Analysis of Intraclass Correlation Coefficients for Correlated Binomial Data from Several Treatment Groups

Krishna Saha* Debaraj Sen†

Abstract
The intraclass correlation coefficient for correlated binary responses arising in many applications of biological investigations is often of interest in measuring the precision of the treatment effect in clinical trials. Although inference procedures concerning the intraclass correlation have been well developed for single-sample problems, little attention has been paid to extend this inference procedures for multiple-sample problems. In this paper, we construct several confidence interval procedures for a common intraclass correlation of several treatment groups. Our simulation results indicate that the generalized pivot based confidence interval approach performs better compared to other asymptotic approaches considered here. An application to a solar protection study is used to illustrate the proposed methods.

Key Words: beta-binomial, clustered binary data, confidence interval, intraclass correlation

1. Introduction

Binary outcome data in many biomedical, toxicological, clinical medicine, and epidemiological research often exhibit extra-binomial variability due to the correlated responses within the sampling units (or clusters). This intraclass correlation has been widely used to measure the efficiency of hospital staff in health care delivery research, the familial aggregation of disease in genetic epidemiological studies, and the level of interobserver agreement in reliability studies. Inference procedures concerning the intraclass correlation have been well developed for single-sample problems. Several techniques for the point estimation of the intraclass correlation have been developed based on beta-binomial, quasi-likelihood, quadratic estimating equations, generalized estimating equations, unbiased estimating equation, analysis of variance, method of moments, direct probabilistic method, etc.; see Paul and Islam (1998), Ridout et al. (1999), Paul (2001), Paul et al. (2003), Lee (2004), and Saha and Paul (2005). For the construction of the confidence interval, several procedures have also been developed. For example, Lui et al. [18] derived the CI estimates for the intraclass correlation on the basis of the ratio of between-cluster and within-cluster mean squares in equal cluster sampling. Zou and Donner [8] studied the CI of the intraclass correlation parameter based on the ANOVA estimator, the Pearson pairwise estimator with constant weights, and the kappa-type estimator (see details of these three estimators in Paul et al. [16]) by obtaining closed-form asymptotic variance formulas for these three point estimators of this parameter. Saha (2012) generalized the results of the four point estimators recommended by Paul et al. (2003) and Lee (2004) to construct asymptotic confidence intervals using closed-form asymptotic and sandwich variance expressions. He also introduced the Fishers-transformation approach on the intraclass correlation coefficient, the profile likelihood approach based on the beta-binomial model, and the hybrid profile variance approach based on the quadratic estimating equation for constructing the confidence intervals of the intraclass correlation for binary outcome data.

*Department of Mathematical Sciences, Central Connecticut State University, 1615 Stanley Street, New Britain, CT 06050, USA

†Department of Mathematics and Statistics, Concordia University, 1455 de Maisonneuve Blvd. West, Montreal, QC H3G 1M8, Canada

In many applied research, inference procedure for a common intraclass correlation in the analysis of several treatment groups is often of interest that one needs to develop and compare. For example, in a common teteratogenesis laboratory experiment, pregnant animals are assigned to a control or one of several dose groups to study the reproductive and development toxicity of a substance. Kupper & Hasemen (1978) discussed that the litter effect is an inherent characteristic of reproductive and development data and this can be measured by the intraclass correlation parameter. This raises question as to whether the litter effect differs among the several dose groups. In this paper, we focus on developing confidence interval procedures to address this question.

2. Confidence intervals for a common ICC

2.1 The CI based on ML

Let y_{ij} $(j = 1, \ldots, m_i;$ i = 1,..., k) be a random sample of the number of affected individuals among the n_{ij} individuals drawn from the ith beta-binomial population, with the expected number of affected individuals $\mathrm{E}(Y_{ij}) = n_{ij}\pi_i$ and variance $n_i\pi_i(1-\pi_i)\{1 + (n_i - 1)\phi_i\}$, where π_i is the expected proportion of affected individuals in the ith population and ϕ_i is the intraclass correlation coefficient in the ith population. The probability mass function of the ith beta-binomial population, denoted by $BB(\pi_i, \phi_i)$, is

$$P(y_{ij}|\pi_i, \phi_i) = \begin{pmatrix} n_{ij} \\ y_{ij} \end{pmatrix} \frac{\prod_{r=0}^{y_{ij}-1}[(1-\phi_i)\pi_i + r\phi_i] \prod_{r=0}^{n_{ij}-y_{ij}-1}[(1-\pi_i)(1-\phi_i) + r\phi_i]}{\prod_{r=0}^{n_{ij}-1}[(1-\phi_i) + r\phi_i]}$$

