exposure groups. However, it is well known that this presumption is not often met (Rappaport, 1991).

In this study, the validity of exposure to asbestos according to the Harvard JEM compared with self-reported exposure was, surprisingly, almost identical to the validity reported by Linet *et al.*(1987) (a sensitivity of 0.33 vs 0.26 (cases) and 0.33 (controls) and a specificity of 0.88 vs 0.88 (cases) and 0.91 (controls)). The sensitivity of exposure to solvents according to both JEMs was much lower than the perfect sensitivity assessed in the Italian study (Ferrario *et al.* 1988). The specificity in the present study was slightly higher. However, from the brief description of the Italian study, it is uncertain whether both methods were applied independently.

The validity of the JEMs was compared to exposures reported by the cohort members themselves as the "gold standard". The validity of the latter could not be assessed, because accurate quantitative exposure data were lacking. However, the occurrence of differential misclassification seems unlikely, because men with a diagnosis of lung cancer prior to 1977 and 1978 (the years in which the self-reported exposures were assessed) were excluded. Besides, the description of the 27 chemical/groups of agents are considered reasonable and recognizable in a self-report questionnaire followed by an interview. Ahlborg (1990) recently compared self-reported exposure data on women who worked in a laundry or dry-cleaning shop during pregnancy with information obtained from the employers. The sensitivity and specificity of self-reported exposure to tetrachloroethylene was very high (above 0.93) for both cases and referents. Ahlborg concluded that missing information, and not erroneous reporting of exposure led to misclassification, because the proportion of women who did not know if tetrachloroethylene was used was larger in the case group than in the reference group. Holmes and Garschick (1991) showed that self-reported exposure histories obtained by mail survey methods alone tend to underreport occupational exposure and should be reviewed in more detail as was done in the Zutphen study in 1977/1978.

The question of which of the JEMs performed better is not easy to answer. The sensitivity of both JEMs is low. Although the sensitivity of the MRC JEM is, on average, higher than the sensitivity of the Harvard JEM, the effect on the estimated hazard ratios is not substantial, because given the overall low prevalence of exposure, the specificity determines to a great extent the outcome from the analysis. Aggregating specific exposures in broader exposure groups (such as "at least one exposure") leads to increased sensitivity but very low specificity when the less stringent exposure assignment classification is used. The more stringent B classification with lower sensitivity but higher specificity is then preferred.

For a few self-reported exposures (asbestos, pesticides, and welding fumes), the analysis of the 7-year lung cancer incidence showed distinctly elevated hazard ratios for lung cancer that were not confirmed for the same exposures generated by the JEMs. The same phenomenon was present in the results of the analysis of the 25-year lung cancer incidence. The exposures to dust, soldering, and welding fumes generated by the population-specific JEM had significantly elevated hazard ratios which were absent when the other two JEMs were used. In the 7-year follow-up analysis, the reverse was seen as well. The hazard ratios for subjects exposed to coal tar, oils, organic solvents, printing inks, and wood dust according to the JEMs were higher than those for subjects who reported those exposures themselves. Interpretation is difficult, because the hazard ratio estimates have large confidence intervals as a result of the small number of lung cancer cases and the limited follow-up period.

The formula of Flegal *et al.* (1986) enabled comparison of the performance of the JEMs from a more theoretical point of view. In that formula, the mean sensitivity and specificity of the JEMs was used. Figure 5 shows the observed relative risk for both JEMs as a function of the true prevalence of exposure within a cohort, given a true relative risk of 4. This figure shows that the MRC JEM performs better than the Harvard JEM when the stringent B classification is used in situations with low prevalence of exposure (less than 40 percent). The bias in the risk estimate is yet quite substantial. Using either the lenient (A) or the more stringent (B) classification of the Harvard JEM leads to an almost identical bias in the risk estimates. The population-specific JEM, that was used in the analysis of the 25-year lung cancer incidence data, had a mean sensitivity of 0.79 and a mean specificity of 0.91.

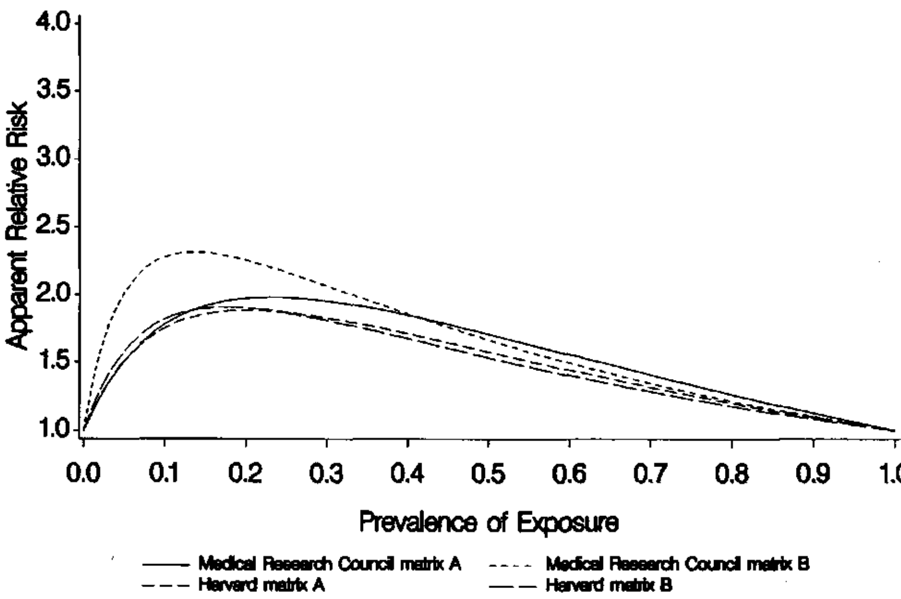

Figure 5. Observed relative risk of lung cancer as a function of the prevalence of exposure: The Zutphen Study. Observed relative risk was estimated with a true relative risk of 4 and using a mean sensitivity and specificity of 0.51 and 0.90, 0.27 and 0.98, 0.33 and 0.94, 0.20 and 0.97 for the Medical Research Council matrix lenient classification (A), the Medical Research Council matrix strict classification (B), the Harvard matrix lenient classification (A), and the Harvard matrix strict classification (B), respectively.

Applying these values in the formula resulted in a better performance than the MRC B classification only when the prevalence of exposure was above 10 percent. The performance of this JEM, however, is highly dependent on which criterion is used for assigning an exposure to a specific job. The criterion used here was that 10 percent of subjects performing a specific job had to report the exposure. Increasing this percentage would lower the sensitivity but increase the specificity. Siemiatycki *et al.* (1989) have suggested tailoring the cut-point for each exposure separately to optimize power.

The population-specific JEM, which was previously described as the "interview JEM" for case-control studies (Siemiatycki *et al.*, 1989), might be an alternative for JEMs developed elsewhere in general population cohort studies. Assuming a true prevalence of exposure of, at most, 10 percent, the performance of a population-specific JEM will only exceed the performance of the MRC JEM when it has a specificity of at least 0.98 and a sensitivity above 0.30.

The results of in-depth interviews on occupational exposures of a by job- and eventually region-stratified sample of the cohort can be used to build a population-specific JEM. Subsequently, this population-specific JEM can be used to generate exposures for the remaining cohort members. The merits of this method will only outweigh the extra costs needed for the interviews when the JEM's structure and exposure assignment leads to a minimum of misclassification.

Designers of any JEM should make explicit the criteria that were used to assess exposure (levels). Moreover, it is obvious from the results of the present study that sound validation of the exposure data within a JEM is needed if the JEM is to be the powerful tool promised by its developers. Although it has to be acknowledged that the respective general JEMs were not designed to be used in the Netherlands, the results seem to confirm the belief that use of general JEMs will hardly ever give sufficiently detailed information on occupational exposures at the individual level (Olsen, 1988).

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Chapter 3

Agreement between semiquantitative exposure estimates and quantitative exposure measurements[1]

[1] Revised version of the paper: H. Kromhout, Y. Oostendorp, D. Heederik, J.S.M. Boleij. *American Journal of Industrial Medicine* **12** (1987) 551-562

ABSTRACT

A method for semi-quantitative estimation of the exposure at task level was used and validated with actual measurements in five small factories. The results showed that occupational hygienists were in general the most successful raters. Plant supervisors and workers handled the estimation method less successfully because of more misclassification of the tasks.

The method resulted, in general, in a classification of tasks in four exposure categories ranging from no exposure to high exposure. The exposure categories correlated positively with mean concentrations, but showed overlapping exposure distributions. This resulted in misclassification of the exposure for individual workers when a relatively large interindividual variability in exposure levels within an exposure category was present.

The results show that this method can be used for workplace exposure zoning, but that the usefulness of the estimates for epidemiological purposes is not clear-cut and depends strongly on the actual exposure characteristics within a workplace.

A combination of the semi-quantitative exposure estimation method together with assessment of the exposure levels by measurements makes a rearrangement of tasks or individual workers possible and could improve the validity of this method for epidemiological purposes.

INTRODUCTION

Semiquantitative exposure estimates are often used in retrospective epidemiologic studies when appropriate quantitative data are not available. Occasionally these semiquantitative exposure estimates are used in prospective health information systems set up by multinational companies (Lynch *et al.*, 1982; Socha *et al.*, 1979;

Langner *et al.*, 1979; Greenburg and Tamburro, 1981). The main advantage of semiquantitative exposure estimates are that they are obtained inexpensively and that it is possible to be reasonably comprehensive compared to quantitative exposure measurements. Until now no results have been published from epidemiologic studies using semiquantitative data from these health information systems, which are gathered prospectively. However, several investigators have used estimation techniques for epidemiological studies resulting in semiquantitative exposure estimates generated just for the occasion by different raters such as workers (doPico, 1982; Rom *et al.*, 1983; Hertzman *et al.*, 1986), occupational hygienists (Blum *et al.*, 1978; Rosenstock *et al.*, 1984; Hawkins & Evans 1989), plant supervisors (DeFonso and Kelton, 1976; Wald *et al.*, 1984), chemists (Gérin *et al.*, 1985), or so called occupational health teams (Woitowitz *et al.*, 1970). (Cross) Validation of these semiquantitative exposure estimates has been carried out in several ways:

The first is by using the semiquantitative estimates in dose-effect studies of known effects such as angiosarcoma and vinylchloride. Greenburg and Tamburro (1981) concluded that a system of rank-ordered individual exposure indices for highly suspected chemicals can identify a known causative relationship between exposure and the development of a disease. These indices were constructed by combining job history and level of exposure (semiquantitatively on a six-point scale) per area and job. The serially additive expected dose (SAED) model, which uses time-specific exposure data to construct cumulative exposures for members of an industrial cohort, was validated by applying it in the presence of well-established occupational carcinogens. The strongest association indicated that for angiosarcoma the jobs with high excursional exposures from leaks or spills may have been the most dangerous (Waxweiler and Smith, 1984).

The second way to validate estimates is by comparing the estimates of various raters. Lynch (1982) described a study in which an experienced occupational hygienist semiquantitatively estimated the past exposure of a long list of job categories also using a six-point scale. This was validated in a second study in which the original occupational hygienist and a panel of plant supervisors repeated those estimates. These two new estimates were compared with the original one by calculating the level of agreement (Fleiss, 1981). The results showed that the ability of occupational hygienists to retrospectively reconstruct exposure was doubtful. After the six-degree exposure estimation scheme was reduced to three degrees and the job categorization was simplified, the agreement became fair-to-good between the three different estimates. However, as Maclure and Willett (1987) showed, such an increase of Kappa values is an intrinsic characteristic of Cohen's Kappa, which is greatly influenced by the number of categories. By collapsing categories the Kappa increases but cannot be compared with the Kappa of the original number of categories. Whether the agreement really improved after merging the six catogories into three is therefore doubtful.

Gérin *et al.* (1985) reported substantial agreement between different exposure raters (chemists and plant specialists), considering only those exposure estimates of which the raters were highly confident, using a three-point scale for level of exposure. These results were confirmed by Goldberg *et al.* (1986) in a more extensive survey of the inter-rater agreement in the same study (Kappa ranging from 0.5 to 0.7 for a dichotomous classification of exposure). Hertzman *et al.* (1986) also reported reliable estimates of frequency (on a five-point scale) and of duration (on a six-point scale) after comparing the results of 11 workers, which estimated their chlorophenate exposure levels by job title.

The third way to validate estimates is by comparing the semiquantitative exposure estimates with quantitative exposure measurements. doPico (1982) asked workers to estimate their dust exposure during the work shift as less than average, average, or more than average. He found a statistically significant correlation between the actual measured dust level and workers' subjective estimation. He concluded then that workers are capable of detecting dust levels that fluctuate within a narrow range. Rom *et al.* (1983) asked workers participating in their study of dermatitis in trona (sodium sesquicarbonate) miners and millers to code on a scale of 1 to 4 their job exposure to raw trona dust. Afterwards a mean score was determined for all employees in each job category. Scores were assigned exposure ratings as follows: 1.0-2.0, low; 2.1-3.0, medium; and 3.1-4.0, high. Personal samples for dust differed by a factor 4 between high and medium and between medium and low. Woitowitz *et al.* (1970) assessed semiquantitative exposure estimates for dust by classifying departments and tasks from no exposure to heavy exposure (on a three-point scale). A lineair relationship existed between the semiquantitative exposure estimates and dust measurements in a factory where asbestos was used. The mean concentrations per exposure category had ratios of 0.5:1.0:1.5 mg/m^3. The standard deviations of the concentrations per exposure category increased with increasing exposure category.

Most of the authors of these studies presented their methods of semiquantitative exposure assessment as rather valid and therefore useful for epidemiologic purposes. However, only very limited attention was given to important aspects such as overlapping exposure distributions between exposure categories and misclassification of individual workers. These aspects could be important elements when a lack of association between exposures and health effects has been detected.

In a study carried out for the Dutch Labour Inspectorate dealing with the standardization of occupational hygiene surveys, we tested and validated a method of semiquantitative estimation of exposure levels. The objective of this study was to see how reliable and valid the "guestimates" (Gérin *et al.*, 1985) from several raters were compared with each other and compared with actual measurements of the exposure. Unlike the studies mentioned above, our goals focused upon two issues related to the uniformity of exposures within groups.

First, we wanted to see whether it was possible to group tasks by the level of exposure for several chemicals so that exposures would be the same for all workers within an exposure category. That is, we wanted to use our estimation method as a zoning strategy, as described by Corn and Esmen (1979). Such zones can be used to maximize the effectiveness of the industrial hygienists sampling to assess potential risk.

Second, we wanted to gain insight into the usefulness of these exposure estimates for epidemiologic purposes. It was assumed that the validity of the estimates and therefore their usefulness for epidemiologic research would highly depend upon the ratio of the interindividual (worker to worker) variance to the intraindividual (day to day) variance in exposure. With information on these variance components the amount of misclassification between exposure categories could be determined. By means of repeated measurements the two variance components could be estimated.

In this article we will present our estimation method and its validity, which were tested in five small companies.

MATERIALS AND METHODS

Experimental protocol

The method was tested in five small factories (30-160 production workers). The products made and production methods used were different; this made it possible to see whether the same method could be used in different workplaces. The five small factories were a paint producing factory, a carbohydrates and proteins

Table 1. Main characteristics of the studied factories

Factory	Departments	Tasks	Production workers	Chemicals
1. Paint	11	14	29	±200
2. Carbohydrates and proteins	5	17	58	32
3. Nonwoven materials	5	24	164	±400
4. Truck cabins	4	30	44	36
5. Trailers	4	12	100	23

processing factory, a non-woven materials manufacturing factory, and two coach-works. The two coach works had different production layouts. One was producing truck cabins in a modern assembly line with several welding stations; in the other, trailers were produced individually. Table 1 gives the main characteristics of the five workplaces.

Exposures to chemicals were rated *a priori* after the identification of tasks in each department had taken place. In every factory the following groups of raters filled in the self-administered questionnaires: workers, plant supervisors (foremen, production managers), and occupational hygienists, using a four-point scale for level of exposure (Table 2). The supervisors and occupational hygienists estimated exposures to all chemicals present for every task. The workers only estimated the exposure of the task they were performing at the time of the study. Either trademarks or chemical names were used in the questionnaires. Products or chemicals had to be grouped in the paint factory and in the nonwovens factory because of the enormous number of products used in these workplaces.

Following the *a priori* evaluation of exposure, personal measurements were performed during 1 week. In the paint factory the exposure to solvents was sampled using charcoal tubes as personal monitors (NIOSH 1977). In the other four factories, personal dust samples were taken with a sampling device as described by van der Wal (1983). Full shift samples were taken on almost every occasion. The total workforce or a sample of the workforce stratified by task was sampled twice. The days of measurement were distributed at random over the population sampled. In the truck cabin factory, each worker was sampled five times during the week. Tasks were assumed to cover the entire shift.

Statistical analysis

The quantitative exposure data were lognormally distributed (Filliben's test on normality, Filliben 1975, $p<.05$). Descriptive statistics were generated for tasks and exposure categories based on the semiquantitative exposure estimates using the

Table 2. Semiquantitative exposure estimates

Estimate	Definition
1 = No exposure	No contact; chemical is present, but this task is not involved
2 = Minor exposure	Minor contact; chemical is handled in a closed system; there are no special activities in this task, which enhance exposure; exposure takes place because of presence in this department
3 = Medium exposure	Varying and mainly passive contact; chemical is in a closed system, but now and then handwork is needed through which exposure is enhanced
4 = High exposure	Regular contact; because of the character of the production process and necessary handwork, regular contact is needed

log-transformed data.

Single-factor analysis of variance (ANOVA) was performed with the estimates of the different raters as explanatory factor using the GLIM system (Royal Statistical Society 1978) to assess the best rater of the exposure per task within each factory. Interindividual and intraindividual components of variance in exposure levels were obtained by using the Reliability procedure from SPSSX software (SPSSX 1983).

The overall agreement between all semiquantitative exposure estimates of different (groups of) raters was calculated in pairs for each factory using the formula for Cohen's Kappa described by Fleiss (1981).

RESULTS

Distribution of measurements

Table 3 shows the overall results of the measurements in each factory. The numbers of personal samples collected together with the geometric means (GM) and geometric standard deviations (GSD) of the measured concentrations are presented. The overall GSD was rather high in every factory, indicating a large

Table 3. Geometric mean (GM) and standard deviation (GSD) of observed concentrations per factory (mg/m^3)

Factory	n[*]	GM	GSD	Specimen
1	58	211	2.6	Total solvents
2	43	7.4	4.2	Dust (organic)
3	90	1.6	3.1	Dust (fibers)
4	205	0.6	2.4	Dust (welding fume)
5	83	2.4	2.2	Dust (welding fume)

[*] n= No. of measurements

range in measured concentrations.

Persons and tasks

A one-way analysis of variance model was fitted to the data from each factory to see whether there were differences in exposure between workers. The same model was used to detect differences in exposure between tasks. The results of these analyses are given in Table 4. As shown, there were significant differences in exposure between both persons and tasks in every factory. The day of measurement (Monday, Tuesday, etc) did not result in significant differences in exposure in a similar analysis.

Table 4. Differences in exposure between workers and tasks analysed by a one-way analysis of variance for each factory[*]

		Workers			Tasks		
Factory	n	$n_{workers}$	F	Adjusted R^2	n_{tasks}	F	Adjusted R^2
1	58	30	22.03[a]	0.92	14	15.63[a]	0.77
2	43	30	4.48[a]	0.71	11	8.52[a]	0.65
3	90	48	2.39[a]	0.41	23	4.36[a]	0.46
4	205	49	3.55[a]	0.37	26	5.85[a]	0.37
5	83	42	3.72[a]	0.50	11	4.68[a]	0.31

[*]n, No. of workers.
$n_{workers}$, No. of measured workers.
n_{tasks}, No. of measured tasks.
[a] $P<0.005$.

Semiquantitative exposure estimates

The agreement between the exposure estimates and the exposure measurements differed from factory to factory. The semiquantitative exposure estimates were used in the same way as task and person as factors in a one-way analysis of variance. The results of this analysis (Table 5) revealed interesting information. In most factories (four out of five) the effect of the estimation procedure was highly significant. The variability in concentrations accounted for by the semiquantitative

Table 5. Differences in exposure between exposure categories resulting from the estimation method analysed by a one-way analysis of variance for each factory*

		Outcome variable: Ln(concentration)			
		Adjusted R_2			
Factory	n	OH 1	OH 2	SV	W
1	58	0.58[a]	0.37[a]	0.38	0.56[a]
2	43	0.08	0.16[b]	0.27	0.03
3	90	0.25[a]	0.18[a]	0.15	0.13[a]
4	205	0.25[a]	0.27[a]	0.23	0.14[a]
5	83	0.25[a]	0.26[a]	0.00	0.23[a]

* OH, occupational hygienist; SV = supervisor; W = worker (mode of individual estimates per task).
[a] $P<0.005$; [b] $P<0.05$.

Table 6. Differences in exposure between exposure categories resulting from the estimation method analysed by a one-way analysis of variance for each factory*

		Outcome variable: Ln(concentration)			
		Adjusted R_2 between tasks			
Factory	n	OH 1	OH 2	SV	W
1	58	0.67[c]	0.32[a]	0.35[a]	0.62[c]
2	43	0.00	0.00	0.28	0.00
3	90	0.40[c]	0.25[b]	0.20[a]	0.15[a]
4	205	0.50[c]	0.55[c]	0.52[c]	0.23
5	83	0.63[b]	0.61[a]	0.00	0.53

* OH = occupational hygienist; SV = supervisor; W = worker.
[a] $P<0.05$.
[b] $P<0.01$.
[c] $P<0.005$.

estimates differed approximately by a factor of 2 between the first and three other factories (3,4,5). This could be explained by the fact that the estimates were made at task level within a factory. In the paint factory (factory 1), task accounted for 77% of the total variability in exposure levels (R^2=0.77, Table 4), which was distinctly more than 46%, 37% and 31% in the other three factories. So too for the paint factory, semiquantitative estimates could explain more variability because differences in exposure between the tasks explained most of the variability in the observed exposure distribution. To eliminate this effect the relative explained variability was calculated (Table 6). This is the variability in exposure levels between tasks (intertask) accounted for by the semiquantitative exposure estimates of the different raters.

From Table 6 it is clear that the occupational hygienists made the best semiquantitative exposure estimates as compared with actual measurements of the same exposure. In factories 1 and 5, the workers made better estimates than the supervisors; the supervisors performed better in factories 3 and 4. In the carbohydrates and proteins processing factory (factory 2) none of the estimates had a significant effect, although task on its own explained 65% of the variability in dust concentrations (Table 4).

In Table 7 the arithmetic mean, geometric mean, and geometric standard deviation per exposure category are given for the two best raters for all five factories. It shows that raters were indeed able to group tasks by degree of exposure in such a way that exposure increased with increasing exposure estimate in most of the studied situations. The most successful raters seemed to be the occupational hygienists. The method usually resulted in four exposure categories with significantly different mean concentrations. The geometric standard deviations within the exposure categories were smaller than the overall GSDs (compare Tables 3 and 7). The success of the method depended largely upon a good definition of tasks and the variance in exposure within a task. Unfortunately, the data set was not suited to unravel the intertask and intratask variance in exposure.

Table 7. Arithmetic mean (AM) with its 95% confidence interval (CI), geometric mean (GM), and standard deviation (GSD) per exposure category for the best estimatos in five factories (mg/m$^{3)}$

Factory	Rater	Estimate	n	AM	95% CI	GM	GSD
1	OH 1	1	-	-	-	-	-
		2	8	45	27- 78	37	1.9
		3	26	270	206-355	215	2.0
		4	24	433	342-549	370	1.8
1	W	1	8	46	27- 78	37	1.9
		2	8	178	126-251	164	1.5
		3	17	349	251-486	284	1.9
		4	25	419	312-555	327	2.0
2	OH 2	1	7	2.5	1.4- 4.2	2.1	1.8
		2	6	12.3	4.3-35.1	7.5	2.7
		3	22	43.3	21.6-86.8	12.6	4.8
		4	8	9.9	3.8-25.6	5.2	3.1
2	SV	1	3	3.9	-	3.8	1.3
		2	10	3.5	1.6- 7.5	2.0	2.9
		3	30	29.1	17.8-47.5	12.3	3.7
		4	-	-			
3	OH 1	1	6	0.6	0.4- 0.7	0.6	1.3
		2	49	1.8	1.3- 2.3	1.1	2.6
		3	14	7.5	3.7-14.9	3.6	3.3
		4	21	5.0	3.2- 7.7	3.2	3.2
3	OH 2	1	15	1.0	0.7- 1.4	0.7	1.9
		2	28	2.8	1.7- 4.5	1.3	3.4
		3	30	3.4	2.5- 4.8	2.3	2.4
		4	17	5.4	3.0- 9.5	2.9	3.0
4[b]	OH 1	1	61	0.5	0.4- 0.6	0.4	2.2
		2	25	0.7	0.5- 1.0	0.5	2.4
		3	27	0.8	0.6- 1.0	0.6	2.2
		4	57	1.6	1.3- 1.9	1.1	2.2
4[b]	OH 2	1	61	0.5	0.4- 0.6	0.4	2.2
		2	25	0.7	0.5- 1.0	0.5	2.4
		3	53	1.0	0.8- 1.2	0.7	2.2
		4	31	1.9	1.4- 3.1	1.5	2.0
5	OH 1	1	-	-	-	-	-
		2	6	1.6	1.1- 2.4	1.3	2.0
		3	54	3.2	2.7- 3.8	2.5	2.0
		4	13	6.2	4.2- 9.2	5.0	1.9
5	OH 2	1	4	1.7	0.5- 6.0	1.2	2.2
		2	8	1.0	0.7- 1.5	0.9	1.6
		3	54	3.3	2.7- 3.9	2.6	2.0
		4	17	5.1	3.5- 7.4	3.9	2.1

[a] OH = occupational hygienist; SV = supervisor; W = worker.
[b] Exposure for only a limited No. of tasks was estimated.

It was, however, possible to estimate the interindividual and intraindividual variance in exposure by factory. The results are presented in Table 8. The solvent exposures of the workers in factory 1 showed limited day-to-day variation; in factory 2, most of the observed variance in exposure was also due to differences between workers (differences in task, work style, work environment). In the other three factories the variance in exposure owing to differences between workers was almost equal to the variance in exposure owing to differences between days.

Table 8. Percentages of intraindividual and interindividual variability in concentrations per factory*

		Variance components	
Factory	n x k	Percent Intraindividual	Percent Interindividual
1	28 x 2	7	93
2	14 x 2	28	72
3	41 x 2	43	57
4	27 x 5	50	50
5	40 x 2	44	56

Interrater agreement

The comparison between semiquantitative exposure estimates and quantitative exposure measurements was not complete. In each factory only one component of the total exposure was measured and compared with the estimates. The reliability of the estimates of all other exposures was assessed by calculating interrater agreement within each factory except for factory 4. The results of these are shown in Table 9. The Kappa-values between the occupational hygienists considering all tasks and all exposures present in each factory ranged from .23 to .50 indicating fair-to-moderate agreement (Landis, 1977). The agreement between other pairs of raters was generally less. Differences in agreement that were due to the number of chemicals listed on the estimation forms (as in factory 3) were not detected.

Table 9. Interrater agreement per factory

Factory	OH1 vs OH2	OH1 vs SV	OH2 vs SV	OH1 vs W	OH2 vs W	SV vs W
1	0.42	0.26	0.26	0.21	0.38	0.27
2	0.50	0.16	0.27	0.27	0.16	0.36
3A[A]	0.40	0.28	0.36	0.17	0.33	0.29
3B[A]	0.32	0.26	0.34	0.36	0.15	0.17
5	0.23	0.24	0.29	0.29	0.36	0.35

[a]Two different forms were used: A, compiled list of chemicals and B, complete list of chemicals.

DISCUSSION

Semiquantitative exposure estimates for zoning

From this study it has become clear that the estimation method can result in the definition of four exposure categories, which consist of tasks within a factory or a department. The exposure categories have increasing mean concentrations and show less variability than the overall variability. However, substantial overlap of the exposure distributions between exposure categories is possible as can be seen in Fig. 1. This overlap can be due to two causes. First, misclassification of tasks can result in inhomogeneous exposure categories with a large range in exposure levels (high GSDs). Second, large differences in exposure of workers with the same task that are due to, for instance, work style or ventilation, can also result in inhomogeneous exposure categories with high GSDs. On the other hand, a small interindividual variance in exposure results in a homogeneous exposure without misclassification of individual workers. Therefore, even in situations where the estimation method does not explain a distinct amount of variability in exposure levels between tasks because of a large intraindividual variance in exposure, it still can be useful for zoning purposes as long as it results in homogeneous categories with significantly different mean concentrations and a reduction of the variability.

The fact that the estimates made by occupational hygienists were the best was in a

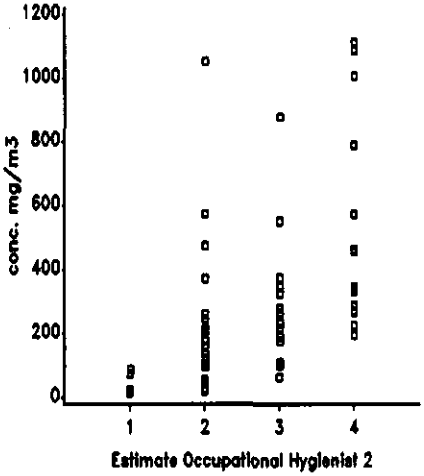

Fig. 1. (a) Distribution of individual exposure levels per semiquantitative exposure estimate of occupational hygienist 2 in factory 1

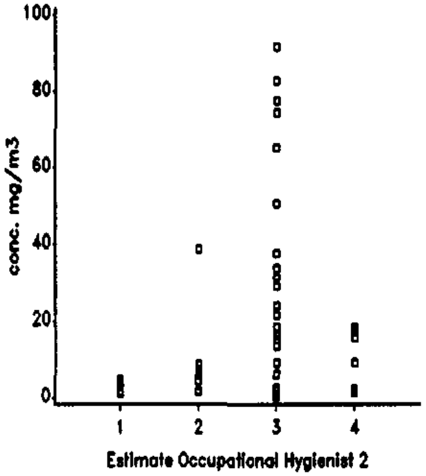

Fig. 1. (b) Distribution of individual exposure levels per semiquantitative exposure estimate of occupational hygienist 2 in factory 2

sense expected. The definitions of the exposure estimates used were not always clear to non-insiders such as supervisors and workers, and moreover, the occupational hygienists had used the method extensively. Extension of the definitions of the exposure estimates with, for instance, the environmental control measures present in the workplace, will prevent misclassification but will also result in a more complicated estimation method. Another point of attention is the amount of agreement between the estimates of the different raters. Only the agreement found between the two occupational hygienists was comparable to the findings of Lynch (1982) and was slightly less than the agreement that Gérin *et al.* (1985) found between his raters using only the estimates of exposures that they were highly confident about. From our experience it has become clear that exposures to products or chemicals that are not constantly used in the workplace, will lead to disagreement.

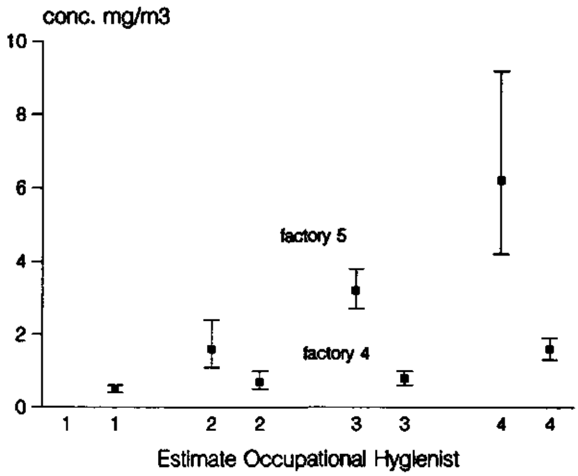

Fig. 2. Arithmetic mean (AM) with its 95% confidence interval (CI) per semiquantitative estimate of occupational hygienist 1 in both coach-works (factories 4 and 5)

Semiquantitative exposure estimates for epidemiological purposes

Although these estimates are often used in epidemiological studies, great care hasto be taken when actually using them. Even when the estimation method results in exposure categories with different mean concentrations, which will be proper estimates of a long-term exposure for every task (person) when the exposure groups are homogeneous (a small interindividual variance in exposure), problems still can be expected. In Fig. 2, these problems are illustrated. The estimation method only gives a relative classification of tasks from no to high exposure within a factory. From the results in the two coach-works it can be seen that the mean concentrations are different in corresponding categories, and the increase in mean exposure with increasing category is not the same in both factories. This, together with the observed misclassification of individual exposures between categories makes the usefulness of these estimates *a priori* doubtful. Of course this estimation method was not exclusively constructed to be used in an epidemiological study in different factories from a specific industry. The earlier-mentioned extension of the definitions of the exposure estimates or a combination of semiquantitative exposure estimation methods and a select assessment of the exposure levels by measurements followed by rearrangement of tasks or individual workers, if necessary, could improve the method for this purpose.

The successful use of semiquantitative estimates of exposure in epidemiological studies in the past is, according to our findings, more likely the outcome of a clear-cut relation between a specific agent than a result of agreement between these estimates and quantitative exposure measurements.

A thorough look at the misclassification of the exposure and overlap of exposure distributions might therefore be very important in the case of a negative epidemiological finding.

ACKNOWLEDGMENTS

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Chapter 4

Semiquantitative estimates of exposure to methylene chloride and styrene: the influence of quantitative exposure data[1]

[1] Revised version of the paper: W. Post, H. Kromhout, D. Heederik, D. Noy, R. Smit Duijzentkunst. *Applied Occupational and Environmental Hygiene* **3** (1991) 197-204.

ABSTRACT

Nine occupational hygienists semiquantitatively estimated the exposure to methylene chloride and styrene in a small polyester factory. They ranked the jobs from low to high exposure, and subsequently classified them into three exposure categories (0-½TLV, ½TLV-TLV, and > TLV). The influence of quantitative exposure data on the results of the estimations was studied. Therefore, three estimations were performed. The first estimation was made after a visit to the workplace; the second and third were made after limited exposure data were presented. The ranking of styrene exposure was, in general, poor compared to the ranking of methylene chloride exposure. Physical properties such as perception of smell, application in the process, and level of exposure might be the reasons for this striking difference. Classification of exposure into quantitative exposure categories was poor without knowledge of actual exposure data. No differences in the performance of the occupational hygienists between the two solvents were present.

The results suggest that the success of an exposure estimation method depends on the type of exposure (kind of chemical, use, appearance), the available information on jobs and process, and the kind of estimate (ranking or classification). Semiquantitative classification of exposure by occupational hygienists appears to be better if they have a limited set of air sampling data at their disposal. Ranking of jobs can be performed successfully without exposure data, but a detailed description of the workplace and tasks is needed. More insight is needed concerning the influence of the chemical type, exposure pattern(s), and raters' experience on the results of semiquantitative ranking methods.

INTRODUCTION

Occupational hygienists often lack the time and money needed for thorough air monitoring of the workplace to evaluate workers' exposures. Instead, they often perform an inventory walk-through survey to gather information about the materials and chemicals used, the process, and the working conditions. The walk-through survey often leads to the selection of a restricted number of workers with a high probability of exposure, and eventually, a limited number of spot samples are taken. The information collected by means of the walk-through survey, the results of the spot samples, and professional experience are used to assess the possibility of exposure and workers' health risks.

