A LOGNORMAL DISTRIBUTION-BASED EXPOSURE ASSESSMENT METHOD FOR UNBALANCED DATA

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Abstract—We present a generalization of existing statistical methodology for assessing occupational exposures while explicitly accounting for between- and within-worker sources of variability. The approach relies upon an intuitively reasonable model for shift-long exposures, and requires repeated exposure measurements on at least some members of a random sample of workers from a job group. We make the methodology more readily applicable by providing the necessary details for its use when the exposure data are unbalanced (that is, when there are varying numbers of measurements per worker). The hypothesis testing strategy focuses on the probability that an arbitrary worker in a job group experiences a long-term mean exposure above the occupational exposure limit (OEL). We also provide a statistical approach to aid in the determination of an appropriate intervention strategy in the event that exposure levels are deemed unacceptable for a group of workers. We discuss important practical considerations associated with the methodology, and we provide several examples using unbalanced sets of shift-long exposure data taken on workers in various sectors of the nickel-producing industry. We conclude that the statistical methods discussed afford sizable practical advantages, while maintaining similar overall performance to that of existing methods appropriate for balanced data only.

NOMENCLATURE

Symbol | Definition
---|---
\(X_{ij}\) | A shift-long exposure measurement, presumed to be lognormally distributed
\(Y_{ij}\) | \(\ln(X_{ij})\), the natural logarithm of a shift-long measurement, presumed to be normally distributed
\(k\) | The number of workers randomly sampled from the job group under study
\(m_i\) | The number of shift-long exposure measurements taken on the \(i\)th worker
\(N\) | The total number of exposure measurements taken
\(\mu_y\) | The expected value, or mean, of \(Y_{ij}\)
\(\beta_i\) | Random deviation of \(i\)th worker's mean natural logged exposure from \(\mu_y\)
\(\mu_x\) | Mean natural logged exposure for \(i\)th worker
\(\varepsilon_{ij}\) | Random deviation of \(Y_{ij}\) from \(\mu_y\)
\(\sigma^2_{\mu_y}\) | Between-worker variance component of \(Y_{ij}\)
\(\sigma^2_{\varepsilon}\) | Within-worker variance component of \(Y_{ij}\)
\(\mu_x\) | The expected value, or mean, of \(X_{ij}\)
\(\hat{\mu}_x\) | A point estimator of \(\mu_x\)
\(\mu_e\) | Mean exposure for \(i\)th worker
\(\theta\) | The probability that an arbitrary worker's mean exposure exceeds the OEL
\(\hat{\theta}\) | A point estimator of \(\theta\)
\(A\) | A specified value against which it is desired to compare the value of \(\theta\)
\(\hat{R}\) | An estimated restriction used for hypothesis testing

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INTRODUCTION

A previous paper (Rappaport et al., 1995) described a five-level protocol for assessing occupational exposures accounting for between- and within-worker variation in exposure. The approach is based on applying a well-known and intuitively reasonable statistical model to a set of shift-long exposure data containing repeated measurements on each of several workers randomly sampled from a job group. A major emphasis of the protocol is a rigorous statistical test of a null hypothesis involving the unknown probability that an arbitrary worker from the job group experiences a mean exposure level above the occupational exposure limit (OEL) for the toxicant in question. If there is insufficient evidence that exposure levels are acceptable for the group under consideration, a rule of thumb is applied that makes use of predicted values of mean exposure for individual workers, together with approximate confidence limits for the overall population mean, in order to prescribe an appropriate intervention strategy. We justify this focus on individuals’ mean exposure by citing the fact that the risk of chronic disease may often be taken as proportional to a worker’s cumulative exposure to the toxicant (Rappaport, 1991, 1993).

In the previous paper, we recommended a balanced sampling strategy (that is, the collection of an equal number of repeated shift-long exposure measurements on each randomly selected worker), and we described the statistical aspects of the protocol assuming balanced data. However, few existing databases contain completely balanced exposure data, and the practical issues of environmental sampling often make the attainment of balanced data problematic. Hence, the purpose of this paper is to provide statistical details allowing for the application of our hypothesis testing strategy in the unbalanced case. The basic background and the fundamental protocol discussed in Rappaport et al. (1995) remain unchanged.

In Section 2, we review the model for shift-long exposures and the hypothesis testing strategy proposed by Rappaport et al. (1995). We then provide an appropriate test statistic for use with unbalanced data, with suggested procedures that may be applied in the event of a negative estimate of the between-worker
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variance component. In Section 3, we provide a method for predicting true mean exposure for individual workers, based on the assumed model for shift-long exposure. We describe an intuitively reasonable statistical strategy for deciding whether engineering or administrative controls may be preferable to modification of tasks or practices for individual workers in order to reduce exposure levels. We also provide examples using real shift-long exposure data in Section 4, and discuss important implications in Section 5.

