

Multiple Comparisons of Several Log-normal Means under Heteroscedasticity

Guoyi Zhang¹ and Bose Falk² and Zhongxue Chen³

¹Department of Mathematics and Statistics
University of New Mexico
Albuquerque, NM, 87131-0001
gzhang@unm.edu

²DKMS gemeinnützige GmbH, Germany
bosefalk@gmail.com

³Department of Epidemiology and Biostatistics School of Public Health
Indiana University
Bloomington, IN, 47405
zc3@indiana.edu

ABSTRACT

This research considers several log-normal distributions when variances are heteroscedastic and group sizes are unequal. We proposed fiducial generalized pivotal quantities (FGPQ)-based simultaneous confidence intervals for pairwise multiple comparisons of ratios of the means. We also proved that the proposed confidence intervals have correct asymptotic coverage. Simulation results show that the proposed methods work well in terms of coverage probabilities.

Keywords: Log-normal, Fiducial Generalized Pivotal Quantities (FGPQ), Multiple Comparison, Simulations, Unequal Variances.

2000 Mathematics Subject Classification: 97K70.

1 Introduction

Log-normal distribution is widely used to describe the distribution of positive random variables that exhibit skewness in biological, medical, and economical studies. The problem of equality and multiple comparisons of the group means are common interests in many observational and experimental data arising from several populations. Unfortunately, if sample variances are unequal, the standard ANOVA tests don't apply for log-normal distributions even after transformation, since the null hypothesis based on log-transformed outcomes is not equivalent to the one based on the original outcomes (Zhou, Gao, & Hui, 1997).

Simultaneous confidence intervals for certain log-normal parameters are useful in many areas. In pharmaceutical statistics, it is often of interest to compare the mean responses of two or

several drugs to ensure that they are (more or less) equally effective. For example, twenty-three healthy male subjects each followed randomly allocated sequences of five treatments (with one week washout period between different treatments to ensure no carry-over effects), either no treatment or one of four active treatments from the same drug class was used to treat the same illness (Bradstreet & Liss, 1995). One of the subjects are missing under treatment 2, which leads to an unbalanced case. Since data followed a log-normal distribution, to find out if there are any of the four active treatments similar to no treatment, or similar to each other, we require a new method on multiple comparison procedure (MCP) for several log-normal distributions.

In standard analysis of variance, Scheffé's method (Scheffé, 1959), the Bonferroni inequality-based method, and Tukey method (Tukey, 1953) are widely used for simultaneous pairwise comparisons (SPC). When variances are heteroscedastic and group sizes are unequal, exact frequentist tests are unavailable. In such situations, parametric bootstrap and generalized p-value (Tsui & Weerahandi, 1989) procedures are commonly used. Weerahandi (1993) introduced the concept of a generalized pivotal quantity. Later, Hannig, Iyer, and Patterson (2006) introduced a subclass of Weerahandi's generalized pivotal quantity, called fiducial generalized pivotal quantities (FGPQs), which is essentially based on invertible pivotal relationships. In their paper, they have described three general approaches for constructing FGPQs. Using the idea of FGPQ, Hannig (2006) provided a method to construct MCP of means in the one-way layout under heteroscedasticity. Xiong and Mu (2009) proposed two kinds of simultaneous intervals based on FGPQ for all pairwise comparisons of treatment means in a one-way layout under heteroscedasticity. Xiong and Mu (2009) pointed out that if sample sizes are sufficiently large, Hannig (2006)'s simultaneous confidence intervals are equal to one of their proposed intervals. Otherwise, Xiong and Mu (2009) methods perform better than Hannig (2006)'s methods. Using FGPQ for vector parameters, Zhang (2014) proposed MCP of means from inverse Gaussian distribution. Zhang and Chen (2015) developed generalized confidence intervals (GCI) and hypothesis tests for the correlation coefficients, and extended the results to compare two independent correlations based on FGPQs. In this research, we propose FGPQ-based MCP for ratios of means from several log-normal populations under heteroscedasticity.

This paper is organized as follows. In Section 2, we review notation of generalized variable approach. In Section 3, we propose FGPQ-based simultaneous confidence intervals for ratios of means from several log-normal distributions. In Section 4, we present simulation studies. Section 5 gives conclusions.

2 Background: generalized variable approach

The principles of GCI are outlined by Weerahandi (1993). The idea of GCI is to construct confidence intervals for cases where exact confidence intervals based on sufficient statistics are not available. For example, we want to compare two means from the exponential distribution, or from the log-normal distribution.