There are two important estimation processes inherent in this assessment method. The first involves selecting individuals, jobs, tasks or areas for spot sampling. Ranking the jobs from low to high exposure is an important step in this selection procedure. The second element is assessment of the actual exposure level as part of a health risk assessment.

It is important that the assessment of workers' exposure is as accurate as possible. However, the accuracy of semiquantitative exposure estimates by occupational hygienists has hardly been evaluated. In a few studies, the validity of exposure estimates by different raters (occupational hygienists, workers, supervisors) and their estimation methods and procedures have been evaluated by measuring the reproducibility or by comparing estimates with actual measurements. These studies show that exposure estimates may be correct, but that success may depend upon both the situation and several conditions such as training of the rater, the nature of production processes, and other available information (Woitowitz *et al.*, 1970; Kromhout *et al.*, 1987; Hertzman *et al.*, 1988; Hawkins and Evans, 1989). Two of these studies examined the ability of occupational hygienists to estimate exposure (Kromhout *et al.*, 1987; Hawkins and Evans, 1989).

The study of Kromhout *et al.* (1987) focused at the semiquantitative estimation of the exposure for certain tasks. The estimates were made by occupational hygienists, workers and plant supervisors. They had to assign tasks in five different factories to four semiquantitative categories by degree of exposure: none, minor, medium, and high. Afterwards, personal monitoring was conducted to establish the actual exposure received from performing the tasks. The semiquantitative exposure categories correlated positively with the mean exposure but showed wide ranges of exposures which overlapped between categories. The agreement between the exposure estimates and the exposure measurements differed from factory to factory. The best agreement was obtained for the occupational hygienists, while that of the other raters suffered due to a greater misclassification of the tasks. It was concluded that the success of this estimation method depended strongly on good definitions of the tasks and small amounts of interindividual variation in exposure within tasks. The authors indicated that classification of tasks into semiquantitative exposure categories was possible, but sampling data would improve the estimates (Kromhout *et al.*, 1987).

Hawkins and Evans (1989) evaluated the ability of occupational hygienists to assess actual exposure levels. Twenty-four occupational hygienists with experience in assessing exposures from batch chemical processing operations were asked to predict the distribution of toluene exposures for a defined group of workers in a chemical plant. The distribution of personal exposures had been measured before and was used as a reference for determining the validity of the predictions. During a personal interview, according to a standard protocol, occupational hygienists reviewed chemical process information and then assessed toluene exposure for the first time. The second assessment was made after presentation of limited quantitative exposure data. The study indicated that quantitative exposure estimates, based on experience and professional judgement, may be reasonably accurate but only after the raters were provided with quantitative measurement data (Hawkins and Evans, 1989).

The goal of the present study was to verify whether it is possible to make valid predictions of exposures in the workplace, based on information and a limited set of sampling data. The two earlier identified elements of the exposure estimation process were investigated: ranking jobs from low to high exposure and assessment of actual exposure level by classification of the jobs into exposure groups. The suggestion of Kromhout *et al.* (1987), that a combination of a semi-quantitative exposure estimation method together with measurement of exposure levels could improve the validity of the estimation method, was evaluated by examining the influence of actual exposure data on the results of the estimation method.

METHODS

Nine occupational hygienists were invited to estimate exposures in a small reinforced-plastics factory. The workers in the factory were exposed to styrene (used as solvent of the polyester resins) and to methylene chloride (used as a cleaning agent).

The occupational hygienists estimated the workers' exposure to styrene and methylene chloride in two different ways: by ranking jobs from lowest to highest exposed and then by classifying those same jobs in quantitative exposure categories. By assessing the exposures to both chemicals separately, it was possible to determine whether differences between the solvents (physical properties, application in the process) affected the estimates.

Production lay-out and job description

Based on a pilot study, three departments in the factory were selected for the study: the moulding shop, the preparation department, and the laboratory. In the moulding shop, workers were exposed to styrene vapour outgassing from the moulds containing the uncured products. In the preparation department, exposure to styrene occurred during the mixing of resins and forming of the polyester sheets. There was also exposure to methylene chloride, which was used to remove resins from the tools and equipment. In the laboratory, exposure to both solvents also occurred during various procedures for testing the products and resins.

All departments were spatially separated but were contained under the same roof. Natural ventilation was present most of the year through open doors. Local exhaust ventilation was present but was ineffective because of poor design and a lack of maintenance.

In the preparation department, a pre-impregnated polyester sheet was prepared from a mixture of unsaturated polyester resins (containing 38-40% styrene), glass fibres, and several additives. The composition of the mixture depended on the kind of product made. Blending of the polyester mixture was partially automated; the resin tanks were controlled by computer, but several additives (including additional styrene) were added by hand. This job was always performed by the same person ("mixer").

The pigments and pastes were weighed, dissolved in resins (also containing styrene) and blended. This was normally done by the "color mixer", but when production was low, it became an extra task for the mixer. Before production of another batch with a different color could take place, the barrels and blenders were cleaned with methylene chloride.

The mixture was automatically transported from the blending cask to the machine where the polyester sheet was formed and coated with thin layers of plastic on both sides. During the production of polyester sheets, other jobs were mainly involved in process control: the "first machine operator", the "second machine operator", and the "forklift operator". These jobs rotated daily. The first machine operator controlled and adjusted the speed of a machine which folded the polyester sheets on a pallet or in boxes. When a pallet or box was filled, the sheet was cut into two pieces by a second machine operator. At the same time, a sample of the sheet was removed, weighed, and wrapped in plastic. The samples were analyzed in the laboratory. The pallets and boxes containing the polyester sheets were then wrapped in plastic by the forklift operator and stored in racks to cure.

After production, the machine and supply equipment was cleaned by the machine cleaners and the supply cleaners over about three hours. They were the same men as mentioned above (except for the mixers). These jobs rotate as well. Another person, without production tasks, thoroughly cleaned the spare parts of the machine and the blending casks. This job will be referred to as "cleaner". Most of the time, the cleaner remained in the room where methylene chloride was stored. Before cleaning started, the cleaner was involved in filling buckets with methylene chloride. Occasionally equipment was cleaned immediately after use, but ordinarily the buckets were used for cleaning after production.

After the polyester sheets had cured, they were transported to the moulding shop where the sheets were unwrapped, cut into smaller parts, and wrapped up again. The plastic coating was not removed during the cutting. Smaller polyester sheets were transported to the moulding machines directly. These sheets were unwrapped and the plastic coating removed. Sheets were then cut into smaller pieces and, according to a pattern, placed in the moulding machine. After moulding at a temperature of approximately 150 °C, the finished product was polished and drilled.

In the laboratory all production materials, polyester mixtures, sheets (m^2-pieces) and products were tested and inspected.

Table 1. Jobs exposed to methylene chloride per department

Job	Task(s)
Preparation department	
Mixer	No cleaning tasks, but helped color mixer
Color mixer	Cleaned blenders, barrels and floor (now and then)
Machine cleaner	Cleaned machine
Supply cleaner	Cleaned supply and blending casks above the machine
Cleaner	Cleaned the spare parts of the machine, filled buckets with methylene chloride, cleaned blending casks thoroughly.
Laboratory	
Laboratory	Cleaned used tools and machines

Table 2. Jobs exposed to styrene per department

Job	Task(s)
Preparation department	
Mixer	Controlled the blending process and added additives partly by hand
Color mixer	Made the color mixture
Machine operator 1	Checked the first part of the machine
Machine operator 2	Checked the last part of the machine, cut the sheet in two and cut, weighed and wrapped up a laboratory sample
Forklift operator	Wrapped up and places filled pallet/boxes in racking
Moulding shop	
Cutter	Unwrapped polyester sheets, operated cutting machine, wrapped sheets up
Moulder 1	Unwrapped and removed plastic coats, cut sheets, put sheets in mould, operated moulding machine
Moulder 2	Took polyester product out press, finishing (polishing, drilling)
Laboratory	
Laboratory	Inspection and control materials and (half)products

The description of the jobs in the three departments is summarized in Tables 1 and 2.

Quantitative exposure assessment

Personal, 8-hour time-weighted average (TWA) measurements were taken using the charcoal tube sampling method (NIOSH, 1977). Peak exposures were measured by means of gas detection tubes (Dräger). Tables 3 and 4 show the overall results of the 8-hour exposures for each job. Figs 1 and 2 show the arithmetic mean and range of the exposures per job. These data provided a reference for assessing the accuracy of the exposure estimates made by the nine occupational hygienists (hereafter referred to as raters).

Semiquantitative exposure estimation methods

Before the rating took place, written information about the factory, the production lay-out, and the jobs was given to the raters. The raters then visited the factory. After the visit, they were asked to estimate the exposure to styrene and methylene chloride for the different jobs. Two different estimates were made: a relative ranking and an actual exposure estimate. The relative estimate consisted of ranking jobs

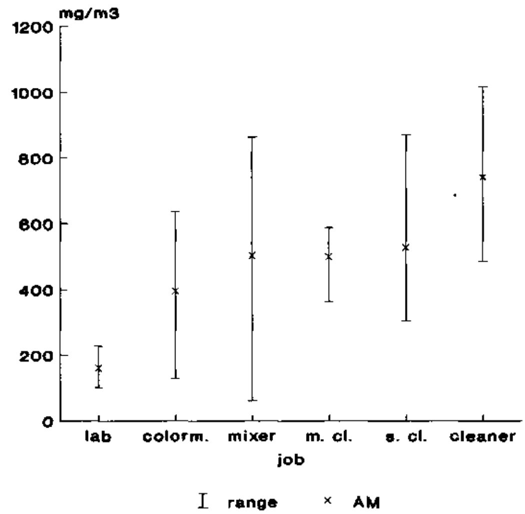

Fig. 1. Arithmetic mean and range of exposure to methylene chloride per job

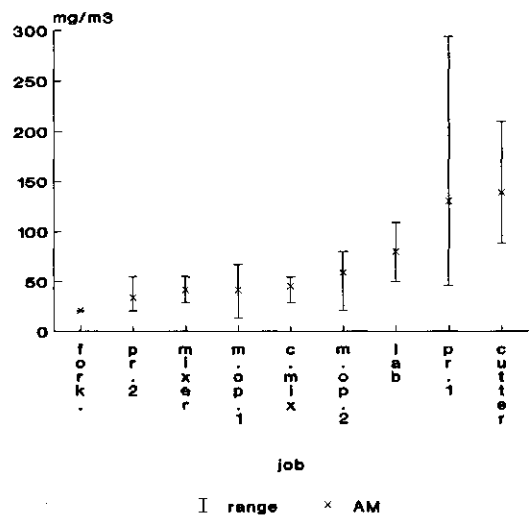

Fig. 2. Arithmetic mean and range of exposure to styrene per job

from the lowest to the highest exposure (mean 8-hour TWA). When jobs were thought to have equal exposures, mean ordinals could be given. For the estimate of actual exposure, each job was assigned into one of three exposure categories. Jobs in category 1 had an exposure to methylene chloride that ranged from 0 to 175 mg/m^3 , category 2 from 175 to 350 mg/m^3, and category 3 above 350 mg/m^3. For styrene, these categories were, respectively, 0-210 mg/m^3, 210-420 mg/m^3, and above 420 mg/m^3. (The Dutch TLV for methylene chloride is 350 mg/m^3 and for styrene 420 mg/m^3.)

After the first assessment the raters could request a limited number of personal exposure data. There were two restrictions: 1) only 4 measurements of styrene exposure and 3 measurements of methylene chloride exposure could be requested and 2) only one of the measurements could be an 8-hour TWA measurement. The other data were spot sample results. If a particular type of measurement was not available or if no special conditions were specified by the rater, the rater received the result of one randomly chosen exposure measurement collected for the specified job. After receiving these data, a second estimate had to be made. A third estimate was made after each rater had received another set of exposure measurements in the same way as described above.

Statistical analyses

All statistical analyses were performed on a VAX computer using procedures from the SAS statistical package (SAS, 1983). The raters' rankings were correlated (Spearman correlation) to a ranking based on the arithmetic mean TWA per job. Exposures of jobs were arbitrarily considered equal when the arithmetic means were within the same range ($\pm$30 mg/m^3 methylene chloride; $\pm$10 mg/m^3 styrene). The Page distribution-free test for ordered alternatives (Page, 1963) was used to evaluate the influence of the quantitative exposure data on the relative estimates of all raters simultaneously.

Agreement between raters' classification into three exposure categories and the arithmetic mean TWA per job was expressed as the percentage of jobs grouped in the same category.

To examine whether the total number of correct classifications of all occupational hygienists could be explained by chance, the probability of success was calculated assuming a binomial distribution (Snedecor and Cochran, 1982). Success was defined as classification of a job by a rater in the same exposure category as indicated by the mean TWA per job.

Next, the influence of the knowledge of exposure data on the classification was examined. This was done by calculating the agreement of the raters' classification with a classification of the jobs based on the exposure data with which the raters were supplied. This classification differed from the previous one, because it was based on an individual measurement per job and not on the overall mean value used in the classification above. The proportion of agreement (P_o) was used as a measure of agreement (Fleiss, 1981). The agreement before the raters had any knowledge of exposure levels was compared with the agreement afterwards. A difference was made between the TWA data and the grab sample results.

RESULTS

Correlation between ideal ranking and raters' ranking

Tables 3 and 4 give the ranking of the jobs based on the personal exposure data. Fig. 3 shows the results of the individual raters for both solvents. The average correlation coefficient and the range are shown in Fig. 4. The mean correlations of the rankings of methylene chloride (0.69, 0.73, 0.67) were significantly higher than those of styrene (0.13, 0.12, 0.29) (Student's T-test, $p<0.001$). The variation between the raters was higher for styrene than for methylene chloride. Ranking hardly improved after exposure data became available. The ranking of methylene chloride exposure by the raters as a group was clearly not attributable to chance

Table 3. Arithmetic mean (AM), geometric mean (GM), geometric standard deviation (GSD) of 8-hour twa methylene chloride concentrations per job (mg/m^3) and ideal ranking and classification

Department	Job	n[A]	AM	GM	GSD[B]	Rank[C]	Class[D]
Preparation	Mixer	3	504	315	4.1	4	3
	Color mixer	3	396	326	2.3	2	3
	Machine cleaner	6	501	494	1.2	4	3
	Supply cleaner	6	529	497	1.5	4	3
	Cleaner	4	742	707	1.4	6	3
Laboratory	Laboratory	6	161	151	1.4	1	1

[A] Number of measurements.
[B] $GSD_{between\ jobs}$ = 1.7.
[C] Ideal ranking.
[D] Ideal classification.

Table 4. Arithmetic mean (AM), geometric mean (GM), geometric standard deviation (GSD) of 8-hour twa styrene concentrations per job (mg/m^3) and ideal ranking and classification

Department	Job	n[A]	AM	GM	GSD[B]	Rank[C]	Class[D]
Preparation	Mixer	3	42	42	1.4	4	1
	Color mixer	3	46	46	1.4	4	1
	Machine operator 1	4	42	34	2.3	4	1
	Machine operator 2	4	59	50	1.9	6	1
	Forklift operator	2	21	21	1.0	1	1
Laboratory	Laboratory	6	80	76	1.4	7	1
Moulding shop	Cutter	5	139	134	1.4	8.5	1
	Moulder 1	14	130	113	1.8	8.5	1
	Moulder 2	4	34	29	1.6	2	1

[A] Number of measurements.
[B] $GSD_{between\ jobs}$ = 1.8.
[C] Ideal ranking.
[D] Ideal classification.

($p<0.001$), and did not improve after quantitative exposure data became available.

The first two rankings of styrene exposure were not statistically significant. Only the third ranking was not attributable to chance ($p<0.05$). The mean correlation between the ideal ranking and the raters' third ranking was still very poor.

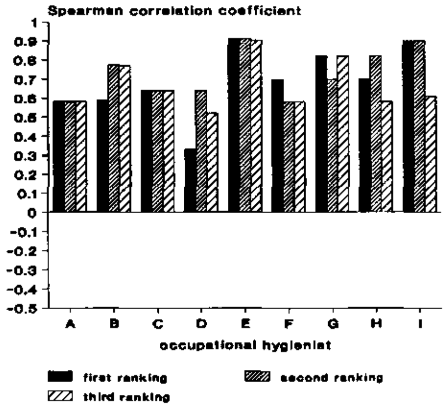

Fig. 3. (a) Spearman correlation coefficient per ranking of methylene chloride exposure per occupational hygienist

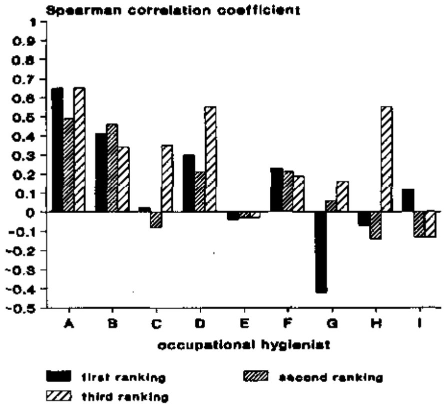

Fig. 3. (b) Spearman correlation coefficient per ranking of styrene exposure per occupational hygienist

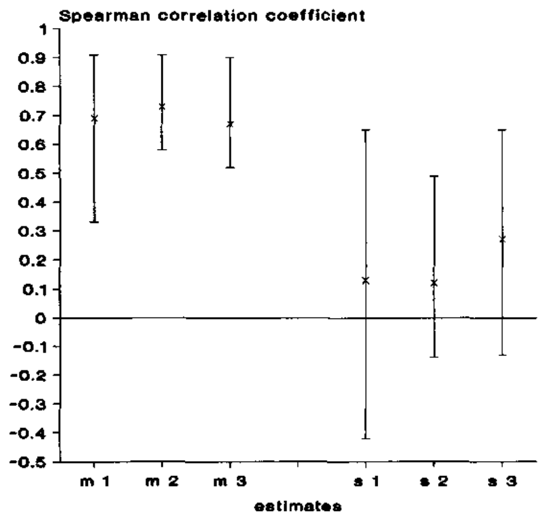

Fig. 4. Mean and range of Spearman correlation coefficient per ranking of methylene chloride (m_x) and styrene exposure (s_x)

The results suggest that it was possible to rank jobs correctly based on walk-through information, but the result depended strongly on the exposure considered. A limited set of additional exposure data did not seem to have a distinct influence on the results of the ranking.

Agreement between ideal classification and raters classification

Tables 3 and 4 show the classification of the jobs based on the arithmetic mean of TWAs per job. The classification of the raters was compared with the classification of the jobs based on the mean TWA per job. Fig. 5 shows the percentage of correctly classified jobs per rater for each solvent after each classification. Fig. 6 gives the means and ranges. The successive methylene chloride and styrene classifications showed an increasing agreement (42.6%, 59.2%, 68.5% for methylene chloride; 45.7%, 67.9%, 76.6% for styrene). The exposure to methylene chloride was, in general, underestimated in the first classification. The percentage of misclassification of two categories dropped from 19.5 to 4 percent and within one category from 39 to 28 percent. The job of the mixer was often misclassified. The level of styrene exposure was overestimated. The percentage of misclassification of two categories dropped from 21 to 4 percent and within one category from 33 to 20 percent. The raters overestimated the styrene exposure of the color mixer and the first machine operator. From this and Fig. 6, it is obvious that classification of workers' exposure, based solely on information about production process and jobs, was poor. Additional quantitative data improved the classification. There were great differences between the results of the individual raters, but the overall results were similar for methylene chloride and styrene exposure. Years of experience as an occupational hygienist or with comparable exposures in similar workplaces did not seem to be a determinant for the differences in performance between the raters. However, the range in years of professional experience was rather small (5-10 years). In all cases, the probability was less than 0.05 that the total number of correct classifications by the raters as a group after each estimate was attributable to chance.

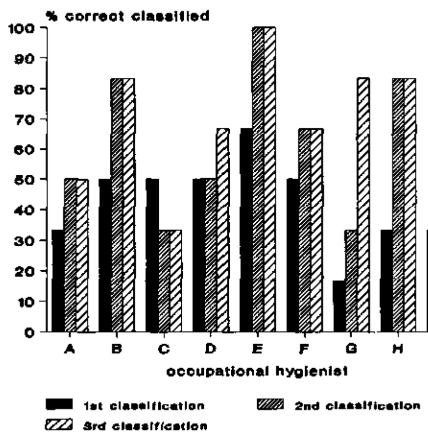

Fig. 5. (a) Proportion of agreement (P_o) per classification of methylene chloride exposure per occupational hygienist

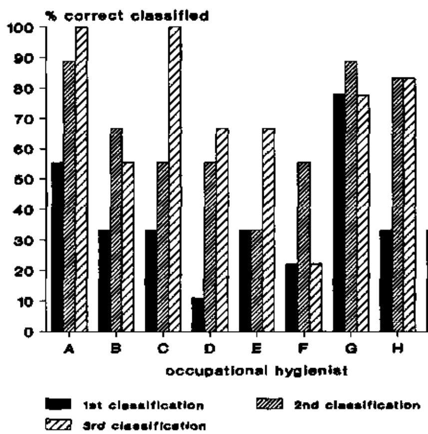

Fig. 5. (b) Proportion of agreement (P_o) per classification of styrene exposure per occupational hygienist

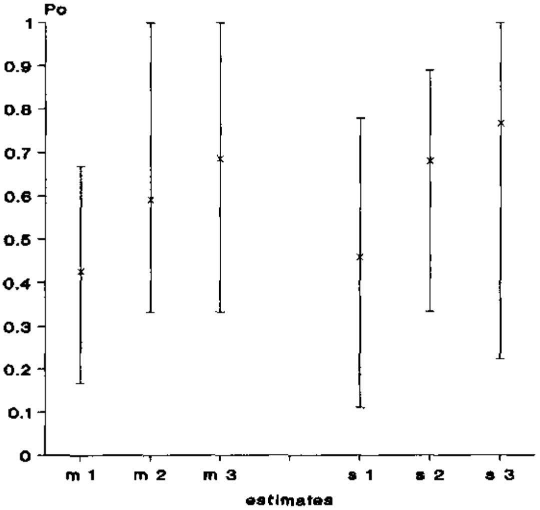

Fig. 6. Mean and range of proportion of agreement (P_o) per classification of methylene chloride (m_x) and styrene exposure (s_x)

Table 5 shows the agreement between the raters' classification of jobs for which they received exposure data and a classification of these jobs based on the individual measurement result received. The increase in agreement after receiving the quantitative exposure data suggests that the raters were directly influenced by the supplied exposure data. Table 5 also shows that the raters were strongly influenced in their classification by the TWA data. The grab sample results seemed to play a negligible role.

Table 5. Proportion of agreement between raters' classification of jobs for which exposure data was received and classification of the jobs based on the received exposure data before and after exposure data was received

	Methylene chloride		Styrene	
	Before	After	Before	After
First set of data				
twa	0.63	1.00	0.13	0.88
grab samples	0.19	0.31	0.36	0.50
Second set of data				
twa	0.50	0.75	0.63	0.88
grab samples	0.31	0.44	0.52	0.65

CONCLUSION AND DISCUSSION

The ranking of the jobs exposed to methylene chloride was more successful than the ranking of the styrene exposure. This might be due to differences in chemical and physical properties, e.g., the limit of perception by smell. Methylene chloride has a high odor threshold (1050 mg/m^3) (Fasset and Irish, 1963). All 8-hour TWAs were below this level. Styrene, on the contrary, has an extremely low odor threshold (0.2-0.4 mg/m^3) (Härkonen, 1978). All jobs had mean TWA exposures above this level. Another possible explanation might be the difference in appearance within the polyester plant. The exposure pattern of styrene consists of a continuously moderate level of exposure, in contrast to a pattern of peak exposures during cleaning operations with methylene chloride. The frequency, duration and level of exposure of these cleaning tasks might be easier to estimate. Furthermore, these cleaning operations are job-specific making it relatively easy to rank the jobs from lowest to highest methylene chloride exposure. The frequency, duration, and association between styrene exposure and specific tasks was less obvious. In addition, the overall exposure to styrene was lower than to methylene chloride. However, the variation in exposure between the jobs for both solvents was essentially the same (GSD between jobs: 1.7 and 1.8, Tables 3 and 4).

Exposure data did not seem to play an important role in ranking the jobs. The ranking hardly improved when exposure data became available. This might be explained by the way the occupational hygienists seemed to rank the jobs from lowest to highest exposure. The jobs were presumably compared with each other and eventually ranked. Exposure data were not necessary for this comparison.

Classifying jobs into categories of levels of exposure without knowledge of exposure data was difficult and resulted generally in poor estimates. After supplying actual exposure data, this classification improved considerably. The data seemed to have an effect on the result of classification. There was little difference between the classification of styrene and methylene chloride exposure, although the exposure to methylene chloride was at first underestimated and the styrene exposure overestimated. The raters apparently used the provided data (especially the TWA concentrations) to adjust and improve their classification.

This study tends to support the conclusions of Kromhout *et al.* (1987) that it is possible to rank jobs from low to high exposure without quantitative data. However, the success of the ranking seems to depend on the particular chemical in question.

The study of Hawkins and Evans (1989) showed that experienced occupational hygienists were able to estimate the average exposure quantitatively, especially after reviewing limited quantitative data. However, it must be noted that the conditions of their study were favourable to success. That is, a group of experienced and specialized occupational hygienists were able to predict the exposure of a well-defined, homogeneous group of workers with incidental toluene exposures. When exposure frequency, duration and level of exposure per task is known, it is relatively easy to predict the workers' exposure.

In our study nine occupational hygienists, most of them unfamiliar with the production process, estimated the exposure of nine jobs exposed to styrene and six jobs exposed to methylene chloride. Despite the differences, our results tend to support the contention of Hawkins and Evans conclusion that occupational hygienists are able to estimate exposure (semi)quantitatively. However, limited exposure data are needed, especially when dealing with occupational hygienists unfamiliar with the production process.

The number of samples which were used for the ideal ranking and classification were rather small. Differences in exposure level between jobs were, in general, not statistically significant, except for the jobs with extreme exposures. Using alternative ideal rankings changed the correlation coefficients only slightly. The large difference between the ranking results for styrene and methylene chloride always remained.

Since the variation in exposure level within jobs was quite small (most GSDs were below 1.5), more measurements would have resulted in more precise mean exposure levels and therefore more significant differences between jobs, but not in different mean levels. This is also based on the production process, which was quite stable over time.

In conclusion it might be stated that the success of an exposure estimation method depends on the type of exposure (kind of chemical, use, appearance), the available information, and the kind of estimate (relative or absolute). To broaden the insight in the validity of exposure estimation methods further, studies focused at the influence of the kind of chemicals (physical and chemical properties), the exposure pattern, and the influence of the raters' experience are recommended.

ACKNOWLEDGEMENTS

This research was an initiative of the Working Group on Monitoring Strategies of the Dutch Occupational Hygiene Association (Nederlandse Vereniging voor Arbeidshygiëne). We wish to thank all occupational hygienists who participated in this study.

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Chapter 5

Empirical modelling of chemical exposure in the rubber manufacturing industry[1]

[1] H. Kromhout, P. Swuste and J.S.M. Boleij, *Annals of Occupational Hygiene* in press.

ABSTRACT

As part of a study of working conditions chemical exposure was assessed in 10 rubber-manufacturing plants in The Netherlands. Personal exposures to airborne particulates, rubber fumes and solvents, and also dermal contamination, were measured. To identify factors affecting exposure the personal exposure levels and information on tasks performed, ventilation characteristics, and production variables were used in multiple linear regression models.

The exposure was generally very variable. The specific circumstances in each department of each plant determined the actual levels of exposure to a large extent. The factors affecting exposure turned out to be different for each of the types of exposure considered. The model for exposure to airborne particulates explained 40% of the total variability and incorporating the actual time spent on a task only slightly improved the model (R^2=0.42). The handling of chemicals in powder form was the main factor affecting exposure, forced ventilation having a negligible effect. The model for exposure to curing fumes (measured as the cyclohexane-soluble fraction of the particulate matter) explained 50% of the variability. Both curing temperature and pressure determined the level of rubber fumes. Local exhaust ventilation showed a significant exposure reducing effect. The effect of curing different elastomers was not statistically significant. Dermal exposure to cyclohexane-soluble matter could only be explained to a limited extent (R^2=0.22). Tasks with frequent contact with (warm) compound and maintenance tasks in the engineering services departments resulted in high dermal exposure. Tasks in which solvents were directly used explained 56% of the variation in solvent exposures.

Exposure data together with information on tasks, methods of work, ventilation and production throughout a branch of industry, can be used to derive empirical statistical models which occupational hygienists can apply to study factors affecting exposure. These determining factors are of crucial importance, whenever hazard control or epidemiologic research is the ultimate goal.

INTRODUCTION

Exposure to chemical agents in the rubber manufacturing industry has been the focus of attention for at least two decades. Extensive occupational hygiene surveys focused on exposure to airborne particulates, rubber fumes and solvent vapours were conducted in the U.K. (Parkes *et al.*, 1975; Nutt, 1976; HSE, 1981). In the United States the exposure to airborne particulates and solvent vapours was studied as part of large epidemiologic studies (Williams *et al.*, 1980; van Ert *et al.*, 1980). The National Institute for Occupational Safety and Health (NIOSH) performed a large study on control measures to reduce exposure to dust, vapours and fumes (McKinnery and Heitbrink, 1984). In Germany the exposure to *N*-nitrosamines was evaluated on a large scale in the rubber manufacturing industry (Spiegelhalder and Preussmann, 1983; Wolf, 1989) and the Dutch Labour Inspectorate measured the exposure to *N*-nitrosamines, polycyclic aromatic hydrocarbons, airborne particulates and the benzene-soluble fraction of the particulate matter in seven rubber-manufacturing plants (van de Riet, 1985).

The above studies described the exposure throughout the industry and the influence of control measures on the exposure levels. In this paper the results of an assessment of the chemical exposure of workers employed in The Netherlands' rubber-manufacturing industry are described. Its objective was to serve as a starting point for workplace improvement. Before working conditions could be improved it was necessary to locate likely sources of exposure and to quantify their effect on exposure. This was realized by a measurement strategy which made it possible to identify those factors which affect exposure to chemical hazards. The exposure assessment was carried out during the first half of 1988 as part of a study dealing with labour conditions and company policies in this sector of industry in The Netherlands (Kromhout *et al.*, 1989).

MATERIALS AND METHODS

The rubber-manufacturing industry in The Netherlands is relatively small. In 1985 employment totalled 6700-6800 workers, including 550 women. In 1987 of the plants with more than 10 employees, 10 made tyres, 29 made general rubber goods, and nine were retreading plants. About half of the plants had less than 75 employees and the largest company had approximately 2700 employees. The plants chosen for the survey had to form a representative cross-section of the industry and this determined the two most important selection criteria: the size of the workforce and the nature of production (tyres, general goods, etc.). The characteristics which were preferred within the selected groups included: presence of an occupational health unit, of a works council, of union representatives and the use of workplace improvement subsidies. Out of 10 companies approached, nine agreed to participate in the study. One company refused and was replaced by a company that fulfilled the selection criteria. Because of this modification, no plant producing car tyres was involved in the study. The general characteristics of the plants studied are presented in Table 1.

Table 1. General characteristics of surveyed plants

SBI-code*	No. of workers	Production
3111	370	bicycle tyres
3111	220	belting, hose
3112	360	mould and extruding articles, roller covering, metal to rubber bonded articles
3112	220	high pressure hose, compounds, battery containers (ebonite)
3112	80	mould articles
3112	60	mould and extruding articles, rubber foil, compounds
3112	60	mould articles, roller covering, metal to rubber bonded articles
3112	60	mould and extruding articles, metal to rubber bonded articles
3121	90	truck and industrial tyres, compounds
3121	30	truck, industrial and passenger car tyres

* Dutch Standard Industrial Classification: 3111 rubber tyre; 3112 general rubber goods; 3121 retreading.

Production processes in the rubber-manufacturing industry vary from plant to plant. To make it possible to compare working conditions throughout the industry, these processes were analysed using a design analysis described elsewhere by van den Kroonenberg and Swiers (1983) and by Swuste *et al.* (1993). The production function was classified in accordance with the classification of occupational title groups (OTGs) developed by Gamble *et al.* (1976). The OTG classification was widely used in epidemiological research in the rubber-manufacturing industry in the United States. This general classification, which was also used in the exposure studies in the United States mentioned earlier, divides workers of the rubber-manufacturing industry in accordance with job titles, which are subsequently classified in exposure groups (occupational title groups) depending on the exposure concerned.

From a pilot study in a retreading plant (de Haan *et al.*, 1988; Bos *et al.*, 1989) it appeared that within a job title exposure could vary substantially from day to day. Therefore a repeated measurement strategy was chosen in order to obtain a reasonable estimate of the mean exposure within each exposure group, and to make it possible to identify the factors which determined the exposure variability. All production and supporting departments were involved in the survey. In Table 2 the most important characteristics of the monitoring strategy and measuring methods are summarized. The total fieldwork lasted from February to June 1988. For each plant the measurements and observations took 4 days a week (Tuesday-Friday). In each company a sample of the total workforce, stratified by production function involved and by the job done, was monitored on randomly chosen days during the course of the measurement period. At the end of a shift a worker was interviewed about separate tasks performed, the time spent on each task, the use of personal protection devices, ventilation characteristics (general and local exhaust ventilation) and process characteristics (polymers used, hardness, number of units produced, temperature and pressure of curing presses used, etc.).

Table 2. Characteristics of sampling and analytical methods

Exposure	Sampling method	Analytical method	No. of plants	Prod. funct.	Planned No. of persons & samples	Collected No. of samples
Particulate	PAS6[1]	Gravimetric	10	All	269 x 3	666
Curing fumes	PAS6	Gravimetric/CSF[2]	10	Curing	75 x 3	163
Solvent vapours	Charcoal[3]	GC[4]	9	All	79 x 2	137
Skin exposure	Pad[5]	CSF	10	All	260 x 3	669

[1] inspirable particulate sampling device, described by ter Kuile (1984).
[2] based on NIOSH-method P&CAM 217 (1977).
[3] based on NIOSH-method P&CAM 127 (1977); activated charcoal was used as adsorbent.
[4] gas chromatography.
[5] 24 layers of surgical gauze (cotton) with a surface of 9 cm^2, worn on the lower side of the wrist of the hand of preference, method described by Durham and Wolfe (1962).