for $y_{ij} = 0, 1, 2, \ldots, n_{ij}$; $0 \leq \pi_i \leq 1$ and $\max(\frac{-1}{n_{ij}-1}) < \phi_i < 1$. Although the main analysis of this study is making inferences about the proportions π_i, $i = 1, \ldots, k$, it depends on the assumption of the equality of the intraclass correlations ϕ_i, $i = 1, \ldots, k$ among several treatment groups. Here we wish to test $H_0 : \phi_1 = \ldots = \phi_k = \phi$, where ϕ is unspecified, against H_1 : at least two ϕ_i's are unequal. The log-likelihood of the k beta-binomial samples under H_0 is given by

$$\begin{aligned} l(\pi_1, \ldots, \pi_k, \phi) &= \sum_{i=1}^{k}\sum_{j=1}^{m_i}\left[\sum_{r=0}^{y_{ij}-1} \ln\{(1-\phi)\pi_i + r\phi\} + \sum_{r=0}^{n_{ij}-y_{ij}-1} \ln\{(1-\pi_i)(1-\phi) + r\phi\}\right. \\ &\qquad \left. - \sum_{r=0}^{n_{ij}-1} \ln\{(1-\phi) + r\phi\}\right]. \end{aligned} \tag{1}$$

The ML estimates $\hat{\pi}_i$ and $\hat{\phi}$ of π_i and ϕ under H_0 can be obtained by maximizing the log-likelihood $l(\pi_1, \ldots, \pi_k, \phi)$ or by solving iteratively the ML estimating equations:

$$\sum_{j=1}^{m_i}\left[\sum_{r=1}^{y_{ij}} \frac{1-\phi}{\pi_i(1-\phi) + (r-1)\phi} - \sum_{r=1}^{n_{ij}-y_{ij}} \frac{1-\phi}{(1-\pi_i)(1-\phi) + (r-1)\phi}\right] = 0, \quad \text{for } i = 1, \ldots, k,$$

and

$$\sum_{i=1}^{k}\sum_{j=1}^{m_i}\left[\sum_{r=1}^{y_{ij}} \frac{(r-1)-\pi_i}{\pi_i(1-\phi) + (r-1)\phi} + \sum_{r=1}^{n_{ij}-y_{ij}} \frac{(r-1)-(1-\pi_i)}{(1-\pi_i)(1-\phi) + (r-1)\phi} - \sum_{r=1}^{n_{ij}} \frac{r-2}{1-\phi+(r-1)\phi}\right] = 0.$$

Based on the inverse of the Fisher information matrix, an asymptotic variance of $\hat{\phi}$ can be obtained as $\mathrm{Var}(\hat{\phi}) = \Gamma_{(k+1)(k+1)}$, where $\Gamma_{(k+1)(k+1)}$ is the $(k+1)$th diagonal element of

Table 1: Coverage probability estimates based on confidence intervals by the methods with nominal level, $1 - \alpha$ = 95%.

(m_1, m_2)	(π_1, π_2)	ϕ	AOV	FC	PP	GP	ML
(19, 27)	(0.1, 0.3)	0.1	0.996	0.977	0.975	0.926	0.907
		0.2	0.991	0.969	0.975	0.932	0.821
		0.3	0.988	0.973	0.975	0.905	0.797
		0.4	0.983	0.968	0.976	0.897	0.781
		0.5	0.981	0.965	0.967	0.867	0.755
	(0.2, 0.4)	0.1	0.994	0.977	0.982	0.933	0.928
		0.2	0.978	0.958	0.952	0.939	0.832
		0.3	0.978	0.966	0.965	0.933	0.828
		0.4	0.971	0.958	0.967	0.912	0.788
		0.5	0.976	0.970	0.967	0.910	0.767
	(0.3, 0.6)	0.1	0.990	0.962	0.964	0.941	0.918
		0.2	0.973	0.950	0.949	0.935	0.835
		0.3	0.969	0.957	0.951	0.920	0.821
		0.4	0.976	0.958	0.961	0.925	0.805
		0.5	0.973	0.972	0.968	0.911	0.806
(73, 87)	(0.1, 0.3)	0.1	0.995	0.990	0.995	0.924	0.850
		0.2	0.996	0.994	0.996	0.938	0.807
		0.3	0.996	0.996	0.996	0.910	0.790
		0.4	0.996	0.994	0.995	0.920	0.760
		0.5	0.992	0.990	0.989	0.889	0.774
	(0.2, 0.4)	0.1	0.995	0.990	0.992	0.944	0.892
		0.2	0.994	0.990	0.992	0.944	0.825
		0.3	0.997	0.995	0.992	0.934	0.801
		0.4	0.988	0.985	0.987	0.940	0.800
		0.5	0.987	0.988	0.988	0.914	0.790
	(0.3, 0.6)	0.1	0.989	0.986	0.982	0.949	0.893
		0.2	0.997	0.991	0.995	0.946	0.843
		0.3	0.993	0.992	0.991	0.948	0.804
		0.4	0.986	0.985	0.984	0.938	0.812
		0.5	0.987	0.984	0.986	0.920	0.802