METHODS FOR WORKPLACE EXPOSURE ASSESSMENT

Model for exposures

Let \(X_{ij}\) represent the \(j\)th \((j=1, \ldots, n_i)\) shift-long measurement obtained on the \(i\)th \((i=1, \ldots, k)\) worker among those randomly sampled from a particular job group. We assume that the one-way random effects ANOVA model (Searle et al., 1992) applies to the natural logged exposures \(\{Y_{ij}\}\):

\[
Y_{ij} = \ln(X_{ij}) = \mu_y + \beta_i + \varepsilon_{ij} \quad (i = 1, \ldots, k; j = 1, \ldots n_i),
\]

where \(\beta_i \sim N(0, \sigma^2_{\beta})\) and \(\varepsilon_{ij} \sim N(0, \sigma^2_{\varepsilon})\). Here, \(\beta_i\) represents the random deviation of the \(i\)th worker's logged-scale mean \((\mu_{yi} = \mu_y + \beta_i)\) from the population logged-scale mean \((\mu_y)\), and \(\varepsilon_{ij}\) represents the random deviation of the \(j\)th exposure measurement on the \(i\)th worker from \(\mu_{yi}\). As usual, all these random effects are assumed to be mutually independent. The subscript \('i'\) on \('n_i'\) emphasizes the fact that there are different numbers of measurements taken on different workers. The parameters \(\sigma^2_{\beta}\) and \(\sigma^2_{\varepsilon}\) represent the between- and within-worker components of variability, respectively. The above model assumes that the shift-long exposures \(\{X_{ij}\}\) are lognormal, which is consistent with much of the previous literature. Indeed, model (1) appears to provide an adequate description of many of the occupational data sets that we have examined.

Null and alternative hypotheses

Note that \(\mu_{yi}\) is the conditional mean of \(Y_{ij}\) for fixed \(\beta_i\). Analogously, we define the \(i\)th worker's mean exposure (on the original lognormal scale) as \(\mu_{xi} = \exp(\mu_y + \beta_i + \sigma^2_{\varepsilon}/2)\), which is the conditional mean of \(X_{ij}\) for fixed \(\beta_i\). We take this individual mean as the exposure index most directly related to the risk of chronic health effects. Unconditionally, \(\mu_{xi}\) is itself a lognormal random variable.

Rappaport et al. (1995) propose a simple decision rule for assessing whether or not the overall exposure distribution for an entire group of workers is in compliance with specified regulatory guidelines. This rule is based upon the following null and alternative hypotheses, where the parameter \(\theta = \Pr(\mu_{xi} > OEL)\) denotes the probability that the mean exposure for an arbitrary worker (that is, \(\mu_{xi}\) for arbitrary \(i\)) exceeds the OEL:

\[
H_0 : \theta \geq A \quad \text{vs} \quad H_1 : \theta < A.
\]

Spear and Selvin, 1989 previously asserted the relevance of the parameter \(\theta\) in the occupational setting. For overall regulatory compliance based upon our decision rule, there must be strong evidence in the data against the state of nature \(\theta \geq A\),
where \( A \) is some small probability defined a priori. Rappaport et al. (1995) considered \( A = 0.10 \) for initial applications of their protocol.

**Calculation of the test statistic**

As for the balanced case discussed by Rappaport et al. (1995), the most conveniently calculated test statistic for use with \( H_0 \) is a Wald-type statistic (Rao, 1965). While such a test statistic is typically a function of maximum likelihood (ML) estimates of unknown parameters, we have found through computer simulation studies that the familiar (and more easily evaluated) estimators \( \hat{\mu}_y, \hat{\sigma}^2_w \) and \( \hat{\sigma}^2_h \) given in Appendix A exhibit slightly better behaviour in conjunction with our decision rule.

The Wald-type test statistic, generalized to the unbalanced case, is given by

\[
\hat{Z}_w = \frac{\hat{R}}{\sqrt{\hat{V}(\hat{R})}},
\]

(2)

where

\[
\hat{R} = \hat{\mu}_y + \frac{\hat{\sigma}^2_w}{2} + \hat{\sigma}_h z_{1-A} - \ln(OEL)
\]

(3)

and

\[
\hat{V}(\hat{R}) = \hat{a} + \frac{\hat{b} + z_{1-A}}{4\hat{d}_h} \left( 2\hat{c} + \frac{\hat{d} z_{1-A}}{\hat{d}_h} \right).
\]

(4)

In these expressions, \( z_{1-A} \) represents the 100(1 - \( A \))th percentile of the standard normal distribution \( \hat{\sigma}_h = \sqrt{\hat{\sigma}^2_h} \), and \( \hat{a}, \hat{b}, \hat{c} \) and \( \hat{d} \) are the algebraic expressions presented in Appendix A. If the ML estimators are utilized to compute \( \hat{Z}_w \), then statistical theory dictates that the distribution of \( \hat{Z}_w \) approaches the standard normal under the equality condition in \( H_0 \) as the number of workers studied becomes large. Again, based on empirical studies assuming moderate sample sizes (see also the commentary in Section 5), we suggest the use in practice of the ANOVA estimators given in Appendix A, although they are not identical to the ML estimators. Hence, for an approximately size \( \alpha \) test, we reject \( H_0: \theta \geq A \) in favour of \( H_1: \theta < A \) when \( \hat{Z}_w < z_\alpha \) (typically, \( \alpha \) will be 0.05). We note that when \( n_i \) is the same for all workers (that is, the data are balanced), \( \hat{Z}_w \) in (2) is identical to the Wald-type statistic proposed by Rappaport et al. (1995).