All information collected and the exposure data were subsequently used in linear regression models in order to unravel factors affecting exposure. In the empirical models continuous variables (such as curing pressure and temperature, time spent performing a task, etc.), as well as dummy variables (i.e. variables which take the values 0 or 1, indicating factors such as tasks performed, the use of personal protection devices, the presence of local exhaust ventilation, etc.) were used. The general equation of the statistical model was as follows:

$$\ln[\text{concentration}] = C + \beta_1 X_1 + \beta_2 X_2 + \ldots\ldots + \beta_n X_n$$

in which the dependent variable ln[concentration] is the natural logarithm of the 8-h TWA exposure concentration, the β_i are the regression coefficients, and the X_i the independent variables; the intercept C represents the background exposure level in these models. The regression coefficients represent the contribution to the exposure concentration per unit of the independent variable (for instance: the increase in rubber fume concentration per °C curing temperature increase). The coefficient of a dichotomous dummy variable is the contribution to the exposure concentration of a factor such as task, presence of local exhaust ventilation or use of personal protection devices, and represents an estimate of the difference in exposure between workers with and without the specified task, local exhaust ventilation or personal protection. For each production function significant factors were initially obtained separately, using standard stepwise regression techniques. Subsequently, models were created for the complete industry by using significant factors from the first analysis in a second stepwise procedure. At both stages, to enter the model each variable had to meet a significance level of 0.50 and was kept in the model if its significance was below 0.10. Model adequacy was tested with standard regression techniques such as residual plots and outlier detection. All statistical analyses were performed with the SAS package (SAS, 1983) on a VAX computer using the GLM procedure.

RESULTS

Airborne particulates

The 8-h TWA geometric mean particulates concentration varied from 0.8 to 1.9 mg/m^3 and from 0.2 to 2.0 mg/m^3 when analysed by plant and production function, respectively (Table 3). The variance of exposure to airborne particulates was only partially explained by these two factors (R^2=0.13). To a great extent, the particulate exposure appeared to be determined by specific circumstances in each production function in each plant (Fig. 1). There was significant interaction between plant and production function (with the addition of the interaction term in the model R^2 became 0.39).

The statistical analysis with tasks performed, and the presence of local exhaust ventilation as variables yielded a model which explained 40% of the total exposure variance (R^2=0.40). The tasks done and local exhaust ventilation systems which contributed to a significantly lower or higher exposure than the background are presented in Table 4, in which the estimated geometric mean concentration and its 95% confidence interval based on the linear model are given for each factor with an exposure significantly different from the background level of 0.8 mg/m^3. The estimated geometric mean represents the median exposure a worker would have

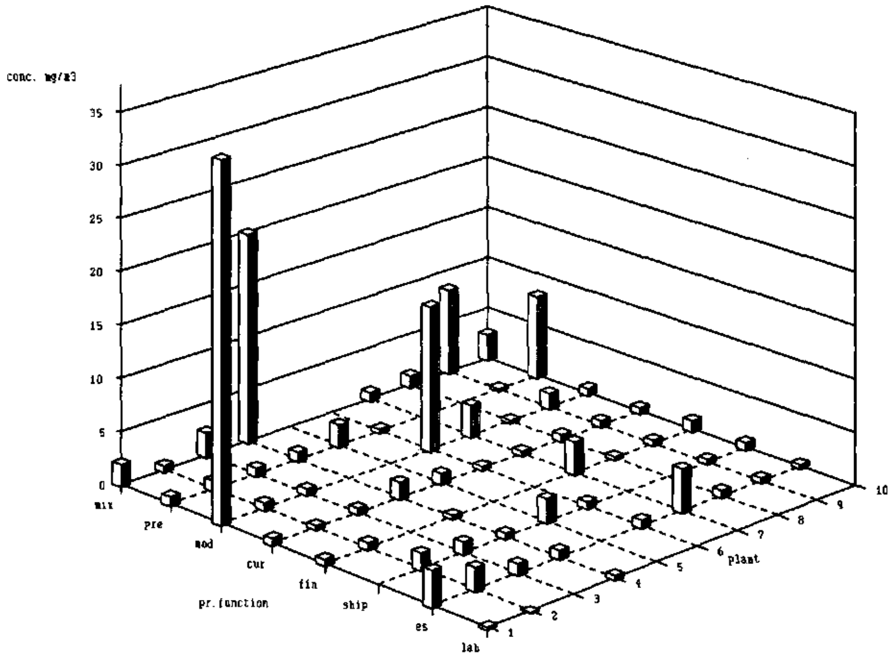

Fig. 1. Geometric mean particulate exposure for each production function in each plant

received if he or she performed only the specified task throughout a complete shift. If more than one task was performed during a shift the median exposure was determined by linear interpolation between the estimated coefficients. For instance, a worker who operated a two-roll mixing mill but also cleaned the workplace would have had an estimated median exposure to airborne particulates of 2.2 mg/m^3 based on the (multiplicative) linear model. [The model yielded regression coefficients of -0.1685, 0.3694, and 0.6088, respectively, for background, cleaning and mixing on a two-roll mixing mill, which leads to: exp(-0.1685) x exp(0.3694) x exp(0.6088) = 0.84 x 1.45 x 1.84 = 2.2 mg/m^3.]

Table 3. Airborne particulates, rubber fumes, dermal CSF and total-solvent concentrations in eight production functions and 10 plants in the rubber-manufacturing industry in The Netherlands

Group	Airborne particulates (mg/m^3)				Rubber fumes (CSF) ($\mu g/m^3$)				Dermal (CSF) ($\mu g/cm^2$/8-h)				Total solvents (mg/m^3)			
	No.	AM	GM	GSD	No.	AM	GM	GSD	No.	AM	GM	GSD	No.	AM	GM	GSD
Compounding-mixing	99	5.4	2.0	3.4	-				105	378	89	4.2	4	10.4	1.3	10.1
Pre-treating	62	2.2	1.0	2.6	-				67	101	59	2.9	31	62.0	34.6	3.8
Moulding	130	41.0	1.8	7.5	-				132	208	106	2.8	19	15.1	6.3	5.4
Curing	184	1.2	0.7	2.4	163	584	392	2.2	165	165	74	3.2	49	6.2	2.2	4.1
Finishing	90	4.7	1.0	4.2	-				90	85	53	2.7	19	5.5	1.5	4.8
Shipping	43	1.8	1.1	2.6	-				47	50	37	2.3	-			
Engineering services	50	1.5	0.9	2.4	-				55	424	177	3.2	13	3.7	1.8	3.5
Laboratory	8	0.3	0.2	2.3	-				8	28	26	1.4	2	0.4	0.4	1.1
Plant 1	60	64.3	1.7	7.5	14	343	299	1.6	60	546	70	5.2	-			
Plant 2	64	1.5	0.9	2.7	1	287	287	-	67	77	55	2.2	12	51.1	46.9	1.6
Plant 3	53	1.6	1.0	2.3	8	361	325	1.6	51	106	67	2.7	17	48.8	23.7	3.7
Plant 4	43	5.5	1.2	3.4	17	1510	1160	2.1	44	83	52	2.4	13	3.5	1.8	3.2
Plant 5	17	3.1	1.9	2.5	4	428	356	2.0	20	184	122	2.7	5	14.6	12.0	2.2
Plant 6	50	7.9	0.8	4.0	17	352	327	1.5	63	197	87	3.4	10	20.6	7.0	6.1
Plant 7	104	8.1	1.6	5.4	31	733	618	1.6	114	123	84	2.3	21	3.9	1.7	2.8
Plant 8	67	1.2	0.8	2.5	12	1280	831	2.5	67	209	71	4.1	18	0.9	0.5	2.1
Plant 9	112	7.5	0.9	4.1	41	259	214	1.7	84	219	90	3.4	20	38.0	15.3	3.6
Plant 10	96	3.4	1.0	3.2	18	297	258	1.8	99	255	94	4.0	21	3.9	1.2	4.6

Table 4. Statistically significant[1] factors affecting inspirable particulate exposure (mg/m^3) for each production function (analysis with dummy task and dummy local exhaust ventilation variables; 620 observations; R^2=0.40)

Production function	Factors related to high exposure	GM[2](95% CI)[3]	Factors related to low exposure	GM(95% CI)
General	Cleaning	1.2 (0.9- 1.6)		
	Transport	1.2 (0.9- 1.6)		
Compounding-mixing	Weighing	3.5 (2.5- 5.1)		
	Open mill	1.6 (0.9- 2.6)		
	Internal mill	1.4 (0.9- 2.3)		
Pre-treating	Repair buffing	1.9 (1.1- 3.4)		
Moulding	Jointing	12.7 (7.2-22.4)	Calendering	0.5 (0.3-0.7)
	Heating mill	2.5 (1.6- 3.9)	Assembling machine	0.4 (0.2-0.9)
			Manual assembling	0.4 (0.3-0.6)
			Extruding-slicing	0.3 (0.1-0.8)
			Braiding machine	0.3 (0.1-0.7)
			Lead extrusion	0.3 (0.1-0.8)
Curing	Autoclave without LEV[4]	4.5 (2.5- 7.8)	UHF curing	0.3 (0.2-0.6)
	Autoclave with LEV	1.1 (0.5- 2.1)[5]		
Finishing	Punching powdered products	23.6 (7.6-73.4)	Rubber cutting	0.7 (0.5-0.9)
			Unrolling	0.5 (0.3-0.9)
	Tube inspection	22.8 (7.3-71.0)	Weighing products	0.3 (0.1-0.8)
			General trimming	0.1 (0.1-0.3)
Shipping	Packing powdered products	22.9 (5.7-92.0)	Loading-unloading	0.4 (0.2-0.8)
	Packing	1.4 (0.9- 2.0)		
Engineering services	Bench fitting	1.9 (1.1- 3.1)	Breakdown work	0.6 (0.4-0.8)
Laboratory			Laboratory work	0.3 (0.1-0.5)

[1] Significance level of coefficients < 0.05, except *rubber cutting*, and *assembling machine* (P < 0.10), and *autoclave with LEV* (P > 0.10); background level 0.8 mg/m^3.
[2] GM, estimated geometric mean.
[3] CI, confidence interval.
[4] LEV,local exhaust ventilation.
[5] The local exhaust ventilation had a significant negative effect, but the estimated geometric mean of autoclave curing with LEV was not significantly different from the background concentration.

A second model which used the actual time spent on a task, and the presence of local exhaust ventilation yielded comparable results. In Table 5 the estimated regression coefficients and standard errors are given. The number of significant

Table 5. Statistically significant[1] factors affecting inspirable particulate exposure (mg/m^3) for each production function (analysis with continuous task duration variables and dummy local exhaust ventilation variable; 599 observations; R^2=0.42)

Production function	Factors related to high exposure	ß[2] (SE)[3]	Factors related to low exposure	ß (SE)
General	Manual transport	1.87 (0.69)		
	Supervisor	0.76 (0.34)		
Compounding-mixing	Weighing	2.31 (0.30)		
	Emptying bags	2.21 (0.97)		
	Open mill	1.53 (0.49)		
	Internal mill	1.00 (0.46)		
Pre-treating	Repair buffing	0.99 (0.58)		
Moulding	Jointing	4.14 (0.36)	Manual assembling	-0.71 (0.31)
	Heating mill	1.56 (0.33)	Braiding machine	-1.24 (0.66)
Curing	Autoclave without LEV[5]	6.66 (1.20)	UHF curing	-1.16 (0.56)
	Autoclave with LEV	5.05 (0.94)		
Finishing	Punching powdered products	4.44 (0.74)	Unrolling	-1.80 (0.61)
			Weighing products	-2.24 (1.38)
	Polishing-grinding	4.16 (1.18)	General trimming	-4.61 (1.39)
	Tube inspection	3.60 (0.60)		
Shipping	Packing powdered products	2.65 (0.78)		
	Packing general	0.94 (0.30)		
Engineering services	Welding	1.34 (0.58)	Oiling	-1.39 (0.65)
Laboratory			Laboratory work	-1.96 (0.70)

[1] Significance level of coefficients < 0.05, except *repair buffing*, *weighing products*, and *braiding machine* (P < 0.10); background level 0.8 mg/m^3.

[2] ß, coefficient ($\exp^{(ß \times \text{proportion of shift})}$ yields a factor with which the background level should be multiplied to calculate the estimated geometric mean; e.g. a worker weighing during a full shift would have an estimated exposure of $\exp^{(2.31 \times 1.0)} \times 0.8 = 8.1$ mg/m^3, while a colleague only weighing for a half shift and milling the rest of the shift would have an estimated exposure of $\exp^{(2.31 \times 0.5 + 1.00 \times 0.5)} \times 0.8 = 4.2$ mg/m^3 based on the multiplicative model)

[3] SE, standard error.

[4] LEV, local exhaust ventilation.

factors affecting exposure was slightly less (25 against 29), but explained a similar amount of variance (42%). When the proportion of sampling time assigned to six tasks (manual transport, supervising, emptying chemical bags, polishing-grinding, welding, and oiling) was incorporated in the model they appeared to be significant factors. All these tasks were performed during a limited time period of a shift, which was apparently the reason that their contribution to an 8-h TWA concentration was not statistically significant and therefore did not show in the first model.

The significantly high mean particulate concentrations are generally related to work with chemicals in powder form (weighing, emptying bags, and operating an internal or an open mixing mill) and application of anti-tacking agents such as talc and zinc stearate in powder form (re-warming milling, extruding, jointing of uncured tubes, autoclave curing of profiles, and inspection and packing of dusty products). An inventory of almost 60 different accelerators, retarders and anti-degradants used in nine of the 10 plants surveyed showed that 22% were used in powder form (29% of the accelerators, 22% of the retarders and 7% of the anti-degradants).

A more detailed picture emerged when the particulate exposure was modelled for each production function separately. Even in production functions involving low particulate exposure (e.g. curing), tasks with statistically significant higher and significantly lower exposure existed, but these results are not presented.

Ventilation had little effect, and only autoclave curing with local exhaust ventilation apparently reduced particulate exposure. However, this might have been a spurious effect. The relatively high particulate exposure for autoclaves without local exhaust ventilation was caused by excessive use of anti-tacking agents near one of these autoclaves. By coincidence, this did not happen near autoclaves with local exhaust ventilation. The use of anti-tacking agents by autoclave curers could not be adjusted for in the statistical models, because it was not systematically recorded.

Curing fumes

Monitoring of curing fumes was restricted to the production function involving curing. In Table 3 the average exposure to rubber fumes measured as the cyclohexane-soluble fraction of the airborne particulates is presented for each plant. In three plants the British standard of 600 $\mu g/m^3$ was exceeded (plants 4, 7 and 8).

The geometric mean concentration of curing fumes varied from 214 to 1160 $\mu g/m^3$ (Table 3).

In Table 6 the most important factors for exposure to rubber fumes are presented. This model explained 50% of the exposure variability. The production factors curing temperature and closing pressure significantly increased exposure. The presence of local exhaust ventilation showed a two-fold reduction in exposure in this model. Operating injection moulding presses, which are operated at high temperatures and under relative high pressures (up to 250 bar), was therefore also related to higher exposure levels. The effect of closing pressure (range 0-500 bar) was 1.5 per 100 bar and for curing temperature (range 0-225 °C) 1.6 per 100 °C with a background level of 140 $\mu g/m^3$. The effect of curing different elastomers was not statistically significant. In the model, curing compounds based on NR/SBR, SBR, EPDM elastomers seemed to give rise to higher curing fume concentrations while compounds based on NBR elastomer showed an opposite effect.

Dermal exposure

The variation in dermal exposure to cyclohexane-soluble agents was also very large and traceable to a significant interaction between plant and production function

Table 6. Statistically significant[1] factors affecting rubber fumes exposure (cyclohexane-soluble matter) in the production function curing (analysis with dummy ventilation variable and continuous production variables; 59 observations; R^2=0.50)

Production function	Factors related to high exposure	β^2 (SE)[3]	Factors related to low exposure	β (SE)
Curing	Pressure[4] Temperature[6]	0.42 (0.10) 0.49 (0.23)	LEV[5]	-0.68 (0.19)

[1] Significance level of coefficients < 0.05; background level 140 $\mu g/m^3$.
[2] β, coefficient ($\exp^{(\beta \times \text{proportion of shift})}$ yields a factor with which the background level should be multiplied to calculate the estimated geometric mean).
[3] SE, standard error.
[4] Per 100 bar.
[5] LEV, local exhaust ventilation.
[6] Per 100 °C.

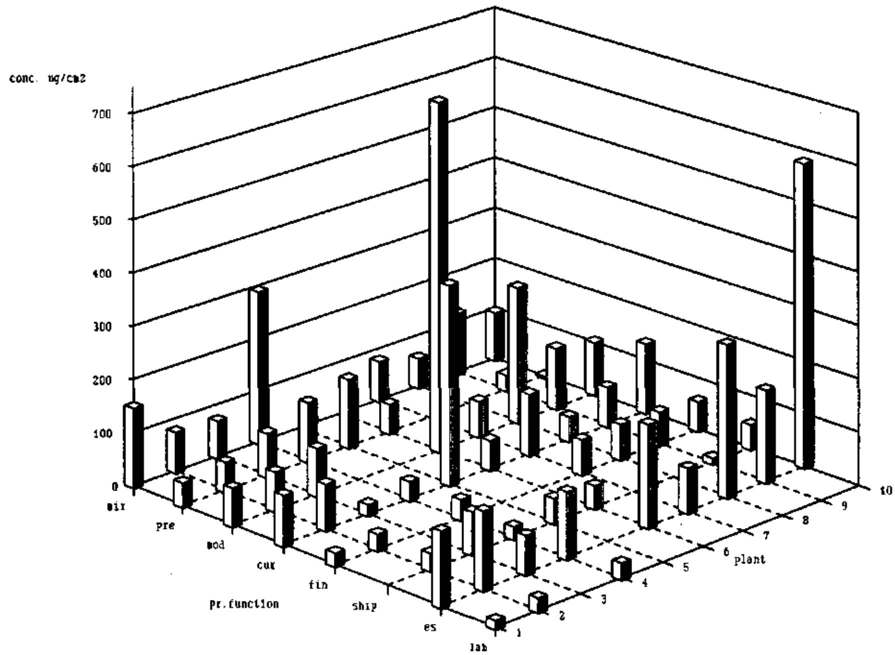

Fig. 2. Geometric mean dermal exposure to cyclohexane-soluble agents for each production function in each plant

(Fig. 2). The 8-h TWA geometric mean dermal exposure to cyclohexane-soluble matter varied across the plants from 52 to 122 $\mu g/cm^2/8$-h, and across production functions from 26 to 177 $\mu g/cm^2/8$-h (Table 3). A crude estimate of the potential total dermal exposure showed a considerably higher exposure through the skin than by inhalation. For instance, a press operator at plant 4 with a dermal exposure of 80 $\mu g/cm^2$ and an exposure to curing fumes of 1500 $\mu g/m^3$ (Table 3), assuming a 10 m^3 of air inhaled during an 8-h shift and a total surface of the skin of hands and wrists of 1280 cm^2 and 100% uptake, would have experienced an uptake through the skin almost seven times higher than that by inhalation. The situation in the curing departments of plant 4 was very extreme, with relatively low dermal exposure and the highest exposure to rubber fume. The ratio of the uptake through the skin to that by inhalation would have been higher in most other situations surveyed.

In Table 7 the results of the statistical analyses with tasks performed and personal protection devices used are presented. This model explained only 22% of the total variance. The background level was 65 $\mu g/cm^2$ (8-h geometric mean). High dermal exposure occurs in workplaces and during tasks where repetitive direct contact with (warm) mostly uncured compound takes place (such as wrapping of warm profiles, tyre presses, mixing on an open two-roll mill, operating of an extruder, grinding). The high dermal exposure of workers in the engineering services is caused by lubricating machinery without gloves, by breakdown work, and by operating lathes. The very high dermal exposure involved in 'operating the paint cabin' is due to direct contact with the release agent (named 'paint' in the particular factory), deposited on the transport cart. The effect of the use of gloves and towels did not follow unambiguously from the analyses. Oiling with gloves significantly reduced dermal exposure, and the low dermal exposure of operators of the curing presses (injection moulding) was presumably due to the use and regular replacement of gloves because of the exposure to heat from the presses and cured products. At work-places where gloves were not regularly replaced their use led to a higher dermal exposure (for instance, mixing on a open two-roll mill and operating a re-warming mill).

Another model, in which the actual time a task was performed was included, explained 24% of the variation in dermal exposure (Table 8). The tasks which appeared in this model and were not present in the former one, were on average performed during only a short time within a shift. Other tasks, like injection moulding, inspecting, and general trimming were no longer present as significant factors, most likely due to the fact that time spent in these tasks hardly varied among workers.

Table 7. Statistically significant[1] factors affecting dermal exposure to cyclohexane-soluble matter ($\mu g/cm^2$/8-h) for each Production Function (analysis with dummy task and personal protection variables; 669 observations; R^2=0.22)

Production function	Factors related to high exposure	GM[2](95% CI)[3]	Factors related to low exposure	GM(95% CI)
General			Supervisor	45 (34-61)
Compounding-mixing	Refiner	372 (131-1055)	Granulating	15 (6-38)
	Oil weighing	211 (76- 585)		
	Open mill	119 (69- 203)		
	Weighing	108 (72- 162)		
Pre-treating				
Moulding	Extruding	117 (89- 155)		
Curing	Paint spray cabin	413 (189- 901)	Injection moulding	43 (30- 62)
	Tyre press	194 (118- 316)	Inspecting	41 (30- 55)
	Wrapping profiles	107 (76- 150)		
Finishing	Grinding bench	113 (73- 175)	General trimming	27 (11- 68)
Shipping				
Engineering services	Lubricating without gloves	396 (181- 868)	Lubricating with gloves	57 (19-170)[4]
	Breakdown work	134 (89- 202)		
	Bench fitting	108 (65- 179)		
Lab			Laboratory work	29 (14- 61)

[1] Significance level of coefficients < 0.05, except *trimming* and *bench fitting* (P < 0.10); background level 65 $\mu g/cm^2$/8-h.
[2] GM, estimated geometric mean.
[3] CI, confidence interval.
[4] The estimated geometric mean exposure of oiling with gloves differed significantly from the estimated exposure without gloves, but was not significantly different from the background level.

Solvents

The quantitative assessment of exposure to solvents was restricted to paraffins, aromatics, chlorinated hydrocarbons, ketones, alcohols and esters. These were chosen on the basis of information on solvents, cements, and release and bonding agents used in the 10 plants.

Table 8. Statistically significant[1] factors affecting dermal exposure to cyclohexane-soluble matter ($\mu g/cm^2/8$-h) for each production function (analysis with time variables and dummy personal protection variable; 643 observations; $R^2=0.24$)

Production function	Factors related to high exposure	ß[2] (SE)[3]	Factors related to low exposure	ß (SE)
General	Cleaning	1.40 (0.46)	supervisor	-0.79 (0.38)
Compounding-mixing	Oil weighing	6.28 (3.15)	Granulating	-2.58 (0.70)
	Refiner	1.66 (0.77)		
	Weighing	1.05 (0.35)		
	Open mill	0.96 (0.54)		
Pre-treating				
Moulding	Extruding	1.02 (0.26)		
	Heating mill	0.80 (0.36)		
Curing	Paint spray cabin	5.99 (1.55)		
	Autoclave	2.27 (0.77)		
	Tyre press	1.56 (0.42)		
	Mould changing	1.36 (0.48)		
	Wrapping profiles	0.97 (0.42)		
Finishing	Tyre trimming	6.11 (3.73)		
	Grinding bench	1.02 (0.40)		
Shipping				
Engineering services	Oiling without gloves	4.80 (0.78)	Mould grinding	-1.68 (0.88)
	Oiling with gloves	3.41 (0.78)		
	Outdoor work	4.69 (1.63)		
	Welding	1.49 (0.64)		
	Breakdown work	1.47 (0.32)		
	General	1.40 (0.68)		
Lab			Laboratory work	-1.31 (0.77)

[1] Significance level of coefficients < 0.05, except *open mill*, *laboratory work*, *trimming*, and *mould grinding* ($P < 0.10$); background level 60 $\mu g/cm^2/8$-h.
[2] ß, coefficient ($\exp^{(\beta \times \text{proportion of shift})}$ yields a factor with which the background level should be multiplied to calculate the estimated geometric mean).
[3] SE, standard error.

The compounds chosen were:

(1) aliphatic hydrocarbons: hexane, heptane and octane;

(2) aromatic hydrocarbons: toluene, xylene, trimethylbenzene, naphthalene and isopropylbenzene;

(3) chlorinated hydrocarbons: trichloroethylene and 1,1,1,-trichloro-ethane; and
(4) ketones, alcohols and esters: methylisobutylketone, 2-ethoxyethanol, and isobutylacetate.

The presence of particular solvents was in general directly related to the use of solvents in rubber cements, bonding and release agents. This greatly affected exposure variability. The variance in exposure was therefore largely attributable to differences between plants, and as a result it was difficult to analyse differences in level of exposure to specific solvents between the production functions. After adjusting for differences between plants, workers involved in pre-treating seemed to be the most exposed, though the measured mean concentrations were low (< ¼ of the Dutch TLVs). The highest 8-h TWA geometric mean concentrations were

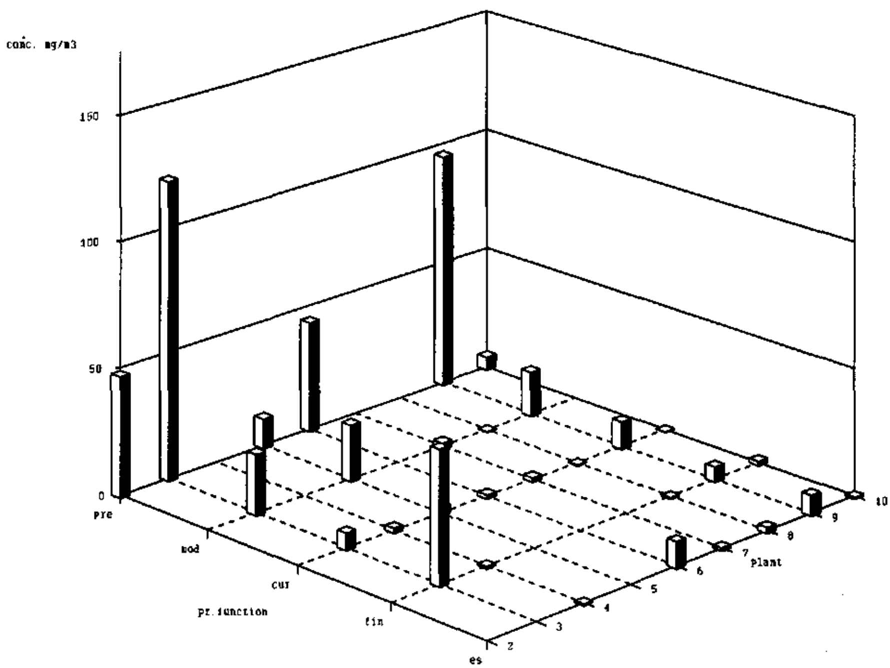

Fig. 3. Geometric mean total solvent exposure for each plant for each production function

respectively: 7 mg/m^3 hexane; 14 mg/m^3 heptane; 1 mg/m^3 octane; 18 mg/m^3 toluene; 17 mg/m^3 xylene; 90 mg/m^3 1,1,1,-trichloro-ethane and 4 mg/m^3 trichloro-ethylene.

Total solvent exposure varied between plants from 0.5 to 47.6 mg/m^3 and between production functions from 1.5 to 34.6 mg/m^3 (Table 3). Fig. 3 shows that the exposure to solvents is greatest in pre-treating and moulding and that in some of the plants (2, 3, 5, 6 and 9) higher solvent exposures were typical. Total solvent exposure was used as the dependent variable in the statistical models, because modelling of exposure to specific solvents was possible only for certain combinations of the 10 plants. Table 9 lists the significant factors. This model explained 56% of the total solvent exposure variance. From Table 9 it is clear that high solvent exposure was restricted to pre-treating, moulding and finishing, in which several tasks led to exposure concentrations above the background level of 1.5 mg/m^3.

In the tasks degreasing, cement application and jointing solvent use was obvious. Application of cements with a brush without local exhaust ventilation led to the highest concentrations, followed by cement spraying (which was performed exclusively in spraying booths), and finally cement application with a brush in a ventilated booth. Solvents were also used by operators of extruders in cleaning operations involving the extruder head and during cleaning of the final products in the finishing departments. From further analyses which included the additional factors of general ventilation or of open doors, it appeared that these were associated with solvent concentrations higher by a factor of 1.7 (this model explained 61% of the total exposure variance).

The significant factors of the model were similar when allowance was made for time spent on a task, but explained only 44% of the variance (Table 10). Cement mixing and degreasing had by far the largest effect on the exposure per unit of time, but in the situations studied cement mixing was performed during only a limited period

Table 9. Statistically significant[1] factors affecting total solvent exposure (mg/m^3) for each production function (analysis with dummy task and dummy local exhaust ventilation variables; 131 observations; R^2=0.57)

Production function	Factors related to high exposure	GM[2](95% CI)[3]	Factors related to low exposure	GM(95% CI)
General				
Compounding-mixing				
Pre-treating	Cementing with brush without LEV	14.5 (6.5-32.4)		
	Degreasing	13.3 (3.8-45.8)		
	Cement spraying	7.5 (3.0-18.9)		
	Cementing with brush with LEV[4]	4.6 (1.9-10.8)		
Moulding	Extruding	10.5 (5.3-20.8)		
	Jointing	4.0 (1.4-11.4)		
Curing				
Finishing	Polishing-grinding	9.5 (2.8-32.0)		
	Rubber cutting	9.4 (3.5-25.1)		
	Grinding bench	5.0 (2.0-12.7)		
Shipping			Packing	0.7 (0.2-1.8)
Engineering services				

[1] Significance level of coefficients < 0.05, except *jointing* and *packing* (P < 0.10); background level 1.53 mg/m^3.
[2] GM, estimated geometric mean.
[3] CI, confidence interval.
[4] LEV, local exhaust ventilation.

of time (less than 30 min during a shift) and took place in separate buildings. The mixers were automatically operated and exposure occurred only during loading and unloading of the mixers. Degreasing of metal parts took place in ventilated vapour degreasers. Exposure occurred while unloading the metal parts from the vapour degreaser and refilling the vapour degreaser by hand.

Table 10. Statistically significant[1] factors affecting total solvent exposure (mg/m^3) for each production function (analysis with time variables and dummy local exhaust ventilation variable; 131 observations; R^2=0.44)

Production function	Factors related to high exposure	ß[2] (SE)[3]	Factors related to low exposure	ß	(SE)
General					
Compounding-mixing	Cement mixing	21.88 (11.31)			
Pre-treating	Degreasing	32.53 (12.07)			
	Cement spraying	3.45 (1.10)			
	Cementing with brush without LEV[4]	3.37 (0.76)			
	Cementing with brush with LEV	2.85 (0.89)			
Moulding	Extruding	2.29 (0.68)			
Curing					
Finishing	Polishing-grinding	8.21 (2.45)			
	Rubber cutting	3.15 (1.19)			
	Grinding bench	1.21 (0.65)			
Shipping					
Engineering services					

[1] Significance level of coefficients < 0.05, except *grinding bench*, and *cement mixing* (P < 0.10); background level 1.84 mg/m^3.
[2] ß, coefficient (exp$^{(ß \times \text{proportion of shift})}$ yields a factor with which the background level should be multiplied to calculate the estimated geometric mean).
[3] SE, standard error.
[4] LEV, local exhaust ventilation.

DISCUSSION AND CONCLUSIONS

When the results of this study are compared with earlier published results of similar studies a few remarkable facts emerge. It seems that the large differences in exposure to airborne particulates between the tyre and general goods sector observed by others (Parkes *et al.*, 1975; HSE, 1981; van de Riet, 1985) was absent in this study. The large differences observed by Williams *et al.* (1980) between workers in front and back processing was also absent. A partial reconstruction of the dust hazard in compounding-mixing through replacement of chemicals in the form of powders by chemicals in other forms is the most likely explanation of this phenomenon. In the Dutch rubber-manufacturing industry the exposure to solvents was not restricted to 'rubber solvent' and was low and readily explained in relation to the tasks involved. The variability in curing fume concentrations was comparable with the results obtained by the Dutch Labour Inspectorate (van de Riet 1985). The variability in exposure could be partly explained by different curing methods and differences in process characteristics like temperature and pressure. Increasing curing temperature and pressure were both significantly related to higher curing fume concentrations. The dermal exposure to cyclohexane-soluble agents was evaluated for the first time on a large scale: its importance is so far unknown, in spite of the recently published study by Bos *et al.* (1989) in which a relation between the dermal exposure and urinary mutagenicity was demonstrated in a retreading plant and earlier mentioning of this route by Falck (1983) and Kilpikari (1981). Skin absorption must be regarded as an important subject for future exposure studies in the rubber-manufacturing industry.

Statistical linear models have previously been successfully applied to a wide variety of situations in indoor air studies as well as in occupational hygiene settings (Wadden and Scheff, 1983; Eisen *et al.*, 1984; Hansen and Whitehead, 1988; Hawkins *et al.*, 1992; Ulin *et al.*, 1992). Eisen *et al.* (1984) and Kalliokoski (1990) used statistical models to describe long-term exposure to dust and toluene. The model of Eisen *et al.* (1984), which incorporated job, shed, season, survey year and several interaction terms explained 46% of the total variance in dust levels measured in the Vermont granite sheds, similar to that of particulate levels in the presented study. Hansen and Whitehead (1988), Kalliokoski (1990) and Hawkins *et al.* (1992) used statistical models to describe the relationship between solvent exposure and solvent emission rates and were able to explain 50-70% of the variance in concentrations. The statistical models described here for solvent exposure explained slightly less exposure variance (R^2=0.44 and 0.56), which is probably attributable to the fact that the models developed were for solvent exposure data collected industry-wide, whereas the models in the other studies described single specific processes using production characteristics.

The monitoring strategy applied, with subsequent statistical modelling of measured exposure concentrations, has several limitations. For instance, it was impossible to make reliable estimates of the contributions of activities that occurred only infrequently. Besides, a lot of variance in exposure levels remained unexplained in the linear models, because of differences in work-style, differences in task content from plant to plant, and other factors not accounted for. Next to this, the independent variables have to vary and therefore a large number of measurements might be necessary. In the models with the time variables for instance some tasks did not show up any longer in the model because the time spent on them hardly varied among workers. However, the models with duration of tasks revealed tasks with a high exposure that had not previously been found because they had such short duration that they were not significant to the 8-h TWA and therefore had not shown up in the models with tasks irrespective of their duration as explanatory variables. Changes in duration of these tasks might lead to higher future 8-h TWAs and they are therefore important to identify.

Despite the limitations, a relatively small investment in time and labour for collecting ancillary information during and after the measurements produced very valuable information, which enabled us to identify factors affecting exposure. The identification of those factors will prove its value during the improving of labour conditions in the rubber-manufacturing industry in The Netherlands, which has already started. Application of new methods using real-time data evaluation as described by Gressel *et al.* (1988) and Cooper and Gressel (1992) can use tasks that has been identified as affecting exposure as a starting point to evaluate specific task contents and work practices leading to high exposures. Appropriate redesign and modification of process characteristics and work practices will eventually lead to a reduction of workers' exposure.

It can be argued that other measurement strategies, including task-specific sampling, might have resulted in similar results for hazard control purposes in a more cost-effective way, but this would not have resulted in an overview of average exposure levels and exposure variability throughout the industry. This overview will be very useful for epidemiological studies. The use of factors affecting exposure and collected exposure data in the design of future epidemiological research in this sector of industry will be the subject of a forthcoming paper. Finally, this study in the Dutch rubber-manufacturing industry showed that it is possible to combine multiple goals within one measurement strategy in an industry-wide study.

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Chapter 6

Occupational epidemiology in the rubber industry Implications of exposure variability[1]

[1] H. Kromhout & D. Heederik. Submitted to *American Journal of Industrial Medicine*.

