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Generalized P-Values and Confidence Intervals: A Novel Approach for Analyzing Lognormally Distributed Exposure Data

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The problem of assessing occupational exposure using the mean of a lognormal distribution is addressed. The novel concepts of generalized p-values and generalized confidence intervals are applied for testing hypotheses and computing confidence intervals for a lognormal mean. The proposed methods perform well, they are applicable to small sample sizes, and they are easy to implement. Power studies and sample size calculation are also discussed. Computational details and a source for the computer program are given. The procedures are also extended to compare two lognormal means and to make inference about a lognormal variance. In fact, our approach based on generalized p-values and generalized confidence intervals is easily adapted to deal with any *parametric function involving one or two lognormal distributions. Several examples involving industrial exposure data are used to illustrate the methods. An added advantage of the generalized variables approach is the ease of computation and implementation. In fact, the procedures can be easily coded in a programming language for implementation. Furthermore, extensive numerical computations by the authors show that the results based on the generalized p-value approach are essentially equivalent to those based on the Land's method. We want to draw the attention of the industrial hygiene community to this accurate and unified methodology to deal with any parameter associated with the lognormal distribution.*

Keywords confidence interval, hypothesis test, Type 1 error

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INTRODUCTION

It has been well established that occupational exposure data and pollution data very often follow the lognormal distribution. Since Oldham's[1] 1953 report that the distribution of dust levels in coal mines is approximately lognormal, several authors have postulated the lognormal model for studying and analyzing workplace pollutant data.[2–8] The most common explanation for this phenomenon is as follows: workplace concentrations are related to rates of contaminant generation and ventilation rates that are variable. Workers move around in this nonuniform environment, and their activity patterns also vary from day to day. The workers' exposures are related to the above factors in a multiplicative manner. Irrespective of the distribution of contaminant generation rates, ventilation rates, and worker activity patterns, their multiplicative interactions typically lead to exposure distributions that are right skewed and described well by the lognormal probability distribution.

The validity of lognormality assumption for a given data set can be easily tested. The fact that the data $y_1, \ldots, y_n$ are said to follow a lognormal distribution if $\ln(y_1), \ldots, \ln(y_n)$ follow a normal distribution (where "ln" denotes the natural logarithm) allows us to adequately validate the assumption of lognormality of a given data set. Thus, testing for lognormality is simply a matter of validating the normality assumption for the logged data, and this can be done using many widely available software programs such as Minitab, SPSS, and SAS or using some popular methods such as Shapiro-Wilks test or Anderson-Darling test.

If we let y denote the lognormally distributed exposure measurement of an employee, then $x = \ln(y)$ is distributed normally with mean and standard deviation to be denoted by μ_l and σ_l, respectively, and the mean of the lognormal distribution (say, μ) is given by

$$\mu = \exp(\eta), \text{ where } \eta = \mu_l + \sigma_l^2/2. \quad \textbf{(1)}$$

If repeated exposure measurements are available from a single worker, then μ can be viewed as the mean of the worker, and our approach can be used to estimate the individual worker's mean. Our approach is also applicable to estimate the mean of a similarly exposed group (SEG) of workers if only one exposure measurement is obtained per worker

NOMENCLATURE

$y_1, \ldots, y_n$	sample from a lognormal distribution	σ^2	variance of the lognormal distribution; $\sigma^2 = \exp(2\mu_l + \sigma_l^2)[\exp(\sigma_l^2) - 1]$
$x_1, \ldots, x_n$	logged data; $x_i = \ln(y_i), \quad i = 1, \ldots, n$		
μ_l	population mean of the logged data	σ_g	geometric standard deviation; $\sigma_g = \exp(\sigma_l)$
σ_l	population standard deviation of the logged data	$\bar{x}$	sample mean of the logged data
μ	mean of the lognormal distribution; $\mu = \exp(\mu_l + \sigma_l^2/2)$	s	sample standard deviation of the logged data

or to estimate the mean contaminant level in a workplace. If multiple measurements exist for each worker, and both between- and within-worker variability are significant and need to be accounted for, then one should use the random effects model.[9,10,11]

The sample mean exposure can be used as an estimate of the long-term average exposure or the average exposure for a SEG of workers over an extended period of time. For substances that cause health effects due to chronic exposures, day-to-day variability in long-term exposures is less health relevant than the long-term mean. For such exposures, the arithmetic mean is the best measure of cumulative exposure over a biologically relevant time period, since the body would have integrated exposures over this time period.[9] The long-term mean is of relevance in occupational epidemiology where the estimated value of the long-term mean is assigned to all workers in a SEG. Once lognormality has been verified for an exposure sample, inferences on the parameters of the lognormal distribution can be made. Whereas there are currently only a few legal standards and threshold values based on long-term averages, some researchers have explored the statistics of exposures exceeding long-term limits.[3] To show that the mean exposure does not exceed the long-term average exposure limit (LTA-OEL), we may want to test the hypotheses

$$H_0 : \mu \geq \text{LTA-OEL} \quad \text{vs.} \quad H_a : \mu < \text{LTA-OEL} \qquad \textbf{(2)}$$

Note that the null and alternative hypotheses in Eq. 2 are set up to look for evidence in favor of H_a. Rejection of the null hypothesis in Eq. 2 implies that the exposure level is acceptable.