**Point estimates of \( \theta \) and the overall mean exposure**

One may calculate a rough point estimate of the parameter \( \theta = \Pr(\mu_{xi} > OEL) \) using the following formula:

\[
\hat{\theta} = 1 - \Phi \left( \frac{\ln(OEL) - \hat{\mu}_y - \hat{\sigma}^2_w/2}{\hat{\sigma}_h} \right),
\]

where \( \Phi(t) \) denotes the probability that a standard normal random variate falls below the value \( t \). A point estimate of the overall (lognormal scale) population mean exposure (that is, the expected value of \( X_{ij} \)) for the group in question is given by
The term ‘population’ refers to the hypothetical large population of workers who could eventually enter the group in question during the assessment study period. The estimators depicted in these two formulae are not unbiased; however, the resulting estimates can be informative in conjunction with the proposed hypothesis testing strategy.

Negative estimates of $\sigma_b^2$

Even when data are generated directly using model (1), negative ANOVA estimates of $\sigma_b^2$ occasionally occur. While certain estimation techniques prescribe setting such a negative estimate equal to 0, this strategy is not recommended in the current context (Lyles et al., 1995). Rappaport et al., 1995 suggest an *ad hoc* method for handling the occurrence of a negative estimate of $\sigma_b^2$ in conjunction with the Wald-type test for balanced data. In a more detailed statistical treatment of the hypothesis testing portion of their protocol for assessing occupational exposure levels based on balanced exposure data, Lyles et al. (1995) provide an alternative approach to this *ad hoc* method, an approach that tends to exhibit better properties in numerical studies. Both procedures rely upon the calculation of an approximate upper bound on the parameter $\sigma_b^2$.

The *ad hoc* procedure suggested by Rappaport et al. (1995) involves simply substituting a 60% upper bound on $\sigma_b^2$ ($\hat{\sigma}_{b,0.60}^2$) in place of $\sigma_b^2$ when calculating the test statistic (2). More specifically, $\hat{\sigma}_{b,0.60}^2$ is chosen so that, approximately, $\Pr(\sigma_b^2 \leq \hat{\sigma}_{b,0.60}^2) = 0.60$. This method is rough, and can be disadvantageous because it is possible for this 60% upper bound itself to be negative.

The preferred approach is somewhat more complex, and its derivation is provided elsewhere (Lyles et al., 1995). It involves evaluating the following null and alternative hypotheses in place of the original $H_0$ and $H_1$, under the assumption that the data on each worker constitute a *random sample* from a lognormal distribution (that is, the intra-worker correlation is small enough that it may be ignored):

$$H_0^1 : \mu_x \geq \hat{c}^{*}(OEL). \quad \text{vs} \quad H_1^1 : \mu_x < \hat{c}^{*}(OEL).$$

In the above, $\mu_x$ is simply the overall population mean shift-long exposure for the group of workers in question. The multiplier $\hat{c}^{*}$ is given by

$$\hat{c}^{*} = \exp\{\hat{\sigma}_{b,0.95}^2/2 - z_{1-\alpha/2}^2\},$$

where $\hat{\sigma}_{b,0.95}^2$ is an estimated 95% upper bound on $\sigma_b^2$, provided that this upper bound is less than $z_{1-\alpha}^2$. If the value of the 95% upper bound is greater than or equal to $z_{1-\alpha}^2$, then we set $\hat{\sigma}_{b,0.95}^2 = z_{1-\alpha}^2$ and obtain $\hat{c}^{*} = \exp\{-z_{1-\alpha}^2/2\}$.

The incorporation of $\hat{c}^{*}$ is based upon the assumed validity of the underlying model (1) for exposures, despite the fact that $\hat{\sigma}_b^2 < 0$ in the observed data. Since $\hat{c}^{*}$ is just a constant given the exposure data, the evaluation of $H_0^1$ simply reduces to testing a population mean against a given value [namely, $\hat{c}^{*}(OEL)$], based on a random sample of $N = \sum_{i=1}^{k} n_i$ observations from a lognormal distribution. There are several methods for conducting such a hypothesis test (for example, Land, 1973; Rappaport and Selvin, 1987; Lyles and Kupper, 1996). Lyles et al. (1995) provide a numerical study incorporating one of these methods in the event that $\hat{\sigma}_b^2 < 0$ for a balanced set of exposure data. Clearly, the same procedure can be performed with...
unbalanced data, given an appropriate 95% upper bound for $\sigma^2$. To implement this procedure, we reject $H_0$ in favour of $H_1$ (and hence, $H_0$ in favour of $H_1$) if and only if the following inequality holds:

$$
\hat{\tau} = \overline{Y}_n + d^* S_Y < \ln(\hat{c}^*\text{OEL}).
$$

(5)

Here, $\overline{Y}_n$ is the sample mean of the $N(= \sum_{i=1}^k n_i)$ logged exposure measurements, and $S_Y$ is the sample standard deviation of these $N$ measurements. Also,

$$
d^* = (S_Y \sqrt{N - 1})/(2\chi_{N-1,\alpha}) + t_{N-1,1-\alpha}/\sqrt{N},
$$

(6)

where $\chi_{N-1,\alpha}$ is the square root of the 100th percentile of the chi-squared distribution with $(N-1)$ degrees of freedom, and $t_{N-1,1-\alpha}$ is the 100th percentile of the central $t$ distribution with $(N-1)$ degrees of freedom. The expression for $d^*$ stems from existing work by Halperin (1963). For those interested in the derivation of this method and its potential advantages, see Lyles and Kupper (1996).