ABSTRACT

The implications of exposure variability were examined for the design of occupational epidemiology studies in the rubber industry. The efficiency of different grouping schemes for exposure to particulates, dermal exposure to cyclohexane-soluble contaminants, and exposure to solvents was assessed. Statistical parameters for contrast in average exposure and precision of average exposure were developed to enable comparison of different grouping schemes. Groupings based on job title, plant, factors affecting exposure, published classifications, and the ISCO-ILO classification were compared.

Grouping of exposure to particulates and dermal exposure appeared to be less efficient than grouping of exposure to solvents. Grouping of solvent exposure using either occupational title groups, existing classification schemes, and schemes based on factors affecting exposure showed comparable high resolution in exposure levels. Even the most detailed grouping schemes based on the combination of plant and occupational title group showed relative modest resolution in particulate and dermal exposure levels. Groupings based on factors affecting exposure showed for these exposures similar resolution, but were more efficient because of a higher precision due to a smaller number of groups.

It was concluded, that application of optimal exposure grouping strategies will benefit new research on cancer among rubber workers. Eventually, this might resolve the unwanted situation in which a complete industry was included on the list of proven human carcinogens.

INTRODUCTION

Epidemiologic cohort studies in the rubber-manufacturing industry were numerous from the late 1960s through the 1980s in Europe (Fox *et al.* 1974, Fox *et al.* 1976, Waterhouse *et al.* 1979, Baxter and Werner 1980, Bovet *et al.* 1980, Parkes *et al.* 1982, Kilpikari *et al.* 1982, Holmberg *et al.* 1983, Norseth *et al.* 1983, Gustavsson *et al.* 1986, Sorahan *et al.* 1986, Bernardinelli *et al.* 1987, Sorahan *et al.* 1989, Negri *et al.* 1989) and in the USA (Mancuso *et al.* 1968, Michael *et al.* 1974, Monson *et al.*1976a, Monson *et al.* 1976b, McMichael *et al.* 1976a, McMichael *et al.* 1976b, Andjelkovich *et al.* 1976, Monson *et al.* 1978, Andjelkovich *et al.* 1978, Delzell *et al.* 1981a, Delzell *et al.* 1981b, Symons *et al.* 1982). The first studies were initiated because of an elevated risk of bladder cancer among rubber compounders that was revealed by accident (Case and Hosker, 1954). Studies in the United Kingdom were originally performed to prove the elimination of this risk by replacing bladder carcinogens by other non-carcinogenic chemicals (Fox *et al.* 1974, Waterhouse *et al.* 1979). During the course of these studies, and later studies in the United States, several other elevated risks were reported for leukaemia, cancer of the lung, renal tract, stomach, pancreas, oesophagus, liver, skin, colon, larynx and brain (IARC 1987). Results from these studies were contradictory in nature and did not elucidate causative agents for these risks or even reach a firm conclusion regarding whether these risks were present at all. IARC, however, decided to include the "rubber industry" on the list of proven human carcinogens (IARC 1987).

The chemical environment in which rubber workers perform their duties is highly variable in a qualitative and quantitative sense (van Ert *et al.* 1980, Williams *et al.* 1980, Kromhout *et al.* 1993). Therefore, exposure classification schemes based on general descriptors like job title might not have been informative with regard to exposure to chemical agents. Regardless, in almost all cohort studies, the occupational title of the longest performed job was used as a proxy measure of exposure, most likely due to the retrospective character of the cohort studies. Gamble and Spirtas (1976) introduced the occupational title group (OTG), which was constructed by allocating jobs with a comparable exposure profile into the same exposure group, as a more direct classification of exposure. Spirtas and Fendt (1982) presented an algorithm for linking job titles with individual exposures based on the OTG concept. The cohort members of the Health and Safety

Executive study (Fox *et al.* 1974) were divided into three qualitative exposure groups representing potential exposure to specific bladder carcinogens based on employment in companies who used specific carcinogenic anti-oxidants. All factories were inspected for use of the suspected anti-oxidants and cohort members were assigned to these three exposure groups dependent on their date of entrance into the rubber industry. In some of the cohort studies, length of employment within an occupational title group was used as a surrogate for dose (Sorahan *et al.* 1986, McMichael *et al.* 1976b). Nonetheless, almost all exposure estimates used in the cohort studies were based on occupational title.

Within the case-referent studies, which were nested within the cohort studies in the United States, researchers attempted to describe the exposure to specific solvents with use of different sources of information (Arp 1979, Arp *et al.* 1983, Checkoway *et al.* 1984, Wilcosky *et al.* 1984). These exercises resulted in semiquantitative exposure groups consisting of occupational titles or occupational title groups. An example of such a grouping scheme for exposure to solvents can be found in McMichael *et al.* (1975). Jobs were grouped based on the *a priori* expected likelihood of exposure to solvents. Goldsmith (1980) presented a similar grouping scheme of occupational title groups for exposure to particulates (metal oxides and organic accelerators).

In this paper the use of different exposure measures in epidemiologic research in the rubber industry is critically reviewed in the light of the results of an extensive exposure survey in ten rubber factories in the Netherlands (Kromhout *et al.* 1993, Swuste *et al.* 1993). In the survey, an exposure assessment strategy with repeated measurements per worker was utilized. This enabled estimation of between- and within-worker components of exposure variance both for each individual plant and for each occupational title group throughout the plants. The repeated measurement design also permitted an evaluation of different exposure grouping schemes (i.e. plant, occupational title group, and classifications used in previous case-referent studies in the rubber industry) in terms of clarity of contrast between groups and precision of average exposure estimated for each group. Contrast in exposure level between exposure groups is a prerequisite for detection of any exposure-response relationship in an epidemiologic analysis. As early as 1954, while discussing grouping of observations in regression analysis, Prais and Aitchinson (1954) recognised that maximizing between-group variance and minimising within-group variance optimizes the grouping of observations. Next to contrast, precision of the exposure estimate plays a crucial role, because imprecise exposure estimates will introduce non-differential misclassification that will obscure an existing exposure-response relationship. Therefore, in order to describe the optimal grouping of present exposure measurements in the rubber industry both precision and contrast were taken into consideration.

MATERIALS AND METHODS

Exposure information from a large industry-wide survey of the rubber industry in the Netherlands was used. Characteristics of this study have been described elsewhere (Kromhout *et al.* 1993). Only data from randomly chosen workers with repeated measurements were used for this analysis. Also, observations of workers with either a particulate exposure measurement or dermal exposure measurement missing for a given day were excluded, to enable direct comparisons between grouping schemes for these two different types of exposure. The number of observations reported herein is, therefore, different from that presented earlier by Kromhout *et al.* (1993).

Within- and between-worker components of exposure variance were estimated from the log-transformed exposure concentrations employing a one-way nested random-effects ANOVA model:

$$Y_{ij} = \ln(X_{ij}) = \mu_y + \beta_i + \epsilon_{ij}, \text{ for } (i=1,2, \ldots,k) \text{ and } (j=1,2, \ldots,n_i)$$

where

X_{ij} = exposure concentration of the i-th worker on the j-th day,

μ_y = mean of Y_{ij},

β_i = random deviation of the i-th worker's true exposure ($\mu_{y,i}$) from μ_y, and

ϵ_{ij} = random deviation of the i-th worker's exposure on the j-th day from his true exposure, $\mu_{y,i}$.

It is assumed under the model that both β_i and ϵ_{ij} are normally distributed; i.e., $\beta_i \sim N(0, \sigma_B^2)$, and $\epsilon_{ij} \sim N(0, \sigma_W^2)$. The underlying distribution of exposures (X_{ij}) is assumed to be lognormal. Also, β_i and ϵ_{ij}, are assumed to be statistically independent of each other.

The resulting ANOVA-table makes estimation of the within- and between-worker variance components possible:

Factor	SS	DF	Mean Squares	Expected Values
worker	$SS_{between}$	k-1	$SS_{between\text{-}worker}/k\text{-}1$	$\sigma_{WW}^2 + n'\sigma_{BW}^2$
error:worker	SS_{error}	N-k	$SS_{within\text{-}worker}/N\text{-}k$	σ_{WW}^2

SS, sum of squares.
DF, degrees of freedom.
k, number of workers.
N, total number of observations.
in the case of balanced data $n' = n$ (number of repeats per worker).
in the case of unbalanced data $n' = (N - \Sigma_{i=1}^{k} n_i^2 / N) / k - 1$, with $N = \Sigma_{i=1}^{k} n_i$.
σ_{BW}^2, variance component due to workers.
σ_{WW}^2, variance component due to days (error).

The estimates of the variance components σ_{BW}^2 and σ_{WW}^2 will be designated as ${}_{BW}S_y^2$ and ${}_{WW}S_y^2$, respectively. From these variance components the standard deviations were estimated for the between-worker (${}_{BW}S_y$) and within-worker distributions (${}_{WW}S_y$). These standard deviations were used to estimate the corresponding geometric standard deviations (${}_{BW}S_g = \exp({}_{BW}S_y)$, and ${}_{WW}S_g = \exp({}_{W}S_y)$) and the ratios of the 97.5th and 2.5th percentiles of the log-normally distributed exposures of each group of workers (Rappaport, 1991). These ratios, estimated as ${}_{BW}\hat{R}_{.95} = \exp(3.92\ {}_{BW}S_y)$ provide information regarding the ranges of exposures experienced among workers within a group.

Contrast in exposure levels among exposure groups was defined as the ratio of the between-group variance component and sum of the between-group and within-group variance components ($_{BG}S_y$ / ($_{BG}S_y$ + $_{WG}S_y$)), which were estimated by applying a two-way random effects model. This ratio (referred to as elasticity) will by definition reach unity if each worker constitutes a unique exposure group. This, however, will not be the case in most occupational epidemiology studies since not every worker of interest will have been sampled. Applying a group's average exposure to the individuals within the group is therefore often required. At the other extreme, if the grouping strategy has no value, then this ratio will approach the null value.

Precision of each group's mean exposure was also calculated from the variance components estimated in a two-way nested random effects model.

The two-way random-effects ANOVA model had the following features:

$Y_{ijk} = \ln X_{ijk} = \mu_y + \alpha_i + \beta_{ij} + \epsilon_{ijk}$, for ($i=1,2, ...,g$), ($j=1,2, ...,k_i$), and ($k=1,2, ...,n_{ij}$)

where

X_{ijk} = exposure concentration of the i-th group's j-th worker on the k-th day,

μ_y = mean of Y_{ijk},

α_i = random deviation of the i-th group's true exposure ($\mu_{y,i}$) from μ_y

β_{ij} = random deviation of the j-th worker's true exposure ($\mu_{y,ij}$) from $\mu_{y,i}$, and

ϵ_{ijk} = random deviation of the i-th group's j-th worker's exposure on the k-th day from his true exposure, $\mu_{y,ij}$.

It is assumed under the model that α_i, β_{ij} and ϵ_{ijk} are normally distributed; i.e., $\alpha_i \sim N(0, \sigma^2_{BG})$, $\beta_{ij} \sim N(0, \sigma^2_{BW})$, and $\epsilon_{ijk} \sim N(0, \sigma^2_{WW})$. The underlying distribution of exposures (X_{ij}) is assumed to be lognormal. Also, α_i, β_{ij} and ϵ_{ijk}, are assumed to be statistically independent of each other. In this model, α_i, β_{ij} and ϵ_{ijk} are all considered to be random effects of respectively group, worker, and day. An individual observation Y_{ijk} is depending on an overall underlying mean (μ), a random group (α_i) effect for the i-th group, a random worker (β_{ij}) effect for the i-th group's j-th worker, and a random day (e_{ijk}) effect for the k-th day of the j-th worker in the i-th group. Worker is supposed to be nested in a group, and day in both group and worker. The ANOVA table resulting from this model enables the estimation of the three variance components, the between-group variance, the pooled within-group variance which is analogous to the between-worker variance, and the pooled within-worker or day-to-day variance (Searle 1961):

Factor	SS	DF	Mean Squares	Expected Values
group	$SS_{between}$	g-1	$SS_{between\text{-}group}/g\text{-}1$	$\sigma^2_{WW} + n'\sigma^2_{WG} + n'k'\sigma^2_{BG}$
worker: group	SS_{within}	K-g	$SS_{within\text{-}group}/K\text{-}g$	$\sigma^2_{WW} + n''\sigma^2_{WG}$
error: group,worker	SS_{error}	N-K	$SS_{within\text{-}worker}/N\text{-}K$	σ^2_{WW}

g, number of groups.
K, total number of workers.
N, total number of observations.
in the case of unbalanced data:
$k' = (N - \Sigma_{i=1}^{g} n_{i.}^2 / N) / n' (g - 1)$.
$n' = (\Sigma_{i=1}^{g} (\Sigma_{j=1}^{k} n_{ij}^2 / n_{i.}) - \Sigma_{i=1}^{g} \Sigma_{j=1}^{k} n_{ij}^2 / N) / (g - 1)$.
$n'' = (N - (\Sigma_{i=1}^{g} (\Sigma_{j=1}^{k} n_{ij}^2 / n_{i.})) / K - g$.
$N = \Sigma_{i=1}^{g} \Sigma_{j=1}^{ki} n_{ij}$ (total number of observations).
$K = \Sigma_{i=1}^{g} k_i$ (total number of workers).
in the case of balanced data, $k' = k$ (number of workers in a group) and $n', n'' = n$ (number of repeats per worker).
σ^2_{BG}, variance component due to groups.
σ^2_{WG}, variance component due to workers.
σ^2_{WW}, variance component due to days (error).

The estimates of the variance components σ^2_{BG}, σ^2_{WG}, and σ^2_{WW} will be designated as ${}_{BG}S_y^2$, ${}_{WG}S_y^2$, and ${}_{WW}S_y^2$, respectively. From these variance components the standard deviations were estimated for the between-group (${}_{BG}S_y$), within-group (${}_{WG}S_y$), and within-worker distributions (${}_{WW}S_y$). These standard deviations were used to estimate the corresponding geometric standard deviations (${}_{BG}S_g = \exp({}_{BG}S_y)$, ${}_{WG}S_g = \exp({}_{WG}S_y)$, and ${}_{WW}S_g = \exp({}_{WW}S_y)$) and the ratios of the 97.5th and 2.5th percentiles of the log-normally distributed exposures of each grouping. These ratios, designated as ${}_{BG}\hat{R}_{.95} = \exp(3.92\ {}_{BG}S_y)$ provide information regarding the ranges of exposures experienced between different groups.

Also, the following statistics were derived using the variance components estimates:

elasticity (ϵ) = ${}_{BG}S_y^2$ / (${}_{BG}S_y^2$ + ${}_{WG}S_y^2$), and

precision (π) = ((${}_{WG}S_y^2$ / k + ${}_{WW}S_y^2$ / kn)$^{1/2}$)$^{-1}$, in which k is the number of workers and kn the number of observations in a group. The precision was estimated for each group separately and the median precision of all g groups of a grouping is presented.

All statistical analyses were performed with the SAS (SAS Institute, Cary, NC) package on a VAX computer. Variance components were estimated using Proc Nested.

Grouping schemes were compared for exposure to particulates, exposure to total-solvents, and dermal exposure to cyclohexane-soluble contaminants. In Table 1 and Appendix 1 the different evaluated grouping schemes are described.

RESULTS

Within- and between-worker exposure variability

In Table 2 the descriptive statistics of the analyzed exposure data are shown. In Table 3 estimates of within- and between-worker exposure variability of exposure to particulates, dermal exposure to cyclohexane-soluble matter, and exposure to total-solvents are shown for the complete group and for each of the occupational title groups and plants separately. The between-worker exposure variability for the complete population was highest for exposure to solvents when compared to exposure to inspirable particulates and dermal exposure to cyclohexane-soluble matter (${}_{BW}S_g$ 5.48 versus 3.05 and 2.36, respectively). The within-worker exposure variability for dermal exposure (${}_{WW}S_g$ 2.29) almost equalled the between-worker exposure variability, indicating a substantial day-to-day variation.

Table 1. Evaluated grouping schemes*

Scheme	No. Groups	Description
particulates, dermal csf		
otg	7	compounding, pre-treating, moulding, curing, finishing, shipping, engineering services
plant	10	representative sample of plants present in the Netherlands
otg and plant	53	some OTGs were not present in some plants
isco-ilo	6	90120, 90125, 90130, 90135, 90140, 90190
augmented isco-ilo	17, 18	each of the isco-codes was augmented with a digit 1, 2, or 3, which stand for respectively low, medium, and high exposed based on the presence or absence of factors affecting exposure for each worker (Kromhout *et al.* 1993); occupational title groups with the same isco code were separated
exposure group	3	grouping solely based on factors affecting exposure (last digit of augmented isco-ilo code)
particulates		
Goldsmith	4	high: batch preparation; medium: service to batch preparation, drop milling, skilled metal working, milling, calendering; low: tuber, tread and tube extrusion; curing: reclaim, fabrication of tires and beads, tubes, flaps and bladders inspection and cure preparation; unspecified: maintenance, general service, janitoring, shipping and receiving, metal and steel products, synthetic rubber, salary (hourly workers at some stage holding salaried jobs), unknown
total solvents		
otg	5	pre-treating, moulding, curing, finishing, engineering services
plant	9	no personal exposures available for one plant
otg and plant	24	some OTGs were not present in some plants
isco-ilo	4	90130, 90135, 90140, 90190
augmented isco-ilo	8	each of the four isco-codes was augmented with a digit 1, 2 or 3, which stand for respectively low, medium and high exposed based on the presence or absence of factors affecting exposure for each worker (Kromhout *et al.* 1993); occupational title groups with the same isco code were separated
McMichael	4	high: tread cementing, calender tending, cement mixing; medium: calender operating, curing preparation, finishing, inspection, repair, maintenance & service; light: bead building, plystock preparation, tire building; no: compounding, mixing, milling, curing, warehouse, powerhouse, freight yards, janitors, others

* the exact coding scheme for otg, isco-ilo, and augmented isco-ilo can be found in Appendix 1

Table 2. Airborne particulates, dermal cyclohexane soluble agents (csf), and total-solvents concentrations in seven production functions and ten plants in rubber-manufacturing industry in the Netherlands

		particulates (mg/m^3)			dermal (csf) ($\mu g/cm^2/8\text{-}hr$)			total-solvents (mg/m^3)			
group	No.	AM	GM	GSD	AM	GM	GSD	No.	AM	GM	GSD
total	552	7.2	1.0	3.5	192	74	3.3	107	22.9	5.4	6.4
compounding/mixing	88	3.0	1.7	2.8	318	79	4.1	-			
pre-treating	53	2.4	1.0	2.7	82	50	2.8	29	63.9	34.6	4.0
moulding	107	27.9	1.3	6.1	204	104	2.8	14	16.7	8.9	4.1
curing	134	0.9	0.7	2.1	161	70	3.2	38	7.7	2.9	4.1
finishing	83	4.3	0.9	3.8	86	52	2.8	16	2.4	1.1	3.6
shipping	39	1.8	1.0	2.7	47	35	2.3	-			
engineering services	48	1.4	0.9	2.4	442	177	3.3	10	3.5	1.7	3.5
plant 1	48	44.1	1.2	4.6	444	58	4.4	-			
plant 2	57	1.6	1.0	2.4	72	52	2.1	9	56.1	51.3	1.7
plant 3	42	1.7	1.0	2.5	113	69	2.8	14	51.9	22.1	4.1
plant 4	31	1.1	0.9	2.0	63	46	2.1	10	4.0	1.9	3.6
plant 5	14	3.2	1.9	2.8	175	120	2.5	4	17.4	16.3	1.5
plant 6	44	8.9	0.8	4.3	164	80	3.3	8	24.3	8.4	6.8
plant 7	92	7.8	1.5	5.1	117	81	2.3	16	4.9	2.2	2.9
plant 8	62	1.2	0.8	2.5	220	72	4.3	12	1.1	0.6	2.4
plant 9	71	2.2	0.9	3.4	217	87	3.5	20	38.0	15.3	3.6
plant 10	91	3.2	1.0	3.0	266	92	4.2	14	4.8	1.6	4.9

No., number of measurements.
AM, arithmetic mean.
GM, geometric mean.
GSD, geometric standard deviation.

Dividing the population into seven occupational title groups decreased the between-worker particulate exposure variability for most groups (compounding, pre-treating, curing, shipping, and engineering services). The between-worker exposure variability for the groups "moulding" and "finishing" increased substantially, however. This implies large differences in exposure levels among workers within these groups or even within these groups within plants. The picture for dermal exposure was slightly less favourable because the between-worker exposure variability only decreased for the groups "moulding", "finishing", "shipping", and "engineering services". The between-worker exposure variability for the other groups (compounding, pre-treating, and curing) stayed rather high (${}_{BW}S_g$ 2.41, 2.40, and 2.53, respectively). Classifying the workers' solvent exposure in five occupational title groups resulted overall in a smaller between-worker exposure variability (${}_{BW}S_g$ range 2.56-3.41), but in an absolute sense the differences between workers within these five occupational title groups were still high (${}_{BW}\hat{R}_{.95}$ range 40-123).

If workers were classified according to the plant they worked in, large differences between factories were apparent. Three factories had very high between-worker particulate exposure variability (${}_{BW}S_g$ range 4.04 - 4.77), while the between-worker exposure variability of the other factories decreased (${}_{BW}S_g$ range 1.43 - 2.93). Grouping by factory was even less beneficial for dermal exposure. Only four factories showed less (${}_{BW}S_g$ range 1.71 - 2.25) and six showed more (${}_{BW}S_g$ range 2.46 - 3.00) between-worker exposure variability. For solvents, on the contrary, only the between-worker variability for plant 6 increased. In this plant large differences in exposure to solvents existed (${}_{BW}S_g$ 7.46, ${}_{BW}\hat{R}_{.95}$ 2640!).

Within- and between-group exposure variability for several grouping schemes

The elasticity and precision of different (combinations of) grouping variables are presented in Table 4 for the three measured exposures. Considering exposure to particulates, it is obvious from Table 4 that grouping workers by the combination of occupational title group and plant is one of the best grouping strategies in terms of contrast in exposure level (ϵ 0.23). However, the differences between these group

Table 3. Within- and between-worker exposure variability of exposure to particulates, dermal cyclohexane-soluble matter, and total solvents for each production function and plant

group	N	k	particulate exposure $_{ww}S_g$	$_{BW}S_g$	$_{BW}\hat{R}_{.95}$	dermal csf exposure $_{ww}S_g$	$_{BW}S_g$	$_{BW}\hat{R}_{.95}$	total solvent exposure N	k	$_{ww}S_g$	$_{BW}S_g$	$_{BW}\hat{R}_{.95}$
total group	552	206	1.73	3.05	78.9	2.29	2.36	29.1	107	51	2.17	5.48	785
compounding	88	34	1.68	2.44	33.2	3.05	2.41	31.2	-	-	-	-	-
pre-treating	53	19	1.81	2.26	24.6	1.75	2.40	30.9	29	13	2.33	3.08	82.5
moulding	107	39	1.93	5.51	802	2.22	1.91	12.6	14	7	2.39	3.26	103
curing	134	51	1.49	1.86	11.3	1.98	2.53	38.6	38	19	2.06	3.41	123
finishing	83	30	1.77	3.42	123	2.41	1.71	8.1	16	8	1.68	3.37	117
shipping	39	15	1.75	2.32	27.1	2.03	1.53	5.3	-	-	-	-	-
eng. services	48	18	1.77	1.97	14.3	2.50	2.20	22.2	10	5	2.47	2.56	40.0
plant 1	48	20	1.99	4.04	237	2.82	2.96	70.6	-	-	-	-	-
plant 2	57	21	1.79	1.90	12.5	1.70	1.71	8.2	9	4	1.73	1.00	1.0
plant 3	42	15	1.64	2.22	22.6	1.74	2.46	34.3	14	6	1.66	4.07	246
plant 4	31	12	1.81	1.43	10.2	1.62	1.83	10.8	10	5	1.63	3.50	136
plant 5	14	6	1.66	2.53	38.1	1.65	2.25	23.8	4	2	1.30	1.50	5.0
plant 6	44	15	1.63	4.07	245	1.92	2.75	53.1	8	3	2.42	7.46	2640
plant 7	92	36	1.71	4.77	455	1.85	1.78	9.6	16	8	2.35	1.95	13.7
plant 8	62	22	1.57	2.23	23.4	2.81	2.87	62.6	12	6	2.14	1.58	6.0
plant 9	71	26	1.87	2.93	68.0	3.06	1.76	9.2	20	10	2.41	2.66	46.0
plant 10	91	33	1.75	2.63	44.5	2.55	3.00	74.1	14	7	2.91	3.43	125

N, number of measurements in a group.
k, number of workers in a group.
$_{ww}S_y$, estimated standard deviation of within-worker distribution of log-transformed exposures.
$_{BW}S_y$, estimated standard deviation of between-worker distribution of log-transformed exposures.

$_{BW}\hat{R}_{.95}$, ratio of the 97.5th and 2.5th percentiles of the between-worker distribution.

Table 4. Between- and within-group exposure variability for several grouping schemes

grouping variable	g	$_{WG}S_g$	$_{BG}S_g$	$_{BG}R_{.95}$	elasticity	precision
particulates exposure (n=552)						
occupational title group	7	2.95	1.35	3.2	0.07	4.2
plant	10	3.06	1.00	1.0	0.00	4.3
occupational title group + plant	53	2.66	1.72	8.3	0.23	3.0
isco-ilo	6	2.88	1.51	5.0	0.13	5.6
augmented isco-ilo	19	2.81	1.55	5.6	0.15	3.7
exposure group	3	2.80	1.72	8.5	0.22	8.3
Goldsmith classification	4	2.94	1.42	3.9	0.09	6.3
dermal csf exposure (n=552)						
occupational title group	7	2.17	1.50	4.9	0.22	6.3
plant	10	2.36	1.09	1.4	0.01	4.2
occupational title group + plant	53	2.05	1.62	6.6	0.31	3.0
isco-ilo	6	2.34	1.15	1.7	0.03	5.9
augmented isco-ilo	18	2.08	1.60	6.3	0.29	4.5
exposure group	3	2.13	1.72	8.3	0.34	8.3
total solvent exposure (n=107)						
occupational title group	5	3.22	4.10	252	0.59	2.2
plant	9	2.93	4.04	239	0.63	2.7
occupational title group + plant	24	1.99	4.87	496	0.84	2.9
isco-ilo	4	5.32	1.48	4.7	0.05	2.7
augmented isco-ilo	8	3.25	3.93	214	0.57	2.2
exposure group	2	3.92	4.33	314	0.54	3.2
McMichael classification	4	3.21	4.22	283	0.60	2.9

g, number of groups
$_{WG}S_g$, estimated standard deviation of within-group distribution of log-transformed exposures
$_{BG}S_g$, estimated standard deviation of between-group distribution of log-transformed exposures
$_{BG}\hat{R}_{.95}$, ratio of the 97.5th and 2.5th percentiles of the between-group distribution

are relatively modest ($_{BG}\hat{R}_{.95}$ is only 8.3). A large within-group exposure variability and a large number of groups (53) leads in this grouping scheme to the lowest precision (π 3.0). The so-called exposure grouping, which was based on factors affecting exposure, yielded comparable contrast (ϵ 0.22), but with only three groups this grouping scheme produced more precise estimates of average exposure (8.3 versus 3.0). Surprisingly, the standard ISCO-ILO classification performed better than both a straightforward occupational title group classification and a classification of jobs used by Goldsmith (1980) (ϵ 0.13 vs ϵ 0.07 and ϵ 0.09, respectively). Grouping workers based on plants they work in appeared not to be meaningful in terms of exposure to particulates.

For dermal exposure, preference was given to exposure grouping based on factors affecting exposure. This grouping yielded the most contrast (ϵ 0.34) and the highest precision (π 8.3). Using OTG and plant resulted in nearly the same contrast (ϵ 0.31) , but again a loss of precision resulted from a larger number of groups. Grouping by OTG solely led to reasonable results as did grouping workers by augmented ISCO-ILO code. Both had higher precision than grouping by combination of OTG and plant, but somewhat lower contrast. Grouping either by plant or by standard ISCO-ILO code did not lead to an effective classification of worker's dermal exposure (ϵ 0.01 and ϵ 0.03, respectively).

From Table 3 it follows that differences in solvent exposure among workers can be very large within the complete population (${}_{BG}\hat{R}_{.95}$ 785). Table 4 shows once again that grouping rubber workers by combination of OTG and plant yielded the largest differences in average exposure between exposure groups, but, in contrast with the other two types of exposure, also resulted in a relatively high precision (π 2.9). Grouping only by OTG or plant still led to relatively large differences in mean exposure (${}_{BG}\hat{R}_{.95}$ 252 and 239, respectively). Between-group exposure variability was substantially greater than within-group exposure variability for all grouping schemes except the standard ISCO-ILO code. This indicates that overlap in exposure distributions between groups is smaller than differences in mean exposure between the groups. The grouping scheme used by McMichael (1975) was meaningful to classify workers in groups with different levels of solvent exposure.

DISCUSSION AND CONCLUSIONS

Exposure assessment strategies for epidemiologic research are almost always based on grouping workers into exposure categories. This strategy is essential where assessment of an individual study subject's exposure is not feasible, for instance because of logistic or financial reasons. Assessing a group's exposure is based on the assumption that workers share common occupational experiences. Within an occupational cohort, workers can belong to the same job group, environment, or plant within the same time frame. Thus, it is generally assumed that the assessed exposure level of a sample of workers can be assigned to each member of the group (including the unmeasured workers). The OTG concept has been extensively used for assigning exposures in studies in the rubber industry. Another example is the job-exposure matrix, which, in its simplest, form attributes the same exposure estimate to each individual with the same job title. More elaborate matrices take time period and plant into consideration, but will still attribute the same exposure estimate to all workers within a particular cell of a matrix (Goldberg *et al.* 1993).

Given the necessity of using grouping methods, it is essential to know what the efficiency of a grouping scheme will be in terms of resolution in exposure level. Only then, can alternative approaches be compared and the level of success be quantified. This was the rationale behind the present study. Exposure information from an industry-wide survey of the rubber industry enabled testing of different grouping schemes. Some of them were quite obvious and reflect common practice (e.g. OTG, plant, isco-ilo code), others were borrowed from past epidemiologic studies. Next to these, the efficiency of grouping schemes based on factors affecting exposure (actual performed tasks, control measures, ventilation characteristics) were evaluated as well. These factors had been identified in a previous study of the same industry (Kromhout *et al.* 1993).

Parameters based on ideas presented by Praise and Aitchinson (1954) were developed to compare different grouping schemes. Therefore an extension of the one-way random effects model, which has been used by several authors in the past to estimate within- and between worker exposure variability, was used (Brunekreef *et al.* 1986, Kromhout *et al.* 1987, Rappaport 1991, Heederik *et al.* 1991a). The two-way nested random effects model assumes random effects for group, worker, and days. In the case of workers and days this seems to be justified, because they were randomly chosen. The choice of a random grouping effect is more debatable but finds support in the notion that there exists, at least in principle, an infinite number of possible grouping schemes. The model also assumes homogeneity of the between-worker and within-worker component of variance across groups, but from Table 3 it is clear that these variance components did vary to some extent across production functions and plants.

Two grouping parameters were designed to optimize the groups, i.e., contrast and precision. Contrast is important to end up with workers with different exposures and these estimates should be precise to prevent non-differential bias of the exposure-response relationship towards the null. Some authors (e.g. Seixas *et al.* 1988) have argued that whatever the grouping scheme, the relationship between exposure and response is unbiased and refer to a special case of Berkson type error as described by Durbin (1954). This case of Berkson type error deals with grouping of data in a fixed rank order. Grouping in that case has an *a posteriori* character and deals with the actual classification of observed concentrations. However, groupings based on *a priori* determined factors like OTG, plant, tasks, etc., which deal only indirectly with observed concentrations, can still lead to non-differential misclassification of workers, and consequently to a negative bias of the true exposure response relationship. Also, the estimated exposure response relationship will be less precise.

From the results it is clear that variability of exposure in the rubber industry can be considerable, especially for exposure to solvents. Furthermore, it seems that grouping of workers exposed to solvents can be much more efficient than those exposed either to particulates or to cyclohexane-soluble contaminants which are absorbed through the skin. Although within-group variability for exposure to solvents is smaller than between-group variability under most grouping schemes, in absolute terms it is still higher than the within-group variance components associated with particulate and dermal exposures. Nevertheless, between-group differences are large enough to make an epidemiologic evaluation of risks associated with exposure to solvents meaningful. This may not be the case regarding particulate and dermal exposure when classified by standard grouping schemes (OTG, plant, OTG within a plant, ISCO-ILO). The character of the exposure variability in the latter two cases suggests that a more detailed grouping scheme based on real factors affecting exposure or an actual prospective exposure assessment strategy based on estimated variance components.

The case of solvent exposure in the rubber industry shows that exposure-response relationships can be found even when the groups have large within-group variances as long as the differences among groups are even larger than the within-group variances. Therefore, a strict definition of a uniformly exposed group is not a prerequisite for identifying a relationship between an exposure and a health outcome (Rappaport, 1991, Heederik *et al.* 1991b), but it will be helpful to be able to estimate the relationship more precise.

Only one other study has reported ratios of between-group and within-group variances. Heederik *et al.* (1991a) mentioned a ratio of within-group to between-group variance (λ) of 1.24 and 0.97 for exposure to dust and endotoxin, respectively, in the animal feed industry. Recalculating these ratios yielded an elasticity (ϵ) of 0.44 and 0.51, respectively. These figures are much higher than elasticity ratios presented here for grouping of exposure to particulates and dermal exposure by OTGs in the rubber industry. For grouping of exposure to solvents by OTGs, however, the elasticity ratio is somewhat higher (ϵ 0.59) in the present study. Therefore, classification of workers' exposure to dust and endotoxin in the animal feed industry is more effective, based on job or occupational title, than classification of workers' exposure to particulates and dermal contaminants in the rubber industry, but is less effective than for workers exposure to solvents in this industry. Precision, which is highly dependent on the number of measurements taken, was not taken into account in this comparison.

The ability to detect exposure-response relationships in studies using a grouping strategy depends upon both the contrast or resolution in average exposure and the precision of average exposures. Lack of precision and lack of contrast will both diminish the likelihood of detecting exposure-response relationships. Both aspects are closely related. Grouping strategies resulting in uniformly exposed workers in groups with different mean exposures will show good contrast and good precision. On the contrary, non-efficient strategies leading to non-uniformly exposed workers in groups with overlapping exposure distributions will result in poor contrast and precision. However, precision can always be optimized by increasing the number of observations, whereas contrast can only be improved by better classification of workers. There is an obvious need for more research to determine the influence of both contrast and precision on the evaluation of exposure-response relationships.

Finally, anyone considering an epidemiologic study in the rubber industry should realize that this paper focused entirely on the quantitative aspects of occupational exposures in the rubber industry. The qualitative aspects of these exposures are also variable, because the chemicals used and intermediates produced during the processes are multitudinous and are changing over time. It is, however, not intended to discourage future epidemiologic studies in this branch of industry. Past studies, which were based on only (imprecise) proxy measures of exposures, have led to the situation in which the whole industry was put on the list of proven human carcinogens. Since abolishment of this industry can not be anyone's goal, development and application of better exposure assessment methods in new epidemiologic studies are urgently needed if we are to solve the problem of cancer in the rubber industry.