The confidence interval is constructed using a pivotal quantity (Weerahandi, 1993, page 900). Let R be a function $r(\mathbf{X}; \mathbf{x}, \mathbf{v})$, where $\mathbf{X} = (X_1, \dots, X_n)$ is a random sample, \mathbf{x} are the ob-

served values of \mathbf{X} , and $\mathbf{v} = (\theta, \delta)$, where θ is an unknown parameter of interest from \mathbf{X} and δ is a vector of nuisance parameters. \mathbf{R} is called a generalized pivotal quantity (GPQ) if it has the following two properties:

Property A: R has a probability distribution free of unknown parameters,

Property B: The observed pivotal, defined as $r_{obs} = r(\mathbf{x}; \mathbf{x}, \mathbf{v})$ does not depend on the nuisance parameter δ .

Consider the problem of testing population parameter θ of a log-normal distribution,

$$H_0 : \theta \leq \theta_0 \quad \text{vs.} \quad H_\alpha : \theta > \theta_0, \quad (2.1)$$

where θ_0 is a specified value of θ . The generalized test statistic $T(\mathbf{X}; \mathbf{x}, \theta; \delta)$ has the same properties of A and B as GPQ as well as one additional:

Property C: T is monotonically increasing or decreasing in θ .

If T is stochastically increasing in θ , The generalized p-value for testing the hypothesis in (2.1) is defined by $P = P[T(\mathbf{X}; \mathbf{x}, \theta, \delta) \geq T(\mathbf{x}; \mathbf{x}, \theta, \delta) | \theta = \theta_0]$. If T is stochastically decreasing in θ ,

The generalized p-value for testing the hypotheses in (2.1) is defined by $P = P[T(\mathbf{X}; \mathbf{x}, \theta, \delta) \leq T(\mathbf{x}; \mathbf{x}, \theta, \delta) | \theta = \theta_0]$.

As pointed out by Weerahandi (1993), the problem of finding an appropriate generalized pivotal quantity is a non-trivial task. There is no systematic approach that can be used to find pivotal quantities for all problems. Interested readers may refer to Iyer and Patterson (2002) for generalized pivotal quantities of a large class of practical problems. In the following, we give an example of constructing GPQ and GCI for log-normal distribution.

Example 1: Let Y_{ij} , $i = 1, \dots, k, j = 1, \dots, n_i$ be a random sample from k log-normal distributions with parameters μ_i and σ_i^2 , and let $X_{ij} = \log Y_{ij}$. By definition, $X_{ij}, j = 1, \dots, n_i$ is an independent random sample from the k populations and has a normal distribution of $N(\mu_i, \sigma_i^2)$.

For each sample, the sample mean and variance are defined as follows

$$\bar{X}_i = \frac{\sum_{j=1}^{n_i} X_{ij}}{n_i}, S_i^2 = \frac{1}{n_i - 1} \sum_{j=1}^{n_i} (X_{ij} - \bar{X}_i)^2.$$

Let

$$Z_i = \sqrt{n_i}(\bar{X}_i - \mu_i)/\sigma_i \quad \text{and} \quad U_i^2 = (n_i - 1)S_i^2/\sigma_i^2.$$

It is well known that $Z_i \sim N(0, 1)$ and $U_i^2 \sim \chi_{(n_i-1)}^2$ and they are independent. For each population, define

$$M_i = E(Y_{ij}) = e^{\mu_i + \sigma_i^2/2} \quad \text{and} \quad \theta_i = \log(M_i) = \mu_i + \sigma_i^2/2. \quad (2.2)$$

Krishnamoorthy and Mathew (2003) suggested the following GPQ for μ_i and σ_i^2 :

$$T_{\mu_i} = \bar{x}_i - \frac{\bar{X}_i - \mu_i}{S_i/\sqrt{n_i}} s_i/\sqrt{n_i} = \bar{x}_i - \frac{Z_i}{U_i/\sqrt{n_i-1}} s_i/\sqrt{n_i} = \bar{x}_i - \sqrt{\frac{n_i-1}{n_i}} \cdot \frac{Z_i s_i}{U_i}, \quad (2.3)$$

and

$$T_{\sigma_i^2} = \frac{s_i^2}{S_i^2} \sigma_i^2 = \frac{s_i^2}{U_i^2/(n_i-1)}, \quad (2.4)$$

where \bar{x}_i and s_i^2 are the observed values of \bar{X}_i and S_i^2 .

To obtain a generalized confidence interval for θ_i , define

$$T_{\theta_i} = T_{\mu_i} + \frac{1}{2}T_{\sigma_i^2} = \bar{x}_i - \sqrt{\frac{n_i - 1}{n_i}} \frac{Z_i s_i}{U_i} + \frac{1}{2} \frac{s_i^2}{U_i^2 / (n_i - 1)}. \quad (2.5)$$

The distribution of T_{θ_i} is free of any unknown parameters. The $100(1-\alpha)\%$ GCI for θ_i is (T_α, ∞) , where T_α is the $100 \times \alpha$ th percentile of T_{θ_i} . If θ_0 is within the GCI, we don't reject H_0 in (2.1), otherwise, reject H_0 . Similarly, a two sided $100(1 - \alpha)\%$ GCI for θ_i is given by $(T_{\alpha/2}, T_{(1-\alpha/2)})$.