In previous work (Rappaport et al., 1995; Lyles et al., 1995) considering balanced data, we cited an appropriate method due to Williams (1962) for obtaining a bound on $\sigma^2$. Approximate upper bounds on $\sigma^2$ derived from unbalanced data may be based on the methodology of Burdick and Eickman (1986). In Appendix B, we give the details necessary for computing $\sigma^2_{0.95}$ in the unbalanced case, and we show the required calculations using a real set of shift-long exposure data.

GUIDELINES FOR INTERVENTION STRATEGIES

Rappaport et al. (1995) propose the use of empirical Bayes-like estimates of the random variables $\{\mu_i\}$ as part of a rule of thumb for determining an appropriate intervention strategy in the event that exposure levels are unacceptable based on the hypothesis test described in Section 2. A direct extension of their result for balanced data to the unbalanced case suggests the following estimated predictor for the $i$th worker:

$$
\tilde{\mu}_{xi} = \exp \left\{ \frac{(n_i \hat{Y}_i + \hat{\mu}_y + \hat{c}^2 \sigma^2_w/2)}{(n_i \hat{y} + 1)} + \hat{c}^2 \sigma^2_w/2 \right\},
$$

(7)

where $\hat{y} = \hat{c}^2 \sigma^2_w/\sigma^2_w$, $\hat{Y}_i = (n_i)^{-1} \sum_{j=1}^{n_i} Y_{ij}$, and $\hat{\mu}_y$, $\hat{\sigma}^2_w$ and $\hat{\sigma}^2_w$ are estimated as described in Appendix A. If $\hat{c}^2 \sigma^2_w < 0$, we recommend the following alternative calculation: $\tilde{\mu}_{xi} = \exp\{\hat{Y}_i + [(n_i - 1)/(2n_i)]\hat{c}^2 \sigma^2_w\}$. The quantity in Equation (7) is an estimator of a predictor for worker-specific mean exposure that has certain optimal characteristics based on statistical considerations reviewed by Searle et al. (1992); we are currently studying its properties in more detail. In conjunction with estimated predictors for balanced data that are analogous to those determined according to Equation (7), Rappaport et al. (1995) recommend calculating an approximate 100(1 - 1/k)% confidence interval (CI) for the overall population mean exposure $\mu_x$. Again, proper extension of their result is required; such extension leads to the following CI for $\mu_x$ assuming unbalanced data:
\[
\left\{ \hat{\mu}_x \exp \left( z_{\alpha'/2} \sqrt{\text{Var} \ln(\hat{\mu}_x)} \right), \hat{\mu}_x \exp \left( z_{1-\alpha'/2} \sqrt{\text{Var} \ln(\hat{\mu}_x)} \right) \right\}. \tag{8}
\]

In expression (8), we have \(\hat{\mu}_x = \exp(\hat{\mu}_y + (\hat{\sigma}_b^2 + \hat{\sigma}_w^2)/2)\) and \(\alpha^* = 1/k\). Also, the required estimated variance is given by

\[
\text{Var} \ln(\hat{\mu}_y) = \{\hat{\alpha} + (\hat{\beta} + 2\hat{c} + \hat{d})/4\},
\]

where \(\hat{\alpha}, \hat{\beta}, \hat{c}\) and \(\hat{d}\) are the same algebraic expressions that were used to calculate \(\hat{Z}_w\) as described in Section 2 (see Appendix A).

In accordance with Rappaport et al. (1995), a plot that depicts the estimated values \(\hat{\mu}_{xi}\) calculated according to Equation (7) with the upper and lower limits of the estimated CI in expression (8) may be used to help determine a promising intervention strategy for reducing workplace exposures. If all the \(\hat{\mu}_{xi}\) values lie within the confidence bounds for the overall mean, we contend that overall engineering or administrative controls aimed at reducing exposure for the entire group in question may be called for. If one or more of the \(\hat{\mu}_{xi}\) values are outside the interval, then it may be of benefit to consider control measures focusing on the work habits and tasks of specific workers.

The measures described above are intended as a rough guideline; for further discussion, see Rappaport et al. (1995). The graphical procedure is illustrated in Appendix C, based on actual shift-long exposure data that are the subject of the first example presented in the following section.

**EXAMPLES**

In Appendix D, we provide tables containing three sets of actual (logged) shift-long exposure data obtained on workers in the nickel producing industry. The first set (Table D1; \(k = 12, N = 27\)) represents total nickel dust exposures (encompassing all forms of nickel as measured by the so-called total dust method) of furnacemen in the refinery of a nickel-producing complex. The second (Table D2; \(k = 23, N = 34\)) and third (Table D3; \(k = 20, N = 28\)) sets represent total nickel dust exposures of two separate groups of maintenance mechanics, respectively in the smelting and milling operations of the same nickel-producing complex. The applicable OEL for nickel dust is taken to be 1 mg m\(^{-3}\), which represents the 1995 Threshold Limit Value (ACGIH, 1995).