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APPENDIX

Table A1. ISCO-ILO codes rubber industry

code	description
90120	rubber millman
90125	rubber calender operator
90130	rubber extruding-machine operator
90135	rubber moulding-press operator
90140	rubber goods assembler
90190	other rubber and plastics products makers (except tire makers and tire vulcanisers)

Table A2. Occupational title groups in Dutch study

otg*	description	isco-ilo
1	compounding/mixing	90120
2	moulding	90125, 90130, 90140
3	pre-treating	90190
4	curing	90135
5	finishing	90190
7	engineering services	90190
9	shipping	90190

* otg 6 "raw materials handling" was included in otg 1 "compounding/mixing; otg 8 "laboratory worker" was excluded for this analysis, because of the small number of observations

Table A3. Augmented isco-ilo codes for exposure to particulates

otg code	isco-ilo code	augmented code	factors affecting exposure
1	90120	901203	weighing, open mill, internal mill, cleaning, transport
		901202	other
2	90125 or 90130 or 90140	901503	jointing, heating mill, cleaning, transport
		901502	other
		901501	calendering, extruding/slicing, manual assembling, assembling machine, braiding machine, lead extrusion
3	90190	901933	repair buffing, cleaning, transport
		901932	other
4	90135	901353	autoclave-lev (powdering), cleaning, transport
		901352	other
		901351	uhf curing
5	90190	901953	punching powdered products, tube inspection, cleaning, transport
		901952	other
		901951	general trimming, rubber cutting, unrolling, weighing products
7	90190	901973	bench fitting, cleaning, transport
		901972	other
		901971	breakdown work
9	90190	901993	packing powdered products, general packing, cleaning, transport
		901992	other
		901991	loading/unloading

Table A4. Augmented isco-ilo codes for dermal exposure to cyclohexane-soluble contaminants

otg code	isco-ilo code	augmented code	factors affecting exposure
1	90120	901203	refiner, oil weighing, open mill, weighing
		901202	other
		901201	granulating, supervisor
2	90125 or 90130 or 90140	901503	extruding
		901502	other
		901501	supervisor
3	90190	901932	other
		901931	supervisor
4	90135	901353	paint spray cabin, tire press, wrapping profiles
		901352	other
		901351	injection moulding, inspecting, supervisor
5	90190	901953	grinding bench
		901952	other
		901951	general trimming, supervisor
7	90190	901973	lubricating without gloves, breakdown work, bench fitting
		901972	other
		901971	supervisor
9	90190	901992	other
		901991	supervisor

* *no supervisor in the engineering services was measured*

Table A5. Augmented isco-ilo codes for exposure to total solvents

otg code	isco-ilo code	augmented code	factors affecting exposure
2	90130 or 90140	901503	extruding, jointing
		901502	other
3	90190	901933	cementing with brush, degreasing, cement spraying
		901932	other
4	90135	901352	all
5	90190	901953	polishing/grinding, rubber cutting, grinding bench
		901952	other
7	90190	901972	all

Chapter 7

A comprehensive evaluation of within- and between-worker components of occupational exposure to chemical agents[1]

[1] H. Kromhout, E. Symanski, and S.M. Rappaport, *The Annals of occupational Hygiene* **37** (1993) 253-270.

ABSTRACT

A database of approximately 20,000 chemical exposures has been constructed in close co-operation between the School of Public Health of the University of North Carolina at Chapel Hill and the Department of Air Pollution of the Wageningen Agricultural University. A special feature of this database is that only multiple measurements of exposure from the same workers were included. This enabled estimation of within- and between-worker variance components of occupational exposure to chemical agents throughout industry.

Most of the groups were not uniformly exposed as is generally assumed by occupational hygienists. In fact only 42 out of a total of 165 groups (25%), based on job title and factory, had 95% of individual mean exposures within a two-fold range. On the contrary, about 30% of the groups had 95% of individual mean exposures in a range which was greater than 10-fold.

Environmental and production factors were shown to have distinct influences on the within-worker (day-to-day) variability, but not on the between-worker variability. Groups working outdoors and those working without local exhaust ventilation showed more day-to-day variability than groups working indoors and those working with local exhaust ventilation. Groups consisting of mobile workers, those working with an intermittent process and those where the source of contamination was either local or mobile also showed great day-to-day variability. In a multivariate regression model, environment (indoors-outdoors) and type of process (continuous-intermittent) explained 41% of the variability in the within-worker component of variance. Another model, in which only type of process (continuous-intermittent) had a significant effect, explained only 13% of the variability in the between-worker component of variance.

INTRODUCTION

The importance of the within- and between-worker components of variability in occupational exposure has only been recognized recently (Kromhout *et al.*, 1987, Spear *et al.*, 1987, Rappaport *et al.*, 1988). In reviews of methods for assessing exposure Rappaport (1991a,b) summarized the variance components of occupational exposures in 31 groups of workers from nine types of facilities. Although these summaries suggested that both components of variance can be large, the database was too small to allow the results to be generalized. In order to overcome this problem a much larger database consisting of about 20,000 chemical exposures obtained from over 500 groups of workers in a variety of industries was developed. Since the exposures of all workers were measured by personal sampling on at least two occasions we were able to estimate the within- and between-worker components of variance. In this paper we will describe the database, summarize the variance components, and report on factors which contributed significantly to the variances including, type of exposure, type of industry, group size, type of measurement strategy, and production and environmental characteristics.

MATERIALS AND METHODS

The database consists of 83 sets of personal exposure data collected in 45 studies. The majority of the studies (58%) were performed either by or under the supervision of the authors. Some of the data were provided by other researchers (24%) and by industry (9%) and a few sets were extracted from the literature (9%) (Lindstedt *et al.*, 1979; Cope *et al.*, 1979; Goller and Paik, 1985; Hansen and Whitehead, 1988). Results of half of the studies have been reported in the open literature (Lindstedt *et al.*, 1979; Cope *et al.*, 1979; Goller and Paik, 1985; Kromhout *et al.*, 1987; Spear *et al.*, 1987; Hansen and Whitehead, 1988; Hollander *et al.*, 1988; Bos *et al.*, 1989; Marquart *et al.*, 1989; Buringh *et al.*, 1990; Kateman *et al.*,

Table 1. Information in the database

Variable	Description
Set	Unique number
Origin	Research group
Country	Country of origin
Factory	Unique number
Industry	Description of industry
Industry code	International Standard Industrial Classification (ISIC)
Job	Description of job
Jobcode	Original coding of jobs
Class	Original classification of jobs (*a priori*)
Occupation	International Standard Classification of Occupations (ISCO)
Date	Date of measurement
Worker	Unique identity number
Type	Type of exposure (agent)
Exposure type	Physical appearance
Concentration	Measured concentration
Detection limit	Below (=0) or at or above (=1) detection limit
Unity	Unity of measurement (e.g. mg/m^3)
Sampling time	Duration of measurement
Sample of workers	Non-random (=0); random (=1); volunteers (=2); everybody (=3)
Sample of days	Non-random (=0); random (=1); fixed days (=2); all days (=3)
Environment	Outdoors (=0); indoors (=1) (most of the time)
Local exhaust ventilation	Not present (=0); present (=1)
Process	Intermittent (=0); continuous (=1)
Mobility of worker	Stationary (=0); mobile (=1)
Mobility of source	Stationary (=0); mobile (=1)
Source	Local (=0); general (=1)

1990; Galvin *et al.*, 1990; Waters *et al.*, 1991; Geuskens *et al.*, 1992; Petreas *et al.*, 1992; Smid *et al.*, 1992; Yager *et al.*, 1992, Kromhout *et al.*, 1993). The data within the database were collected over the years 1974-1989. Two of the authors (E. Symanski and H. Kromhout) elaborated the database, which comprises the variables listed in Table 1. Coding of the production and environmental factors was often done by consulting the original investigators. However, complete information on all variables was available for only about half of the groups. Workers were grouped by job title and by factory (location). The variance components were estimated for each group, having at least five workers with at least two measurements per worker. Thus, at least 10 measurements were required for each group. Measurements with an averaging time less than 4 h were excluded. Groups with more than 25% of their observations below the detection limit were also excluded.

The analysis-of-variance (ANOVA) methods, which were used to estimate the components of variance, are described extensively elsewhere (Rappaport *et al.*, in preparation). The fit of the ANOVA model to each group was evaluated with *ad hoc* procedures, based upon statistical methods to detect influential observations (Christensen *et al.*, 1992) and to test the normality of the between-worker exposure distribution of log-transformed exposures (Lange and Ryan, 1989). Details of our applications of these procedures are also described elsewhere (Rappaport *et al.*, in preparation). Two of the authors (H. Kromhout and S.M. Rappaport) independently judged the goodness of fit of the ANOVA model for each of the groups and excluded either a worker or an individual measurement after consensus was reached.

The database exists as a SAS (SAS Institute, Cary, North Carolina, U.S.A.) data file which was created with DBMSCOPY (Conceptual Software, Inc., Houston, Texas, U.S.A.) out of several individual files created by Lotus-123 (Lotus Development Corporation, Cambridge, Massachusetts, U.S.A.), Excel (Microsoft Corporation, Redmond, Washington, U.S.A.), or SPSS-PC (SPSS, Inc., Chicago, Illinois, U.S.A.). Variance components were estimated from the log-transformed exposure concentrations employing the random-effects ANOVA model from Proc NESTED and the goodness of fit plots were made with Proc GPLOT and Proc GREPLAY using SAS System Software PC Version 6.04. The random-effects ANOVA model is specified by the following expression,

$$Y_{ij} = \ln(X_{ij}) = \mu_y + \beta_i + \epsilon_{ij}, \text{ for } (i=1,2, ...,k) \text{ and } (j=1,2, ...,n_i)$$

where

X_{ij} = the exposure concentration of the i-th worker on the j-th day,
μ_y = mean of Y_{ij},
β_i = the random deviation of the i-th worker's true exposure $\mu_{y,i}$ from μ_y, and
ϵ_{ij} = the random deviation of the i-th worker's exposure on the j-th day from his or her true exposure, $\mu_{y,i}$.

It is assumed under the model that both β_i and ϵ_{ij} are normally distributed; i.e., $\beta_i \sim N(0, \sigma_B^2)$, and $\epsilon_{ij} \sim N(0, \sigma_W^2)$. The underlying distribution of exposures (X_{ij}) is assumed to be log-normal. Also, β_i and ϵ_{ij}, are assumed to be statistically independent of each other. Thus, the parameters σ_B^2 and σ_W^2 are referred to as the components of the total variance $\sigma_T^2 = \sigma_B^2 + \sigma_W^2$, and $Y_{ij} \sim N(\mu_y, \sigma_T^2)$. The estimates of σ_T^2, σ_W^2 and σ_B^2 will be designated as ${}_TS_y^2$, ${}_WS_y^2$ and ${}_BS_y^2$, respectively. From the variance components the standard deviations were estimated for the total (${}_TS_y$), within-worker (${}_WS_y$) and between-worker distributions (${}_BS_y$). These standard deviations were used to estimate the corresponding geometric standard deviations [${}_TS_g = \exp({}_TS_y)$, ${}_BS_g = \exp({}_BS_y)$ and ${}_WS_g = \exp({}_WS_y)$] and the ratios of the 97.5th and 2.5th percentiles of the log-normally distributed exposures of each group of workers (Rappaport, 1991a, b). These ratios, designated as ${}_B\hat{R}_{0.95} = \exp(3.92\ {}_BS_y)$ and ${}_W\hat{R}_{0.95} = \exp(3.92\ {}_WS_y)$ provide information regarding the ranges of exposures experienced between workers and within workers, from day to day, respectively. The distributions of the within- and between-worker variance components were evaluated independently for several variables, including number of workers and measurements per group, type of measurement strategy, and production and environmental characteristics. Wilcoxon's rank sum test (Snedecor and Cochran, 1980) was used to test the significance of shifts of location in the distributions of total-, within- and between-worker variance components (Proc NPAR1WAY, SAS PC Version 6.04). Finally, a multivariate regression model (Proc GLM) was built to identify factors which contributed significantly to these variance components.

RESULTS

General characteristics of the database

In Table 2 the basic characteristics of the database are presented. Within the 45 studies 83 sets of measurements were collected from more than 3,200 workers yielding almost 20,000 observations. The total number of groups based on job title and factory (location) was 522. The data originated mainly from The Netherlands

Table 2. Basic characteristics of the database

Number of studies:	45
Number of measurement series:	83
Number of groups:	522
Number of workers:	3243
Number of observations:	19845

Country	No. of measurements	No. of groups
The Netherlands	7601 (38%)	455 (87%)
U.K.	7523 (38%)	5 (1%)
U.S.A.	4021 (20%)	59 (11%)
Sweden	592 (3%)	1 (0%)
P.R. China	108 (<1%)	2 (2%)

ISIC	Industry	No. of measurements	No. of groups
35	Chemical	15028 (76%)	181 (35%)
351	*Industrial chemicals*	9409 (47%)	27 (5%)
352	Other chemicals	243 (1%)	21 (4%)
353	Refineries	2797 (14%)	22 (4%)
355	Rubber products	1962 (10%)	76 (15%)
356	Plastic products	617 (3%)	35 (7%)
31	Food	2014 (10%)	141 (27%)
38	Metal manufacturing	1266 (6%)	72 (14%)
37	Basic metal	510 (3%)	5 (1%)
32	Textile manufacturing	263 (1%)	32 (6%)
36	Brick manufacturing	243 (1%)	27 (5%)
71	Transport	227 (1%)	27 (5%)
95	Dry cleaning	171 (1%)	27 (5%)
34	Printing	115 (1%)	6 (1%)
11	Agriculture	8 (0%)	4 (1%)

(38%), the U.K. (38%) and the United States (20%). The majority of the groups were of Dutch origin (87%). The data sets from the U.K. and the United States were generally much larger in terms of either workers in a group or measurements per worker. It is also clear from Table 2 that the majority of the data (76%) originated from several sectors in the chemical industry. The majority of the groups was also from the chemical industry (35%), but considerable numbers of groups were from the food (27%) and metal manufacturing industries (14%).

The chemical agents are listed in Table 3. Over two-thirds (68%) of the measure-

Table 3. Agents present in the database

Agent	No. of observations	%
Gaseous	13423	67.6
Alkyl lead	176	0.9
Benzene	2409	12.1
Diphenyl	121	0.6
Diphenylether	195	1.0
Ethanal	43	0.2
Formaldehyde	131	0.7
Heptane	29	0.1
Hexane	29	0.1
Hydrogen fluoride	36	0.2
Mercury inorganic	592	3.0
Nitrogendioxide	137	0.7
Octane	37	0.2
Organic vapour	7523	37.9
Perchloroethylene	216	1.1
Styrene	617	3.1
Sulfur dioxide	36	0.2
Toluene	638	3.2
Total solvents	188	0.9
Trichloroethane	87	0.4
Trichloroethylene	55	0.3
Xylene	128	0.6
Gaseous and particulate	34	0.2
Total fluoride	34	0.2
Particulate	5519	27.8
Chromium inspirable	80	0.4
Copper inspirable	80	0.4
Copper respirable	110	0.6
Dust inspirable	2936	14.8
Dust respirable	276	1.4
Dust total	55	0.3
Endotoxin inspirable	669	3.4
Fluoride dust	36	0.2
Iron inspirable	80	0.4
Lead inorganic	177	0.9
Lead inspirable	79	0.4
Lead respirable	110	0.6
Nicotine inspirable	189	1.0
Quartz respirable	93	0.5
Welding fume inspirable	156	0.8
Zinc inspirable	283	1.4
Zinc respirable	110	0.6
Dermal	869	4.4
Pyrazofos	8	0.0
Cyclohexane soluble fractions	861	4.3

ments involved gases and vapours and about one-third (28%) involved particulate matter. Dermal exposures, measured with so-called pads carried on the lower parts of the wrists in two studies in the rubber industry, comprised only a very small part of the database (4%) (Bos *et al.*, 1989, Kromhout *et al.*, 1993).

Exposure groups and variance components

Grouping the workers by job title and factory and excluding groups, workers and individual observations based on the criteria mentioned earlier left 165 groups with 1574 workers and 13945 measurements. In Fig. 1 the distributions of the within- and between-worker values of $\hat{R}_{0.95}$ are shown for these 165 groups. Only 42 groups (25%) had 95% of the individual mean exposures lying within a factor 2 (${}_{B}\hat{R}_{0.95} \leq 2$). Almost 30% of the groups had values of ${}_{B}\hat{R}_{0.95} > 10$ and 10% of the groups had ${}_{B}\hat{R}_{0.95} > 50$. The day-to-day variability was generally larger than the between-worker variability, indicating larger differences in exposures between work shifts than between workers with the same job title and factory. The median values for the total, within- and between-worker geometric standard deviations were respectively, 2.41, 2.00 and 1.43.

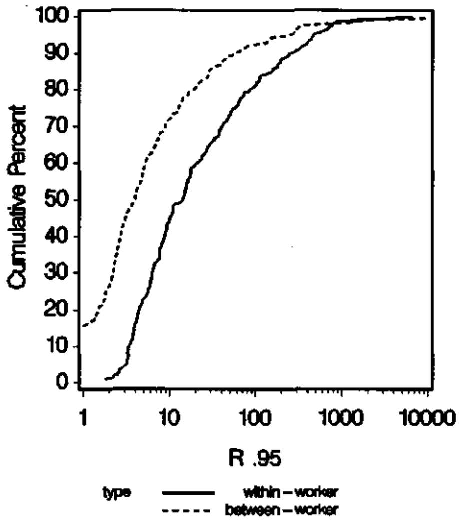

Fig. 1. Cumulative distributions of ${}_{W}\hat{R}_{0.95}$ (solid line) and ${}_{B}\hat{R}_{0.95}$ (dashed line) for all 165 groups of workers based on job title and factory.

Influence of group size and number of observations

In Figs 2(a)-(d) the influence of the number of measurements and workers on the distributions of the within- and between-worker values of $\hat{R}_{0.95}$ is shown. The influence of both the number of measurements and the number of workers in a group on ${}_B\hat{R}_{0.95}$ is negligible [Figs 2(a) and (b)]. However, the influence of sample size on ${}_W\hat{R}_{0.95}$ is significantly higher ($P<0.05$, Wilcoxon rank sum test) for the groups with more measurements (more than 25) and more workers (more than seven) [Figs 2(c) and (d)]. The increase in ${}_W\hat{R}_{0.95}$ with number of measurements may reflect a longer period of observation, which in some cases extended over several years. The increase in ${}_W\hat{R}_{0.95}$ with the number of workers on the other hand, may point to larger underlying populations and workplaces. However, given the many combinations of coded variables which comprise the database such conjectures are difficult to confirm.

Influence of type of industry and exposure

The results of subdividing the 165 groups by industry and type of chemical agent are summarized in Table 4. Breaking the 165 groups down by type of chemical agent revealed no differences in the variance components (median ${}_WS_g$ 2.05 and 1.97, median ${}_BS_g$ 1.34 and 1.44, respectively, for gases and vapours and particulate exposures). The 23 groups with dermal exposures had a median ${}_WS_g$ of 2.07 and a median ${}_BS_g$ of 1.76. The latter was significantly higher than what was seen for gases and vapours ($P<0.05$, Wilcoxon rank sum test).

Dividing the groups by type of industry showed a significantly lower ${}_BS_g$ ($P<0.05$, Wilcoxon rank sum test) for the non-chemical industry (median ${}_BS_g$ 1.30 vs 1.49) but indicated no difference for the ${}_WS_g$ (median ${}_WS_g$ 2.05 vs 1.99). Subdividing the groups by type of chemical agent and industry, showed significantly higher ${}_WS_g$ and ${}_BS_g$ distributions for gaseous exposures in the chemical industry (respectively $P<0.001$ and $P<0.01$). The ${}_BS_g$ distribution was also significantly higher for particulate exposure in the chemical industry ($P<0.01$), while the ${}_WS_g$ distribution was not significantly different from that observed in the non-chemical industry.

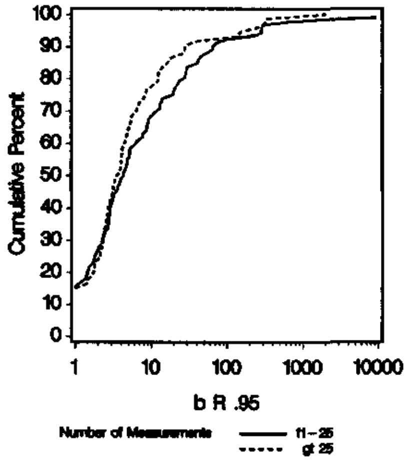

Fig. 2. (a) Cumulative distributions of ${}_B\hat{R}_{0.95}$ for 92 groups with 11-25 measurements (solid line) and 73 groups with more than 25 measurements (dashed line).

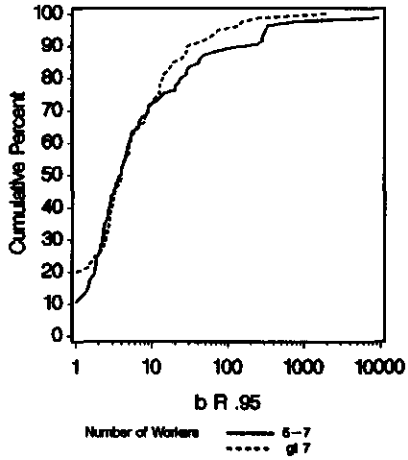

Fig. 2. (b) Cumulative distributions of ${}_B\hat{R}_{0.95}$ for 85 groups with five to seven workers (solid line) and 80 groups with more than seven workers (dashed line).

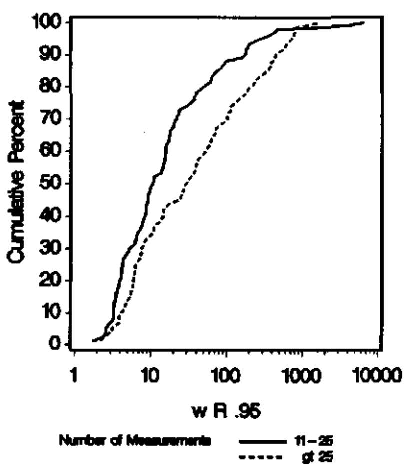

Fig. 2. (c) Cumulative distributions of ${}_W\hat{R}_{0.95}$ for 92 groups with 11-25 measurements (solid line) and 73 groups with more than 25 measurements (dashed line).

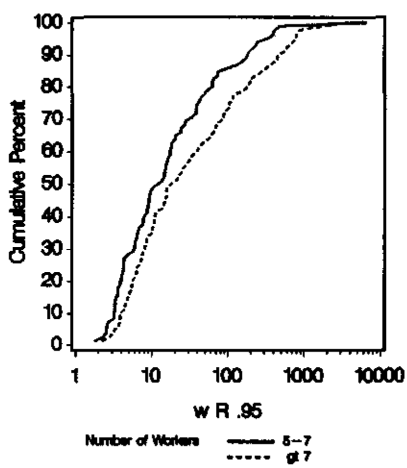

Fig. 2. (d) Cumulative distributions of ${}_W\hat{R}_{0.95}$ for 85 groups with five to seven workers (solid line) and 80 groups with more than seven workers (dashed line).

Table 4. Median of total, within- and between-worker geometric standard deviations by type of industry and type of chemical agent (Number of groups in parentheses)

	total chemical (96)	total non-chemical (69)	total gases-vapours (60)	chemical gases-vapours (50)	non-chemical gases-vapours (10)	total particulate (81)	chemical particulate (23)	non-chemical particulate (58)	total dermal (23)
k	8	6	9.5	10	6	6	6	6.5	7
N	27	22	46	55.5	18	22	18	23.5	19
${}_{T}S_{g}$	2.47	2.23	2.29	2.65	1.43	2.34	2.08	2.56	2.56
${}_{W}S_{g}$	2.05	1.99	2.05	2.48	1.36	1.97	1.67	2.05	2.07
${}_{B}S_{g}$	1.49	1.30	1.34	1.43	1.17	1.44	1.59	1.35	1.76

k, number of workers.
N, number of measurements.
${}_{T}S_{g}$, estimated geometric standard deviation of the total distribution.
${}_{W}S_{g}$, estimated geometric standard deviation of the within-worker distribution.
${}_{B}S_{g}$, estimated geometric standard deviation of the between-worker distribution.

Influence of measurement strategy

The influence of measurement strategy on the distributions of the within- and between-worker variability is depicted in Fig. 3. Groups with non-randomly chosen workers (67 groups) and groups measured on non-randomly chosen days (112 groups) had significantly lower between-worker variability [median ${}_{B}S_{g}$ 1.33 vs 1.56 (P<0.01, Wilcoxon rank sum test) and 1.36 vs 1.75 (P<0.01, Wilcoxon rank sum test), respectively]. Groups measured on non-randomly chosen days had, however, significantly higher day-to-day variability than groups measured on randomly chosen days (median ${}_{W}S_{g}$ 2.12 vs 1.75, P<0.01, Wilcoxon rank sum test). The difference for groups consisting of non-randomly chosen workers was in the same direction, but not statistically significant (median ${}_{W}S_{g}$ 2.02 vs 1.94). No significant differences were seen for the total variability (median ${}_{T}S_{g}$ 2.20 vs 2.32 for non-random and random workers and 2.27 vs 2.26 for non-random and random days).

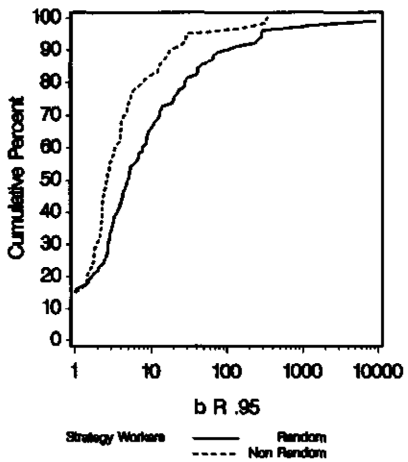

Fig. 3. (a) Cumulative distributions of $_B\hat{R}_{0.95}$ for 116 groups comprised of randomly chosen workers (solid line) and 67 groups comprised of non-randomly-chosen workers (dashed line).

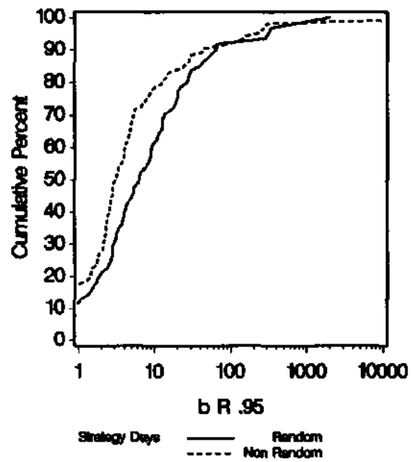

Fig. 3. (b) Cumulative distributions of $_B\hat{R}_{0.95}$ for 71 groups measured on randomly chosen days (solid line) and 112 groups measured on non-randomly-chosen days (dashed line).

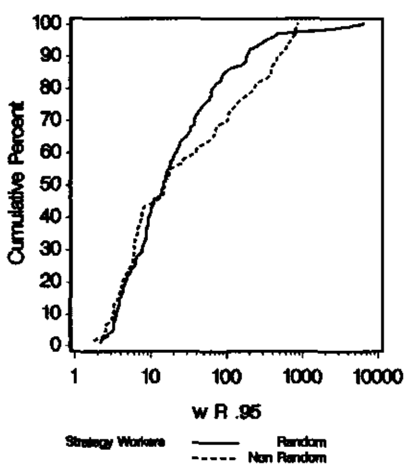

Fig. 3. (c) Cumulative distributions of $_W\hat{R}_{0.95}$ for 116 groups comprised of randomly chosen workers (solid line) and 67 groups comprised of non-randomly-chosen workers (dashed line).

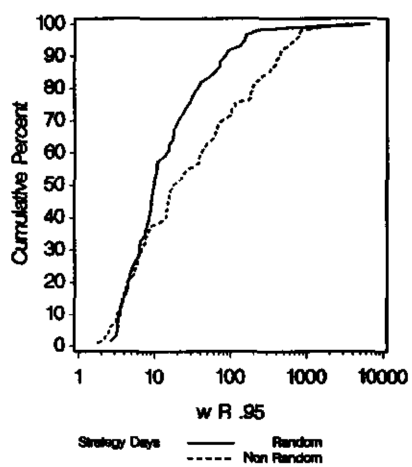

Fig. 3. (d) Cumulative distributions of $_W\hat{R}_{0.95}$ for 71 groups measured on randomly chosen days (solid line) and 112 groups measured on non-randomly-chosen days (dashed line).

Table 5. Median of total, within- and between-worker geometric standard deviation by environmental factors (Number of groups in parentheses)

	total (87)	indoors (62)	outdoors (25)	local exhaust ventilation (24)	no local exhaust ventilation (63)
k	8	8	15	9	8
N	29	24	74	36	29
$_TS_g$	2.28	1.87	3.46***	1.69	2.71***
$_WS_g$	2.07	1.73	3.27***	1.57	2.53***
$_BS_g$	1.30	1.25	1.43**	1.17	1.39**

k, number of workers.
N, number of measurements.
$_TS_g$, estimated geometric standard deviation of the total distribution.
$_WS_g$, estimated geometric standard deviation of the within-worker distribution.
$_BS_g$, estimated geometric standard deviation of the between-worker distribution.

** $P<0.01$.
*** $P<0.001$.

Influence of environmental and production factors

In Table 5 the results are summarized for the environmental factors "indoor-outdoor work" and "presence of local exhaust ventilation", on the estimated variance components. Groups in which the work was outdoors had significantly higher exposure variability ($P<0.001$), particularly for the within-worker component ($P<0.001$). Similarly, groups working in situations without local exhaust ventilation had significantly higher exposure variability ($P<0.001$), again, primarily due to the within-worker component ($P<0.001$).

The effect of production variables is given in Table 6. Groups with an intermittent process, or with mobile workers, or with a local source tended to have significantly higher day-to-day variability ($P<0.001$ for "process" and "worker mobility", $P<0.01$ for "type of source") and between-worker variability ($P<0.001$ for "process", $P<0.05$ for "worker mobility" and "type of source"). The differences for the factor "source mobility" were not statistically significant, but was again in the *a priori* assumed direction.

Table 6. Median of total, within- and between-worker geometric standard deviation by production factors (Number of groups in parentheses)

	total (87)	continuous process (43)	intermittent process (44)	mobile worker (54)	stationary worker (33)	general source (25)	local source (62)	mobile source (52)	stationary source (35)
k	8	7	10	10	7	6	9	13	8
N	29	24	48	41.5	22	24	29	50	24
$_TS_g$	2.28	1.70	3.62***	3.07	1.73***	1.76	2.79**	2.50	2.05ns
$_WS_g$	2.07	1.60	3.19***	2.72	1.60***	1.68	2.54**	2.37	1.84ns
$_BS_g$	1.30	1.23	1.46***	1.41	1.24*	1.23	1.35*	1.34	1.26ns

k, number of workers.
N, number of measurements.
$_TS_g$, estimated geometric standard deviation of the total distribution.
$_WS_g$, estimated geometric standard deviation of the within-worker distribution.
$_BS_g$, estimated geometric standard deviation of the between-worker distribution.

* $P<0.05$.
** $P<0.01$.
*** $P<0.001$.
ns not significant.

Multivariate analyses

The results of the multivariate analysis are given in Table 7. A model with environment and process as independent variables explained 41% of the day-to-day variance component. Other process-, environmental- and measurement strategy-related variables did not contribute significantly. This model predicts the largest within-worker geometric standard deviation for groups of workers working outdoors and with an intermittent process ($_WS_g$=3.54). The smallest within-worker component of variability can be expected for groups of workers working indoors and exposed in a continuous process ($_WS_g$=1.76).

For the between-worker variance component process was the only significant factor in the model. The model predicted that groups of workers exposed in a continuous process had lower between-worker variability ($_BS_g$=1.26), while those exposed in an intermittent process had greater between-worker variability ($_BS_g$=1.76). However, this model explained only 13% of the variability of the between-worker variance component and the fit was very poor. Thus, it can be

Table 7. Multivariate models and predictions of within- and between-worker variability

Within-worker variability					
Source	DF	SS	MS	*F* Value	*P*
Model	2	56.10	28.05	29.39	0.0001
Error	83	79.21	0.95		
R-squared	0.41				
Situation				Estimate ($_wS_g$)	SEE
Indoors & continuous process				1.76	0.15
Indoors & intermittent process				3.13	0.22
Outdoors & intermittent process				3.54	0.20
Between-worker variability					
Source	DF	SS	MS	*F* Value	*P*
Model	1	5.40	5.40	12.92	0.0005
Error	84	35.53	0.42		
R-squared	0.13				
Situation				Estimate ($_BS_g$)	SEE
Continuous process				1.26	0.10
Intermittent process				1.76	0.10

DF, degrees of freedom.
SS, sum of squares.
MS, mean squares.
F value, value of *F* test.
P, significance.
R-squared, explained variability.
SEE, standard error of estimate.

concluded that the variables coded in the database only marginally affected the between-worker variance component.

DISCUSSION

The database described in this paper provides a comprehensive overview of within- and between-worker components of occupational exposure to chemical agents throughout industry. The median value of the geometric standard deviation ($_TS_g$) of

165 groups based on job title and factory was 2.41 (gases and vapours: ${}_{T}S_{g}$=2.29; particulate matter: ${}_{T}S_{g}$=2.34). Leidel *et al.* (1975) reported much lower median values of ${}_{T}S_{g}$ of 1.55 and 1.65 for gases and vapours and particulate matter, respectively. It is unlikely that the variability of occupational exposures has increased dramatically over the last two decades. Rather, we suspect that the small database of Leidel *et al.* (1975) was comprised of more homogeneous exposure situations or industries. Our findings are more consistent with those reported by Buringh and Lanting (1991), where 2.02 $\leq$ mean ${}_{W}S_{g}$ $\leq$ 2.41 depending on the number of measurements. Our mean value of ${}_{W}S_{g}$ for 165 groups of workers was only slightly higher: 2.47.

In the chemical industry the between-worker variability was significantly higher than in the non-chemical industry (median ${}_{B}S_{g}$ 1.49 vs 1.30). This feature was seen both for aerosols and gases and vapours. The day-to-day variability was more ambiguous with higher day-to-day variability observed for gases and vapours (median ${}_{W}S_{g}$ 2.48 vs 1.36) than for aerosols (median ${}_{W}S_{g}$ 1.67 vs 2.05). However, since the number of measurements and workers in the groups from the chemical industry was by far the highest for exposure to gases and vapours, the apparent comparison might be confounded.

The notion expressed by Roach (1991), that exposures tend to vary more with aerosols (dust, fumes and mists) than with gases and vapours, was not corroborated within this database. However, the small number of dermal exposures within the database showed a larger total variability (median ${}_{T}S_{g}$=2.56) suggesting that dermal exposure is more influenced by personal behaviour than is exposure to air contaminants. However, this finding should be interpreted with caution, because the number of groups with measured dermal exposures was very small (23) and all those groups stemmed from a single industry (rubber manufacturing).