3 FGPQ-based multiple comparison procedure

The FGPQ introduced by Hannig et al. (2006) is a subclass of Weerahandi's GPQ. It has a stronger version of condition in the definition of a GPQ. FGPQ is essentially based on invertible pivotal relationships. To check if a GPQ is also an FGPQ, we only need to check if $T(\mathbf{x}, \mathbf{x}, \theta, \delta) = \theta$. Notice that in Example 1, when $\mathbf{X}_i = \mathbf{x}_i$ and $S_i^2 = s_i^2$, T_{μ_i} in (2.3) reduces to μ_i and $T_{\sigma_i^2}$ in (2.4) reduces to σ_i^2 . As a result, $T_{\theta_i} = \mu_i + 1/2 * \sigma_i^2 = \theta_i$. Hence, T_{θ_i} is an FGPQ. Interested readers may refer to Hannig et al. (2006), in which the authors suggested three general approaches for constructing FGPQs.

In this section, we propose FGPQ-based MCP for means from k log-normal populations under heteroscedasticity. The testing problem is as follows

$$H_0 : M_i = M_j \quad \text{for all } i \neq j \quad \text{versus} \quad H_\alpha : \text{at least one of } M_i \neq M_j. \quad (3.1)$$

Define ratio of the mean as $M_{ij} = M_i/M_j$ and

$$\theta_{ij} = \log M_{ij} = \log \frac{M_i}{M_j} = \log \frac{e^{\mu_i + \sigma_i^2/2}}{e^{\mu_j + \sigma_j^2/2}} = \left(\mu_i + \frac{\sigma_i^2}{2} \right) - \left(\mu_j + \frac{\sigma_j^2}{2} \right).$$

The problem of constructing simultaneous confidence intervals for M_{ij} is equivalent to the problem of constructing simultaneous confidence intervals for θ_{ij} . The multiple comparison problem in (3.1) is equivalent to the hypothesis tests

$$H_0 : \theta_{ij} = 0 \quad \text{versus} \quad H_\alpha : \text{not all } \theta_{ij} = 0. \quad (3.2)$$

Follow Hannig et al. (2006) and Xiong and Mu (2009), we define the FGPQs for μ_i and σ_i^2 for $i = 1, \dots, k$ as follows

$$R_{\mu_i} = \bar{X}_i - \sqrt{\frac{n_i - 1}{n_i}} \cdot \frac{S_i Z_i}{U_i}, \quad R_{\sigma_i^2} = \frac{(n_i - 1)S_i^2}{U_i^2}, \quad i = 1, \dots, k. \quad (3.3)$$

Since $\theta_i = \log(E(Y_{ij})) = \mu_i + \sigma_i^2/2$, the pivotal variable for θ_i follows immediately as

$$R_{\theta_i} = R_{\mu_i} + \frac{R_{\sigma_i^2}}{2} = \bar{X}_i - \sqrt{\frac{n_i - 1}{n_i}} \cdot \frac{S_i Z_i}{U_i} + \frac{(n_i - 1)S_i^2}{2U_i^2}.$$

As a result,

$$R_{\theta_{ij}} = R_{\theta_i} - R_{\theta_j} = \bar{X}_i - \bar{X}_j - \sqrt{\frac{n_i - 1}{n_i}} \cdot \frac{S_i Z_i}{U_i} + \sqrt{\frac{n_j - 1}{n_j}} \cdot \frac{S_j Z_j}{U_j} + \frac{(n_i - 1)S_i^2}{2U_i^2} - \frac{(n_j - 1)S_j^2}{2U_j^2}$$

Let $\bar{\mathbf{X}} = (\bar{X}_1, \bar{X}_2, \dots, \bar{X}_k)$, $\mathbf{S}^2 = (S_1^2, S_2^2, \dots, S_k^2)$.

