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Commentary

To celebrate the British Occupational Hygiene Society's fiftieth anniversary this year, we are reproducing in our on-line edition 'classic papers' from past issues of the Annals, with accompanying commentaries in the print and on-line edition. For this issue, the classic paper we reproduce is Kromhout H, Symanski E, Rappaport SM. (1993) A comprehensive evaluation of within- and between-worker components of occupational exposure to chemical agents. Ann Occup Hyg; 37: 253–70.

Variability in Workplace Exposures and the Design of Efficient Measurement and Control Strategies

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Kromhout *et al.*'s (1993) well-cited publication presented detailed information on statistical procedures to estimate the magnitude of exposure variability within and between workers, drawing from a large database on chemical exposures throughout industry. It convincingly demonstrated that the construct of homogeneous exposure groups often does not hold true and suggested ways to improve measurement strategies. The authors hit a rich vein of research, and many publications, not at least by the authors themselves, followed in the decade after publication. In recent years the principles of estimating the variation in exposure have been applied in new methods for optimization of sampling strategies, for compliance testing, for quantifying exposures in epidemiologic studies, and for identifying important sources of emissions and suggesting strategies for controlling exposures. Many occupational hygienists across the globe have adopted these new methods as powerful tools in their exposure assessment strategies.

Keywords: exposure assessment; variability

INTRODUCTION

An essential tool of occupational hygiene has always been the assessment of exposures to potentially hazardous chemicals in the workplace. The purpose of occupational exposure assessment strategies can be manifold, ranging from diagnostic monitoring to reveal the sources and tasks that pose the largest exposures in a workplace to characterizing the distribution of exposures of workers at risk. One of the first authoritative documents on evaluation of workplace exposures was the well-known NIOSH Occupational Exposure Sampling Strategy Manual from 1977 (Leidel *et al.*, 1977). In this manual, emphasis was placed on procedures to demonstrate that exposure at the workplace would not exceed the threshold limit value. A formal compliance test was advocated, based on a limited number of exposure measurements on employees believed to experience the highest exposure (worst-case approach). Within a few years this NIOSH Manual had become the most cited and discussed publication in occupational hygiene.

A fundamental criticism of the NIOSH compliance test was that decisions would only be reasonable if the air concentration experienced by a worker was more or less constant. It became clear that the worst-case sampling strategy was surrounded with large uncertainties, partly stemming from the inability to

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a priori select workers with the highest exposure. Hence, attention shifted towards strategies where personal monitoring was performed on a sample of workers with similar exposure profiles (Burdorf , 1993). Different techniques were developed to assign workers to homogeneous exposure groups, depending on information collected on work processes, chemicals, jobs, tasks and actual layout of the workplace (Corn and Esmen, 1979; Hawkins *et al.*, 1991).

Measurement strategies based on homogeneous exposure groups have become very popular. This concept is at the core of many workplace surveys, especially in risk assessments for legal requirements and epidemiological studies. The growing insight in variability of exposure, and its impact on the homogeneity of occupational exposure groups, spurred research into quantification of specific parameters of exposure distributions within occupational groups. In 1993, Kromhout and colleagues published a comprehensive evaluation of determinants of exposure variability and convincingly demonstrated that many occupational groups were not uniformly exposed as was generally assumed by occupational hygienists (Kromhout *et al.*, 1993). Similarities in environmental conditions, work environments, job tasks and identifiable exposures may not always be sufficient to assign workers to homogeneous exposure groups without availability of quantitative exposure data. The phenomenon of variability of exposure over time and among persons needs to be understood since it affects the basic elements of any measurement strategy. It was exactly this message of Kromhout and co-authors that attracted attention and their publication soon became a source of inspiration for many researchers and practitioners alike. This paper describes the results of this classic paper and analyses its impact on newly developed measurement and control strategies in occupational hygiene.