The between-worker component of variability was shown to be smaller than the within-worker component (median ${}_{B}S_{g}$=1.43 vs median ${}_{W}S_{g}$=2.00) suggesting that day-to-day differences in exposure to chemical agents were more prominent than differences in mean exposures between workers. The percentage of groups with a ${}_B\hat{R}_{0.95} \leq 2$ [uniformly exposed group as defined by Rappaport (1991a)] was higher than presented by Rappaport (1991a) for 31 groups (25 vs 10%). Nevertheless, for almost 30% of the groups within the database the individual mean exposure differed by a factor greater than 10. Apparently, grouping workers by job title and factory does not lead automatically to uniformly exposed groups, as is often assumed (Rappaport *et al.*, in press).

Sampling on randomly chosen days from randomly-chosen workers seems to have an effect on the variance components, particulary for the between-worker variability. Both randomly chosen workers and days resulted in larger between-worker variability, while groups with randomly-chosen days had smaller within-worker variability. The data suggest that non-random sampling can lead to problems of interpretation and should be avoided if possible.

It was shown that several factors had an influence on the within- and between-worker variance components of occupational exposure. The number of workers and the number of measurements per group were shown to have distinct effects on the day-to-day variability. A greater number of measured exposures in a group led to a larger estimated within-worker component of variance. Such behaviour would be consistent with the notion that the number of measurements per worker is proportional to the time period over which monitoring is conducted. If this time period is small (e.g. within 1 week) then it is possible that measurements can be positively autocorrelated since they might reflect only a limited set of conditions, activities and practices which are inherent in the process (Francis *et al.*, 1989, Buringh and Lanting, 1991). This would lead to an underestimation of the variance. However, if the period of observation is large, the variation can also be large, not only because the full range of conditions, etc., is sampled, but also because the underlying distribution of exposures might have changed (Roach, 1991). In either case, the estimated variance should be larger than that obtained from a short period.

The influence of environmental and production factors on the variance components was significant for all but "stationary-mobile source" and was in all cases in the *a priori* expected direction. The effect was largest for the within-worker component. In the multivariate models the size of the group, type of industry and measurement strategy were not significant. In the case of the within-worker variability two production factors: indoors-outdoors and intermittent-continuous process explained 41% of the variance. Based on the model a two-fold difference in day-to-day variability ($_{W}S_{y}$) can be predicted between the two extreme situations "groups working indoors and exposed in a continuous process" and "groups working outdoors and exposed in an intermittent process". Although the differences in between-worker variability were also in the *a priori* expected direction (for instance groups with mobile workers were more variable), no suitable multivariate model could be built. A model with "type of process" as independent variable showed a two-fold difference in between-worker variability ($_{B}S_{y}$) for "groups exposed in a continuous process" vs "groups exposed in an intermittent process". However, this model explained only 13% of the variance and had a poor fit. Apparently, differences between workers within a group are hardly predictable based on general environmental and production characteristics. More likely, differences between workers are more influenced by factors like work style and the mix of tasks involved (Rappaport *et al.*, 1993).

Given the fact that coding of the environmental and production factors was done retrospectively, we consider the results remarkable. The quality of the codings also depended greatly on details of the actual surveys which were gleaned from reports and interviews with the original investigators. Unfortunately, complete information on all variables was only available for 50% of the groups.

The findings have consequences for measurement strategies both for hazard control and occupational epidemiology. Unfortunately, it seems impossible to predict which groups, based on job title and factory, are more-or-less homogeneously exposed. Therefore, *a priori* assessment of homogeneity is not feasible and measurement strategies must require repeated measurements from the same individuals (Rappaport *et al.*, 1993). Day-to-day variability seems to be more prominent in situations where workers are exposed outdoors in an intermittent process. In order to estimate the group's mean exposure with the same precision 4-5 times more measurements are needed than in a situation were workers work indoors in a continuous process [since the day-to-day exposure variability (${}_{W}S_{y}$) will be 2.2 times as high]. Also, groups with a larger day-to-day variability will show a higher peak-to-mean concentration ratio (considering shift-long average exposure concentrations). This can be very important in the case of exposures resulting in acute effects.

The results of our database show that simple characteristics related to the environment and the process can explain almost half of the within-worker component of variance. Thus, it is now possible, for the first time, to infer the day-to-day fluctuations in exposure based upon information which can be obtained easily. This knowledge can be very useful in the design of strategies for assessing occupational exposure. For example, sample sizes can be selected prior to monitoring of a particular workplace, based upon the nature of the process and the environment.

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APPENDIX

Table A1. Characteristics of 165 groups (based on job title and factory) which fit the random-effects model

Group	k	N	${}_wS_y$	${}_w\hat{R}_{0.95}$	${}_BS_y$	${}_B\hat{R}_{0.95}$	Chemical agent	Industry
1	5	25	0.305	3.3	0.213	2.3	Perchloroethylene	Dry cleaning
2	5	35	0.661	13.3	0.952	41.8	Inspirable dust	Wool mill
3	5	23	0.326	3.6	0.189	2.1	Inspirable dust	Wool mill
4	12	24	0.610	10.9	0.259	2.8	Inspirable dust	Vehicle manufacture
5	8	16	0.590	10.1	0.287	3.1	Inspirable dust	Vehicle manufacture
6	12	24	0.534	8.1	0.229	2.5	Inspirable iron	Vehicle manufacture
7	7	14	0.345	3.9	0.086	1.4	Inspirable iron	Vehicle manufacture
8	11	22	0.862	29.4	0.000	1.0	Inspirable zinc	Vehicle manufacture
9	8	16	1.155	92.6	0.754	19.2	Inspirable zinc	Vehicle manufacture
10	12	24	0.698	15.5	0.569	9.3	Inspirable copper	Vehicle manufacture
11	8	16	0.384	4.5	0.378	4.4	Inspirable copper	Vehicle manufacture
12	5	22	0.727	17.3	0.000	1.0	Inspirable dust	Vehicle manufacture
13	5	22	0.487	6.7	0.104	1.5	Inspirable zinc	Vehicle manufacture
14	9	36	1.444	287.7	0.000	1.0	Respirable zinc	Brass foundry
15	5	15	1.536	411.3	0.000	1.0	Respirable zinc	Brass foundry
16	6	27	0.687	14.8	0.365	4.2	Inspirable dust	Animal feed prod.
17	5	18	0.527	7.9	0.676	14.2	Inspirable dust	Animal feed prod.
18	5	21	0.810	24.0	1.455	300.1	Inspirable dust	Animal feed prod.
19	6	26	0.989	48.4	0.242	2.6	Inspirable dust	Animal feed prod.
20	5	18	0.679	14.3	0.852	28.2	Inspirable dust	Animal feed prod.
21	5	12	1.175	100.3	2.617	28577	Inspirable dust	Animal feed prod.
22	9	27	1.206	113.2	1.415	256.7	Inspirable dust	Animal feed prod.
23	6	26	0.928	38.0	0.496	7.0	Inspirable dust	Animal feed prod.
24	8	25	1.078	68.5	0.000	1.0	Inspirable dust	Animal feed prod.
25	6	24	0.764	20.0	0.263	2.8	Insp. endotoxin	Animal feed prod.
26	5	17	0.553	8.7	0.556	8.8	Insp. endotoxin	Animal feed prod.
27	5	21	1.323	179.0	1.442	284.6	Insp. endotoxin	Animal feed prod.
28	6	26	1.329	183.1	0.490	6.8	Insp. endotoxin	Animal feed prod.
29	5	18	0.686	14.7	1.187	105.0	Insp. endotoxin	Animal feed prod.
30	5	12	1.358	204.9	2.331	9306.4	Insp. endotoxin	Animal feed prod.
31	9	27	1.043	59.8	1.260	139.5	Insp. endotoxin	Animal feed prod.
32	6	26	1.055	62.6	0.307	3.3	Insp. endotoxin	Animal feed prod.
33	8	24	2.099	3743.5	0.405	4.9	Insp. endotoxin	Animal feed prod.
34	5	20	0.929	38.2	0.401	4.8	Inspirable dust	Grain mill
35	10	33	1.139	86.8	0.000	1.0	Inspirable dust	Grain mill
36	8	24	0.981	46.7	0.523	7.8	Inspirable dust	Grain mill
37	6	15	0.552	8.7	0.806	23.6	Inspirable dust	Grain mill
38	5	20	1.570	470.1	0.374	4.3	Insp. endotoxin	Grain mill
39	10	32	1.880	1586.8	0.000	1.0	Insp. endotoxin	Grain mill
40	8	24	1.324	179.7	0.590	10.1	Insp. endotoxin	Grain mill
41	5	12	0.895	33.4	0.327	3.6	Insp. endotoxin	Grain mill
42	7	14	1.060	63.8	1.399	240.5	Inspirable dust	Grain elevator
43	10	20	1.344	194.5	0.952	41.8	Inspirable dust	Grain elevator
44	8	16	1.483	334.4	0.000	1.0	Inspirable dust	Grain elevator

Table A1 continued

Group	k	N	$_wS_y$	$_w\hat{R}_{0.95}$	$_BS_y$	$_B\hat{R}_{0.95}$	Chemical agent	Industry
45	9	18	0.793	22.4	1.099	74.2	Inspirable dust	Grain elevator
46	8	24	0.704	15.8	0.277	3.0	Inspirable dust	Tobacco products
47	5	15	0.710	16.1	0.422	5.2	Inspirable dust	Tobacco products
48	10	29	0.468	6.3	0.295	3.2	Inspirable dust	Tobacco products
49	7	21	0.371	4.3	0.255	2.7	Inspirable dust	Tobacco products
50	8	24	0.432	5.4	0.000	1.0	Insp. nicotine	Tobacco products
51	5	15	0.349	3.9	0.224	2.4	Insp. nicotine	Tobacco products
52	10	28	0.348	3.9	0.102	1.5	Insp. nicotine	Tobacco products
53	7	21	0.356	4.0	0.000	1.0	Insp. nicotine	Tobacco products
54	6	17	0.927	37.9	0.979	46.4	Inspirable dust	Rubber manufacture
55	18	36	0.829	25.8	0.369	4.3	Inspirable dust	Rubber manufacture
56	5	14	0.251	2.7	0.180	2.0	Inspirable dust	Rubber manufacture
57	6	18	0.736	17.9	0.768	20.3	Inspirable dust	Rubber manufacture
58	8	22	0.547	8.5	0.465	6.2	Inspirable dust	Rubber manufacture
59	6	18	0.368	4.2	0.268	2.9	Inspirable dust	Rubber manufacture
60	5	13	0.327	3.6	0.155	1.8	Inspirable dust	Rubber manufacture
61	5	11	0.467	6.2	0.767	20.2	Inspirable dust	Rubber manufacture
62	5	14	0.482	6.6	0.653	13.0	Inspirable dust	Rubber manufacture
63	5	12	0.303	3.3	0.855	28.6	Inspirable dust	Rubber manufacture
64	6	18	0.473	6.4	0.335	3.7	Inspirable dust	Rubber manufacture
65	6	13	0.403	4.9	0.293	3.2	Inspirable dust	Rubber manufacture
66	7	21	0.521	7.7	0.428	5.4	Inspirable dust	Rubber manufacture
67	9	25	0.337	3.7	1.019	54.2	Inspirable dust	Rubber manufacture
68	7	21	0.572	9.4	0.249	2.7	Inspirable dust	Rubber retreading
69	5	14	0.739	18.1	1.067	65.5	Inspirable dust	Rubber retreading
70	6	13	0.569	9.3	0.483	6.6	Inspirable dust	Rubber manufacture
71	12	32	0.516	7.6	1.939	1999.3	Inspirable dust	Rubber manufacture
72	11	28	0.397	4.7	0.000	1.0	Inspirable dust	Rubber manufacture
73	6	16	0.763	19.9	1.716	833.4	Inspirable dust	Rubber manufacture
74	7	20	1.407	248.6	0.000	1.0	Cycloh. sol. derm.	Rubber manufacture
75	7	19	1.056	62.9	0.616	11.2	Cycloh. sol. derm.	Rubber manufacture
76	8	21	0.781	21.4	0.671	13.9	Cycloh. sol. derm.	Rubber manufacture
77	5	13	1.097	73.7	0.136	1.7	Cycloh. sol. derm.	Rubber manufacture
78	6	18	1.294	159.8	0.948	41.1	Cycloh. sol. derm.	Rubber manufacture
79	8	22	0.419	5.2	0.349	3.9	Cycloh. sol. derm.	Rubber manufacture
80	6	16	0.296	3.2	0.024	1.1	Cycloh. sol. derm.	Rubber manufacture
81	7	20	0.948	41.1	0.412	5.0	Cycloh. sol. derm.	Rubber manufacture
82	6	13	2.239	6473.0	0.306	3.3	Cycloh. sol. derm.	Rubber manufacture
83	5	14	1.014	53.2	1.442	285.1	Cycloh. sol. derm.	Rubber manufacture
84	5	16	0.560	9.0	0.522	7.7	Cycloh. sol. derm.	Rubber manufacture
85	6	14	0.321	3.5	0.874	30.8	Cycloh. sol. derm.	Rubber manufacture
86	9	25	0.701	15.6	0.653	12.9	Cycloh. sol. derm.	Rubber manufacture
87	12	25	0.606	10.8	0.000	1.0	Cycloh. sol. derm.	Rubber manufacture
88	8	23	1.134	85.4	1.066	65.2	Cycloh. sol. derm.	Rubber manufacture
89	10	27	0.898	33.7	0.847	27.7	Cycloh. sol. derm.	Rubber manufacture
90	6	14	0.729	17.5	0.563	9.1	Cycloh. sol. derm.	Rubber manufacture
91	9	27	0.592	10.2	0.606	10.7	Cycloh. sol. derm.	Rubber retreading
92	5	14	0.306	3.3	0.110	1.5	Cycloh. sol. derm.	Rubber retreading
93	7	19	0.567	9.2	0.795	22.5	Cycloh. sol. derm.	Rubber manufacture

Table A1 continued

Group	k	N	${}_{W}S_{y}$	${}_{W}\hat{R}_{0.95}$	${}_{B}S_{y}$	${}_{B}\hat{R}_{0.95}$	Chemical agent	Industry
94	15	40	0.554	8.8	0.545	8.5	Cycloh. sol. derm.	Rubber manufacture
95	15	39	0.611	11.0	0.643	12.4	Cycloh. sol. derm.	Rubber manufacture
96	5	14	0.809	23.8	0.000	1.0	Cycloh. sol. derm.	Rubber manufacture
97	12	77	0.409	5.0	0.411	5.0	Diphenyl	Synthetic yarn man.
98	5	28	0.236	2.5	0.249	2.7	Diphenyl	Synthetic yarn man.
99	12	77	0.436	5.5	0.432	5.4	Diphenyl ether	Synthetic yarn man.
100	5	29	0.298	3.2	0.193	2.1	Diphenyl ether	Synthetic yarn man.
101	11	48	0.946	40.8	0.678	14.3	Inspirable dust	Pesticides formulation
102	13	57	0.489	6.8	0.309	3.4	Inspirable dust	Pesticides formulation
103	5	91	0.961	43.2	0.000	1.0	Nitrogen dioxide	Fertilizer manufacture
104	10	28	1.562	455.6	0.000	1.0	Styrene	Reinforced plastics
105	8	23	0.617	11.2	0.859	29.0	Styrene	Reinforced plastics
106	8	32	0.462	6.1	0.357	4.0	Styrene	Reinforced plastics
107	7	18	0.704	15.8	0.000	1.0	Styrene	Reinforced plastics
108	8	24	0.507	7.3	0.000	1.0	Styrene	Reinforced plastics
109	10	30	0.204	2.2	0.269	2.9	Styrene	Reinforced plastics
110	6	18	0.208	2.3	0.392	4.6	Styrene	Reinforced plastics
111	8	24	0.267	2.8	0.422	5.2	Styrene	Reinforced plastics
112	6	29	0.457	6.0	0.218	2.4	Welding fume	Locomotive manuf.
113	6	29	0.459	6.0	0.147	1.8	Welding fume	Locomotive manuf.
114	6	29	0.521	7.7	0.206	2.2	Welding fume	Locomotive manuf.
115	6	29	0.446	5.8	0.211	2.3	Welding fume	Locomotive manuf.
116	10	27	0.440	5.6	0.427	5.3	Diphenyl ether	Synthetic yarn man.
117	6	16	0.377	4.4	0.354	4.0	Diphenyl ether	Synthetic yarn man.
118	5	14	0.584	9.9	0.557	8.9	Diphenyl ether	Synthetic yarn man.
119	9	21	0.309	3.4	0.000	1.0	Ethanal	Synthetic yarn man.
120	7	21	0.146	1.8	0.148	1.8	Solvent vapours	Printing plant
121	14	68	0.470	6.3	0.471	6.3	Styrene	Reinforced plastics
122	6	33	1.095	73.0	1.469	316.3	Styrene	Reinforced plastics
123	8	48	1.284	153.7	0.734	17.7	Styrene	Reinforced plastics
124	6	27	1.251	134.7	1.488	341.7	Styrene	Reinforced plastics
125	53	382	1.022	54.9	0.530	8.0	Toluene	Petroleum refining
126	5	39	0.845	27.4	0.353	4.0	Toluene	Petroleum refining
127	6	176	0.848	27.8	0.393	4.7	Tetraalkyl lead	Alkyl lead manuf.
128	6	177	0.614	11.1	0.153	1.8	Inorganic lead	Alkyl lead manuf.
129	38	201	1.184	103.8	0.264	2.8	Benzene	Petroleum refining
130	17	89	0.683	14.5	0.193	2.1	Benzene	Petroleum refining
131	18	57	0.693	15.1	0.152	1.8	Benzene	Petroleum refining
132	38	164	1.208	113.8	0.285	3.1	Benzene	Petroleum refining
133	17	74	1.556	445.3	0.557	8.9	Benzene	Petroleum refining
134	16	50	0.733	17.7	0.222	2.4	Benzene	Petroleum refining
135	5	44	1.492	346.9	0.385	4.5	Benzene	Petroleum refining
136	10	54	1.620	571.7	0.824	25.3	Benzene	Petroleum refining
137	8	68	1.671	699.5	0.299	3.2	Benzene	Petroleum refining
138	22	145	1.705	799.0	0.715	16.5	Benzene	Petroleum refining
139	17	118	1.072	66.7	0.243	2.6	Benzene	Petroleum refining
140	18	90	1.348	197.2	0.134	1.7	Benzene	Petroleum refining
141	25	105	0.820	24.9	0.404	4.9	Benzene	Petroleum refining
142	14	87	0.936	39.3	0.355	4.0	Benzene	Petroleum refining

Table A1 continued

Group	k	N	$_{W}S_{y}$	$_{W}\hat{R}_{0.95}$	$_{B}S_{y}$	$_{B}\hat{R}_{0.95}$	Chemical agent	Industry
143	13	73	1.183	103.1	0.249	2.7	Benzene	Petroleum refining
144	15	87	1.092	72.2	0.360	4.1	Benzene	Petroleum refining
145	15	167	1.522	390.0	0.649	12.8	Benzene	Petroleum refining
146	14	38	1.699	781.8	1.278	149.6	Benzene	Petroleum refining
147	13	50	1.403	244.8	0.642	12.4	Benzene	Petroleum refining
148	15	36	0.344	3.9	0.000	1.0	Sulphur dioxide	Aluminum reduction
149	16	38	0.539	8.3	0.000	1.0	Total dust	Aluminum reduction
150	14	34	0.347	3.9	0.089	1.4	Total fluoride	Aluminum reduction
151	14	34	0.385	4.5	0.000	1.0	Fluoride dust	Aluminum reduction
152	15	36	0.293	3.2	0.205	2.2	Hydrogen fluoride	Aluminum reduction
153	26	79	0.880	31.5	0.000	1.0	Formaldehyde	Resin manufacture
154	8	24	0.668	13.7	0.259	2.8	Formaldehyde	Resin manufacture
155	6	54	1.390	232.6	0.000	1.0	Organic vapour	Pesticide manufacture
156	5	1139	1.525	394.3	0.435	5.5	Organic vapour	Pesticide manufacture
157	16	5076	1.723	856.3	0.341	3.8	Organic vapour	Pesticide manufacture
158	62	1162	1.638	615.4	0.857	28.8	Organic vapour	Pesticide manufacture
159	16	592	0.517	7.6	0.232	2.5	Inorganic mercury	Chloralkali production
160	6	18	0.367	4.2	0.091	1.4	Benzene	Spray painting
161	6	18	0.308	3.3	0.212	2.3	Benzene	Spray painting
162	6	18	0.245	2.6	0.165	1.9	Toluene	Spray painting
163	6	18	0.694	15.2	0.000	1.0	Toluene	Spray painting
164	6	18	0.363	4.1	0.060	1.3	Xylene	Spray painting
165	6	18	0.241	2.6	0.270	2.9	Xylene	Spray painting

k, number of workers in a group.
N, number of measurements in a group.
$_{W}S_{y}$, estimated standard deviation of within-worker distribution of log-transformed exposures.
$_{W}\hat{R}_{0.95}$, ratio of the 97.5th and 2.5th percentiles of the within-worker distribution.
$_{B}S_{y}$, estimated standard deviation of between-worker distribution of log-transformed exposures.
$_{B}\hat{R}_{0.95}$, ratio of the 97.5th and 2.5th percentiles of the between-worker distribution.

Chapter 8

Assessment and grouping of occupational magnetic field exposure in five electric utility companies[1]

[1] H. Kromhout, D.P. Loomis, G.J. Mihlan, L.A. Peipins, R.C. Kleckner, R. Iriye, D.A. Savitz. Assessment and grouping of occupational magnetic field exposure in five electric utility companies. Submitted Scandinavian Journal of Work Environment & Health.

ABSTRACT

A large survey of occupational exposure to 60 Hz magnetic fields was conducted among randomly selected workers in five electric power companies. The design of the study facilitated the examination of exposure variability and provided the base for a job-exposure matrix (JEM) for linking health outcomes and occupational magnetic field exposures in the epidemiological study of employees of these companies. Almost 3,000 successful measurement attempts indicated average exposures ranging from 0.11 μT for 'Senior Managers' to 1.50 μT for 'Cable Splicers'. The differences among the five companies were relatively small with the more urban companies showing somewhat higher average exposures. The day-to-day component of variance exceeded the within- and between-group components of variance. The final JEM consisted of five groups with average exposure levels of 0.12, 0.21, 0.39, 0.62, and 1.27 μT, respectively. Given the variance in exposure, even this optimal grouping showed considerable overlap in exposure between adjacent groups. Nevertheless, the JEM incorporated the differences in exposure level within occupational categories between companies in the most efficient way and provides an objective and statistically based method for estimation of cumulative magnetic field exposure.

INTRODUCTION

Concern about occupational exposure to 50 and 60 Hz power-frequency electric and magnetic fields has intensified since epidemiological surveys a decade ago suggested excess cancer mortality among workers in electrical occupations (Milham, 1982; Wright *et al.*, 1982; Coleman *et al.*, 1983; McDowall *et al.*, 1983). Although further studies of health risks among electrical workers have been conducted (Theriault, 1991), quantitative data concerning the level of occupational exposure to power frequency electromagnetic fields remain relatively sparse and of limited quality (Kromhout, 1992a).

In one earlier study, Deadman and colleagues (1988) assessed 60 Hz electric and magnetic field exposures over 7-days among 36 electric utility workers in Canada, providing information on both occupational and non-work exposures. Flynn and others (1991) presented data describing workshift magnetic field exposures from a similar survey of 134 electric utility workers in the United States. Bowman and colleagues (1988) obtained 141 area spot measurements of occupational electric and magnetic field exposures among workers in selected electrical occupations and a sample of other jobs in the Los Angeles area.

These studies indicated high exposures to electric or magnetic fields, but have important limitations: few workers were monitored in each job, subjects were not randomly selected, and, in the Los Angeles study, only short-term measurements were taken. Other exposure assessments were performed in conjunction with epidemiological studies, but only limited information concerning exposure has been published (Sahl *et al.*, 1993; Matanoski *et al.*, 1993). Additional occupational exposure studies have been conducted, including a very large one among electric utility volunteers, but the results have not yet appeared in widely available, refereed publications (Bracken, 1990; Bowman *et al.*, 1992).

Previous assessments of occupational exposure to power frequency electromagnetic fields have particular deficiencies with regard to two key methodological points. Variability between workers and over time is increasingly recognized as an aspect of occupational exposure with importance for both research and regulation (Oldham and Roach, 1954; Rappaport, 1991, Kromhout and Heederik, 1993). Some data concerning exposure variability are available from two studies of exposures in electric utilities (Deadman *et al.*, 1988; Bracken, 1990; Kromhout *et al.*, 1992), but may be compromised by non-random selection of subjects and using consecutive measurement days. This issue has not been thoroughly considered in other assessments of occupational electric and magnetic field exposure. The need to reduce exposure misclassification through the appropriate grouping of workers for epidemiological analysis has also been recognized as an important determinant of validity, but objective techniques for doing so have not been addressed in any previous study of occupational electric and magnetic field exposure.

We conducted a large survey of occupational exposure to 60 Hz magnetic fields among randomly selected workers in 28 job categories in five electric utility companies (Loomis *et al.*, 1994a; Savitz *et al.*, 1988). Relative to earlier assessments of occupational magnetic field exposure, this study has several design advantages that facilitate the examination of exposure variability. These include large sample size, random selection of workers and measurement days, and the use of full-shift personal monitoring. Here we report the results of that survey describing magnetic field exposures among electric utility workers. In addition, we analyze aspects of exposure variability within and between occupational groups and workers, and present a statistically optimal job-exposure matrix (JEM) for linking health outcomes and occupational magnetic field exposures in the epidemiological study of the employees of these companies.

MATERIALS AND METHODS

Details of the sampling design and field methods of the magnetic field exposure survey have been described elsewhere (Loomis *et al.*, 1994a) as have the classification and organization of the work history data from the cohort (Loomis *et al.*, 1994b). A brief description of the survey is provided here.

Sampling design

Initially, occupational categories were constructed to organize thousands of job titles at five electric utility companies participating in a cohort mortality study into logical and homogeneous groups. Using experience gained from two preliminary surveys, the 28 occupational categories were then aggregated into three ordinal levels of presumed magnetic field exposure (Table 1). A goal of 4,000 full-shift magnetic field measurements was set, based principally on considerations of time, cost, and tolerance of the participating companies. The number of measurements to be made in each

Table 1. Characteristics of TWA magnetic field exposure (in μT) for 28 occupational categories

Level	Occupational Category	N	AM	SE	GM	${}_TS_g$	Range
Low	Senior Managers	58	0.11	0.10	0.09	1.9	0.03-0.66
	Engineers	70	0.23	0.64	0.12	2.3	0.03-5.32
	Field/Craft/Trade Supervs	95	0.24	0.47	0.15	2.2	0.04-4.28
	Administrative Supervs	59	0.16	0.19	0.11	2.0	0.03-1.26
	Adm. Support/Clerical Wrkrs	65	0.25	0.46	0.14	2.5	0.02-3.37
	Sales, Market. & Bus. Wrkrs	66	0.12	0.07	0.10	1.8	0.03-0.37
	Services	96	0.41	0.69	0.22	2.8	0.01-4.10
	Telecommunications Techs	35	0.35	0.55	0.21	2.7	0.01-3.26
	Riggers	35	0.38	0.37	0.27	2.4	0.04-1.56
	Auto and Truck Mechs	47	0.20	0.21	0.14	2.3	0.03-0.94
	Painters	9	0.45	0.45	0.30	2.6	0.09-1.30
	Heavy Vehicle Operators	69	0.23	0.27	0.15	2.3	0.03-1.58
	Labourers	57	0.25	0.31	0.16	2.5	0.03-1.66
	Other Crafts/Trades Wrkrs	100	0.21	0.25	0.15	2.3	0.01-1.26
Medium	Technical Workers	175	0.36	0.62	0.18	3.0	0.09-5.68
	Mechanics (plant and subst)	100	0.23	0.30	0.15	2.4	0.01-2.24
	Machinists	138	0.72	1.95	0.26	3.3	0.01-13.5
	Boilermakers/Steamfitters	132	0.41	1.05	0.16	3.0	0.04-7.74
	Instrument. & Control Techs	150	0.40	1.12	0.21	2.6	0.03-13.1
	Relay Technicians	63	1.34	2.34	0.59	3.7	0.02-14.5
	Power Plant Operators	191	0.79	2.34	0.29	3.4	0.01-26.4
	Substation Operators	84	0.80	1.13	0.41	3.3	0.01-6.87
	Pipe Coverers	12	0.28	0.44	0.17	2.6	0.06-1.65
	Welders	76	0.80	1.08	0.40	3.3	0.04-6.03
	Material Handlers	196	0.23	0.74	0.12	2.4	0.01-10.1
High	Electricians	264	1.11	2.18	0.45	3.8	0.01-23.2
	Linemen	251	0.65	1.59	0.23	3.9	0.01-20.8
	Cable Splicers	149	1.50	3.12	0.40	4.8	0.01-15.6

N: number of measurements
AM: arithmetic mean TWA
SE: population standard error
GM: geometric mean TWA
${}_TS_g$: *geometric standard deviation of the total distribution*
range: range of individual measurements

occupational category was a function of the total number of measurements projected, arbitrary weights of one, three, or five for the three exposure levels, and a second set of weights proportional to person-years of employed experience contributed by each of the five companies. The rationale for the weights of one, three, and five was that groups with higher average exposures would also have more variable exposures, requiring more measurements to obtain equally precise estimates of average exposures.

To enable estimation of within- and between-worker components of exposure variance, each individual selected for monitoring in the 'medium' and 'high' exposure groups was measured on two randomly selected days no more than 12 months apart. The temporal variability in exposure in the 'low' exposure group was expected to be small, so study resources were conserved by measuring workers in these occupational categories only once.

Instrumentation

A small integrating personal magnetic field exposure meter, the AMEX 3-D (Kaune *et al.*, 1992) was used to measure magnetic field exposure. This meter yields an estimate of cumulative magnetic field exposure which can be translated to a time weighted average (TWA). The AMEX 3-D does not provide time-specific magnetic field data and does not measure electric fields in contrast to the EMDEX-100 (Bracken, 1990) and the IREQ dosimeter used by Deadman *et al.* (Deadman *et al.*, 1988; Héroux, 1991).

Survey protocol and data handling

Given the number of measurements to be made in each occupational category within each company, workers were randomly selected based on payroll rosters. A number of additional workers were chosen to replace workers who could not be located or were absent on the day of measurement.

Workers and management personnel conducted the exposure survey in the field. Exposure meters were generally distributed to the selected workers by company mail. Workers who chose to participate in the survey wore the meter for a full shift and returned it after recording the on and off times. The meters were read by a field coordinator and the results recorded. The meters were periodically tested for correct functioning and calibration.

When a meter or reader failed the calibration test, all measurements obtained with that instrument since its last successful test were excluded. The data were checked for missing or out-of-range values, logical inconsistency, and data entry errors. Also, a check was performed on correct assignment of the sampled jobs to occupational categories based in part on information collected during walk-through surveys in the companies.

Statistical analysis

After exclusion of erroneous measurement data, descriptive statistics were generated using SAS System Software PC Version 6.04 (SAS Institute, Cary, NC, USA). Further statistical analyses were done to obtain measures of 'average' exposure and exposure variance for groups of workers. Assuming a random-effects ANOVA model, the within-worker variance component (${}_{WW}S_Y^2$) and between-worker variance component (${}_{BW}S_Y^2$) were estimated by applying Proc Nested for each occupational category with repeated measurements (Kromhout *et al.*, 1993). The fit of the random-effects ANOVA model was graphically judged by utilizing recently developed statistical procedures with the help of a SAS-Graph program (Kromhout *et al.*, 1993).

The effect of different grouping strategies was assessed by applying a two-way nested random-effects ANOVA model (Kromhout and Heederik, 1993). The goal of this procedure was to arrive at the most efficient grouping for subsequent estimation of magnetic field exposure to be used in a exposure-response analysis of mortality data. The ratio (ϵ) of the between-group (${}_{BG}S_Y^2$) and the sum of the within-group and between-group variance components (${}_{BG}S_Y^2$ + ${}_{WG}S_Y^2$) was used as a measure of resolution in exposure level. This ratio has a range of 0 to 1, with a value of 1 indicating the most homogeneous possible grouping in which each worker comprises a unique group. The precision (π) of the average exposure level for each of the groups was estimated by taking the median of the reciprocal of the standard error of the average exposure of each group.

Different *a priori* groupings based on exposure level, occupational category, company, and possible combinations of these variables were compared, as was an *a posteriori* grouping based on the actual measured level in each of the occupational categories of the five companies. The *a posteriori* grouping was based on the distribution of the arithmetic mean exposure of each of the occupational categories measured successfully in each company (N=120). The 25, 50, 75, and 87.5 percentiles were chosen as arbitrary cut-off points for the five *a posteriori* groups.

RESULTS

Measurements

The exposure survey was conducted between November 1990 and December 1992. The majority of the measurements were done during the last 11 months, with approximately 300 AMEX-3D meters in use at the end of the survey. Of the 4094 measurement attempts on eligible workers 446 (11%) did not produce usable data due to absence of the worker, 121 (3%) of the workers refused, 346 (8%) were omitted due to procedural errors, and 10 (0.2%) measurements were lost because of total instrument failure. Another 286 (7%) measurements were unusable due to failure to meet the calibration criteria. An additional 43 (1%) measurements were excluded from the analyses due to the fact that the measurements lasted less than 4 hours or more than 12 hours. This left 2842 measurements in the analysis. Incorrectly coded jobs had to be re-coded within the data base in 66 cases (2%). The 662 repeated measurements were performed on average 120 days after the initial measurement (range: 1-649 days).

Magnetic field exposure by a priori exposure level and occupational category

The three exposure levels assigned *a priori* resulted in substantially different arithmetic mean exposures of 1.03, 0.54, and 0.24 μT for the presumed high, medium, and low

Table 2. Characteristics of TWA magnetic field exposure (in μT) for three *a priori* assigned exposure levels.

A priori level	N	AM	SE	GM	${}_TS_g$	Range
Low	861	0.24	0.42	0.15	2.4	0.01-5.32
Medium	1317	0.54	1.44	0.22	3.2	0.01-26.4
High	664	1.03	2.27	0.34	4.2	0.01-23.3

N: number of measurements
AM: arithmetic mean TWA
SE: population standard error
GM: geometric mean TWA
${}_TS_g$: geometric standard deviation of the total distribution
range: range of individual measurements

levels of exposure respectively (Table 2). The ranges of arithmetic mean TWA exposures for the five companies within high, medium, and low groups was 0.67-1.61, 0.44-0.61, and 0.21-0.28 respectively (data not shown in Table 2). Although the arithmetic mean exposures for the three *a priori* levels of exposure were significantly different, it can be seen from Table 1 that some occupational categories had exposures lower or higher than expected based on the means of the groups. In the high exposure group the category 'Linemen' had an arithmetic mean exposure of 0.65 μT, half the level measured for 'Electricians' and 'Cable Splicers', which had levels of 1.11 and 1.50 μT, respectively. Arithmetic mean magnetic field exposures for 'Material Handlers' and 'Plant and Substation Mechanics' also were lower than others in the medium exposure group, at only 0.23 μT. 'Relay Technicians' appeared to have higher exposures than others in the medium exposure group with an arithmetic mean magnetic field exposure of 1.34 μT. Exposures of 'Telecommunication Technicians', 'Riggers', 'Service Workers', and 'Painters' also were somewhat higher than others in the low exposure group, with arithmetic mean magnetic field exposure of 0.35, 0.38, 0.41, and 0.45 μT respectively.