Another method of assessing workplace exposure, suggested by some investigators,[2,5,8] is based on the proportion of exposure data in excess of the LTA-OEL. Because the proportion of the measurements that are above the LTA-OEL is equal to the proportion of the logged measurements that are above ln(LTA-OEL), this approach reduces to the problem of hypothesis testing about an upper quantile of a normal distribution. This hypothesis testing can be carried out using an appropriate tolerance limit of the normal distribution, and it has been well addressed in the context of assessing occupational exposure by Tuggle,[2] Selvin et al.,[5] and Lyles and Kupper.[8]

In the context of exposure assessment, the problem of comparing two lognormal means will arise when we want to compare exposure levels of two similarly exposed groups of workers, or when we want to compare two exposure assessment methods or two different sampling devices. Thus, let y_1 and y_2 be lognormally distributed random variables denoting exposure levels at two different sites or measurements obtained by two different methods, and let μ_{l1}, μ_{l2} and σ_{l1}^2, σ_{l2}^2 denote the respective means and variances of the normally distributed random variables $\ln(y_1)$ and $\ln(y_2)$. Then the means of x_1 and x_2, say μ_1 and μ_2, respectively, are given by

$$\mu_1 = \exp(\eta_1), \text{ and } \mu_2 = \exp(\eta_2), \quad \text{where } \eta_1 = \mu_{l1} + \sigma_{l1}^2/2 \text{ and } \eta_2 = \mu_{l2} + \sigma_{l2}^2/2. \qquad \textbf{(3)}$$

For comparing the exposure levels at the two sites, it is of interest to test the hypotheses

$$H_0 : \mu_1 \leq \mu_2 \text{ vs. } H_a : \mu_1 > \mu_2. \qquad \textbf{(4)}$$

Land[12] has proposed exact methods for constructing confidence intervals and hypothesis tests for the lognormal mean. His methods, however, are computationally intensive and depend on the standard deviation of the logged data, which makes the necessary tabulation difficult. For this reason, Rappaport and Selvin[3] proposed a simple approximate method that is satisfactory as long as $\sigma_l^2 \leq 3$ and $n > 5$. Zhou and Gao[13] reviewed and compared several approximate methods and concluded that all the approximate methods are either too conservative or liberal, except for large samples, in which case, a method developed by Cox[12] is satisfactory. Armstrong[14] compared four approximate methods for estimating the confidence intervals (CI) with Land's[12] exact interval. These were the (a) "simple t-interval," (b) the "lognormal t-interval," (c) the Cox interval proposed by Land,[15] and (d) a variation of the Cox interval. Armstrong[14] found that whereas some of these approximate intervals were adequate for large sample sizes ($n \geq 25$) or small geometric standard deviations ($\sigma_g = 1.5$), none of them were accurate for small sample sizes and large σ_g—precisely the situations that are commonly encountered in occupational exposure assessment. Hewett and Ganser[16] have developed procedures that considerably simplify the calculation of Land's exact confidence interval. In a recent article, Taylor and colleagues[17] evaluated several approximate confidence intervals in terms of their coverage probabilities and also suggested an improved approximation. Very little work is available on the problem of comparing two lognormal means. A large sample test is derived in Zhou et al.[18] for testing the equality of two lognormal means.

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The purpose of this article is to illustrate the application of a novel approach for carrying out tests and confidence intervals for a single lognormal mean, for the ratio of two lognormal means, for a single lognormal variance, and for the ratio of two lognormal variances. The approach is based on the concepts of generalized p-values and generalized confidence intervals, collectively referred to as the generalized variables method. The generalized variables methodology is already described in Krishnamoorthy and Mathew[19] for obtaining tests and confidence intervals for a single lognormal mean, and for comparing two lognormal means; however, the lognormal variance is not considered in that article. In this article, we extend this approach for obtaining confidence intervals for the lognormal variance. Even though the lognormal mean is addressed by Krishnamoorthy and Mathew, we shall first briefly review the generalized variables procedure for the lognormal means described in their article and then apply it to the lognormal variance. We want to draw the attention of the industrial hygiene community to an accurate and unified methodology to deal with any parameter associated with the lognormal distribution. An added advantage of the generalized variables approach is the ease of computation and implementation. In fact the procedures can be easily coded in a programming language for implementation. Furthermore, extensive numerical results by the authors[19] show that for one-sided tests concerning a single lognormal mean, the results based on the generalized p-value approach are essentially equivalent to those based on the Land's[12] method.

The concept of generalized p-value was originally introduced by Tsui and Weerahandi,[20] and the concept of generalized confidence intervals was introduced by Weerahandi.[21] A later book by Weerahandi[22] illustrates several nonstandard statistical problems where the generalized variable approach produced remarkably useful results. Because the concepts are not well known, we have presented them in a brief outline in Appendix 1. In this article, we first present generalized variables for making inferences about a normal mean and variance. We then outline the hypothesis testing and interval estimation procedures for a single lognormal mean and then for the difference between two lognormal means. The necessary algorithms and Fortran and SAS programs to carry out our procedures are posted at http://www.ucs.louisiana.edu/∼kxk4695 and are available as an appendix to the online version of this article on the JOEH website. In a later section, we also address the problem of obtaining tests and confidence intervals concerning a single lognormal variance, or the ratio of two lognormal variances. A confidence interval for the lognormal variance should be of interest to assess the variability among exposure measurements.

We have used two examples to illustrate our methods. The first example involves the sample of air lead levels data collected from a lab by the National Institute of Occupational Safety and Health (NIOSH) health hazard evaluation staffs. The problem is to assess the contaminant level within the facility based on a sample. We also illustrate the generalized variable method for testing the equality of the means of measurements obtained by two different methods. For this purpose we used the data presented in O'Brien et al.[23]

Generalized Variables for the Mean and Variance of a Normal Distribution

As the mean of a lognormal distribution is a function of the mean and variance of a normal distribution, we present the generalized variables for the mean and variance of a normal population. The details of construction of generalized variables can be found in Krishnamoorthy and Mathew[19] or in Weerahandi,[22] and for easy reference they are provided in Appendix 1. Let $X_1, ..., X_n$ be a sample from a normal population with mean μ_l and variance σ_l^2, $N(\mu_l, \sigma_l^2)$. The sample mean and the variance of the X_is are respectively given by

$$\bar{X} = \frac{1}{n}\sum_{i=1}^{n} X_i \text{ and } S^2 = \frac{1}{n-1}\sum_{i=1}^{n}(X_i - \bar{X})^2. \quad \textbf{(5)}$$