By inverse chi squared distribution properties, if $X \sim \chi^2(v)$, then $1/X \sim \text{Inv}\chi^2(v)$ and

$$E(1/X) = \frac{1}{v-2}, \text{Var}(1/X) = \frac{2}{(v-2)^2(v-4)}.$$

In our case,

$$U_i^2 \sim \chi^2(n_i - 1), \quad \frac{1}{U_i^2} \sim \text{Inv}\chi^2(n_i - 1)$$

so that

$$E\left(\frac{1}{U_i^2}\right) = \frac{1}{n_i - 3}, \quad \text{Var}\left(\frac{1}{U_i^2}\right) = \frac{2}{(n_i - 3)^2(n_i - 5)} \quad (3.4)$$

Since $Z_i \sim N(0, 1)$, $E\left(E\left(\frac{Z_i}{U_i} \mid U_i\right)\right) = E\left(\frac{1}{U_i} E(Z_i)\right) = 0$, The conditional expectation and variance of $R_{\theta_{ij}}$ can be derived as follows

$$\begin{aligned} \eta_{ij} &= E(R_{\theta_{ij}} \mid \bar{\mathbf{X}}, \mathbf{S}^2) \\ &= \bar{X}_i - \bar{X}_j + 0 + 0 + \frac{n_i - 1}{2} S_i^2 E(1/U_i^2) - \frac{n_j - 1}{2} S_j^2 E(1/U_j^2) \\ &= \bar{X}_i - \bar{X}_j + 0 + 0 + \frac{n_i - 1}{2(n_i - 3)} S_i^2 - \frac{n_j - 1}{2(n_j - 3)} S_j^2 \end{aligned}$$

By equation (3.4),

$$\begin{aligned} V_{ij} = \text{Var}(R_{\theta_{ij}} \mid \bar{\mathbf{X}}, \mathbf{S}^2) &= \frac{n_i - 1}{n_i(n_i - 3)} S_i^2 + \frac{(n_i - 1)^2}{2(n_i - 3)^2(n_i - 5)} S_i^4 \\ &+ \frac{n_j - 1}{n_j(n_j - 3)} S_j^2 + \frac{(n_j - 1)^2}{2(n_j - 3)^2(n_j - 5)} S_j^4 \end{aligned}$$

Now let ξ_{ij} be the variance of η_{ij} , and let $R_{\xi_{ij}}$ be the pivotal variable of ξ_{ij} . By the fact that $\text{Var}(S_i^2) = 2\sigma_i^4/(n_i - 1)$, we can derive the following:

$$\begin{aligned} \xi_{ij} &= \text{Var}\{E(R_{\theta_{ij}} \mid \bar{\mathbf{X}}, \mathbf{S}^2)\} \\ &= \frac{\sigma_i^2}{n_i} + \frac{\sigma_j^2}{n_j} + \left(\frac{n_i - 1}{2(n_i - 3)}\right)^2 \frac{2\sigma_i^4}{n_i - 1} + \left(\frac{n_j - 1}{2(n_j - 3)}\right)^2 \frac{2\sigma_j^4}{n_j - 1} \\ &= \frac{\sigma_i^2}{n_i} + \frac{(n_i - 1)}{2(n_i - 3)^2} \sigma_i^4 + \frac{\sigma_j^2}{n_j} + \frac{(n_j - 1)}{2(n_j - 3)^2} \sigma_j^4. \end{aligned}$$

Now replace σ_i^2 by $R_{\sigma_i^2}$ in Equation (3.3), we can derive $R_{\xi_{ij}}$ as follows,

$$\begin{aligned} R_{\xi_{ij}} &= \frac{(n_i - 1)S_i^2}{n_i U_i^2} + \frac{(n_i - 1)}{2(n_i - 3)^2} \left(\frac{(n_i - 1)S_i^2}{U_i^2}\right)^2 \\ &+ \frac{(n_j - 1)S_j^2}{n_j U_j^2} + \frac{(n_j - 1)}{2(n_j - 3)^2} \left(\frac{(n_j - 1)S_j^2}{U_j^2}\right)^2. \end{aligned}$$

As pointed out by Xiong and Mu (2009), FGPQs can be used to provide effective approximations of distributions. The distribution of

$$\max_{i < j} \left| \frac{\theta_{ij} - E(R_{\theta_{ij}} \mid \bar{\mathbf{X}}, \mathbf{S}^2)}{\sqrt{\text{Var}(R_{\theta_{ij}} \mid \bar{\mathbf{X}}, \mathbf{S}^2)}} \right| \quad (3.5)$$

can be approximated by the conditional distributions of

$$Q = \max_{i \leq j} \left| \frac{R_{\theta_{ij}} - E(R_{\theta_{ij}} | \bar{\mathbf{X}}, \mathbf{S}^2)}{\sqrt{R_{\xi_{ij}}}} \right|. \quad (3.6)$$

Let $q(\alpha)$ be the conditional upper α th quantile of the distribution of Q . The $(1 - \alpha)100\%$ simultaneous confidence intervals for θ_{ij} are

$$\eta_{ij} \pm q(\alpha)\sqrt{V_{ij}} \quad \text{for all } i < j. \quad (3.7)$$

The following Theorem shows that the confidence intervals (3.7) have asymptotically correct coverage probabilities. Proof is similar as Xiong and Mu (2009) and is included in Appendix.