the inverse of the Fisher information matrix Γ given by

$$\Gamma = \begin{bmatrix} \Gamma_{11} & \Gamma_{12} & \ldots & \Gamma_{1k} & \Gamma_{1(k+1)} \\ \Gamma_{21} & \Gamma_{22} & \ldots & \Gamma_{2k} & \Gamma_{2(k+1)} \\ \ldots & \ldots & \ldots & \ldots & \ldots \\ \Gamma_{k1} & \Gamma_{k2} & \ldots & \Gamma_{kk} & \Gamma_{k(k+1)} \\ \Gamma_{(k+1)1} & \Gamma_{(k+1)2} & \ldots & \Gamma_{(k+1)k} & \Gamma_{(k+1)(k+1)} \end{bmatrix} = \begin{bmatrix} a_1 & 0 & \ldots & 0 & b_1 \\ 0 & a_2 & \ldots & 0 & b_2 \\ \ldots & \ldots & \ldots & \ldots & \ldots \\ 0 & 0 & \ldots & a_k & b_k \\ b_1 & b_2 & \ldots & b_k & c \end{bmatrix}^{-1},$$

where

$$\begin{aligned} a_i &= (1-\phi)^2 \sum_{j=1}^{m_i} \left(A_{1j}^{(2,0)} + A_{2j}^{(2,0)} \right), \text{ for } i = 1, \ldots, k, \\ b_i &= (1-\phi) \sum_{j=1}^{m_i} \left(A_{1j}^{(2,1)} - A_{2j}^{(2,1)} \right) + \sum_{j=1}^{m_i} \left(A_{1j}^{(1,0)} - A_{2j}^{(1,0)} \right), \text{ for } i = 1, \ldots, k, \\ c &= \sum_{i=1}^{k} \sum_{j=1}^{m_i} \left(A_{1j}^{(2,2)} + A_{2j}^{(2,2)} - A_{3j}^{(2,2)} \right), \end{aligned}$$

with, for $j = 1, ..., m_i$; $p = q = 0, 1, 2$,

$$\begin{aligned} A_{1j}^{(p,q)} &= \sum_{r=1}^{n_{ij}} \frac{(r-\pi-1)^q}{[(1-\phi)\pi_i + (r-1)\phi]^p} Pr(Y_{ij} \geq r), \\ A_{2j}^{(p,q)} &= \sum_{r=1}^{n_{ij}} \frac{(r+\pi-2)^q}{[(1-\phi)(1-\pi_i) + (r-1)\phi]^p} Pr(Y_{ij} \leq n_{ij} - r), \\ A_{3j}^{(p,q)} &= \sum_{r=1}^{n_{ij}} \frac{(r-2)^q}{[1 + (r-1)\phi]^p}. \end{aligned}$$

Then, the approximate 100(1 - α)% confidence interval for ϕ is given by

$$\text{ML}: \quad \hat{\phi} - z_{\alpha/2}\sqrt{\widehat{\text{Var}}(\hat{\phi})} \leq \phi \leq \hat{\phi} + z_{\alpha/2}\sqrt{\widehat{\text{Var}}(\hat{\phi})},$$

where $z_{\alpha/2}$ is the upper $\frac{\alpha}{2}$th quantile of the standard normal distribution and $\widehat{\text{Var}}(\hat{\phi})$ is the estimated variance of $\hat{\phi}$ obtained from $\text{Var}(\hat{\phi})$ after replacing the parameters π_i and ϕ by their ML estimates $\hat{\pi}_i$ and $\hat{\phi}$, respectively.