Let Z and V be independent random variables with

$$Z = \frac{\sqrt{n}(\bar{X} - \mu_l)}{\sigma_l} \sim N(0, 1), \text{ and } V^2 = \frac{(n-1)S^2}{\sigma_l^2} \sim \chi^2_{n-1}, \quad \textbf{(6)}$$

where χ^2_r denotes the central chi-square distribution with r degrees of freedom. Let $\bar{x}$ and s be the observed values of $\bar{X}$and S, respectively. Following the procedure outlined in the appendix, a generalized variable for making inferences on μ_l is given by

$$\begin{aligned} G_{\mu_l} &= \bar{x} - \left(\frac{\bar{X} - \mu_l}{\sigma_l/\sqrt{n}}\right)\frac{\sigma_l}{\sqrt{n}}\frac{s}{S} - \mu_l \\ &= \bar{x} - \frac{Z}{V/\sqrt{n-1}}\frac{s}{\sqrt{n}} - \mu_l \\ &= T_{\mu_l} - \mu_l, \end{aligned} \quad \textbf{(7)}$$

where

$$T_{\mu_l} = \bar{x} - \frac{Z}{V/\sqrt{n-1}}\frac{s}{\sqrt{n}}, \quad \textbf{(8)}$$

and Z and V are as defined in (Eq. 6). In the above, G_{μ_l} denotes the generalized test variable for μ_l, and T_{μ_l} denotes the generalized pivot statistic (the statistic that can be used for making inference about the unknown parameter) for μ_l. We shall now show that G_{μ_l} satisfies the three conditions given in (Eq. A3) of Appendix 1: (1) For a given $\bar{x}$ and s, the distribution of G_{μ_l} does not depend on the nuisance parameter σ_l^2; (2) it follows from Step 1 of Eq. 7 that the value of G_{μ_l} at $(\bar{X}, S) = (\bar{x}, s)$ is μ_l; (3) it follows from Step 3 of Eq. 7 that, for a given $\bar{x}$ and$s$, the generalized variable is *stochastically decreasing* with respect to μ_l and hence the generalized p-value for testing $H_0 : \mu_l \geq \mu_{l0}$ vs. H_a:$\mu_l < \mu_{l0}$ is given by

$$\begin{aligned} \sup_{H_0} P(G_{\mu_l} \geq 0) &= P(G_{\mu_l} \geq 0 | \mu_l = \mu_{l0}) \\ &= P(T_{\mu_l} \geq \mu_{l0}) \\ &= P\left(t_{n-1} < \frac{\bar{x} - \mu_{l0}}{s/\sqrt{n}}\right), \end{aligned}$$

which is the p-value based on the usual t-test. To get the last equality, we used the fact that $Z/(V/\sqrt{n-1})$ follows a Student's t distribution with degrees of freedom $n-1$, t_{n-1}.

For a given $\bar{x}$ and s, the lower $\alpha/2$ quantile $T_{\mu_l,\alpha/2}$ of T_{μ_l} and the upper $\alpha/2$ quantile $T_{\mu_l,1-\alpha/2}$ of T_{μ_l} form a $1-\alpha$ generalized confidence interval for μ_l. This generalized CI is indeed equal to the usual t-interval; that is, $(T_{\mu_l,\alpha/2}, T_{\mu_l,1-\alpha/2}) = (\bar{x} - t_{n-1,1-\alpha/2}\frac{s}{\sqrt{n}}, \bar{x} + t_{n-1,1-\alpha/2}\frac{s}{\sqrt{n}})$, where $t_{m,p}$ denotes the $100p$th percentile of the Student's t distribution with m degrees of freedom.

The generalized test variable for the variance σ_l^2 is given by

$$G_{\sigma_l^2} = \frac{s^2}{V^2/(n-1)} - \sigma_l^2 = T_{\sigma_l^2} - \sigma_l^2, \qquad \textbf{(9)}$$

where

$$T_{\sigma_l^2} = \frac{s^2}{V^2/(n-1)} \qquad \textbf{(10)}$$

is the generalized pivot statistic, and V is as defined in Eq. 6. Again, for a given s^2, the generalized $1-\alpha$ CI for σ_l^2 is formed by the lower and upper $\alpha/2$ quantiles of $T_{\sigma_l^2}$ and is equal to the usual CI based on a chi-square distribution with $n-1$ degrees of freedom.

Even though the generalized variable method produced exact inferential procedures for the normal parameters, in general, the generalized variable method is not necessarily exact. In other words, the generalized p-value may not satisfy the conventional properties of the usual p-value. In such cases, the properties (such as Type I error rates of the generalized variable test and coverage probability of the generalized confidence limits) of the generalized variable method should be evaluated numerically.

Suppose we are interested in making inference about a function of μ_l and σ_l^2, say, $q(\mu_l, \sigma_l^2)$. Then, the generalized test variable for $q(\mu_l, \sigma_l^2)$ is given by $q(T_{\mu_l}, T_{\sigma_l^2}) - q(\mu_l, \sigma_l^2)$, and the generalized pivot statistic is given by $q(T_{\mu_l}, T_{\sigma_l^2})$. For a given $\bar{x}$ and s, the variable $q(\mu_l, \sigma_l^2)$ depends only on the random variables Z and V whose distributions do not depend on any unknown parameters. Therefore, Monte Carlo simulation can be used to find a generalized CI for $q(\mu_l, \sigma_l^2)$. This will be illustrated for the lognormal case in the following section.