Theorem 3.1. *Let $X_{i1}, \dots, X_{in_i}, i = 1, \dots, k$ be random samples from k different populations and be mutually independent. Assume that $0 < \sigma_i^2 = \text{Var}(X_{i1}) < \infty, \mu_i = E(X_{i1}), N = \sum_{i=1}^k n_i$ and $\frac{n_i}{N} \rightarrow \lambda_i \in (0, 1)$ as $N \rightarrow \infty$ for all i , then*

$$P(\theta_{ij} \in \eta_{ij} \pm q(\alpha)\sqrt{V_{ij}} \quad \text{for all } i < j) \xrightarrow{P} 1 - \alpha.$$

We propose Algorithm 2 for finding $q(\alpha)$, the conditional upper α th quantile of the distribution of Q to construct the simultaneous confidence intervals.

Algorithm 2:

For given observations $y_{ij}, i = 1, \dots, k, j = 1, \dots, n_i$, compute $x_{ij} = \ln y_{ij}$

Compute \bar{x}_i and $s_i^2, i = 1, \dots, k$

For $l = 1, 2, \dots, L$

Generate Z_i and $U_i^2, i = 1, \dots, k$

Compute $R_{\theta_{ij}}, R_{\xi_{ij}}$, and Q_l .

End l loop.

Compute $q(\alpha)$, the $(1 - \alpha)100\%$ percentile of Q_l .

4 Simulations

In this section, we use simulations to study the MCP for k log-normal distributions under the assumption of heteroscedastic variances and unequal sizes. The simulation settings follow from Li (2009). Statistical software R is used for all computations.

The sample statistics \bar{x}_i and s_i^2 are generated independently as $\bar{x}_i \sim N(0, \sigma_i^2/n_i)$ and $s_i^2 \sim \sigma_i^2 \chi_{n_i-1}^2 / (n_i - 1)$, with $0 < \sigma_i^2 \leq 1, i = 1, \dots, k$. The simulation study was performed with factors: (1) number of levels k : $k = 3$ and $k = 6$; (2) population variance $\sigma = (\sigma_1^2, \dots, \sigma_k^2)$: various combinations; (3) population mean $\mu = (\mu_1, \dots, \mu_k)$: various combinations; (4) Significance level α : 0.01, 0.05 and 0.1; (5) group sizes $\mathbf{n} = (n_1, \dots, n_k)$: various combinations. For a given sample size and parameter configuration, we generated 2000 observed vectors $(\bar{x}_1, \dots, \bar{x}_k, s_1^2, \dots, s_k^2)$ and used 5000 runs to estimate the Type 1 errors (simulated p-value). According to our experience, 5000 runs is sufficient to guarantee the precision of simulated p-value. Algorithm 1 is used to find q_α , the $1 - \alpha$ percentile of the simulated distribution of Q_l . In Tables 1 and 2, the following notation applies. $\mathbf{n} = (n_1, \dots, n_k)$, $k = 3$ or 6 is a vector of unequal group sizes. For $k = 3$, we have $\mathbf{n}_1^{(3)} = (10, 16, 20)$, $\mathbf{n}_2^{(3)} = (10, 10, 10)$, $\mathbf{n}_3^{(3)} =$

Table 1: Simulation results of the proposed FG PQ-based multiple comparison procedure for three groups. Numbers in Table are simulated p-values.

n	$\alpha = .01$			$\alpha = .05$			$\alpha = .1$		
	$C_1^{(3)}$	$C_2^{(3)}$	$C_3^{(3)}$	$C_1^{(3)}$	$C_2^{(3)}$	$C_3^{(3)}$	$C_1^{(3)}$	$C_2^{(3)}$	$C_3^{(3)}$
$\mathbf{n}_1^{(3)}$	0.0105	0.0150	0.0170	0.0475	0.0410	0.0455	0.0840	0.0825	0.0800
$\mathbf{n}_{1*}^{(3)}$	0.0125	0.0165	0.0105	0.0575	0.0470	0.0475	0.1020	0.0995	0.0940
$\mathbf{n}_2^{(3)}$	0.0150	0.0105	0.0140	0.0410	0.0450	0.0385	0.0765	0.0830	0.0830
$\mathbf{n}_{2*}^{(3)}$	0.0100	0.0110	0.0160	0.0500	0.0410	0.0490	0.1030	0.1115	0.0840
$\mathbf{n}_3^{(3)}$	0.0100	0.0090	0.0070	0.0400	0.0335	0.0500	0.0890	0.0720	0.0755
$\mathbf{n}_{3*}^{(3)}$	0.0135	0.0080	0.0100	0.0455	0.0535	0.0510	0.0925	0.1035	0.1015

Table 2: Simulation results of the proposed FG PQ-based multiple comparison procedure for six groups. Numbers in Table are simulated p-values.