ANALYSIS OF EXPOSURE VARIABILITY

Although most analysis of variance techniques stem from the early 1960s, their application in occupational hygiene was not advocated until the late 1980s. Early examples were published by Samuals *et al.* (1985), Spear *et al.* (1987) and Kromhout *et al.* (1987). In his review of methods for exposure assessment, Rappaport (1991) presented detailed guidance on the estimation of the variance components of exposure and their interpretation in defining exposure groups. The analysis described exposure patterns in 31 groups of workers exposed to nine different agents, with exposure information based on repeated measurements on individual workers within each group. He introduced the term ‘monomorphic group’ for a uniformly exposed group, defned as a group in which 95% of the individual mean exposures lie within a factor of 2 (Rappaport, 1991). On the basis of the between-worker variance within a specified group of workers, the ratio of the 97.5th percentile to the 2.5th percentile (range ratio) was estimated. In 27 out of 31 groups this range ratio was >2, ranging from 2.6 to 6230. These results prompted Rappaport to argue that occupational hygienists should move away from compliance testing in worst-case sampling strategies, since variability of exposure would make it almost impossible to identify the most exposed workers by walk-through surveys.

This publication was followed by a discussion on statistical techniques to calculate the within- and between-worker variance. In a letter to the editor, Heederik *et al.* (1991) proposed a more appropriate procedure and suggested expanding the analysis to other occupational groups. This correspondence lead to a collaboration and, subsequently, a more comprehensive evaluation in order to investigate the generalizability of the conclusions. A much larger database was constructed with exposure data from the UK, The Netherlands, the USA, Sweden and China, and a detailed analysis of exposure variability was conducted with approximately 14000 measurements obtained from more than 1500 workers in 165 occupational groups, defined by job title and factory (Kromhout *et al.*, 1993). Exposures were measured by personal sampling on at least two occasions, which enabled the estimation of the within- and between-worker components of variance. Of all occupational groups, only 42 groups (25%) had 95% of the individual mean exposures lying within a factor 2, almost 30% of the groups had a more than 10-fold range, and 10% of the groups showed a range of over 50-fold. Generally, the within-worker variability exceeded the between-worker variability, suggesting even larger differences in exposure between work shifts than among workers with the same job in the same factory. The influence of the measurement strategy was also evaluated, demonstrating that groups with non-randomly chosen workers and workers measured on non-randomly chosen days had significantly lower between-worker variability than in a random sampling strategy but the non-random approach increased the day-to-day variability.

In addition, it was shown that production factors had a clear impact on the within-worker variability, but less on the between-worker variability. The largest day-to-day variability was demonstrated among groups working outdoors, those working without local exhaust ventilation, groups with mobile workers, and groups working with intermittent processes. A regression model with environment (outdoors versus indoors) and type of process (intermittent versus continuous) explained 41% of the variability in the within-worker component of variance. On the basis of these results, the authors concluded that it seemed impossible to predict which occupational groups are more or less homogeneously exposed and, therefore, *a priori* assumptions about of homogeneity were not possible. They strongly advocated using measurement strategies with repeated measurements from the same individuals (Kromhout *et al.*, 1993).

DEVELOPMENT OF NEW MEASUREMENT STRATEGIES

The work of Kromhout, Symanski and Rappaport soon attracted attention and publications quickly followed on components of exposure variability in various working conditions. Within a year their results were corroborated in studies among bakery workers (Burdorf *et al.*, 1994; Nieuwenhuijsen *et al.*, 1994), electric power workers (Loomis *et al.*, 1994) and sodium borate workers (Woskie *et al.*, 1994). The technique of partitioning exposure variability into its main components became a method often used in research (Symanski *et al.*, 2001; Vinzents *et al.*, 2001) and an essential element in evaluation of exposure data in different areas (Kromhout and Vermeulen, 2001; Tielemans *et al.*, 2002; Wild *et al.*, 2002). This new concept in assessment of occupational exposures was soon adopted into optimization of sampling strategies, formalized procedures for compliance testing, measurement strategies in epidemiological studies, and strategies to identify important sources of emissions.

Information on the expected variability in exposure among subjects may guide towards an optimum sampling scheme for exposure measurements. The appropriate number of measurements depends on the relative accuracy, study size and discriminatory power. Formulae have been presented that combine classical equations for determining the discriminatory power of a survey with expressions for evaluating the influence of exposure variability on the precision of the average exposure (Armstrong *et al.*, 1992). The efficiency of increasing the number of repeated measurements or increasing the number of subjects, is partly determined by the variance ratio (Werner and Attfield, 2000). In most surveys, costs considerations will be incorporated in the decision on the required efficiency of the sampling scheme (Lemasters *et al.*, 1996).