Inference about a Lognormal Mean

Let $y_1, \ldots, y_n$ be a sample of exposure measurements and let $x_i = \ln(y_i)$, $i = 1, \ldots, n$. Then, $x_1, \ldots, x_n$ is a random sample from a $N(\mu_l,\sigma_l^2)$ distribution. Since the lognormal mean $\exp(\mu_l + \sigma_l^2/2)$ is a function of μ_l and σ_l^2, the results of the preceding section can be readily applied to construct a generalized test variable and a generalized pivot statistic for the lognormal mean. From the preceding section, we have the generalized test variable for making inference on $\eta = (\mu_l + \sigma_l^2/2)$ as

$$\begin{aligned} G_\eta &= T_{\mu_l} + \frac{T_{\sigma_l^2}}{2} - \eta \\ &= \bar{x} - \frac{Z}{V/\sqrt{n-1}}\frac{s}{\sqrt{n}} + \frac{s^2}{2V^2/(n-1)} - \eta \qquad \textbf{(11)} \\ &= T_\eta - \eta, \end{aligned}$$

where

$$T_\eta = \bar{x} - \frac{Z}{V/\sqrt{n-1}}\frac{s}{\sqrt{n}} + \frac{s^2}{2V^2/(n-1)} \qquad \textbf{(12)}$$

and Z and V are as defined in Eq. 6. For given sample statistics $\bar{x}$ and s, we note that G_η is stochastically decreasing in η, and hence the generalized p-value for testing (Eq. 2) is given by

$$\begin{aligned} P(G_\eta \geq 0 | \eta = \ln(\text{LTA-OEL})) \\ = P(T_\eta \geq \ln(\text{LTA-OEL})). \qquad \textbf{(13)} \end{aligned}$$

The null hypothesis in Eq. 2 will be rejected whenever the probability in Eq. 13 is less than the nominal level α.

The generalized pivot statistic for interval estimation of η is given by T_η. Appropriate quantiles of T_η can be used to obtain confidence intervals for η or for the lognormal mean $\exp(\eta)$. Specifically, if $T_{\eta,p}$, $0 < p < 1$, denotes the pth quantile of T_η, then $(T_{\eta,\alpha/2}, T_{\eta,1-\alpha/2})$ is a $1-\alpha$ generalized confidence interval for η, and $(\exp(T_{\eta,\alpha/2}), \exp(T_{\eta,1-\alpha/2}))$ is a $1-\alpha$ generalized confidence interval for the lognormal mean $\exp(\eta)$. One-sided limits for η and $\exp(\eta)$ can be similarly obtained. In particular, a $1-\alpha$ lower limit for $\exp(\eta)$ is given by $\exp(T_{\eta,\alpha})$.

Through numerical results, Krishnamoorthy and Mathew[17] noted that the confidence limits based on Land's[12] approach and the generalized confidence interval are practically the same. However, computationally, our approach is very easy to implement. The simple algorithm presented in Appendix 2 of Krishnamoorthy and Mathew[19] can be used for computing the generalized p-value and the generalized confidence interval.

Power Studies and Sample Size Calculation for Testing a Lognormal Mean

We shall now discuss the power of the test based on the generalized p-value in Eq. 13. For a given sample size n and for a given value of μ_l and σ_l such that H_a in Eq. 2 holds (i.e., $\eta = \mu_l + \sigma_l^2/2 < \ln(\text{LTA-OEL})$), the power of the test can be estimated by Monte Carlo simulation. In practice, however, practitioners are mainly interested in finding the required sample size to have a specified power at a given level of significance. The sample size can be calculated using an iterative method. For power calculation, an algorithm and Fortran and SAS programs based on the algorithm are posted at http://www.ucs.louisiana.edu/~kxk4695 and are available as an appendix to the online version of this article. Using this program, we computed sample sizes that are required to have a power of 0.90 at the level of significance $\alpha = 0.05$ for various parameter configurations, and these are presented in Table I. As an example, if an employer speculates that the mean exposure level is 40% (the value R in Table I) of the LTA-OEL, and the geometric standard deviation is 2.0, then the required sample size to have a power of at least 0.90 at the level 0.05 is 13.

We observe from Table I that the power of the test increases as the ratio R decreases, which is a natural requirement for a test. We also note that the power decreases as σ_g increases and,

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TABLE I. Sample Size for Testing Equation 2 to Attain a Power of 0.90 at the Level of 0.05, Using the Generalized P-Value Test

	σ_g				
R	**1.5**	**2.0**	**2.5**	**3.0**	**3.5**
0.1	4 (.96)	6 (.94)	8 (.90)	11 (.90)	13 (.91)
0.2	4 (.90)	7 (.91)	11 (.91)	16 (.90)	21 (.91)
0.3	5 (.93)	10 (.91)	16 (.90)	21 (.91)	30 (.90)
0.4	6 (.91)	13 (.90)	23 (.91)	35 (.91)	45 (.90)
0.5	8 (.93)	18 (.91)	33 (.90)	52 (.90)	68 (.90)
0.7	18 (.91)	56 (.90)	99 (.90)	162 (.90)	235 (.90)
0.8	37 (.90)	120 (.90)	241 (.90)	363 (.90)	563 (.90)

Note: $R = \frac{\mu_l}{\text{LTA-OEL}}$; $\sigma_g = \exp(\sigma_l)$ = geometric standard deviation; the numbers in parenthesis represent actual attained powers; LTA-OEL = 1.0; the lognormal mean.

hence, large samples are required to make correct decisions when σ_g is expected to be large.

Comparison of Two Lognormal Means

Consider the independent lognormal random variables y_1 and y_2 so that $x_1 = \ln(y_1) \sim N(\mu_{l1}, \sigma_{l1}^2)$ and $x_2 = \ln(y_2) \sim N(\mu_{l2}, \sigma_{l2}^2)$. Then the lognormal means are given by $E(y_1) = \exp(\eta_1)$ and $E(y_2) = \exp(\eta_2)$, where

$$\eta_1 = \exp\left(\mu_{l1} + \sigma_{l1}^2/2\right) \text{ and } \eta_2 = \exp\left(\mu_{l2} + \sigma_{l2}^2/2\right). \quad \textbf{(14)}$$

Thus, hypothesis tests and confidence intervals for the ratio of the two lognormal means are respectively equivalent to those for the difference $\eta_1 - \eta_2$. We shall now develop generalized p-values and generalized confidence intervals for this problem.