n	$\alpha = .01$			$\alpha = .05$			$\alpha = .1$		
	$C_1^{(6)}$	$C_2^{(6)}$	$C_3^{(6)}$	$C_1^{(6)}$	$C_2^{(6)}$	$C_3^{(6)}$	$C_1^{(6)}$	$C_2^{(6)}$	$C_3^{(6)}$
$\mathbf{n}_1^{(6)}$	0.0125	0.0140	0.0140	0.0530	0.0590	0.0500	0.0995	0.0925	0.0985
$\mathbf{n}_{1*}^{(6)}$	0.0105	0.0115	0.0105	0.0460	0.0520	0.0470	0.1005	0.1055	0.1055
$\mathbf{n}_2^{(6)}$	0.0150	0.0140	0.0115	0.0600	0.0570	0.0580	0.0920	0.0875	0.0895
$\mathbf{n}_{2*}^{(6)}$	0.0110	0.0115	0.0150	0.0460	0.0510	0.0455	0.0990	0.1050	0.1030
$\mathbf{n}_3^{(6)}$	0.0140	0.0185	0.0125	0.0570	0.0600	0.0525	0.0920	0.1050	0.0935
$\mathbf{n}_{3*}^{(6)}$	0.0070	0.0125	0.0125	0.0520	0.0505	0.0580	0.0915	0.084	0.109

$(20, 16, 10)$, $\mathbf{n}_{1*}^{(3)} = (50, 80, 100)$, $\mathbf{n}_{2*}^{(3)} = (50, 50, 50)$, and $\mathbf{n}_{3*}^{(3)} = (100, 80, 50)$. For $k = 6$, we have $\mathbf{n}_1^{(6)} = (10, 12, 12, 16, 16, 20)$, $\mathbf{n}_2^{(6)} = (10, 10, 10, 10, 10, 10)$, $\mathbf{n}_3^{(6)} = (20, 16, 16, 12, 12, 10)$, $\mathbf{n}_{1*}^{(6)} = (50, 60, 60, 80, 80, 100)$, $\mathbf{n}_{2*}^{(6)} = (50, 50, 50, 50, 50, 50)$, and $\mathbf{n}_{3*}^{(6)} = (100, 80, 80, 60, 60, 50)$. Note that $\mathbf{n}_{i*}^{(j)}/\mathbf{n}_i^{(j)} = 5, i = 1, 2, 3, j = 3$ or 6 . $\boldsymbol{\mu} = (\mu_1, \dots, \mu_k)$, $k = 3$ or 6 is a vector of means. For $k = 3$, we consider $\boldsymbol{\mu}_1^{(3)} = (1, 1, 1)$, $\boldsymbol{\mu}_2^{(3)} = (1, 1, 1.25)$, $\boldsymbol{\mu}_3^{(3)} = (1, 1.25, 1.45)$. For $k = 6$, we consider $\boldsymbol{\mu}_1^{(6)} = (1, 1, 1, 1, 1, 1)$, $\boldsymbol{\mu}_2^{(6)} = (1, 1, 1, 1, 1, 0.8)$, $\boldsymbol{\mu}_3^{(6)} = (1, 1, 1, 1, 1, 0.9)$. $\boldsymbol{\sigma} = (\sigma_1^2, \dots, \sigma_k^2)$, $k = 3$ or 6 is a vector of variances with $\boldsymbol{\sigma}_1^{(3)} = (0.1, 0.1, 0.1)$, $\boldsymbol{\sigma}_2^{(3)} = (1, 1, 0.5)$, $\boldsymbol{\sigma}_3^{(3)} = (1, 0.5, 0.1)$, $\boldsymbol{\sigma}_1^{(6)} = (0.1, 0.1, 0.1, 0.1, 0.1, 0.1)$, $\boldsymbol{\sigma}_2^{(6)} = (0.1, 0.1, 0.1, 0.1, 0.1, 0.5)$, and $\boldsymbol{\sigma}_3^{(6)} = (0.1, 0.1, 0.1, 0.1, 0.1, 0.3)$. To simplify notation in the tables, let $C_1^{(3)} = (\boldsymbol{\mu}_1^{(3)}, \boldsymbol{\sigma}_1^{(3)})$, $C_2^{(3)} = (\boldsymbol{\mu}_2^{(3)}, \boldsymbol{\sigma}_2^{(3)})$, $C_3^{(3)} = (\boldsymbol{\mu}_3^{(3)}, \boldsymbol{\sigma}_3^{(3)})$, $C_1^{(6)} = (\boldsymbol{\mu}_1^{(6)}, \boldsymbol{\sigma}_1^{(6)})$, $C_2^{(6)} = (\boldsymbol{\mu}_2^{(6)}, \boldsymbol{\sigma}_2^{(6)})$, and $C_3^{(6)} = (\boldsymbol{\mu}_3^{(6)}, \boldsymbol{\sigma}_3^{(6)})$.