When the exposure levels for each occupational category in each of the five companies (120 groups in total) were considered, the deviations from expected levels became more apparent. For example, for the five company-specific groups of 'Linemen' the arithmetic mean exposures were 0.94, 1.03, 0.69, 0.57, and 0.38 μT. The

Table 3. Characteristics of TWA magnetic field exposure (in μT) for five electric utility companies

Company	Size	Type	N	AM	SE	GM	$_TS_g$	Range
A	Small	Less Urban	272	0.41	0.59	0.21	2.9	0.03-4.28
B	Medium	More Urban	322	0.66	1.82	0.26	3.1	0.01-23.3
C	Large	More Urban	883	0.69	1.90	0.23	3.6	0.01-20.8
D	Large	Rural	931	0.50	1.16	0.19	3.4	0.01-13.1
E	Medium	Less Urban	434	0.47	1.43	0.22	2.9	0.01-26.4

N: number of measurements
AM: arithmetic mean TWA
SE: population standard error
GM: geometric mean TWA
$_TS_g$: geometric standard deviation of the total distribution
range: range of individual measurements

between-company variation for 'Cable Splicers' was even more striking with 0.39 μT for company E and 1.61 and 1.65 for companies C and B, respectively ('Cable Splicers' were not present at companies A and D).

The mean exposure by company was highest for the two more urban companies, although the overall differences among the companies were less than the differences between occupational categories (Table 3).

Within- and between-worker components of variance for occupational categories

Generally, TWA magnetic field exposure varied more on a day-to-day basis within workers than between workers. However, for 'Technical Workers', 'Relay Technicians', and 'Material Handlers' the opposite pattern was observed (Table 4). The largest differences between individual average magnetic field exposures were present for 'Technical Workers', 'Relay Technicians', 'Power Plant Operators', 'Electricians' and 'Cable Splicers' ($_{BW}\hat{R}_{0.95} > 20$). Only the occupational categories 'Mechanics' and 'Welders' could be considered uniformly exposed groups, based on $_{BW}\hat{R}_{0.95} \leq 2$ as defined by Rappaport (1991).

Comparison of grouping schemes

The results of analyses to compare the efficiency of four *a priori* and one *a posteriori*

Table 4. Within- and between-worker components of variance in several occupational categories.

Occupational Category	N	K	AM (μT)	$_{BW}S_g$	$_{BW}\hat{R}_{0.95}$	$_{WW}S_G$
Other Crafts/Trades Wrkrs	100	74	0.21	1.40	3.76	2.13
Technical Workers	175	130	0.36	2.15	24.8	2.06
Mechanics (plant and subst)	100	86	0.23	1.19	1.96	2.37
Machinists	138	96	0.72	1.69	7.86	2.90
Boilermakers/Steamfitters	132	88	0.41	1.46	4.39	2.82
Instrument. & Control Techs	150	102	0.40	1.59	6.17	2.33
Relay Technicians	63	43	1.34	2.66	46.0	2.40
Power Plant Operators	191	148	0.79	2.23	23.5	2.52
Substation Operators	84	55	0.80	1.90	12.4	2.73
Welders	76	58	0.80	1.00	1.00	3.30
Material Handlers	196	121	0.23	1.90	12.3	1.82
Electricians	264	167	1.11	2.27	25.1	2.87
Linemen	251	161	0.65	2.04	16.3	3.20
Cable Splicers	149	97	1.50	2.27	24.7	3.81

N: number of measurements
K: number of workers
AM: arithmetic mean TWA
$_{BW}S_g$: geometric standard deviation for the between-worker distribution
$_{BW}\hat{R}_{0.95}$: ratio of 97.5th and 2.5th percentiles of the between-worker distribution
$_{WW}S_g$: geometric standard deviation for the within-worker distribution

schemes for grouping workers are shown in Table 5. The groupings by occupational category, occupational category plus company and the *a posteriori* grouping (with the 25, 50, 75, and 87.5 percentiles of the distribution of average exposures (AMs) of the 120 occupational category plus company groups as cut-off points) showed the greatest contrast in exposure levels between the created groups as indicated by ϵ and $_{BG}\hat{R}_{0.95}$. The *a priori* grouping gave the highest precision (π=27.8), but relatively poor resolution between groups ($_{BG}\hat{R}_{0.95}$=4.5, ϵ=0.29). The posterior grouping yielded similar precision (π=25.5) but far better resolution between groups ($_{BG}\hat{R}_{0.95}$=8.6, ϵ=0.59) and was selected as the basis of the magnetic field job-exposure matrix (JEM).

Table 5. Grouping efficiency based on all measurements (N=2842).

Grouping	G	K	${}_{BG}S_Y^2$	${}_{BG}\hat{R}_{0.95}$	${}_{WG}S_Y^2$	ϵ	${}_{WW}S_Y^2$	π
A priori	3	2177	0.1452	4.45	0.3606	0.29	0.9843	27.8
OC	28	2180	0.2245	6.41	0.2360	0.49	0.9883	9.9
Company	5	2170	0.0109	1.51	0.4407	0.02	0.9888	19.2
OC-company	120	2180	0.2529	7.18	0.2003	0.56	0.9883	5.0
A posteriori	5	2180	0.3017	8.61	0.2124	0.59	0.9883	25.5

G: number of groups
K: number of workers
${}_{BG}S_Y^2$: variance of the between-group distribution of log-transformed exposures
${}_{BG}\hat{R}_{0.95}$: ratio of 97.5th and 2.5th percentiles of the between-group distribution
${}_{WG}S_Y^2$: variance of the within-group distribution of log-transformed exposures
ϵ: ratio of ${}_{BG}S_Y^2$ and sum of ${}_{BG}S_Y^2$ and ${}_{WG}S_Y^2$
${}_{WW}S_Y^2$: variance of the within-worker distribution of log-transformed exposures
π: median precision
OC: occupational category

Elaborating the magnetic field JEM

Table 6 gives descriptive statistics for the groups resulting from aggregating the 120 occupational category-company combinations into five exposure groups. The confidence intervals were based on both the within- and between-worker components of variance, which were estimated for each of the five exposure groups. The very small number of repeated measurements in the first two groups (group 1 and 2) resulted in very unstable estimates of the within- and between-worker components of variance. From this table it follows that both the between-worker and the within-worker component tended to increase with increasing level of exposure. However, in all cases the within-worker component exceeded the between-worker component.

The fit of the random-effects model for the three highest exposure groups, in which the majority of the repeated measurements were performed, is shown graphically in Figure 1. The plots for the two highest exposure groups (groups 4 and 5) indicate that the estimated variance components are very precise. The plot of the empirical cumulative between-worker distribution function (ECDF) for exposure group 3 suggests a non-normal between-worker exposure distribution (over-representation of workers whose individual means are close to the group's average).

Table 6. Descriptive statistics for *a posteriori* exposure grouping (in μT).

Group	N	K	AM	CI AM	GM	CI GM	$_{T}S_g$	$_{BW}S_g$	$_{BW}\hat{R}_{0.95}$	$_{WW}S_g$	Range of AMs
1	347	331	0.12	0.11-0.13	0.10	0.09-0.11	1.8	1.0	1.0	2.1	0.05-0.15
2	511	441	0.21	0.19-0.23	0.15	0.14-0.16	2.3	1.6	6.3	2.0	0.15-0.30
3	821	621	0.39	0.33-0.45	0.19	0.18-0.20	2.8	1.8	11.0	2.3	0.30-0.48
4	529	363	0.62	0.50-0.74	0.25	0.23-0.28	3.5	1.9	11.8	3.0	0.48-0.80
5	634	424	1.27	1.07-1.48	0.46	0.41-0.51	4.0	2.2	21.3	3.1	0.80-2.00

N: number of measurements
K: number of workers
AM: arithmetic mean TWA
CI AM: 95% confidence interval of arithmetic mean
GM: geometric mean TWA
CI GM: 95% confidence interval of geometric mean
$_{T}S_g$: geometric standard deviation of the total distribution
$_{BW}S_g$: *geometric standard deviation for the between-worker distribution*
$_{BW}\hat{R}_{0.95}$: ratio of 97.5th and 2.5th percentiles of the between-worker distribution
$_{WW}S_g$: geometric standard deviation for the within-worker distribution
range of AMs: range of arithmetic means of occupational category-company combinations

Given that the difference in average exposure level between the highest and lowest exposed groups is about a factor of 10 (see also the estimated $_{BG}\hat{R}_{0.95}$ of 8.61 in Table 5), it is also obvious that overlap in exposure level due to the large within-group (between-worker within a group) variance will still be present; the three highest exposed groups had especially large $_{BW}\hat{R}_{0.95}$ of respectively 11, 12, and 21.

No exposure data were obtained for 14 occupational category-company combinations. Eight groups with few workers were not selected in the random sample and another six were historical groups no longer present. Average exposure levels for those 14 groups were imputed based on a linear model with occupational categories and company as independent factors and the untransformed TWA magnetic field exposure as dependent variable. Due to the large day-to-day variability, this model explained only 7% of the total exposure variance. Based on the estimated exposure these groups were placed in one of the five exposure categories. The 120 sampled occupational category-company combinations were placed in one of the five exposure categories based on their actual measured level of magnetic field exposure (AM). Six occupational category-company combinations had never been present.

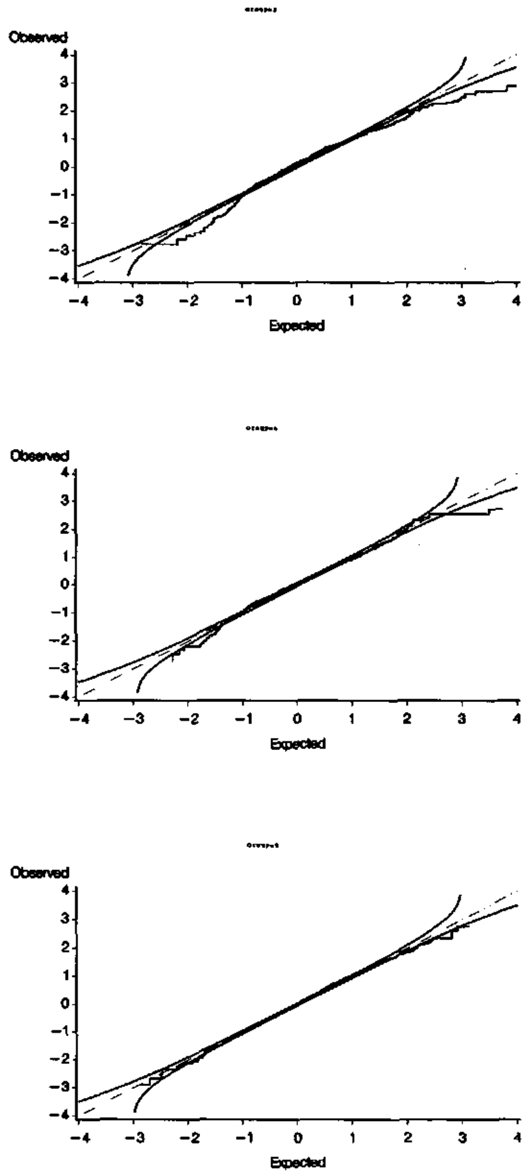

Figure 1. Weighted empirical cumulative between-worker distribution function against the expected cumulative distribution function (so-called Q-Q plot), with adjusted ± 0.75 standard deviation bands for magnetic field exposure data of the highest three *a posteriori* exposure groups.

DISCUSSION AND CONCLUSIONS

Measurement strategy

The measurement strategy required intensive involvement of management personnel and workers. Given the rather limited time-span and the cessation of the survey at the end of December 1992, the number of measurement attempts was considered to be satisfactory despite an estimated rate of measurement of 2.5 usable measurements per meter per month. The main reason for loss of measurements was absence of the worker (11% of the attempts). Some of these may actually have been indirect refusals, because workers who did not arrive at the distribution points for the meters were classified as absent. The number of measurements due to procedural errors was 8% of the attempts, which is rather high. However, one third of this number was due to lost exposure meters, many of which were never returned to the research laboratory at the end of the study. Instrument failure and failed calibration together accounted for 7% of the measurement attempts (Loomis *et al.*, 1994a). Input of research staff (industrial hygienists) in the actual fieldwork could have resulted in larger success rates, with greatest potential to reduce the number of refusals, procedural errors and calibration failures. However, the costs involved in assigning industrial hygienists in the actual field work would have been prohibitive. Finally, some of these successful measurements might have been deliberately falsified, since there was no direct oversight during the actual measurements, but there was no obvious incentive to do so.

Unfortunately, the number of repeated measurements was much smaller than planned. Although the failure rate was similar for first and second measurement attempts on the same worker, the 30% unusable measurements for both first and second measurements restricted the planned number of repeats. Also, the end of the survey period precluded attempts to obtain second measurements for many workers.

As expected, the variability of magnetic field exposure increased with the level of exposure assumed *a priori*. However, the standard error increased by factors of 3.4

and 5.4, respectively for the two higher levels when compared to the lowest level. Therefore, a weighting of 1, 12, and 29 instead of the applied 1, 3, and 5 for the relative number of samples to be collected within the three *a priori* assumed levels would have been required to attain the same precision of average exposure.

We consider the measurement strategy to be feasible in other studies despite its above mentioned shortcomings and potential for improvements. Suitable monitoring devices, careful planning, and the support of management and labour are required for its success, however.

Comparison with other studies

Comparable patterns are seen when comparing the average magnetic fields measured for the pre-assigned exposure levels of 0.24, 0.51 and 1.03 μT with previously published results. Flynn *et al.* (1991) ranked magnetic field exposure *a priori* in three levels for 134 employees of one utility company, which after validation with actual measurements performed with the EMDEX meter showed average exposure levels of 0.10, 0.61, and 1.51 μT for the ranks low, medium, and high, respectively. The fact that the difference between the highest and lowest level assigned was about three times as high in the study of Flynn *et al.* (1.51 over 0.10 μT compared to 1.03 over 0.24 μT) may be partly related to the fact that only one company was involved. Also, individual jobs rather than occupational categories were rated by Flynn *et al.*. Nevertheless, the differences are relatively small in absolute terms.

Lindh and Andersson (1992) ranked occupations into low, medium, and high exposure groups based on measured fields. The resulting average exposure levels were 0.06, 0.28, and 1.47 μT. Their results are less comparable, however, because they applied a procedure of disregarding extreme values and used a different exposure meter (Lindh and Andersson, 1989).

The measured levels for utility workers are notably lower than levels reported by Deadman *et al.* (1988) and Bowman *et al.* (1988). The contrast with the latter study may be explained by the investigators having made non-random spot measurements, leading to upwardly biased exposure levels. The discrepant geometric mean magnetic fields reported by Deadman *et al.* are less readily explained, because they also performed repeated full-shift personal monitoring. It is unlikely that the 5-8 fold difference in exposure seen for such jobs as 'Electricians', 'Cable Splicers', 'Linemen', 'Power Plant Mechanics', and 'Power Plant Operators' can be attributed to differences in work practices and power production and delivery methods between the USA and Canada or to differences due to the time span of five years that has passed since the study by Deadman *et al.*. The more likely reasons are differences between the meters and measurement strategies (random selection of workers and days of measurement in the present study). To our knowledge, no formal comparison of the meter described by Deadman *et al.* (1988) and the AMEX-3D has been carried out, as was done for the AMEX 3-D and the EMDEX-100 meter (Kaune *et al.*, 1992).

This study corroborated the pattern in variability of magnetic field exposure reported by Deadman *et al.* (1988). In their study, the day-to-day component of variance was also greater than the between-worker component of variance for workers exposed at and above background levels, as well as for the subgroup of 10 linemen. The between-worker geometric standard deviation for linemen in our study compared reasonably well with that reported by Deadman *et al.* (2.31 vs 2.05). The day-to-day component of variance was larger in the present study (3.20 vs 2.34), probably due to the relative short measurement period in the Deadman *et al.* study (all measurements were performed within one week).

It is not surprising that the reported levels of exposure compared relatively well with the levels reported in Bracken's study of the same industry (1990), although the congruence seemed to be better for certain occupational categories than for others (Table 7). Since measurements were not taken on random days in the Bracken study, differences for occupational categories in which workers are exposed intermittently (e.g., 'Mechanics', 'Linemen', and 'Substation Operators') are understandable. For chemical exposures, Olsen *et al.* (1991) showed that non-random (worst-case) sampling resulted in a five- to ten-fold increase in level of exposure to solvents, but not

Table 7. Comparison of average magnetic field exposure (in μT) for selected groups in the EMDEX-100 Project (Bracken, 1990) and the present study.

Groups	Bracken N	Bracken AM	Bracken GM	Present N	Present AM	Present GM
Management, Clerical, Professionals	266	0.07-0.58	0.05-0.22	413	0.11-0.25	0.09-0.15
Services	61	0.46	0.26	96	0.41	0.22
Drivers	32	0.32	0.18	69	0.23	0.15
Power Plant Operators	363	0.67	0.23	191	0.79	0.29
Mechanics	161	0.96	0.28	100	0.23	0.15
Linemen	1103	1.15	0.27	251	0.65	0.23
Substation Operators	375	1.88	0.58	84	0.80	0.41
Electricians	667	1.10	0.40	264	1.11	0.45
Welders	42	0.54	0.13	76	0.80	0.40

N: number of measurements
AM: arithmetic mean
GM: geometric mean

in a difference in exposure variability. The latter was also seen in a recent overview of exposure variability by Kromhout *et al.* (1993). Workers in other occupational categories like 'Services', 'Drivers', 'Power Plant Operators', and 'Electricians' are more likely to be exposed through their presence in a certain environment and therefore would have had fewer opportunities to select worst-case days for exposure assessment. 'Welders' were the only occupational category with a markedly elevated exposure in the present survey relative to that reported by Bracken (1990). Another explanation for the differences observed could be in the system of coding jobs; Bracken used 16 groups to classify workers in the utility industry, while we used 28 groups, potentially reducing misclassification. However, the occupational categories presented for comparison in Table 7 were similar in the two studies.

A more extensive comparison is possible for variability patterns in the EMDEX-100 study data (Kromhout *et al.*, 1992). In Table 8 the total variance of magnetic field exposure data is broken down into three variance components for both studies. Although the total variance is similar in both studies, the relative size of two of the three variance components is quite different. In the present study, 70% of the total

Table 8. Comparison of variance components in the EMDEX-100 Project (Bracken, 1990; Kromhout *et al.*, 1992) and the present study.

Grouping	G	N	K	${}_{BG}S_Y^2$	${}_{WG}S_Y^2$	${}_{WW}S_Y^2$	${}_{T}S_Y^2$
job groups (Bracken)	16	4086	2177	0.285	0.712	0.681	1.678
occupational groups (present study)	28	2842	2180	0.225	0.236	0.988	1.449

G: number of groups
N: number of measurements
K: number of workers
${}_{BG}S_Y^2$: variance of the between-group distribution of log-transformed exposures
${}_{WG}S_Y^2$: variance of the within-group distribution of log-transformed exposures
${}_{WW}S_Y^2$: variance of the within-worker distribution of log-transformed exposures
${}_{T}S_Y^2$: total variance

variance was due to day-to-day differences in exposure level, while in the EMDEX-100 study this was only 40%. Consequently, the between-worker component of variance within groups was much larger in the EMDEX-100 study. The classification by job group in the EMDEX-100 study thus showed more overlap between groups and less contrast in exposure level between groups (ϵ=0.28 vs ϵ=0.49). The fact that, in the Bracken study, jobs from 55 utilities had to be aggregated may have resulted in less homogeneous job groups than the present occupational categories, leading to more between-worker variability. The smaller day-to-day component may be explained by the shorter time-period between the repeated measurements in the EMDEX-100 Project (a median value of 1 day compared to a median value of 105 days in the present study). This phenomenon has also been reported for chemical exposures by several authors (Francis *et al.*, 1989; Buringh and Lanting, 1991; Kromhout *et al.*, 1993) and has been attributed to autocorrelation of measurements performed within a small time-period (e.g. a week) and to non-stationary behaviour, for example due to seasonal influence on exposure levels.

The resolution in magnetic field exposure levels for occupational category (ϵ=0.49) is at the higher end of the distribution for similar general grouping variables for chemical exposures. Kromhout (1992b) reported resolutions ranging from 0.00 to 0.59 for nine chemical exposures in six industry-wide exposure surveys. The small differences between companies within the electric power industry (ϵ=0.02) is at the very low end of the distribution for chemical exposures (ϵ=0.00-0.86). The mix of jobs and tasks, their actual content, and the way power is produced and delivered apparently does not lead to distinct differences in average exposure levels between companies. The combination of occupational category and company therefore gives resolution in exposure level (ϵ=0.56) near the middle of the range for chemical exposures (ϵ=0.30-0.84).

Population-specific JEM

The population-specific JEM developed here takes into account the differences in exposure level within occupational categories between companies. Unfortunately 14 cells of the matrix were not measured and had to be estimated based on a statistical model that explained only 7% of the total variability. However, given the very large portion of day-to-day variability (70%) only 30% could have been explained at most by the two factors occupational category and company.

The JEM features only one exposure measure (TWA magnetic field), but several other potential measures like the geometric mean, median, 90th percentile and higher cutoff scores correlate reasonably well with the TWA (Armstrong *et al.*, 1990; Savitz *et al.*, 1993). Using the TWA alone does not sacrifice statistical power in this study of electrical utility workers. However, the correlation of the TWA magnetic fields with lower cutoff scores, electric fields, and high-frequency transients (Armstrong *et al.*, 1990; Savitz *et al.*, 1993) were generally quite weak and may need to be assessed separately.

No measurements of historical magnetic field exposures had been taken and no precise historical data on power generation, power line loads, work patterns, work hours, etc., existed. Therefore, it was decided not to estimate past exposures by adjusting present quantitative exposure levels. General multipliers could not be derived from available information, and the noise inherent in these multipliers may not have generated more reliable estimates for the past. Some evidence, however, was available that the relative ranking of occupational categories, if not the absolute level of exposure, had been stable over the four decades studied (1950-1988). Bowman *et* *al.* (1992) reported few differences between current and historical (past) estimates of exposure based on adjusting for different time-activity profiles.

Conclusions

In conclusion, the measurement strategy used in this study resulted in quantitative estimates of present exposure to 60 Hz magnetic fields for 28 occupational categories in five companies. The population-specific JEM created will enable estimation of cumulative magnetic field exposure. Whether the optimal (given the limitations of the survey) grouping of magnetic field exposure will yield groups of workers with distinctly different levels of cumulative exposure will depend on the distribution of person-years spent in the different occupational categories. However, classifying exposure without any formal consideration of exposure variability might have led to a study with inadequate statistical power to detect relations between magnetic field exposure and cancer.

An extensive comparison of available personal meters for monitoring of magnetic field exposure should be carried out to allow a better understanding to be gained of observed differences between exposure surveys. This will also facilitate the setting and control of future occupational exposure limits if they are needed.

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Chapter 9

General discussion and conclusions

EPIDEMIOLOGICAL STUDY DESIGN AND EXPOSURE ASSESSMENT METHOD

In occupational epidemiology, the choice of the method of exposure assessment will be highly dependent on the study design. Epidemiological studies are either retrospective, prospective, or cross-sectional. In retrospective studies, the researcher has to rely on available exposure data collected in the past or use methods for retrospective exposure assessment to transfer information from the past into exposure levels. In prospective and cross-sectional studies the researcher has greater opportunities to accurately assess exposure. However, in a cross-sectional study the researcher will still be confronted with retrospective exposure assessment when studying chronic health effects. In prospective studies the methods of exposure assessment can be the best available, but studies with such a design are, unfortunately, not very common in occupational epidemiology, due to lack of funding and the long time span between the start of a study and actual results. Notwithstanding, a recent example of the application of a very sophisticated exposure assessment in a cohort study on acute effects of an airborne respiratory irritant can be found in the literature (Wegman *et al.*, 1992).

Another distinction can be made based on the population investigated by a particular study. Epidemiological studies of industry- or even company-specific populations will have great advantage both in terms of access to and quality of exposure information when compared to studies of the general population. As was noticed in the introduction of this thesis, the relatively efficient and cost effective design of hospital-based case-referent studies gave rise to the development of general job-exposure matrices (Hoar *et al.*, 1980; Pannett *et al.*, 1985) and new interview techniques combined with expert opinions (Siemiatycki *et al.*, 1981; Goldberg *et al.*, 1986). Recently, in a case-referent study of leukemia and brain tumors in the general population, exposure to electromagnetic fields was quantitatively assessed in 1,015 different workplaces (Floderus *et al.*, 1993). This unique example shows that even when studying the general population more quantitatively assessment of exposure is possible.

The more quantitative exposure assessment methods have been applied predominantly in industry- or company-specific populations. The first example of extensive quantitative exposure assessment in the course of a large cohort study on pneumoconiosis among miners was already mentioned in Chapter 1 (Oldham and Roach, 1952). Within this context the equivalent American National Study of Coal Workers Pneumoconiosis MSHA (NSCWP) should also be mentioned, although the design of the Mine Safety and Health Administration's (MSHA) exposure assessment strategy was less sophisticated and had elements of hazard control. On top of this, several authors questioned the collected exposure data under the MSHA scheme given the differences in exposure level found between samples collected by inspectors and mining companies themselves (Boden and Gold, 1984; Corn *et al.*, 1985; Seixas *et al.*, 1990; Weeks, 1991).

Another good example of exposure assessment concerns a retrospective cohort study among smelter workers in a copper smelter in Montana (Welch *et al.*, 1982; Lee-Feldstein, 1986). In that study a company specific job-exposure matrix, consisting of job area and calendar year specific quantitative exposure estimates, was based on exposure data collected from 1943-1958 and upon relative rankings of job areas based on data from the early 1960s. In a recent article by Lee-Feldstein (1989), in which a matched case-control was nested within the original cohort, the power of the study with relatively well assessed exposure was clearly demonstrated.

This latter case shows that the terminology used to describe exposure assessment methods can become rather cloudy. Since any cross-classification of jobs and exposure can be called a job-exposure matrix almost all exposure assessment methods except the methods which assess exposure on a case-by-case base can be labelled job-exposure matrices. Therefore, the term job-exposure matrix can not be restricted to situations in which the general population is studied and the cells of the matrix consist of nominal (yes-no) or ordinal (low-medium-high) information, based on qualitative or semiquantitative information. However, the difference between general and industry- or population-specific JEMs (see also Chapters 2 and 8 and Goldberg *et al.*, 1993) will be most noticeable within the contents of the cells made up by both exposure- and job-axis.

The last important distinction, is that between the levels at which the exposure assessment takes place, which again is strongly related to the study design. The exposure assessment (not the actual calculation of a subject's specific exposure measure) can be either on an individual basis or based on a common denominator like, job, zone (Corn and Esmen, 1979), occupational title group (Gamble *et al.*, 1976), or department which was shared by subjects at some point in time. Both approaches have been used in the past. The case-by-case approach has been used predominantly in case-referent studies and cross-sectional studies, although the abundance of quantitative exposure data and the repeated measurement design has enabled application of this approach in the earlier mentioned NSCWP cohort study among miners in the USA (Heederik *et al.*, 1993). Nevertheless, in the vast majority of occupational epidemiological studies of both cohort and case-referent type, exposure is assessed and subsequently applied at group level.

With the previous considerations in mind the results of the studied exposure assessment methods will be discussed.

GENERAL JOB-EXPOSURE MATRICES

The two job-exposure matrices evaluated herein can be identified as first generation JEMs. Hoar (1980) was actually the first to define the cross-classification of jobs and exposures as a job-exposure matrix. The comparison of the matrices showed very meagre concordance in assessed exposure for 25 common exposures. Only exposure to wood dust was assessed by both JEMs for the same jobs and subjects. Little difference was seen when either strict or more lenient criteria were used to define exposure, although for the British MRC JEM the more restrictive way of defining exposure led to better results in analysis of lung cancer morbidity. This was in concordance with what was expected from theory. A high specificity is to be preferred in situations like in the general population in which only a small fraction of the study population is exposed (Flegal *et al.*, 1986; Lagakos, 1988).

It is quite likely that information on which content of the cells of the JEMs was based, played a major role in the discrepancies shown. Also, a difference in detail both for the job axis as for the exposure axis will have contributed. Differences in definitions of jobs, industries, and exposures between the two countries represented by the JEMs, may also have been important. Also, both JEMs were applied on a study base from yet another country. A nice example of misclassification due to this is given by Pouwels *et al.* (1989) who showed that exposure to coal dust for train drivers attributed by the British MRC JEM is very unlikely for train drivers in the Netherlands where the rail network has been almost completely electrified.

A fundamental problem with general JEMs is the inherent notion that workers with the same job title even from different industries will more or less experience the same exposure. While this might be true in general terms, e.g. almost all welders will be exposed to welding fumes, it is probably not generally true when exposures are considered at a more detailed qualitative or (semi)quantitative level. As shown in Chapter 8, only 25% of an industry-wide selection of groups of workers sharing the same environment and jobs, were uniformly exposed (defined as groups with individuals whose exposure levels are within a factor 2). Since these groups were factory-specific, one can only presume that even larger within-group differences would have been seen when workers were grouped across factories or even industries, which is common practice with general JEMs. Furthermore, the assumption of JEMs that exposures remain stationary for periods up to several years should be considered wishful thinking, since exposure levels tend to decline over time (see for instance Huy *et al.*, 1991).

I agree with Olsen's (1988) conclusion that general JEMs will hardly ever give sufficiently detailed information on occupational exposure at the individual level to be very useful in epidemiology. Population-specific JEMs can be an alternative to gather more specific exposure information and will yield more reliable exposure measures. In a prospective design the likelihood of recall bias due to differential under- or over-reporting of certain exposures will be unlikely. On the contrary, the 'interview JEM' proposed by Siemiatycki *et al.* (1989) for hospital-based case-referent studies might be more prone to this bias.

Given the inherent weaknesses of the general JEM approach one can question the results of studies performed with this exposure assessment method. As was shown, non-differential misclassification can not only result in a lack of power to detect a relationship between an exposure and response, but will also bias such a relationship most likely towards the null. The fact that proven lung carcinogens could not be detected in the study of Hinds *et al.* (1985) supports this point.

Application of more detailed questionnaires and interviews on a case-by-case basis might be a more effective method than applying general JEMs in the general population. However, especially in case-referent studies non-differential bias can lead to the detection of spurious relationships between exposure and health effects. For example, the general discussion of the existence of a relationship between chronic non-specific lung diseases (CNSLD) and occupational exposures focussed on the notion of spurious relationships due to non-differential bias (Becklake, 1985; Heederik and Pal, 1993).

The case-by-case approach will make appreciation of between-worker differences in exposure possible. For instance, incorporation of questions on work style, use of personal protection devices, physical form of the chemicals applied, etc., will enable the expert to estimate different exposures for workers with the same job title. The validity and reliability of such (semi)quantitative estimation methods will be essential for the quality of exposure measures resulting from these methods.

SEMIQUANTITATIVE EXPOSURE ESTIMATION

The two studies described in this thesis and a few other studies on semi-quantitative exposure estimation methods have resulted in a rather comprehensive picture on the validity and inherent problems related to these methods. Woitowitz *et al.* (1970) were the first to formalize the subjective estimation of occupational exposure, which in their case was dealing with exposure to asbestos. In a firm processing raw asbestos, a team consisting of an industrial physician, department heads, technical inspectors, industrial health officer, safety engineer and the shop committee classified all parts of the plant and all activities into four main hazard classes. This scheme was subsequently extended into the past to cover all time periods and types of activities which occurred for the entire working histories of the study subjects.

The hazard categories were validated against the exposure measurements collected over the years 1960-1970 in the same plant. The authors showed that "the empirically formed hazard classes and their inner relations are substantially upheld by the dust concentrations as measured". The high, moderate, and heavy classes corresponded to 0.5, 1.0, and 1.5 mg/m^3 dry or ashed asbestos dust. They also noted that the range in dust concentration increased with increasing hazard class, but concluded that their ranking exposure estimation method did have a quantifiable core. However, from the paper it is not exactly clear whether the results of previous dust measurements were actually used to assess the empirical hazard classes. If that had been the case, the observed relationship between hazard classes and dust concentrations might not be that surprising. Regardless, this paper has been very important to the development and validation of semiquantitative exposure estimates in more recent studies.

The two studies presented in Chapter 3 and 4 have clarified several issues related to subjective estimation of occupational exposure. First, it seems that a relative ranking of exposure is feasible within a factory, although chemical and physical properties and occurrence of the chemical within the process may have (a negative) influence on the ability to rank exposures from low to high (see Chapter 4). Extending the assessment to more factories or even assessing exposure industry-wide seems not to be feasible because of severe misclassification due to the relative character of the ranking as was shown in Chapter 3. Second, it seems that over-estimation of exposure level by an expert is common in the absence of quantitative measurement data. This was clearly demonstrated in Chapter 4 and was also seen by Hawkins and Evans (1989). They showed that industrial hygienists overestimated the average exposure to toluene of a group of batch chemical process workers on average by a factor 3 (range 0.25-12). This phenomenon is worrying, since exposure-response relationships based on overestimated exposure estimates will underestimate the risk and subsequently will give rise to occupational exposure limits (OELs), which are not particulary protective.

Stewart and Herrick (1991) showed that weights often arbitrarily assigned to relative classification (for instance, 1, 2, and 3 for respectively low, medium, and high) might not be appropriate for subjective semiquantitative estimates. They calculated average weights of respectively 1, 2, 6, and 5 for the categories none, minor, medium, and high exposure, in which two occupational hygienists grouped full-shift tasks (see Chapter 3). In Table 1 their exercise has been extended and from this table it appears that except for class 4 multiplicative weights seem to be more appropriate than additive weights in this context. In a sense, this is consistent with the idea that exposures are lognormally distributed. The suggestion of Stewart and Herrick to use a more quantitative scale, is not feasible given the relative nature of the subjective estimation. Validation with actual measurements of the exposure, or calibration of the subjective instrument with some quantitative exposure data will be a more promising approach.

Another issue is well demonstrated in a study among brickworkers in South Africa (Myers *et al.*, 1989; Myers, 1989). In that study exposure to dust was subjectively characterized by consensus of the survey team based in part on subjective infor-

Table 1. Empirical weighing factors from several validation studies of subjective semiquantitative exposure estimates.