We shall first consider the testing problem

$$H_0 : \eta_1 \leq \eta_2 \text{ vs. } H_a : \eta_1 > \eta_2. \quad \textbf{(15)}$$

Let $y_{1j}, j = 1, \ldots, n_1$, and $y_{2j}, j = 1, \ldots, n_2$, denote random samples from the lognormal distributions of y_1 and y_2, respectively. Let $x_{1j} = \ln(y_{1j})$, $j = 1, \ldots, n_1$, and $x_{2j} = \ln(y_{2j})$, $j = 1, \ldots, n_2$. The sample means $\bar{x}_1$ and $\bar{x}_2$ and the sample variances s_1^2 and s_2^2 are then given by

$$\bar{x}_i = \frac{1}{n_i}\sum_{j=1}^{n_i} x_{ij} \text{ and } s_i^2 = \frac{1}{n_i - 1}\sum_{j=1}^{n_i}(x_{ij} - \bar{x}_i)^2, \; i = 1, 2. \quad \textbf{(16)}$$

It follows from Eq. 12 that the generalized variable for η_i can be expressed as

$$T_{\eta_i} = \bar{x}_i - \frac{Z_i}{V_i/\sqrt{n_i - 1}}\frac{s_i}{\sqrt{n_i}} + \frac{s_i^2}{2V_i^2/(n_i - 1)}, \; i = 1, 2, \quad \textbf{(17)}$$

where $Z_i \sim N(0, 1)$ and $V_i^2 \sim \chi_{n_i-1}^2$, for $i = 1, 2$, and all these random variables are independent. The generalized test variable for testing (Eq. 15) is given by

$$G_{\eta_1-\eta_2} = T_{\eta_1} - T_{\eta_2} - (\eta_1 - \eta_2) \quad \textbf{(18)}$$

and the generalized pivot statistic to construct CI for $\eta_1 - \eta_2$ for is given by

$$T_{\eta_1-\eta_2} = T_{\eta_1} - T_{\eta_2}. \quad \textbf{(19)}$$

For given sample statistics, $G_{\eta_1-\eta_2}$ is stochastically decreasing in $\eta_1 - \eta_2$. Thus the generalized p-value for testing the hypotheses in Eq. 15 is given by

$$\begin{aligned}\sup_{H_0} P(G_{\eta_1-\eta_2} \leq 0) &= P(G_{\eta_1-\eta_2} \leq 0 | \eta_1 - \eta_2 = 0) \\ &= P(T_{\eta_1-\eta_2} \leq 0). \quad \textbf{(20)}\end{aligned}$$

For given sample statistics, the confidence intervals for $\eta_1 - \eta_2$ can be computed using the percentiles of $T_{\eta_1-\eta_2}$. Because, given $\bar{x}_1, \bar{x}_2, s_1^2$ and s_2^2, the distribution of $T_{\eta_1-\eta_2}$ is free of any unknown parameters, the percentiles of $T_{\eta_1-\eta_2}$ can be estimated using Monte Carlo simulation. We can also construct confidence intervals for the difference between the lognormal means, that is, $\exp(\eta_1) - \exp(\eta_2)$. For this, we can use the percentiles of $\exp(T_{\eta_1}) - \exp(T_{\eta_2})$, where T_{η_1} and T_{η_2} are given in Eq. 17. Note that algorithms similar to Algorithm 1 can be easily developed for computing the above generalized p-values and confidence intervals. An algorithm and Fortran and SAS programs for computing the generalized p-value test and the CI for $\exp(T_{\eta_1}) - \exp(T_{\eta_2})$ are posted at http://www.ucs.louisiana.edu/~kxk4695 and are available as an appendix to the online version of this article.

Power Properties of the Generalized Test for the Two-Sample Case

For given sample sizes n_1 and n_2, parameters $\mu_{l1}, \mu_{l2}, \sigma_{l1}$ and σ_{l2} the powers of the generalized test based on Eq. 20 can be estimated using Monte Carlo method. A Fortran program and SAS codes for computing the power (along with a help file) are posted at http://www.ucs.louisiana.edu/~kxk4695 and are available as an appendix to the online version of this article. The help file also contains an algorithm that can be coded in any desired computing language. Krishnamoorthy and Mathew[19] computed powers for several sample sizes and parameter combinations. It is observed in this article that the generalized test possesses all natural properties. However, the power of the test depends on $\mu_{l1} - \mu_{l2}, \sigma_{l1}$ and σ_{l2}. Therefore, to compute the required sample sizes to attain a specified power, the practitioner should have knowledge about $\mu_{l1} - \mu_{l2}, \sigma_{l1}$, and σ_{l2}.

Inference about a Lognormal Variance and Geometric Standard Deviation

For the assessment of the extent of variability among the exposure measurements, confidence intervals, or tests concerning the variance becomes necessary. If y denotes the lognormally distributed exposure measurements, then $x = \ln(y)$ is distributed normally with mean μ_l and variance σ_l^2.

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TABLE II. Monte Carlo Estimates of the Sizes of the Generalized P-Value Test Based on Equation 24 for Lognormal Variance in Equation 21; Nominal Level = 0.05

	$\sigma_l = 0.5$			$\sigma_l = 1.0$			$\sigma_l = 1.5$		
μ_l	$n = 10$	$n = 15$	$n = 20$	$n = 10$	$n = 15$	$n = 20$	$n = 10$	$n = 15$	$n = 20$
0.00	.050	.041	.047	.047	.048	.046	.050	.044	.049
0.30	.046	.056	.052	.053	.044	.049	.043	.046	.056
0.70	.047	.050	.052	.045	.050	.048	.049	.044	.049
1.00	.050	.050	.054	.048	.049	.050	.048	.044	.049
1.30	.054	.046	.043	.052	.049	.045	.045	.051	.050
1.50	.048	.060	.048	.053	.048	.049	.048	.050	.045
1.70	.053	.053	.051	.043	.045	.048	.052	.048	.042
2.00	.055	.053	.054	.046	.054	.054	.054	.048	.047