Tables 1 and 2 report the simulation results of the proposed MCP under various settings. We can see that simulated p-values of MCP are close to the nominal levels when the group sizes are 10 or more. When group sizes increased by five times, i.e., $\mathbf{n}_{i*}^{(j)}/\mathbf{n}_i^{(j)} = 5$, the simulated p-value comes slightly closer to the nominal level in general, but no significant difference observed. Notice that $\mathbf{n}_2^{(3)}$, $\mathbf{n}_{2*}^{(3)}$, $\mathbf{n}_2^{(6)}$, and $\mathbf{n}_{2*}^{(6)}$ are with equal group sizes, and $C_1^{(3)}$ and $C_1^{(6)}$ are with equal variances. We found that the proposed MCP perform well in terms of coverage probabilities for both unbalanced unequal variance and balanced equal variance cases.

5 Conclusions

In this article, we proposed an FG PQ-based new method to construct simultaneous confidence intervals for ratios of means from several log-normal distributions under heteroscedasticity and unequal group sizes. Simulation studies show that these intervals perform well in terms of coverage probabilities. We also proved that the constructed confidence intervals have correct asymptotic coverage. The proposed methods could be applied to group mean comparisons when data are arising from several log-normal distributions.

Acknowledgment

The authors thank the associate editor and referees for their helpful comments and constructive suggestions to improve the manuscript.

Appendix

Proof of Theorem 1.

Proof. By the central limit theorem, we have

$$\sqrt{N}((\eta_{12} - \theta_{12}), (\eta_{13} - \theta_{13}), \dots, (\eta_{k-1,k} - \theta_{k-1,k})) \xrightarrow{d} N(0, \mathbf{U}),$$

where \mathbf{U} is an $k(k-1)/2 \times k(k-1)/2$ positive definite matrix. Let u_{ab} , $a, b = 1, 2, \dots, k(k-1)/2$ be its (a, b) th entry. It can be shown that

$$u_{aa} = \frac{\sigma_i^2}{\lambda_i} + \frac{\sigma_i^4}{2\lambda_i} + \frac{\sigma_j^2}{\lambda_j} + \frac{\sigma_j^4}{2\lambda_j}$$

and

$$NV_{ij} \rightarrow \frac{\sigma_i^2}{\lambda_i} + \frac{\sigma_i^4}{2\lambda_i} + \frac{\sigma_j^2}{\lambda_j} + \frac{\sigma_j^4}{2\lambda_j}$$

almost surely. Therefore,

$$\left(\frac{\eta_{12} - \theta_{12}}{\sqrt{V_{12}}}, \frac{\eta_{13} - \theta_{13}}{\sqrt{V_{13}}}, \dots, \frac{\eta_{k-1,k} - \theta_{k-1,k}}{\sqrt{V_{k-1,k}}} \right) \xrightarrow{d} N(0, \mathbf{U}^*),$$

where the (a, b) th entry of \mathbf{U}^* is $u_{ab}/\sqrt{u_{aa}u_{bb}}$. Take a random vector $(Z_1, Z_2, \dots, Z_{k(k-1)/2})$ distributed according to $N(0, \mathbf{U}^*)$. By the continuous mapping theorem

$$\max_{i < j} \left| \frac{\theta_{ij} - \eta_{ij}}{\sqrt{V_{ij}}} \right| \xrightarrow{d} \max |Z_a| \quad (5.1)$$

for $1 \leq a \leq k(k-1)/2$.

For $i = 1, \dots, k$, $U_i^2/n_i \xrightarrow{p} 1$. For all $i \neq j$,

$$\begin{aligned} \sqrt{N}(R_{\theta_{ij}} - \eta_{ij}) &= \sqrt{N} \left\{ -\sqrt{\frac{n_i-1}{n_i}} \cdot \frac{S_i Z_i}{U_i} + \sqrt{\frac{n_j-1}{n_j}} \cdot \frac{S_j Z_j}{U_j} \right. \\ &\quad \left. + \frac{(n_i-1)S_i^2}{2U_i^2} - \frac{(n_j-1)S_j^2}{2U_j^2} - \frac{n_i-1}{2(n_i-3)} S_i^2 + \frac{n_j-1}{2(n_j-3)} S_j^2 \right\} \\ &= \frac{\sigma_i}{\sqrt{\lambda_i}} Z_j - \frac{\sigma_j}{\sqrt{\lambda_j}} Z_i + o_p(1) \end{aligned} \quad (5.2)$$

conditionally on $T = (\bar{\mathbf{X}}, \mathbf{S}^2)$ almost surely.