A new compliance testing procedure for agents with chronic health effects has been developed that accounts for within and between sources of variability (Rappaport *et al.*, 1995). This procedure starts with two shift-long measurements randomly collected from each of 10 randomly chosen workers from an occupational group. In the first step it is evaluated whether the selected occupational group may be regarded as a monomorphic group. For monomorphic groups the probability of overexposure is assessed and for non-monomorphic groups alternative grouping should be attempted. For occupational groups with unacceptable exposure levels, resampling is suggested to increase the power of the compliance test. If it appears that workers in the occupational group are uniformly exposed to unacceptable levels, engineering or administrative controls are commended. For non-uniformly exposed workers in a group, interventions at individual level should be considered, such as modifications of tasks and work practices (Rappaport *et al.*, 1995).

The consequences of exposure variability in epidemiological studies have primarily been explored in the context of its effect on the exposure–response relationship. It has been shown that in a study with measurements on all individuals the variance ratio (within-worker variance/between-worker variance) is directly linked to the attenuation in the observed risk estimate (Liu *et al.*, 1978). Hence, the exposure–response function depends on the degree to which the exposure assessment is successful in providing precise estimates of individual exposure levels. In epidemiological surveys it is more common to monitor a random sample of workers in each occupational group under study. In the analysis of an exposure–response relationship all subjects within the same group will be assigned the same exposure level. Kromhout and Kupper have developed mathematical expressions that use estimates of variance components of exposure (within- and between-worker and between-exposure group) for estimating the group-based attenuation and evaluating the effect of different grouping strategies on observed associations between exposure and health outcomes. These formulae were first presented in a keynote lecture at the Exposure Assessment Conference in Lyon, 1994, and subsequently published (Kromhout *et al.*, 1996). The equations were applied to industry-wide surveys in order to study the effects of various sources of exposure variability on choices among different analysis strategies. In general, the individual-based strategies will generate more precise, though biased, estimates, while group-based strategies will result in less precise but essentially unbiased estimates (Tielemans *et al.*, 1998). Several authors have used these mathematical expressions to evaluate the effect of exposure variability within and between occupational groups on risk estimates in epidemiological studies (Van Tongeren *et al.*, 1997; Werner and Attfield, 2000).

The introduction of linear mixed-effects models in standard statistical packages allows the simultaneous estimation of the variance components and determinants of the exposure (Peretz *et al.*, 2002; Rappaport *et al.*, 1999). A mixed-effects model combines fixed and random effects into one model. A fixed effect in such a model assumes that the differences in exposure levels reflect true (constant) differences among workplaces. The random effect evaluates whether the variance within each workplace can partly explain the differences in average exposure among the workplaces. Using these modelling techniques it is possible to identify important determinants of exposure, such as presence of ventilation, type of production process, residence characteristics, and time-activity patterns, while accounting for random within- and between-worker variability. A good illustration of this approach was recently presented by Burstyn and colleagues (2000). A large database on exposure among asphalt workers from 37 different sources in eight countries was constructed. This database enabled the researchers to present three models on the important determinants of bitumen fume, bitumen vapour and polycyclic aromatic hydrocarbon (PAH) exposure intensity among paving workers. These statistical models explained 36–43% of the total variability and revealed strong associations with various production factors, such as surface dressing, oil gravel paving, and asphalt temperature (Burstyn *et al.*, 2000).

CONCLUSIONS

This article has focused on recent developments in occupational hygiene that involve estimation of the variability in exposure as a crucial concept in exposure assessment strategies among occupational groups. The classic papers of Rappaport (1991) and Kromhout *et al.* (1993) have lead to further developments in exposure assessment strategies in the past 10 yr and has resulted in a greater understanding of occupational exposure. The knowledge on estimation procedures for exposure variability have been incorporated in new methods for optimization of sampling strategies, for compliance testing, for quantifying exposures in epidemiologic studies, and for identifying important sources of emissions and determining control strategies. Occupational hygienists and epidemiologists worldwide have adopted these new methods as powerful tools in their assessment strategies.

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