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The variance of y, to be denoted by σ^2, is given by

$$\sigma^2 = \exp\left(2\mu_l + \sigma_l^2\right)\left[\exp\left(\sigma_l^2\right) - 1\right]. \quad \textbf{(21)}$$

As far as we are aware, no procedures (except obvious large sample procedures) are known for computing a confidence interval or for testing hypotheses concerning σ^2. It turns out that the ideas of generalized p-values and generalized confidence intervals provide solutions to this problem, regardless of the sample size. We shall now construct a generalized pivot statistic that can be used to compute a confidence interval for σ^2, and a generalized test variable that can be used for testing the hypotheses

$$H_0 : \sigma^2 \geq \sigma_0^2 \text{ vs. } H_a : \sigma^2 < \sigma_0^2, \quad \textbf{(22)}$$

where σ_0^2 is a known constant. Note that it is by rejecting H_0 that we conclude that the variability is small, that is, below the bound σ_0^2.

Using earlier notations, the generalized test variable for σ^2 is given by

$$\begin{aligned} G_{\sigma^2} &= \exp\left(2T_{\mu_l} + T_{\sigma_l^2}\right)\left[\exp\left(\sigma_l^2\right) - 1\right] - \sigma^2 \\ &= \exp\left(2\left(\bar{x} - \frac{Z}{V/\sqrt{n-1}}\frac{s}{\sqrt{n}}\right) + \frac{s^2}{V^2/(n-1)}\right) \\ &\quad \times \left[\exp\left(\frac{s^2}{V^2/(n-1)}\right) - 1\right] - \sigma^2, \end{aligned} \quad \textbf{(23)}$$

where Z and V are as defined in Eq. 6. The generalized pivot statistic for constructing CI for σ_l^2 is given by

$$\begin{aligned} T_{\sigma^2} &= \exp\left(2\left(\bar{x} - \frac{Z}{V/\sqrt{n-1}}\frac{s}{\sqrt{n}}\right) + \frac{s^2}{V^2/(n-1)}\right) \\ &\quad \left[\exp\left(\frac{s^2}{V^2/(n-1)}\right) - 1\right]. \end{aligned} \quad \textbf{(24)}$$

Arguing as in previous sections, the generalized p-value for testing the hypotheses in Eq. 22 is given by

$$P\left(G_{\sigma^2} \geq 0 \middle| \sigma^2 = \sigma_0^2\right) = P\left(T_{\sigma^2} \geq \sigma_0^2\right). \quad \textbf{(25)}$$

Furthermore, the percentiles of T_{σ^2} can be used for computing a generalized confidence interval for σ^2. An algorithm (similar to Algorithm 1 in Appendix 2) can be easily developed for computing the above generalized p-value and confidence interval. We also note that the above procedure can be easily extended for the purpose of comparing two lognormal variances.

To understand the validity of the generalized test based on Eq. 25, we estimated its sizes (Type I error rates) using Monte Carlo method for various values of μ_l, σ_l and n = 10,15, and 20. The sizes are estimated for testing hypotheses in Eq. 22 at the nominal level 0.05, and they are given in Table II. For a good test, the estimated sizes should be close to the nominal level. We see from Table II that the estimated sizes are very close to the nominal level for all the cases considered.

The generalized variable for a geometric standard deviation $\sigma_g = \exp(\sigma_l)$ is given by

$$G_{\sigma_g} = \exp\left(\sqrt{G_{\sigma_l^2}}\right), \quad \textbf{(26)}$$

where the generalized variable $G_{\sigma_l^2}$ for σ_l^2 is given in Eq. 9. However, it was pointed out earlier that the generalized variable approach gives the same confidence interval for σ_l^2 as the conventional chi-square interval. From this, a confidence interval for the geometric standard deviation is easily obtained as

$$\left(\exp\left(s\sqrt{\frac{(n-1)}{\chi^2_{n-1,1-\alpha/2}}}\right), \exp\left(s\sqrt{\frac{(n-1)}{\chi^2_{n-1,\alpha/2}}}\right)\right), \quad \textbf{(27)}$$

where $\chi^2_{m,p}$ denotes the $100p$th percentile of the central chi-square distribution with df $= m$. The expression in (Eq. 27) is an exact $1 - \alpha$ confidence interval for σ_g.

Similarly, a test for

$$H_0 : \sigma_g \leq c \quad \text{vs.} \quad H_a : \sigma_g > c, \quad \textbf{(28)}$$

is essentially a test concerning the variance σ_l^2, and the usual chi-square test for the variance can be applied.

Illustrative Examples

Example 1

The data represent air lead levels collected by NIOSH at the Alma American Labs, Fairplay, Colorado, for health hazard evaluation purpose (HETA 89-052) on February 23, 1989. The air lead levels were collected from 15 different areas within the facility.

Air Lead Levels (μg/m^3): 200, 120, 15, 7, 8, 6, 48, 61, 380, 80, 29, 1000, 350, 1400, 110

For this data, the mean (=254) is much larger than the median (=80), which is an indication that the distribution is right skewed. The normal probability plots (Minitab 14.0, default method) were constructed for the actual lead levels (Figure 1A) and for the logged lead levels (Figure 1B). It is clear from Figures 1A and 1B that the distribution of the data is far away from a normal distribution (p-value < 0.05), but a lognormal model adequately describes the data (p-value 0.871). The p-values are based on the Anderson-Darling test. Therefore, we apply the methods of this paper to make valid inferences about the mean lead level. Based on the logged data, we have the observed values $\bar{x} = 4.333$ and $s = 1.739$. Using these numbers in Algorithm 1, we computed the 95% upper limit for $\exp(\eta)$ as 2405. We also computed the 95% lower limit for the lognormal mean as 141. That is, the mean air lead level within the facility exceeds 141 μg/m^3 with 95% confidence.