In Table 1, we present the pertinent parameter estimates with the value of the test statistic \(\hat{Z}_w\) for the data in Table D1. As \(\hat{Z}_w\) is much larger than \(z_{0.05} = 1.645\), we are unable to reject \(H_0\) for this group of workers (for \(A = 0.10\)). This conclusion is consistent with the rough point estimates \(\hat{\theta}\) and \(\hat{\mu}_x\), which are well above 0.10 and 1 mg m\(^{-3}\), respectively. Since it would appear that control measures are necessary,

| Table 1. Calculations for exposure data in Table D1* (\(k = 12, N = 27\)) |
|---|---|---|---|---|---|
| \(\hat{\mu}_y\) | \(\hat{\sigma}_b^2\) | \(\hat{\sigma}_w^2\) | \(\hat{Z}_w\) | \(\hat{\theta}\) | \(\hat{\mu}_x\) |
| -0.590 | 0.138 | 1.482 | 0.925 | 0.658 | 1.246 |

*A = 0.10, \(\alpha = 0.05\), \(z_{1-\alpha} = 1.282\), \(z_\alpha = -1.645\), OEL = 1 mg m\(^{-3}\).
we illustrate (see Appendix C) the graphical approach discussed in Section 3. As shown in Fig. 1, no predicted worker-specific mean exposure value falls outside the limits of the approximate 100(1 - 1/k)% CI for the group mean $\mu_x$. Hence, our rule of thumb points in the direction of engineering or administrative control measures to reduce the unacceptable exposure levels for this particular group of furnacemen.

The opposite outcome for the assessment involving the first group of maintenance mechanics (Table D2) is shown in Table 2. Note that $H_0$ is strongly rejected at the $\alpha = 0.05$ level for $A = 0.10$, as $\hat{Z}_w$ is much less than $z_{0.05}$. Again, this is consistent with $\hat{\theta}$ which is scarcely greater than 0, and with $\hat{\mu}_x$, which is far less than 1 mg m$^{-3}$ for this group of workers.

Since the data in Table D3 produce a negative ANOVA estimate of $\sigma_y^2$, we provide the relevant details in Table 3 for applying the alternative procedure recommended in Section 2. Since $\hat{T}$ [computed according to Equation (5)] is clearly less than $\ln(\tilde{c} \times \text{OEL}) = -0.814$, we reject $H_0$ for this set of data assuming $A = 0.10$. More details concerning the calculations for the data in Table D3 are given in Appendix B.

Table 2. Calculations for exposure data in Table D2* ($k = 23, N = 34$)

<table>
<thead>
<tr>
<th>$\hat{\mu}_y$</th>
<th>$\sigma_y^2$</th>
<th>$\sigma_w^2$</th>
<th>$\hat{Z}_w$</th>
<th>$\hat{\theta}$</th>
<th>$\hat{\mu}_x$</th>
</tr>
</thead>
<tbody>
<tr>
<td>-3.693</td>
<td>0.535</td>
<td>0.245</td>
<td>-9.640</td>
<td>$5 \times 10^{-7}$</td>
<td>0.037</td>
</tr>
</tbody>
</table>

* $A = 0.10$, $\alpha = 0.05$, $z_{1-A} = 1.282$, $z_{1-A} = -1.645$, OEL = 1 mg m$^{-3}$. 

Fig. 1. Plot of estimated predictors of mean exposures $\tilde{\mu}_y$ for the data in Table D1, together with an estimate and approximate 100 $(1 - 1/k)$% CI for population mean exposure $(\mu_x)$. 

Fig. 1. Plot of estimated predictors of mean exposures $\tilde{\mu}_y$ for the data in Table D1, together with an estimate and approximate 100 (1 - 1/k)% CI for population mean exposure ($\mu_x$).
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Table 3. Calculations for exposure data in Table D3*† (k = 20, N = 28)

<table>
<thead>
<tr>
<th>( \hat{Y}_n )</th>
<th>( S_p )</th>
<th>( \hat{\sigma}^2_b )</th>
<th>( \hat{\sigma}^2_{b,0.05} )</th>
<th>( \hat{\epsilon}^2 )§</th>
<th>( \hat{\tau}_q )</th>
</tr>
</thead>
<tbody>
<tr>
<td>-4.065</td>
<td>1.087</td>
<td>-0.046</td>
<td>1.331</td>
<td>0.443</td>
<td>-2.952</td>
</tr>
</tbody>
</table>

* \( A = 0.10, \alpha = 0.05, z_{1-\alpha} = 1.282, z_{\alpha} = -1.645, \text{OEL} = 1 \text{mg m}^{-3} \).
† For these data, MSW (= \( \hat{\sigma}^2_w \)) = 1.225.
§ Approximate 95% upper bound on \( \sigma^2_b \) calculated according to Burdick and Eickman (1986).

DISCUSSION

The hypothesis testing strategy outlined in Section 2 provides a simple means of assessing regulatory compliance over a particular sampling period based on repeated shift-long exposure measurements taken on each of a random sample of workers in a job group. The strategy is developed under the notion that cumulative exposure to a toxicant is the key predictor of chronic health effects resulting from a worker’s contact with that toxicant.