2.2 The CI based on GP

By applying the analogy of formulae for continuous data directly, the ANOVA estimator of the intraclass correlation of binary data is also obtained (see, Ridout et al., 1999), which is, for the ith sample, given by

$$\hat{\phi}_i^a = \frac{\text{MSW}_i - \text{MSW}_i}{\text{MSW}_i + (n_i^0 - 1)\text{MSW}_i},$$

where

$$\begin{aligned} \text{MSW}_i &= \frac{1}{m_i - 1} \left[\sum_{j=1}^{m_i} \frac{Y_{ij}^2}{n_{ij}} - \frac{(\sum_{j=1}^{m_i} Y_{ij})^2}{N_i} \right], \\ \text{MSW}_i &= \frac{1}{N_i - m_i} \left[\sum_{j=1}^{m_i} Y_{ij} - \sum_{j=1}^{m_i} \frac{Y_{ij}^2}{n_{ij}} \right], \\ n_i^0 &= \frac{1}{m_i - 1} \left[N_i - \frac{\sum_{j=1}^{m_i} n_{ij}^2}{N_i} \right] \text{ and } N_i = \sum_{j=1}^{m_i} n_{ij}. \end{aligned}$$

Table 2: Expected interval lengths based on confidence intervals by the methods with nominal level, $1 - \alpha$ = 95%.

(m_1, m_2)	(π_1, π_2)	ϕ	AOV	FC	PP	GP	ML
(19, 27)	(0.1, 0.3)	0.1	0.270	0.238	0.247	0.244	0.149
		0.2	0.387	0.347	0.366	0.259	0.176
		0.3	0.455	0.411	0.439	0.280	0.194
		0.4	0.488	0.443	0.480	0.287	0.203
		0.5	0.482	0.439	0.476	0.275	0.198
	(0.2, 0.4)	0.1	0.229	0.206	0.212	0.212	0.142
		0.2	0.327	0.301	0.319	0.248	0.168
		0.3	0.373	0.348	0.374	0.269	0.185
		0.4	0.391	0.368	0.398	0.274	0.193
		0.5	0.391	0.372	0.404	0.265	0.189
	(0.3, 0.6)	0.1	0.221	0.199	0.203	0.210	0.141
		0.2	0.306	0.282	0.298	0.239	0.165
		0.3	0.347	0.324	0.350	0.258	0.181
		0.4	0.364	0.346	0.375	0.263	0.189
		0.5	0.366	0.351	0.382	0.255	0.186
(73, 87)	(0.1, 0.3)	0.1	0.167	0.157	0.164	0.095	0.060
		0.2	0.218	0.205	0.217	0.122	0.077
		0.3	0.243	0.229	0.242	0.139	0.089
		0.4	0.254	0.238	0.252	0.146	0.096
		0.5	0.251	0.235	0.249	0.144	0.097
	(0.2, 0.4)	0.1	0.132	0.127	0.133	0.090	0.058
		0.2	0.171	0.164	0.174	0.115	0.073
		0.3	0.192	0.185	0.195	0.131	0.084
		0.4	0.202	0.194	0.206	0.137	0.091
		0.5	0.202	0.195	0.206	0.135	0.092
	(0.3, 0.6)	0.1	0.121	0.116	0.122	0.084	0.058
		0.2	0.156	0.151	0.159	0.108	0.072
		0.3	0.176	0.170	0.180	0.123	0.082
		0.4	0.185	0.180	0.190	0.129	0.088
		0.5	0.196	0.181	0.191	0.128	0.089

Based on the assumption of exchangeability, an intuitive and simple estimator of π_i for the ith sample is given by $\hat{\pi}_i^a = \sum_{j=1}^{m_i} Y_{ij}/N_i$. Using the exchangeable model and the variance-covariance matrix of a bivariate normal distribution, Zou and Donner (2004) obtained closed-form asymptotic variance formula for the ANOVA estimator of intraclass correlation from a single population, which is, for the ith sample, given by

$$\text{Var}(\hat{\phi}_i^a) = \frac{[(m_i-1)n_i^0 N_i(N_i-m_i)]^2}{\tau_i^4}\left[2m_i + \left(\frac{1}{\pi_i(1-\pi_i)} - 6\right)\sum_{j=1}^{m_i}\frac{1}{n_{ij}} + \Psi_{1i}\phi_i + \Psi_{2i}\phi_i^2 + \Psi_{3i}\phi_i^3\right],$$