Suppose we want to test whether the mean is greater than some arbitrary value (e.g., 120 μg/m^3) that could be a limit value

$$H_0 : \mu \geq 120 \text{ vs. } H_a : \mu < 120,$$

where $\mu = \exp(\eta)$ (with $\eta = \mu_l + \sigma_l^2/2$) denotes the actual unknown mean air lead levels within the lab facility. Using again Algorithm 1, we computed the generalized p-value as

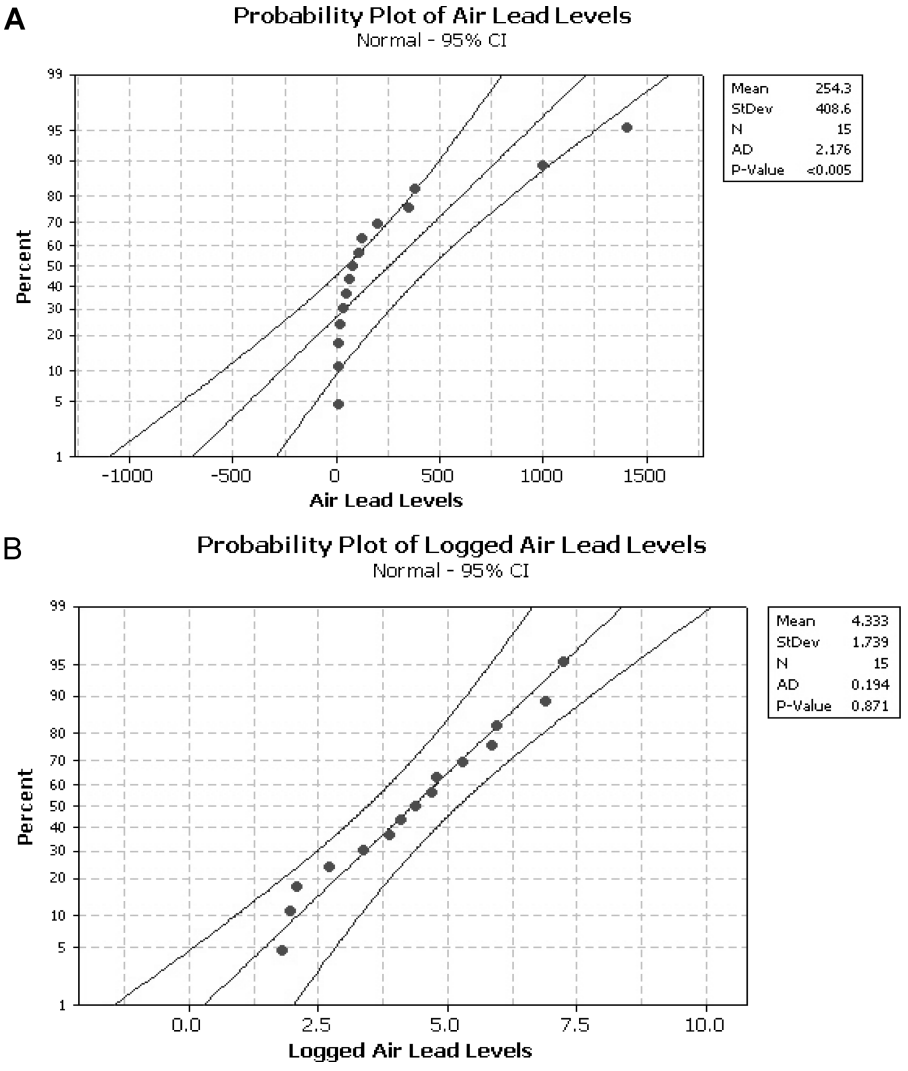

FIGURE 1. Normal probability plots of (A) actual lead levels, and (B) logged air lead levels

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TABLE III. Summary Statistics for Airborne Concentration of Metalworking Fluids (MWF) in 23 Plants

Method	Sample Size	$\bar{x}$	s
Thoracic MWF aerosol (gravimetric analysis)	23	−1.277	0.835
Closed-face MWF analysis	23	−0.979	0.917

Note: $\bar{x}$ = mean of the logged data; s = standard deviation of the logged data.

0.97, and so we conclude that the data do not provide enough evidence to indicate that the mean air lead levels within the facility is less than 120 μg/m^3.

Regarding the lognormal variance, we computed the maximum likelihood estimate as 2337098 μg/m^3. This estimate is obtained by replacing μ_l and σ_l^2 in Eq. 21, respectively, by $\bar{x}$ and $((n-1)s2/n)$. We also computed a 95% confidence interval for the lognormal variance, using the generalized pivot statistic T_{σ^2} in (24), as (128538, 2956026772).

Finally, we computed the 95% CI for the geometric standard deviation using the generalized variable in Eq. 26 as (3.57, 15.49); using the exact formula in Eq. 27, we get (3.57, 15.53).

Example 2

In this example, we shall illustrate the generalized variable procedures for testing the equality of the means of measurements obtained by two different methods. The data were reported in Table I of O'Brien et. al.,[23] and represent total mass of metalworking fluids (MWF) obtained by thoracic MWF aerosol and closed-face MWF aerosol. Normal probability plots of logged data indicated that the lognormality assumption about the original data is tenable. The means and the standard deviations of the logged data are given in Table III. Let μ_t and μ_c denote the true means of the airborne concentrations by thoracic MWF aerosol and closed-face MWF aerosol, respectively. To test the equality of the means, we consider

$$H_0 : \mu_t = \mu_c \text{ vs. } H_a : \mu_t \neq \mu_c.$$

Using the summary statistics in Table III, we simulated $D = \exp(T_{\eta_1}) - \exp(T_{\eta_2})$, where T_{η_1} and T_{η_2} are given in Eq. 17, 100,000 times. The generalized p-value for the above two-tail test can be estimated by $2 \times \min\{\text{proportion of } D\text{s} < 0, \text{proportion of } D\text{s} > 0\}$. Our simulation yielded the generalized p-value of 0.244. The lower 2.5 and the upper 2.5 percentiles of D form a 95% confidence interval for the difference between the means and is computed as (–0.657, 0.145). Thus, at the 5% level, both generalized p-value and the confidence interval indicate that there is no significant difference between the means.