As discussed by Rappaport et al. (1995), model (1) appears to be a reasonable model for shift-long exposure measurements in specific job groups. This is largely due to the physical grouping of workers according to common job titles and locations within plants, which tends to eliminate the need to account for specific fixed factors in the modeling of exposure within such groups. Also, the need to account for possible autocorrelation among repeated exposure measurements is reduced greatly because sampling is done across (as opposed to within) shifts. Still, we recommend that prospective users of our protocol make a serious effort to evaluate the fit of model (1). In this direction, Rappaport et al. (1995) provide several useful references. In particular, they describe an adaptation of existing graphical methods (Lange and Ryan, 1989) for assessing the normality assumption associated with the random worker effects \( \beta_1 \). Such adaptations can also be applied in the case of unbalanced exposure data, though consideration should be given to proper weighting of the points to be plotted. Dempster and Ryan (1985) provide necessary details.

The Wald-type test statistic (2) and the additional procedures for handling the situation when \( \hat{\sigma}^2_b < 0 \) are analogous to those presented by Rappaport et al. (1995) and studied in detail by Lyles et al. (1995) for balanced sets of exposure data. In the latter reference, it is seen that the Wald-type methodology compares favourably with other more complicated test statistics in most cases, with the exception of situations in which the population value of the ratio \( (\sigma^2_b/\sigma^2_w) \) of between- to within-worker components of variability is relatively high. To account for such behaviour (due probably to the reduced accuracy of the normal approximation for small sample sizes), we suggest the following simple adjustment to the rejection rule when applying the Wald-type test statistic \( \hat{Z}_w \) in Equation (2):

If \( \hat{\sigma}_b^2/\hat{\sigma}_w^2 \geq 1 \), then reject \( H_0 \) at the \( \alpha/2 \) level of significance.

Simulation studies (not presented here), involving the random generation of exposure data displaying various degrees of unbalancedness, suggest that this adjustment is effective in controlling the type I error rate of the test at or near the

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nominal level in most situations. Hence, for the example calculations in Table 2 in which \( \frac{\hat{a}_h^2}{\hat{a}_w^2} = 2.18 \), we would do better to compare \( \hat{Z}_w \) with \( z_{0.025} = -1.96 \). Of course, we still strongly reject \( H_0 \) for these data.

Our simulation studies further indicate that the application of the test statistic (2) in conjunction with the above adjustment and the alternative procedure (utilizing \( \hat{a}_{h,0.95}^2 \)) presented in Section 2 maintains near the nominal level the overall type I error rate of our hypothesis testing procedure. Provided that the unbalancedness is not too severe, the power of our recommended testing procedure is roughly equivalent to that of the procedure discussed by Rappaport \textit{et al.} (1995) for balanced data, given the same total number of measurements. This is potentially a valuable observation, since no sample size approximation is available assuming random patterns of unbalancedness in the data. For a reasonably accurate guide as to the overall performance of our hypothesis testing procedure assuming moderate sample sizes for a range of values for the variance components, we refer the reader to the simulation results for balanced data presented by Lyles \textit{et al.} (1995). The empirical properties of the generalized procedure presented in this paper are quite similar in most situations.

In Section 3, we provide the necessary details for the extension of our recommended strategy for determining a promising intervention strategy for reducing workplace exposures. Predicted worker-specific mean exposures calculated via Equation (7) are central to this approach, and are also of benefit in terms of identifying specific workers in the sample who are highly exposed. These estimated predictors are much less likely to be overly distorted by substantial within-worker variability than are more conventional measures (such as worker-specific sample means).

In the design of a study or programme to assess exposures to toxicants associated with chronic health outcomes while accounting for between- and within-worker variability, we still recommend a balanced sampling strategy, with sample size determined according to the approximation given by Rappaport \textit{et al.} (1995). The reasons for this recommendation include its intuitive advantages, facilitation of a priori sample size calculations via existing statistical methodology, and the regulatory appeal associated with allocating an equal measurement effort to each randomly selected worker. However, the methodology presented in this paper allows for the application of the essential features of the assessment protocol of Rappaport \textit{et al.} (1995) to existing and future databases without requiring that the ideal of balanced sampling actually be realized.

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APPENDIX A

Details necessary for calculating the test statistic (2)

Estimating unknown parameters under model (1). For estimating the unknown variance components ($\sigma^2_g$ and $\sigma^2_w$) under model (1), we recommend the usual analysis of variance (ANOVA) estimators (Searle et al., 1992). First, we compute the between- and within-worker mean squares as follows:

$$MSB = \frac{\sum_{i=1}^{k} \sum_{j=1}^{n_i} (Y_{ij} - \bar{Y}_i)^2}{k - 1}$$

$$MSW = \frac{\sum_{i=1}^{k} \sum_{j=1}^{n_i} (Y_{ij} - \bar{Y}_i)^2}{N - k},$$

where $N = \sum_{i=1}^{k} n_i$, $\bar{Y}_i = \frac{1}{n_i} \sum_{j=1}^{n_i} Y_{ij}$, and $\bar{Y} = \frac{1}{N} \sum_{i=1}^{k} \sum_{j=1}^{n_i} Y_{ij}$. The usual ANOVA variance component estimators are then given by the expressions