Recall that $NV_{ij} \rightarrow \frac{\sigma_i^2}{\lambda_i} + \frac{\sigma_i^4}{2\lambda_i} + \frac{\sigma_j^2}{\lambda_j} + \frac{\sigma_j^4}{2\lambda_j}$ almost surely and note that

$$\begin{aligned} NR_{\xi_{ij}} &= N \frac{(n_i - 1)S_i^2}{n_i U_i^2} + N \frac{(n_i - 1)^2}{2n_i(n_i - 3)^2} \left(\frac{(n_i - 1)S_i^2}{U_i^2} \right)^2 \\ &+ N \frac{(n_j - 1)S_j^2}{n_j U_j^2} + N \frac{(n_j - 1)^2}{2n_j(n_j - 3)^2} \left(\frac{(n_j - 1)S_j^2}{U_j^2} \right)^2 \\ &= \frac{\sigma_i^2}{\lambda_i} + \frac{\sigma_i^4}{2\lambda_i} + \frac{\sigma_j^2}{\lambda_j} + \frac{\sigma_j^4}{2\lambda_j} + o_p(1) \end{aligned}$$

conditionally on T almost surely. It can be shown that Equation (5.2) implies

$$\max_{i < j} \left| \frac{\theta_{ij} - \eta_{ij}}{\sqrt{R_{\xi_{ij}}}} \right| \xrightarrow{d} \max_{1 \leq a \leq k(k-1)/2} |Z_a| \quad (5.3)$$

on T almost surely. Let F be the cumulative distribution function of $\max_{1 \leq a \leq k(k-1)/2} |Z_a|$. By the continuity of F

$$\sup_x |F_n(x|T) - F(x)| \rightarrow 0$$

almost surely, where F_n is the conditional distribution function of the left side of (5.3). As a result,

$$\begin{aligned} P \left(\theta_{ij} \in \eta_{ij} \pm q(\alpha) \sqrt{V_{ij}} \quad \text{for all } i < j \right) &= P \left\{ F_n \left(\max_{i < j} \left| \frac{\theta_{ij} - \eta_{ij}}{\sqrt{V_{ij}}} \right| \middle| T \right) \leq 1 - \alpha \right\} \\ &= P \left\{ F \left(\max_{i < j} \left| \frac{\theta_{ij} - \eta_{ij}}{\sqrt{R_{\xi_{ij}}}} \right| \right) + o_p(1) \leq 1 - \alpha \right\} \\ &\xrightarrow{d} 1 - \alpha \end{aligned}$$

□

References

- Bradstreet, T. E., & Liss, C. L. (1995). Favorite data sets from early (and late) phases of drug research - part 4. *Proceedings of the Section on Statistical Education of the American Statistical Association*.
- Hannig, J. (2006). On generalized fiducial inference. *Technical Report, Department of Statistics, Colorado State University*, 101, 254–269.
- Hannig, J., Iyer, H., & Patterson, P. (2006). Fiducial generalized confidence intervals. *Journal of American Statistical Association*, 101, 254–269.
- Iyer, H. K., & Patterson, P. D. (2002). A recipe for constructing generalized pivotal quantities and generalized confidence intervals. *Technical Report*.
- Krishnamoorthy, K., & Mathew, T. (2003). Inferences on the means of lognormal distributions using generalized p-values and generalized confidence intervals. *Journal of Statistical Planning and Inference*, 115, 103–121.

- Li, X. (2009). A generalized p-value approach for comparing the means of several log-normal populations. *Statistics and Probability Letters*, 79, 1404–1408.
- Scheffé, H. (1959). *The analysis of variance*. New York: Wiley.
- Tsui, K., & Weerahandi, S. (1989). Generalized p-values in significance testing of hypotheses in the presence of nuisance parameters. *Journal of the American Statistical Association*, 84, 602–607.
- Tukey, J. W. (1953). The problem of multiple comparisons. *Unpublished manuscript, Princeton University*.
- Weerahandi, S. (1993). Generalized confidence intervals. *Journal of the American Statistical Association*, 88, 899–905.
- Xiong, S., & Mu, W. (2009). Simultaneous confidence intervals for one-way layout based on generalized pivotal quantities. *Journal of Statistical Computation and Simulation*, 79, 1235–1244.
- Zhang, G. (2014). Simultaneous confidence intervals for several inverse gaussian populations. *Statistics and Probability Letters*, 92, 125–131.
- Zhang, G., & Chen, Z. (2015). Inferences on correlation coefficients of bivariate log-normal distributions. *Journal of Applied Statistics*, 42, 603–613.
- Zhou, X., Gao, S., & Hui, S. (1997). Methods for comparing means of two independent log-normal samples. *Biometrics*, 53, 1129–1135.