CONCLUSIONS

Several attempts have been made in the literature for drawing inferences concerning the mean of a single lognormal distribution. To a much lesser extent, attempts have also been made to draw inferences for the ratio of the means of two lognormal distributions. These problems have certain inherent difficulties associated with them, and the available solutions are either approximate, or are applicable only to large samples, or are difficult to compute. In this article, we have explored a novel approach for solving these problems, based on the concepts of generalized p-values and generalized confidence intervals. It turns out that these concepts provide a unified and versatile approach for handling *any* parametric function associated with one or two lognormal distributions. Even though analytic expressions are not available for the resulting confidence intervals or p-values, their computation is both easy and straightforward. We have provided the necessary programs for their computation, and we have also illustrated our approach using several examples dealing with the analysis of exposure data. In writing this article, our intention has been to draw the attention of industrial hygienists to this new methodology.

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APPENDIX 1

The Generalized Confidence Interval and Generalized P-Value

A general setup where the concepts of generalized confidence intervals and generalized p-values are defined is as follows. Consider a random variable X whose distribution depends on a scalar parameter of interest θ and a nuisance parameter (parameter that is not of direct inferential interest) η, where η could be a vector. Here X could also be a vector. Suppose we are interested in computing a confidence interval for θ. Let x denote the observed value of X, that is, x represents the data that has been collected. To obtain a generalized confidence interval for θ, we need a *generalized pivot statistic* (the pivotal quantity based on which inferential procedures will be developed) $T_1(X; x, \theta, \eta)$ that is a function of the random variable X, the observed data x, and the parameters θ and η, and satisfying the following two conditions:

(i) Given x, the distribution of $T_1(X; x, \theta, \eta)$ is free of the unknown parameters θ and η;
(ii) The observed value of $T_1(X; x, \theta, \eta)$, namely, $T_1(x; x, \theta, \eta)$ is equal to θ. **(A1)**

The percentiles of $T_1(X; x, \theta, \eta)$ can then be used to obtain confidence intervals for θ. Such confidence intervals are referred to as generalized confidence intervals. For example, if $T_{1-\alpha}$ denotes the $100(1-\alpha)$th percentile of $T_1(X; x, \theta, \eta)$, then $T_{1-\alpha}$ is a generalized upper confidence limit for θ. A lower confidence limit or two-sided confidence limits can be similarly defined.

Now suppose we are interested in testing the hypothesis

$$H_0 : \theta \le \theta_0 \quad \text{vs.} \quad H_a : \theta > \theta_0, \qquad \textbf{(A2)}$$

where θ_0 is a specified quantity. Suppose we can define a *generalized test variable* $T_2(X; x, \theta, \eta)$ satisfying the following conditions:

(i) For a given x, the distribution of $T_2(X; x, \theta, \eta)$ is free of the nuisance parameter η;
(ii) The observed value of $T_2(X; x, \theta, \eta)$, namely, $T_2(x; x, \theta, \eta)$ is free of any unknown parameters;
(iii) For a given x and η, the distribution of $T_2(X; x, \theta, \eta)$ is stochastically monotone in θ (i.e., stochastically increasing or decreasing in θ). **(A3)**

In general, for a given x and η, $T_2(X; x, \theta, \eta)$ is stochastically decreasing in θ, and the generalized p-value for testing Eq. A2 is given by $P\,(T_2(X; x, \theta, \eta) \le t)$, where $t = T_2(x; x, \theta, \eta)$. On the other hand, if $T_2(X; x, \theta, \eta)$ is stochastically decreasing in θ, then the generalized p-value for Eq. A2 is defined as $P\,(T_2(X; x, \theta, \eta) \ge t)$. In general, the observed value t is equal to θ_0, and as the distribution of $T_2(X; x, \theta, \eta)$ is free of the nuisance parameter η, the generalized p-value at θ_0 can be computed using Monte Carlo simulation.

APPENDIX 2

Algorithm for Computing the Generalized P-Value and the Generalized Confidence Interval

The following algorithm given by Krishnamoorthy and Mathew[17] can be used for computing the generalized p-value and the generalized confidence interval.

For a given logged data set, compute the observed sample mean and variance, namely, $\bar{x}$ and s^2, respectively.

For $i = 1$ to m

Generate a standard normal variate Z

Generate a chi-square random variate V^2 with degrees of freedom $n-1$

$$\text{Set } T_{\eta i} = \bar{x} - \frac{Z}{V/\sqrt{n-1}}\frac{s}{\sqrt{n}} + \frac{s^2}{2V^2/(n-1)}$$

Set $K_i = 1$ if $T_{\eta i} > \ln(\text{LTA - PEL})$, else $K_i = 0$

(end i loop)

$\frac{1}{m}\sum_{i=1}^{m} K_i$ is the generalized p-value for testing the hypotheses in Eq. 2. The $100(1-\alpha)$th percentile of $T_{\eta_1}, \ldots, T_{\eta_m}$, denoted by $T_{\eta,1-\alpha}$, is the $1-\alpha$ generalized upper confidence limit for $\eta = \mu_l + \sigma_l^2/2$. Furthermore, $\exp(T_{\eta,1-\alpha})$ is the $1-\alpha$ generalized upper limit for the lognormal mean.

Based on our experience, we recommend simulation consisting of at least 100,000 (i.e., the value of m) to get consistent results regardless of the initial seed used for random number generation. The above algorithm can be easily programmed in any programming language. A Fortran program and SAS codes for computing generalized p-values for one-tail tests and one-sided confidence limits is posted at http://www.ucs.louisiana.edu/~kxk4695. Interested readers can download these files from this address.