where

$$\begin{aligned}
\tau_i &= \phi_i(N_i-m_i)[N_i - 1 - n_i^0(m_i-1)] + N_i(m_i-1)(n_i^0-1),\\
\Psi_{1i} &= \left\{\frac{1}{\pi_i(1-\pi_i)} - 6\right\}\sum_{j=1}^{m_i}\frac{1}{n_{ij}} - 2N_i + 7m_i - \frac{8m_i^2}{N_i} - \frac{2m_i(1-m_i/N_i)}{\pi_i(1-\pi_i)} + \left\{\frac{1}{\pi_i(1-\pi_i)} - 3\right\}\sum_{j=1}^{m_i} n_{ij}^2,\\
\Psi_{2i} &= \frac{N_i^2 - m_i^2}{N_i\pi_i(1-\pi_i)} - 2N_i - m_i + \frac{4m_i^2}{N_i} + \left\{7 - \frac{8m_i}{N_i} - \frac{2(1-m_i/N_i)}{\pi_i(1-\pi_i)}\right\}\sum_{j=1}^{m_i} n_{ij}^2,\\
\Psi_{3i} &= \left\{\frac{1}{\pi_i(1-\pi_i)} - 4\right\}\left(\frac{N_i-m_i}{N_i}\right)^2\left(\sum_{j=1}^{m_i} n_{ij}^2 - N_i\right).
\end{aligned}$$

Note that there are two typos in the formula given in Zou and Donner (2004). However, we provided here the corrected variance formula for $\hat{\phi}_i^a$ after getting feedback from Dr. Zou. Similar to Mian and Shoukri (1997), we obtain a pooled estimate of the common intraclass correlation ϕ as

$$\hat{\phi}^a = \frac{\sum_{i=1}^k W_{\hat{\phi}_i^a}\hat{\phi}_i^a}{\sum_{i=1}^k W_{\hat{\phi}_i^a}} \quad \text{with} \quad W_{\hat{\phi}_i^a} = \frac{1}{\text{Var}(\hat{\phi}_i^a)|_{\pi_i=\hat{\pi}_i^a,\phi_i=\hat{\phi}_i^a}}.$$

Tian (2005) obtained a potential generalized pivot for the intraclass correlation to continuous data, which was used to construct confidence interval limits for the common intraclass correlation. It can be seen that the formula for the ANOVA estimator of the intraclass correlation for continuous data is directly applied to binary data. Similar to this, we also apply here the generalized pivot for the intraclass correlation for continuous data to binary data and obtain the weighted average of the generalized pivots GP_i $(i = 1, \ldots, k)$ as

$$GP = \frac{\sum_{i=1}^k W_{\hat{\phi}^a}^i GP_i}{\sum_{i=1}^k W_{\hat{\phi}^a}^i} \quad \text{with} \quad W_{\hat{\phi}^a}^i = \frac{1}{\text{Var}(\hat{\phi}_i^a)|_{\pi_i=\hat{\pi}_i^a,\phi_i=\hat{\phi}^a}},$$

where

$$\begin{aligned}
GP_i &= \frac{\text{ssa}_i/u_i - \text{ssw}_i/v_i}{\text{ssa}_i/u_i - (1-n_i^*)\text{ssw}_i/v_i},\\
\text{ssw}_i &= (N_i - m_i)\text{MSW}_i,\\
\text{ssa}_i &= n_i^*\left[\sum_{j=1}^{m_i}\frac{Y_{ij}^2}{n_{ij}^2} - \frac{(\sum_{j=1}^{m_i} Y_{ij}/n_{ij})^2}{m_i}\right],\\
n_i^* &= \frac{m_i}{\sum_{j=1}^{m_i} n_{ij}^{-1}},
\end{aligned}$$

and u_i and v_i follow asymptotically chi-squared distributions with degrees of freedom $m_i - 1$ and $N_i - m_i$, respectively. In order to obtain the confidence limits, we generate u_i and

v_i ($i = 1, \ldots, k$) from the respective chi-squared distributions, and compute GP_i ($i = 1, \ldots, k$) and then GP using the above formulas. We repeat this to compute GP for B times, say $\widetilde{GP}_b$ ($b = 1, \ldots, B$) is the set of values for GP. From this set, we compute the $\alpha/2$th and $(1-\alpha/2)$th quantiles, say $\widetilde{GP}_{\alpha/2}$ and $\widetilde{GP}_{1-\alpha/2}$. Then, the $100(1-\alpha)$% confidence interval based on GP is given by $(\widetilde{GP}_{\alpha/2},\ \widetilde{GP}_{1-\alpha/2})$.