$$\hat{\sigma}_g^2 = \frac{(k - 1)(MSB - MSW)}{(N - \sum_{i=1}^{k} m_i^2/N)}$$

and

$$\hat{\sigma}_w^2 = MSW.$$

For estimating the (log-scale) population mean $\mu$, we use the generalized least squares estimator (Searle et al., 1992), with the ANOVA estimators replacing the unknown variance components:

$$\hat{\mu} = \frac{\sum_{i=1}^{k} (\tilde{Y}_i / \sqrt{\text{var}(\tilde{Y}_i)})}{\sum_{i=1}^{k} (1 / \sqrt{\text{var}(\tilde{Y}_i)})},$$

where $\sqrt{\text{var}(\tilde{Y}_i)} = \sqrt{\hat{\sigma}_g^2 + \hat{\sigma}_w^2/n_i}$.

Calculating $\hat{V}(\hat{R})$. For calculating the estimated variance $\hat{V}(\hat{R})$ in Equation (4), which is in the denominator of the Wald-type statistic (2), we require the following definitions:

$$\hat{a} = \left\{ \sum_{i=1}^{k} \frac{n_i}{\lambda_i} \right\}^{-1}$$

$$\hat{b} = 2\hat{\sigma}_w^2/(N - k)$$
In the above expressions, $\lambda_i = n_i \delta_1^2 + \delta_2^2$, $S_2 = \sum_{i=1}^{k} n_i^2$, and $S_3 = \sum_{i=1}^{k} n_i^3$.

**APPENDIX B**

Details necessary for calculating approximate upper bound on $\sigma_h^2$

The procedure that we recommend for use when a negative ANOVA estimate $(\delta^2_0)$ has been obtained requires estimating an upper bound on $\sigma_h^2$ from the data. To do so under model (1) using an unbalanced set of logged exposure data, we may apply the methodology of Burdick and Eickman (1986).

First, in providing an estimated upper 100(\delta)% bound on $\sigma_h^2$, we will be satisfied with the use of the upper limit of a 100(2\delta - 1)% confidence interval on $\sigma_h^2$. We apply the Burdick and Eickman methodology to obtain this upper confidence limit, making the assumption that their procedure as outlined below provides a roughly symmetric approximate confidence interval. For a 95% upper bound $(\delta^2_{0.095})$, note that $\delta = 0.95$, so that we require the upper limit of a 90% confidence interval.

To calculate the upper limit of the 100(2\delta - 1)% confidence interval, we make the following definitions:

$$ f_1 = \frac{\chi^2_{k-1}(1-\delta)}{k-1}, \quad f_2 = F^+_{N-k}(1-\delta), $$

$$ m = \min\{n_i\}, \quad M = \max\{n_i\}, \quad h = k/\left\{\sum_{i=1}^{k} 1/n_i\right\}, $$

and $S' = (k-1)^{-1}\left\{\sum_{i=1}^{k} \bar{Y}_i^2 - k^{-1}\left\{\sum_{i=1}^{k} \bar{Y}_i\right\}^2\right\}$.

In the above expressions, $\chi^2_{k-1}(\delta)$ represents the 100(\delta)th percentile of the chi-square distribution with (k - 1) degrees of freedom, and $F^+_{N-k}(\delta)$ represents the 100(\delta)th percentile of the F distribution with (k - 1) numerator and $(N-k)$ denominator degrees of freedom. Note also that $m$ and $M$ simply refer, respectively, to the smallest and largest worker-specific numbers of repeated shift-long exposure measurements in the observed set of data.

Based on the above definitions, we now compute the quantity $U = \frac{S'}{f_1/\left(\frac{\chi^2_{k-1}(1-\delta)}{k-1}\right)}$. The upper limit (UL) of the 100(2\delta - 1)% confidence interval is then given by

$$ UL = \frac{hS'U}{f_1(1+hU)}. $$

Simulation studies by Burdick and Eickman (1986) suggest that UL should perform well as an approximate upper 100(\delta)% bound on $\sigma_h^2$.

**Example.** As shown in Table 3, the data on maintenance mechanics in the milling sector (Table D3) produce a negative ANOVA estimate of the between-worker variance component $(\delta^2_0 = -0.046)$. To calculate $\delta^2_{0.95}$, we need the following:

$$ k = 20, \quad N = 28, \quad \delta = 0.95, \quad f_1 = 0.532, \quad f_2 = 0.404, $$

$$ m = 1, \quad M = 4, \quad h = 1.171, \quad \text{and} \quad S' = 1.037. $$

From these values, and using MSW = $\delta^2_0 = 1.225$, we obtain $U = 1.844$ and $UL = \delta^2_{0.95} = 1.331$. Since $\delta^2_{0.95} < \chi^2_{k-1}(\delta)$, we compute $e^* = \exp\left(\frac{\delta^2_{0.95}/2 - z_{1-\delta}^2}{2}\right) = 0.443$.