Study	Class 1	Class 2	Class 3	Class 4	Exposure
Woitowitz *et al.*, 1970	1.0	2.0	3.0	-	asbestos
doPico, 1982	1.0	2.3	7.5	-	grain dust
Rom *et al.*, 1983	1.0	4.0	16.0	-	dust
Kromhout *et al.*, 1987	-	1.0	5.9	9.4	solvents
	1.0	4.9	17.3	4.0	dust
	1.0	3.0	12.5	8.3	dust
	1.0	2.8	3.4	5.4	dust
	1.0	1.4	1.6	3.2	dust
	1.0	1.4	2.0	3.8	dust
	-	1.0	2.0	3.9	dust
	1.0	0.6	1.9	3.0	dust
Myers *et al.*, 1989	1.0	2.1	6.6	-	dust
	1.0	2.8	7.4	-	dust
Flynn *et al.*, 1991	1.0	6.1	15.1	-	magnetic fields
Mean value	1.0	2.5	7.3	5.1	

mation from the workers themselves. Again, it was shown that relative rankings were correct when compared with the results of 135 dust samples from three kilns. Unfortunately, no kiln-specific comparisons were reported. Subsequent use of the individual worker's subjective estimates in an analysis of respiratory symptoms showed stronger relationships for the subjective than the objective estimates of exposure for symptoms of a more acute nature. The opposite was true for more advanced symptomatology. One can argue that in this case the subjective estimates of exposure are probably reflecting estimates of personal susceptibility for the effects of dust exposures than the exposure *per se*. A strong relationship between acute effects and the subjective exposure measures is not surprising but will have only limited value for the relationship between dustiness and respiratory symptoms. Again, this last example shows over-estimation of exposure, but in this case it will be of a differential nature and therefore give rise to a spurious relationship.

Only the study reported in Chapter 3 compared more than two (groups of) raters at the same time (workers, occupational hygienists, and supervisors). Teschke *et al.* (1989) compared the performance of workers with industrial hygienists. It seems from these studies that occupational hygienists are the raters of preference, although experienced seem to perform almost as well. Care has to be taken with supervisors who seem to rely more on their knowledge of how the work should be done, than on how it is actually being done.

Recently, Flynn *et al.* (1991) showed that ranking of non-chemical exposures like exposure to magnetic fields of workers in the utility industry by experts from the industry could be done with comparable results as was seen for chemical exposures. The average levels for the three ranks were not equally spaced, again suggesting that multiplicative weights seem to be more appropriate than additive weights.

It was shown that subjective methods for exposure assessment have some quantitative substance, but only in a relative sense. Thus, ranking of exposures within a factory seems possible for certain chemical agents, but ranking exposures industry-wide not. Subjective classification of exposure in a quantitative way will lead in most cases to overestimation of exposure. Both problems will give rise to misclassification and differential and non-differential bias in industry-wide epidemiological studies and subsequently lead to obscured or spurious exposure-response relationships.

MODELLING OF QUANTITATIVE EXPOSURE DATA

Given the limitations of both the general JEM approach and the subjective semi-quantitative estimation methods it is logical to focus more on quantitative methods of exposure assessment. However, given the variable nature of occupational exposures application of quantitative methods is not always straightforward.

The study in the rubber industry showed that empirical statistical models are capable of unravelling factors affecting exposure. It also showed that these factors are different for different types of exposures. Although, this is not a troublesome finding, it shows that tasks, control measures, production characteristics are better descriptors of exposure than generic proxies like job title. Therefore, it seems logical not to link exposure strictly to the job title, but to relate it to particular tasks, and the presence of control measures for that particular job title.

From the study it is also clear that linear models are only capable of explaining a limited amount of the variability in exposure level. Therefore, using these models to predict exposure concentrations can result in imprecise estimates. Although some improvement in terms of explained variability could be achieved by better coding of explanatory variables, the fact that personal variables like work style and hygienic behaviour were not taken into account will probably prevent significant improvement. Models developed for the rubber industry in the Netherlands, however, have given an impression of relevant factors in terms of exposure. The fact that local exhaust ventilation systems did not show up as significant in the models and therefore did not reduce exposure levels was confirmed in a parallel study in which the local exhaust ventilation systems were evaluated independently on the basis of design, efficiency, and maintenance considerations (Swuste *et al.*, 1993).

Unfortunately, it has not been possible to validate the models with new data. The hypothesis that the models will not predict individual measurements accurately follows directly from the limited amount of explained exposure variability, but on the other hand, the models should be able to predict an average exposure level. This conjecture motivated the development of an observational workplace survey system based on the relationships found in the empirical models. The baseline exposure survey within the rubber manufacturing industry thus lead to some kind of expert system, that was needed to evaluate the chemical hazards present in the other companies not represented in the sample of surveyed companies (van

Tongeren *et al.*, 1993).

The exposure data collected were also used to partition the variance rather than to explain the observed variance. This was done on different levels and resulted eventually in estimates of the between and within group and worker components of variance. The *ad hoc* developed parameters 'resolution in exposure level between groups' and 'precision of the mean exposure of a particular group' do vary for different grouping schemes. So far, unfortunately, it is not clear which of the two parameters is the most important in an epidemiological exposure-response. Recently, Attfield and others (1993) have proposed formulas to facilitate a more formal comparison of different grouping systems. Their formulas focus on the standard error of the regression coefficient of an exposure-response relationship in the case of continuous exposure data. A formula for attenuation in the case of grouped exposure data which incorporates the fact that the classical error model as well as the Berkson model type error play a role, has very recently been developed as well (Kupper, personal communication). Preliminary findings with these new formulas suggest that increasing the resolution in exposure level between groups at the cost of precision is not an efficient way to improve the exposure-response relationship. Also, increasing the number of repeated measurements at the cost of the number of workers sampled within a group will have a negative effect, because the number of workers measured within a group has a larger influence on the precision of the mean exposure within a group.

The recently proposed formulas, have important limitations. They assume equal number of measurements per worker and equal number of workers in each of the groups. This will hardly ever be the case and will not be in line with the observation that only a small (sub)group is generally exposed at relatively high levels, while the groups at low and medium levels are generally larger. Also, the formulas have only been developed for linear exposure-response relationships with a continuous response variable. Alternatively, sensitivity analysis of different methods for calculating exposure measures might be valuable (Heederik *et al.*, 1993), but proclaiming the method that produces the highest risk estimates to be the most valid one should be avoided (Blair and Stewart, 1992). Choosing a particular method of exposure classification should be based on the characteristics of the exposure and not solely on its behaviour in an exposure-response analysis.

EXPOSURE VARIABILITY

The evaluation of exposure variability in a large international database has yielded valuable information and has provided the opportunity to generalize the results to measurement strategies for epidemiological purposes. Both environmental and production factors appeared to influence the day-to-day component of variance and to a much lesser extent the between-worker component of variance. Based on this analysis it can be projected that in situations where workers work outdoors in an intermittent process a 4-5 fold increase in number of repeated measurements will be needed to provide the same precision of the average exposure, compared to a situation where workers are indoors in a continuous process.

No formal model could be established to explain the between-worker component. This result is rather dramatic given the observation that only 25% of the groups based on job title and factory could be considered uniformly exposed. Therefore, *a priori* recognition of so-called homogeneously exposed groups of workers seems to be a rather artful process, in which a good result will be achieved more by chance than good skill. More rigorous application of measurement strategies with repeated random sampling of days and workers within *a priori* assigned groups will have the advantage that the relative size of the variance components can be assessed. By using ancillary data on work methods, work style, production and environmental factors, the reasons for deviations can probably be detected through statistical modelling. *A posteriori* groupings based on factors affecting exposure instead of general proxies like job title, will therefore result in more uniformly exposed groups.

WELL-DESIGNED ASSESSMENT OF OCCUPATIONAL EXPOSURE

The strength of a well-designed assessment of occupational exposure to magnetic fields among electrical utility workers was shown in Chapter 8. Application of a measurement strategy with randomized repeated measurements with limited input of industrial hygiene professionals during the actual fieldwork enabled the collection of a vast amount of personal exposure data within a limited time period and at relatively small cost. However, a major point of discussion will be the extent to which the data might have been deliberately falsified. The extensive protocol used for the collection and handling of the exposure data will not have precluded this. The use of the newly developed graphical method to examine the fit of the random effects model and the distribution of the exposure data enabled the detection of gross outliers and falsified observations, but it will not have had a complete coverage. Despite any drawbacks of this unsupervised measurement strategy, it is believed that the sheer number of randomly collected repeated measurements provided an excellent base for an optimal exposure classification.

CONCLUSIONS AND RECOMMENDATIONS

Exposure assessment in occupational health has long been considered to be more art than science. Through validation and methodological studies, as described in this thesis, some light has been shed on the science of exposure assessment. Although limitations of the methods have become clearer, a lot of work still has to be done. Improvement and validation of existing methods is possible as was shown in this thesis. However, the most profound progress is expected to take place in the field of quantitative exposure assessment. With the increasing availability of simple but accurate measurement devices, the number of measurements should increase. The example of the utility industry survey has shown that large numbers of randomly collected exposure data can be obtained in a relatively short time period and at relatively low cost by limiting the amount of time spent during the actual field work of occupational hygiene professionals. Although the need for randomly collected exposure information of industry-wide populations will be essential for occupational epidemiology, a lot of exposure data will still be collected for compliance purposes. The limitations and uses of these biased data should be further explored in order to find out if and under what conditions, they can be used for epidemiological purposes.

Recently, Droz (1993) has argued that not all good should be expected to come from repeated random sampling of workers and days. In situation with very hazardous but infrequent exposure (e.g. exposure to antineoplastic agents of nurses) a random sampling scheme could result in an imprecise picture of the exposure and should therefore be replaced by task-specific sampling and time-use registration.

Given recent changes in industry exposures might become even more idiosyncratic with the result that the day-to-day variability in exposure will increase. Although, this could lead to more homogeneously or even uniformly exposed workers more repeated measurements might be needed to overcome attenuation of exposure-response relationships. Through more specialisation of workers the opposite picture could be drawn as well. Time will tell, but it will be essential to measure both trends in average exposure level as well as trends in the variability in exposure levels. In doing so, the art of retrospective exposure assessment will become obsolete in the near future making room for more scientific and most likely, more accurate ways of assessment of occupational exposure.

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Summary

In this thesis methods for assessment of occupational exposure are evaluated and developed. These methods range from subjective methods (qualitative and semiquantitative) to more objective quantitative methods based on actual measurement of personal exposure to chemical and physical agents.

In chapter 2, data from a general population cohort of 878 men from the town of Zutphen, the Netherlands, were used to evaluate the performance of two general job-exposure matrices. Exposures, generated by the job-exposure matrices on the basis of job histories, were compared. The validity of those exposures was measured against exposures reported by the participants in 1977/1978. The performance of the different exposure measures was assessed in proportional hazards analyses of lung cancer morbidity incidence. The two general job-exposure matrices generally disagreed with regard to exposure classification because of differences in exposure assessment and the level of detail of the job axis. When compared with self-reported exposures, the sensitivity of both job-exposure matrices was low (on average, below 0.51), while the specificity was generally high (on average, above 0.90). Self-reported exposures to asbestos, pesticides, and welding fumes showed elevated risk ratios for lung cancer, which were absent for exposures generated by the two job-exposure matrices. A population-specific job-exposure matrix was proposed as an alternative to general job-exposure matrices developed elsewhere. Such a matrix can be constructed from the results of in-depth interviews of a job-stratified sample of cohort members. Sound validation and documentation of exposure assessment methods used in job-exposure matrices were recommended.

In chapter 3 a study is described in which a method for semi-quantitative estimation of the exposure at task level was used and validated with actual measurements in five small factories. The results showed that occupational hygienists were in general the most successful raters. Plant supervisors and workers handled the estimation method less successfully because of more misclassification of the tasks. The method resulted, in general, in a classification of

tasks in four exposure categories ranging from no exposure to high exposure. The exposure categories correlated positively with mean concentrations, but showed overlapping exposure distributions. This resulted in misclassification of the exposure for individual workers when a relatively large inter-individual variability in exposure levels within an exposure category was present. The results showed that this method can be used for workplace exposure zoning, but that the usefulness of the estimates for epidemiological purposes was not clear-cut and depended strongly on the actual exposure characteristics within a workplace. A combination of the semiquantitative exposure estimation method together with assessment of the exposure levels by measurements makes a rearrangement of tasks or individual workers possible and could improve the validity of this method for epidemiological purposes.

In chapter 4 the performance is studied of nine occupational hygienists, who semiquantitatively estimated the exposure to methylene chloride and styrene in a small polyester factory. They ranked the jobs from low to high exposure, and subsequently classified them into three exposure categories (0-½TLV, ½TLV-TLV, and > TLV). The influence of quantitative exposure data on the results of the estimations was studied. Therefore, three estimations were performed. The first estimation was made after a visit to the workplace; the second and third were made after limited exposure data were presented. The ranking of styrene exposure was, in general, poor compared to the ranking of methylene chloride exposure. Physical properties, such as perception of smell, application in the process, and level of exposure might be the reasons for this striking difference. Classification of exposure into quantitative exposure categories was poor without knowledge of actual exposure data. No differences in the performance of the occupational hygienists between the two solvents were present. The results suggested that the success of an exposure estimation method depends on the type of exposure (kind of chemical, use, appearance), the available information on jobs and process, and the kind of estimate (ranking or classification). Semiquantitative classification of exposure by occupational hygienists appears to be better if they have a limited set of air sampling data at their disposal. Ranking of jobs can be performed successfully without exposure data, but a detailed description of the workplace and tasks is needed. More insight is needed concerning the influence of the chemical type, exposure pattern(s), and raters' experience on the results of semiquantitative ranking methods.

Chapter 5 describes an exposure survey in 10 rubber-manufacturing plants. Personal exposures to airborne particulates, rubber fumes and solvents, and also dermal contamination, were measured. To identify factors affecting exposure the personal exposure levels and information on tasks performed, ventilation characteristics, and production variables were used in multiple linear regression models. The exposure was generally very variable. The specific circumstances in each department of each plant determined the actual levels of exposure to a large extent. The factors affecting exposure turned out to be different for each of the types of exposure considered. The model for exposure to airborne particulates explained 40% of the total variability and incorporating the actual time spent on a task only slightly improved the model (R^2=0.42). The handling of chemicals in powder form was the main factor affecting exposure, forced ventilation having a negligible effect. The model for exposure to curing fumes (measured as the cyclohexane-soluble fraction of the particulate matter) explained 50% of the variability. Both curing temperature and pressure determined the level of rubber fumes. Local exhaust ventilation showed a significant exposure reducing effect. The effect of curing different elastomers was not statistically significant. Dermal exposure to cyclohexane-soluble matter could only be explained to a limited extent (R^2=0.22). Tasks with frequent contact with (warm) compound and maintenance tasks in the engineering services departments resulted in high dermal exposure. Tasks in which solvents were directly used explained 56% of the variation in solvent exposures. Exposure data together with information on tasks, methods of work, ventilation and production throughout a branch of industry, can be used to derive empirical statistical models which occupational hygienists can apply to study factors affecting exposure. These determining factors are of crucial importance, whenever hazard control or epidemiologic research is the ultimate goal.

In chapter 6 the implications of exposure variability are examined for the design of occupational epidemiology studies in the rubber industry. The efficiency of different grouping schemes for exposure to particulates, dermal exposure to cyclohexane-soluble contaminants, and exposure to solvents was assessed. Statistical parameters for contrast in average exposure and precision of average exposure were developed to enable comparison of different grouping schemes. Groupings based on job title, plant, factors affecting exposure, published classifications, and the ISCO-ILO classification were compared. Grouping of exposure to particulates and dermal exposure appeared to be less efficient than grouping of exposure to solvents. Grouping of solvent exposure using either occupational title groups, existing classification schemes, and schemes based on factors affecting exposure showed comparable high resolution in exposure levels. Even the most detailed grouping schemes based on the combination of plant and occupational title group showed relative modest resolution in particulate and dermal exposure levels. Groupings based on factors affecting exposure showed for these exposures similar resolution, but were more efficient because of a higher precision due to a smaller number of groups. It was concluded, that application of optimal exposure grouping strategies will benefit new research on cancer among rubber workers. Eventually, this might resolve the unwanted situation in which a complete industry was included on the list of proven human carcinogens.

Chapter 7 focuses on within- and between-worker exposure variability. A database of approximately 20,000 chemical exposures was constructed in close co-operation between the School of Public Health of the University of North Carolina at Chapel Hill and the Department of Air Pollution of the Wageningen Agricultural University. A special feature of this database was that only multiple measurements of exposure from the same workers were included. This enabled estimation of within- and between-worker variance components of occupational exposure to chemical agents throughout industry. Most of the groups were not uniformly exposed as is generally assumed by occupational hygienists. In fact only 42 out of a total of 165 groups (25%), based on job title and factory, had 95% of individual mean exposures within a two-fold range. On the contrary, about 30% of the groups had 95% of individual mean exposures in a range which was greater than 10-fold. Environmental and production factors were shown to have distinct influences on the within-worker (day-to-day) variability, but not on the between-worker variability. Groups working outdoors and those working without local exhaust ventilation showed more day-to-day variability than groups working indoors and those working with local exhaust ventilation. Groups consisting of mobile workers, those working with an intermittent process and those where the source of contamination was either local or mobile also showed great day-to-day variability. In a multivariate regression model, environment (indoors-outdoors) and type of process (continuous-intermittent) explained 41% of the variability in the within-worker component of variance. Another model, in which only type of process (continuous-intermittent) had a significant effect, explained only 13% of the variability in the between-worker component of variance.

In chapter 8 the results are reported of a large survey of occupational exposure to 60 Hz magnetic fields conducted among randomly selected workers in five electric power companies. The design of the study facilitated the examination of exposure variability and provided the base for a job-exposure matrix (JEM) for linking health outcomes and occupational magnetic field exposures in the epidemiological study of employees of these companies. Almost 3.000 successful measurement attempts indicated average exposures ranging from 0.11 μT for 'Senior Managers' to 1.50 μT for 'Cable Splicers'. The differences among the five companies were relatively small with the more urban companies showing somewhat higher average exposures. The day-to-day component of variance exceeded the within- and between-group components of variance. The final JEM consisted of five groups with average exposure levels of 0.12, 0.21, 0.39, 0.62, and 1.27 μT, respectively. Given the variance in exposure, even this optimal grouping showed considerable overlap in exposure between adjacent groups. Nevertheless, the JEM incorporated the differences in exposure level within occupational categories between companies in the most efficient way and provides an objective and statistically based method for estimation of cumulative magnetic field exposure.

Finally, in chapter 9 a general discussion and conclusions are given. Through validation and methodological studies, as described in the thesis, some light has been shed on the science of occupational exposure assessment. Although improvement of subjective methods is feasible to some extent, the inherent pitfalls can lead to exposures estimates not accurate enough to be used in epidemiological exposure-response relationships. Statistical models, as developed in this thesis, to unravel factors affecting exposure and to estimate variance components will contribute to more accurate ways of exposure assessment. Application of the developed statistical methods to optimize the grouping of exposure will result in less misclassification and bias and therefore in better exposure-response relationships. Consequently, this will lead to more protective occupational exposure limits. Hopefully, more randomly collected quantitative exposure data will become available to make use of the developed tools. Only then, the widely criticized art of retrospective guessing of occupational exposures will become obsolete.

Samenvatting

VAN SUBJECTIEF SCHATTEN NAAR STATISTISCH MODELLEREN

Methoden voor het karakteriseren van beroepsmatige blootstellingen

In dit proefschrift worden bestaande en nieuwe methoden voor het karakteriseren van beroepsmatige blootstellingen geëvalueerd. De methoden variëren van subjectieve methoden resulterend in kwalitatieve of semi-kwantitatieve blootstellingsmaten tot meer objectieve kwantitatieve methoden gebaseerd op persoonlijke metingen van beroepsmatige blootstellingen.

In hoofdstuk 2 worden gegevens gebruikt van een groep van 878 mannen uit de algemene bevolking van Zutphen om het functioneren van twee zgn. algemene beroepen-blootstellingen matrices te evalueren. De door de matrices gegenereerde blootstellingen op basis van het beroepsverleden werden vergeleken. De validiteit van de gegenereerde blootstellingen werd bepaald aan de hand van vergelijkingen met zelf-gerapporteerde gegevens uit 1977/1978. De verschillende blootstellingsmaten werden vervolgens toegepast in een zgn. 'overlevingsanalyse' van de longkanker morbiditeit incidentie. De mate van overeenkomst tussen de door de twee matrices gegenereerde blootstelling was slecht. Waarschijnlijk is dit te wijten aan verschillen manieren waarop de blootstelling gekarakteriseerd was in de matrices en de mate van detaillering van de beroepen-as van de matrices. Vergeleken met de zelf-gerapporteerde blootstellingen was de sensitiviteit van beide matrices laag (gemiddeld lager dan 0,51), terwijl de specificiteit hoog was (gemiddeld hoger dan 0,90). Zelf-gerapporteerde blootstellingen aan asbest, pesticiden en lasdampen hingen samen met verhoogde risico's voor longkanker. Deze verbanden waren afwezig wanneer dezelfde blootstellingen met behulp van de matrices werden gegenereerd. Als alternatief voor in het buitenland ontwikkelde matrices wordt de zgn. populatie-specifieke beroepen-blootstellingen matrix aanbevolen. Deze matrix kan worden geconstrueerd uit de resultaten van diepte-interviews naar beroepsmatige blootstellingen bij een naar beroep gestratificeerde steekproef van de onderzoekspopulatie. Aanbevolen wordt de blootstellingskarakterisering in een beroepen-blootstellingen matrix degelijk te valideren en te documenteren.

In hoofdstuk 3 wordt een studie beschreven waarin een methode voor semi-kwantitatieve blootstellingsschatting op taakniveau werd ontwikkeld en gevalideerd met metingen in een vijftal kleine bedrijven. Uit de resultaten bleek dat arbeidshygiënisten in het algemeen de beste schatters zijn. Sleutelfiguren (zoals bedrijfsleiders) en werknemers hanteerden de methode minder succesvol, hetgeen leidde tot meer misclassificatie van taken. De methode resulteerde in een classificering van taken in een viertal blootstellingscategorieën variërend van niet tot hoog blootgesteld. De categorieën correleerden positief met de gemeten gemiddelde concentraties, maar vertoonden overlappende blootstellingsverdelingen. Dit resulteerde in misclassificatie van individuele werknemers, wanneer de tussenpersoonsvariatie in blootstelling relatief hoog was. De resultaten geven aan dat de methode gebruikt kan worden voor zoneren, maar dat de bruikbaarheid van de blootstellingsschattingen voor epidemiologisch onderzoek twijfelachtig is en sterk afhangt van het karakter van de blootstelling op de werkplaats. Het combineren van deze semi-kwantitatieve methode met daadwerkelijke metingen van de blootstelling maakt het mogelijk misgeclassificeerde taken of individuele werknemers herin te delen en zodoende de bruikbaarheid voor epidemiologische doeleinden te vergroten.

In hoofdstuk 4 wordt de competentie bestudeerd van negen arbeidshygiënisten, die de blootstelling aan methyleenchloride en styreen in een kleine plastic fabriek semi-kwantitatief moesten schatten. De arbeidshygiënisten rangschikten de functies van laag naar hoog blootgesteld en deelden de functies in drie blootstellingscategorieën in (0-½MAC, ½MAC-MAC en > MAC). De invloed van kwantitatieve meetgegevens op de resultaten van de schatters werd bestudeerd door de schattingen in drievoud uit te voeren. Een eerste schatting werd gemaakt na een werkplekbezoek; de tweede en derde schatting nadat de arbeidshygiënisten de beschikking hadden gekregen over enkele meetgegevens. Het rangschikken van de blootstelling aan styreen verliep zeer matig in vergelijking met het rangschikken van de blootstelling aan methyleenchloride. Fysische kenmerken zoals de reukdrempel, toepassing van de chemische stoffen in het produktieproces en het niveau van de blootstelling kunnen een verklaring vormen voor dit fenomeen. Het classificeren van blootstellingen in meer kwantitatieve categorieën lukte in het algemeen slecht zonder meetgegevens. Verschillen tussen de twee chemische stoffen waren niet aanwezig. De resultaten suggereren dat het succes van een subjectieve methode voor het schatten van blootstelling sterk afhangt van het type blootstelling (soort chemische stof, gebruik, voorkomen op de werkplek), de aanwezige informatie over de functie en het proces en het soort schatting (rangschikken of indelen in klassen). Het indelen in semi-kwantitatieve klassen lukt beter wanneer de arbeidshygiënist kan beschikken over enige meetgegevens. Het rangschikken van functies kan succesvol gebeuren zonder meetgegevens, maar een gedetailleerde beschrijving van werkplekken en taken is nodig. Nader onderzoek naar de invloed van het soort chemische stof, het karakter van de blootstelling en de ervaring van de schatter op de resultaten van semi-kwantitatieve schattingsmethoden wordt aanbevolen.

In hoofdstuk 5 worden de resultaten van een onderzoek naar de chemische blootstelling in 10 rubberverwerkende bedrijven beschreven. De persoonlijke blootstelling aan stof, vulcanisatie-dampen, oplosmiddelen en dermale contaminatie werd uitgebreid gemeten. De meetresultaten tezamen met informatie over uitgevoerde taken, karakteristieken van algmene en gerichte ventilatie en produktiegegevens werden gebruikt in multivariate lineaire regressie modellen om blootstellingsbepalende factoren op te sporen. De blootstelling bleek sterk te variëren. De specifieke omstandigheden in een afdeling in een fabriek bepaalden voor een groot deel het blootstellingsniveau. Significante blootstellingsbepalende factoren waren verschillend voor de verschillende blootstellingen. Het model voor de stofblootstelling verklaarde 40% van de totale variantie. De verklaarde variantie nam licht toe wanneer de tijd gedurende welke een taak werd uitgevoerd in het model werd opgenomen (R^2=0.42). Het omgaan met chemicaliën in poedervorm was de voornaamste blootstellingsbepalende factor te zijn, terwijl gerichte ventilatie geen invloed bleek te hebben. Het model voor blootstelling aan vulcanisatiedampen (gemeten als de cyclohexaan-oplosbare fractie van de deeltjesvormige verontreiniging) verklaarde 50% van de variantie. Vulcanisatietemparatuur en -druk bepaalden de blootstellingsniveaus. Gerichte ventilatie bleek hier wel effectief te zijn. Het effect van het vulcaniseren van verschillende elastomeren was niet statistisch significant. De variatie in dermale blootstelling aan in cyclohexaan oplosbare componenten kon slechts voor een gering deel worden verklaard (R^2=0.22). Taken met frequent contact met warme rubbermengsels en onderhoudswerkzaamheden van de technische dienst resulteerden in hoge dermale blootstellingen. Taken waarin oplosmiddelen werden gebruikt verklaarden 56% van de variatie in de blootstelling aan oplosmiddelen. Blootstellingsgegevens tezamen met informatie over taken, werkmethoden, ventilatie en produktie kunnen gebruikt worden om empirische statistische modellen te ontwikkelen, die door de arbeidshygiënist gebruikt kunnen worden om blootstellingsbepalende factoren te bestuderen en zonodig te elimineren. Kennis van deze factoren is van vitaal belang voor het ontwikkelen van beheersmaatregelen en het uitvoeren van epidemiologisch onderzoek.

In hoofdstuk 6 worden de implicaties van de in de rubberverwerkende industrie geconstateerde variabiliteit in blootstellingsconcentraties bekeken in het licht van epidemiologische studies. De efficiëntie van verschillende manieren van groeperen van de blootstelling aan stof, de dermale blootstelling en de blootstelling aan oplosmiddelen werd bestudeerd. Statistische parameters voor het contrast in gemiddelde blootstelling en voor de precisie van de gemiddelde blootstelling werden ontwikkeld om verschillende manieren van groeperen met elkaar te kunnen vergelijken. Indelingen op basis van functie, bedrijf, blootstelllingsbepalende factoren, indelingen uit de literatuur en de standaard ISCO-ILO indeling werden vergeleken. Het groeperen van de stofblootstelling en van de dermale blootstelling bleek minder efficiënt te zijn dan het groeperen van de blootstelling aan oplosmiddelen. Indelingen van de blootstelling aan oplosmiddelen gebaseerd op functiegroepen, op indelingen uit de literatuur en op blootstellingsbepalende factoren vertoonden een vergelijkbaar groot contrast in gemiddelde blootstelling. Voor de blootstelling aan stof en de dermale blootstelling bleek zelfs de meest gedetailleerde indeling op basis van bedrijf en functiegroep slechts te leiden tot een matig contrast. Indelingen op basis van blootstellingsbepalende factoren vertoonden een gelijk contrast, maar waren meer efficiënt vanwege een hogere precisie door een kleiner aantal groepen. Geconcludeerd wordt, dat het toepassen van een optimale indeling de kans van slagen van nieuwe epidemiologische studies naar kwaadaardige nieuwvormingen bij werknemers in de rubberverwerkende industrie zal verhogen. Uiteindelijk zou dit een einde kunnen maken aan de ongewenste situatie waarin een complete industrietak vermeld staat in de lijst van bewezen humane carcinogenen.

In hoofdstuk 7 worden de binnen- en tussenpersoonsvariantie onderzocht. In een samenwerkingsverband tussen de School of Public Health van de universiteit van North Carolina te Chapel Hill en de vakgroep Luchtkwaliteit van de Landbouwuniversiteit werd een database geconstrueerd met ongeveer 20.000 persoonlijk gemeten chemische blootstellingen. Het speciale van deze database was gelegen in het feit dat slechts werknemers met meerdere metingen in de database werden opgenomen. Dit maakte het mogelijk de binnen- en tussenpersoonsvariantiecomponenten voor beroepsmatige blootstellingen aan chemische stoffen te schatten. Het merendeel van de groepen bleek niet uniform blootgesteld te zijn, in tegenstelling tot wat algemeen gedacht wordt door arbeidshygiënisten. Slechts 42 uit een totaal van 165 groepen (25%) gebaseerd op functie en bedrijf, had 95% van de individuele gemiddelde blootstellingen binnen een bereik van een factor twee. Daartegenover stond, dat ongeveer 30% van de groepen 95% van de individuele gemiddelde blootstellingen binnen een bereik groter dan 10 had. Omgevings- en productiefactoren bleken een duidelijke invloed te hebben op de binnenpersoonscomponent. Groepen die buiten werkten en groepen die werkten zonder gerichte ventilatie vertoonden meer dag-tot-dag variantie, dan groepen die binnen werkten of met gerichte ventilatie. Groepen met mobiele werkers, groepen die werkten in een intermitterend proces en groepen waarbij de bron lokaal of mobiel was, vertoonden ook meer dag-tot-dag variantie. In een multivariable regressie model verklaarden de omgeving (binnen-buiten) en soort proces (continu-intermitterend) 41% van de variatie in de binnen-persoonsvariantiecomponent. Een ander model, waarin alleen het type proces een effect had, verklaarde slechts 13% van de variatie in de tussen-persoonsvariantiecomponent.

In hoofdstuk 8 worden de resultaten gepresenteerd van een omvangrijke studie naar de blootstelling aan 60 Hz magnetische velden, die verricht werd onder willekeurig geselecteerde werknemers in vijf electriciteitsbedrijven in de Verenigde Staten. De opzet van deze studie maakte het mogelijk de blootstellingsvariabiliteit te onderzoeken, die vervolgens de basis vormde voor een beroepen-blootstelling matrix, die gebruikt zal worden in een epidemiologische studie naar gezondheidseffecten tengevolge van blootstelling aan magnetische velden bij werknemers van deze vijf bedrijven. Bijna 3.000 succesvolle metingen resulteerden in gemiddelde blootstellingen die varieerden van 0,11 μT voor 'managers' tot 1,50 μT voor 'kabelsplitsers'. De verschillen in gemiddelde blootstelling tussen de vijf bedrijven waren relatief gering. De meer stedelijke bedrijven hadden een iets hogere gemiddelde blootstelling aan magnetische velden dan de meer rurale bedrijven. De dag-tot-dag variantiecomponent was groter dan de binnengroeps- en tussengroeps-variantiecomponent. De ontwikkelde beroepen-blootstelling matrix bestond uit vijf groepen met gemiddelde blootstellingsniveaus van 0,12, 0,21, 0,39, 0,62 en 1,27 μT. Zelfs deze optimale indeling resulteerde in een aanzienlijke overlap in blootstelling tussen aangrenzende groepen. Desalniettemin houdt de ontwikkelde matrix op de meest efficiënte wijze rekening met verschillen in blootstellingsniveaus tussen bedrijven binnen beroepsgroepen en maakt het een objectieve en statistisch verantwoorde schatting van de cumulatieve blootstelling aan magnetische velden mogelijk.

Tenslotte volgt in hoofdstuk 9 een algemene discussie en de conclusies. Door validatie en methodologische studies, zoals beschreven in dit proefschrift, is inzicht verkregen in de kwaliteit van methoden voor beroepsmatige blootstellingskarakterisering. Ondanks de mogelijkheden om subjectieve methoden voor blootstellingskarakterisering te verbeteren en te valideren, moet gezien de beperkingen en inherente valkuilen rekening gehouden worden met onvoldoende valide blootstellingsmaten voor epidemiologisch onderzoek naar blootstelling-responsrelaties. Statistische modellen, zoals ontwikkeld in dit proefschrift, voor het opsporen van blootstellingsbepalende factoren en voor het schatten van variantiecomponenten zullen bijdragen tot meer valide methoden van blootstellingskarakterisering. Toepassing van de ontwikkelde statistische methode voor het optimaliseren van het groeperen van blootstellingsmetingen zal resulteren in minder misclassificatie en vertekening en bijgevolg in betere blootstelling-responsrelaties. Als gevolg hiervan zullen betere grenswaarden voor beroepsmatige blootstellingen vastgesteld kunnen worden. Het is te hopen, dat op korte termijn meer willekeurig verzamelde kwantitatieve blootstellingsgegevens beschikbaar zullen komen om gebruik te kunnen maken van de ontwikkelde methoden. Slechts in dat geval zullen de alom bekritiseerde retrospectieve gissingsmethoden overbodig worden.

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Curriculum vitae

Johannes Kromhout werd op 5 december 1958 geboren te Rijnsburg (Zuid-Holland). In 1976 behaalde hij het Atheneum B-diploma aan het Christelijk Lyceum Dr. W.A. Visser 't Hooft te Leiden. In hetzelfde jaar werd een aanvang gemaakt met de studie Milieuhygiëne aan de Landbouwhogeschool te Wageningen. De studie werd in september 1983 afgerond. Vanaf 1 januari 1984 tot en met september 1985 vervulde hij zijn vervangende dienstplicht bij de Vakgroep Luchthygiëne en -verontreiniging in een project voor het Directoraat Generaal van de Arbeid van het ministerie van Sociale Zaken en Werkgelegenheid dat als doel had te komen tot standaardisatie van werkplekonderzoek. Daarna trad hij bij dezelfde vakgroep in dienst als universitair docent. In de jaren 1987 en 1988 werd een onderzoek uitgevoerd naar arbeidsplaatsverbetering in de rubberverwerkende industrie. Vanaf mei 1991 tot september 1992 was hij als gastmedewerker verbonden aan de School of Public Health van de University of North Carolina te Chapel Hill. Gedurende deze periode werkte hij aan een door het National Institute of Occupational Health gesubsidieerd onderzoek naar de achtergronden van de variabiliteit van persoonlijke blootstellingsmetingen. Tegelijkertijd was hij betrokken bij een groot epidemiologisch cohortonderzoek naar de gezondheidseffecten van electromagnetische velden bij electriciteitswerkers, dat gesubsidieerd werd door het Energy and Power Research Institute. Na terugkomst werkte hij opnieuw als universitair docent bij dezelfde vakgroep met de nieuwe naam Luchtkwaliteit en coordineert hij momenteel het aandachtsveld Mens en Lucht.