To apply the procedure from Section 2, we must compute the test statistic $T$ in Equation (5). As shown in Table 3, the sample mean and standard deviation of the (logged) exposure measurements provided in
Table D3 are $Y_\cdot = -4.065$ and $S_\cdot = 1.087$, respectively. To compute $d^*$ of Equation (6) assuming $\alpha = 0.05$, we have from standard tables of chi-square and central $t$ critical values that $x_{N-1,\alpha} = \sqrt{16.15} = 4.02$, and $t_{N-1,1-\alpha} = 1.703$. Hence, $d^* = (0.703 + 0.322) = 1.025$. It follows that $T = -2.952$, which is less than $\ln(c^*OEL) = -0.814$. In consequence, we reject $H_0$: ($\theta \geq 0.10$) for these data.

APPENDIX C

Use of a graphical procedure for suggesting an appropriate intervention strategy

To illustrate the calculations described in Section 3, we consider the exposure data in Table D1, which are summarized in Table 1. First, we compute the approximate 100(1 - $1/k$)% ($= 91.7\%$) CI for the overall mean exposure ($\mu_o$) according to expression (8). From Table 1, we have $\bar{\mu}_o = 1.246$. Likewise, the required estimated quantities $\hat{a}$, $\hat{b}$, $\hat{c}$ and $\hat{d}$ according to the expressions cited in Appendix A are as follows: $\hat{a} = 0.070$, $\hat{b} = 0.293$, $\hat{c} = -0.135$, and $\hat{d} = 0.185$. These estimates are used to compute the estimated variance $\operatorname{Var}[\ln(\bar{\mu}_o)] = \{\hat{a} + (\hat{b} + 2\hat{c} + \hat{d})/4\} = 0.122$ as described in Section 3 (as well as in the computation of $Z_{0.025} = 0.925$ as described in Section 2). Also, we note that $\alpha^2 = 1/k = 0.083$, so that the two standard normal critical values required for the approximate 100(1 - $1/k$)% CI for $\mu_o$ in expression (8) are $z_{0.025} = -1.732$ and $z_{1-0.025} = 1.732$. Hence, the estimated CI is (0.680, 2.283); note that this interval is not symmetric about the point estimate $\bar{\mu}_o = 1.246$.

To illustrate the calculation of the estimated predicted mean exposure [Equation (7)] for worker #1 in Table D1, we first note from Table 1 that $\bar{\mu}_y = (1/4) \sum_{j=1}^{4} Y_{ij} = -0.398$ together with the estimates $\bar{\mu}_o$, $\hat{\sigma}^2_o$, and $\hat{\sigma}^2_y$, we compute $\hat{\mu}_y = 1.289$ according to Equation (7). After estimating $\hat{\mu}_y$, similarly for the other 11 workers in Table D1, we produce the plot shown in Fig. 1.

In Fig. 1, the solid line represents the value (1.246) of $\bar{\mu}_o = \exp\{\bar{\mu}_y + (\hat{\sigma}^2_o + \hat{\sigma}^2_y)/2\}$ and the dashed lines represent the upper and lower limits of the approximate 100(1 - $1/k$)% ($= 91.7\%$) confidence interval for $\mu_y$ in expression (8). Clearly, the $\hat{\mu}_y$ values are rather tightly distributed about the point estimate $\bar{\mu}_y$, and all fall within the bounds of the CI. A direct extension of the rule of thumb proposed for balanced data by Rappaport et al. (1995) suggests that engineering or administrative control measures aimed at reducing exposure levels for the group of furnacemen as a whole may be most effective, as the data indicate little variability in the worker-specific mean exposure levels.

APPENDIX D

Exposure data for examples in Section 4

Table D1. Nickel dust* exposures on furnacemen from a refinery at a nickel-producing complex ($k = 12$, $1 \leq n_i \leq 5$)

<table>
<thead>
<tr>
<th>Worker (i)</th>
<th>Measurement (j)</th>
<th>$Y_{ij}^\dagger$</th>
<th>Worker (i)</th>
<th>Measurement (j)</th>
<th>$Y_{ij}$</th>
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</table>

*Dust exposures to all forms of nickel calculated using 'total dust' method.
†$Y_{ij}$ represents the natural log of the jth shift-long exposure measurement on the i th worker.
Table D2. Nickel dust* exposures on maintenance mechanics from a smelter at a nickel-producing complex ($k = 23, 1 \leq n_i \leq 4$)

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<th>Worker ($i$)</th>
<th>Measurement ($j$)</th>
<th>$Y_{ij}$</th>
<th>Worker ($i$)</th>
<th>Measurement ($j$)</th>
<th>$Y_{ij}$</th>
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*Nickel dust exposures to all forms of nickel calculated using 'total dust' method.

$Y_{ij}$ represents the natural log of the $j$th shift-long exposure measurement on the $i$th worker.

Table D3. Nickel dust* exposures on maintenance mechanics from a mill at a nickel-producing complex ($k = 20, 1 \leq n_i \leq 4$)

<table>
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<th>Measurement ($j$)</th>
<th>$Y_{ij}$</th>
<th>Worker ($i$)</th>
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*Nickel dust exposures to all forms of nickel calculated using 'total dust' method.

$Y_{ij}$ represents the natural log of the $j$th shift-long exposure measurement on the $i$th worker.