2.3 The Asymptotic confidence intervals

Instead of obtaining the confidence interval based on analysis of variance (AOV) using generalized pivots, one may obtain the confidence interval of ϕ directly using the asymptotic distribution of $\hat{\phi}^a$. Under the assumption of a common intraclass correlation ϕ, $\hat{\phi}^a$ is asymptotically normally distributed with mean ϕ and variance $1/\sum_{i=i}^k W_{\hat{\phi}_i^a}$, where $W_{\hat{\phi}_i^a}$ is defined in Section 2.2. Following Tian (2005), we obtain the $100(1-\alpha)\%$ asymptotic confidence interval for ϕ based on AOV as

$$\text{AOV}: \quad \hat{\phi}^a - Z_{\alpha/2}\sqrt{1/\sum_{i=i}^k W_{\hat{\phi}_i^a}} \le \phi \le \hat{\phi}^a + Z_{\alpha/2}\sqrt{1/\sum_{i=i}^k W_{\hat{\phi}_i^a}}.$$

For a single population case, Zou and Donner (2004) obtained confidence limits for the intraclass correlation using closed-form asymptotic formulas for the Fleiss-Cuzick (FC) and Pearson pairwise (PP) estimators. In our case, we apply these formulae to obtain the confidence interval for the common intraclass correlation ϕ. In a similar fashion we also obtain asymptotic confidence intervals for ϕ based on FC as

$$\text{FC}: \quad \hat{\phi}^f - Z_{\alpha/2}\sqrt{1/\sum_{i=i}^k W_{\hat{\phi}_i^f}} \le \phi \le \hat{\phi}^f + Z_{\alpha/2}\sqrt{1/\sum_{i=i}^k W_{\hat{\phi}_i^f}},\ \ W_{\hat{\phi}_i^f} = [\text{Var}(\hat{\phi}_i^f)|_{\pi_i=\hat{\pi}_i^a, \phi_i=\hat{\phi}_i^f}]^{-1},$$

where

$$\begin{aligned}
\hat{\phi}^f &= \frac{\sum_{i=1}^k W_{\hat{\phi}_i^f}\hat{\phi}_i^f}{\sum_{i=1}^k W_{\hat{\phi}_i^f}} \quad \text{with} \quad \hat{\phi}_i^f = 1 - \frac{\sum_{j=1}^{m_i} Y_{ij}(n_{ij}-Y_{ij})/n_{ij}}{(N_i - M_i)\hat{\pi}_i^a(1-\hat{\pi}_i^a)}, \\
\text{Var}(\hat{\phi}_i^f) &= (1-\phi_i)\left[\left\{\frac{1}{\pi_i(1-\pi_i)} - 6\right\}\frac{\sum_j 1/n_{ij}}{(N_i - m_i)^2} + \Upsilon_{1i} + \Upsilon_{2i}\phi_i + \Upsilon_{3i}\phi_i^2\right]
\end{aligned}$$

with

$$\begin{aligned}
\Upsilon_{1i} &= \left\{2N_i + 4m_i - \frac{m_i}{\pi_i(1-\pi_i)}\right\}\frac{m_i}{N_i(N-i-m_i)^2}, \\
\Upsilon_{2i} &= \frac{\sum_j n_{ij}^2}{N_i^2\pi_i(1-\pi_i)} - \frac{(3N_i - 2m_i)(N_i - 2m_i)\sum_j n_{ij}^2}{N_i^2(N_i - m_i)^2} - \frac{2N_i - m_i}{(N_i - m_i)^2}, \\
\Upsilon_{3i} &= \left\{4 - \frac{1}{\pi_i(1-\pi_i)}\right\}\frac{\sum_j n_{ij}^2 - N_i}{N_i^2}.
\end{aligned}$$

Based on the PP method, the confidence intervals for ϕ are obtained using the estimated and profile variances of the PP estimator, which are given by

$$\text{PP}: \quad \hat{\phi}^p - Z_{\alpha/2}\sqrt{1/\sum_{i=i}^k W_{\hat{\phi}_i^p}} \le \phi \le \hat{\phi}^p + Z_{\alpha/2}\sqrt{1/\sum_{i=i}^k W_{\hat{\phi}_i^p}},\ \ W_{\hat{\phi}_i^p} = [\text{Var}(\hat{\phi}_i^p)|_{\pi_i=\hat{\pi}_i^a, \phi_i=\hat{\phi}_i^p}]^{-1},$$

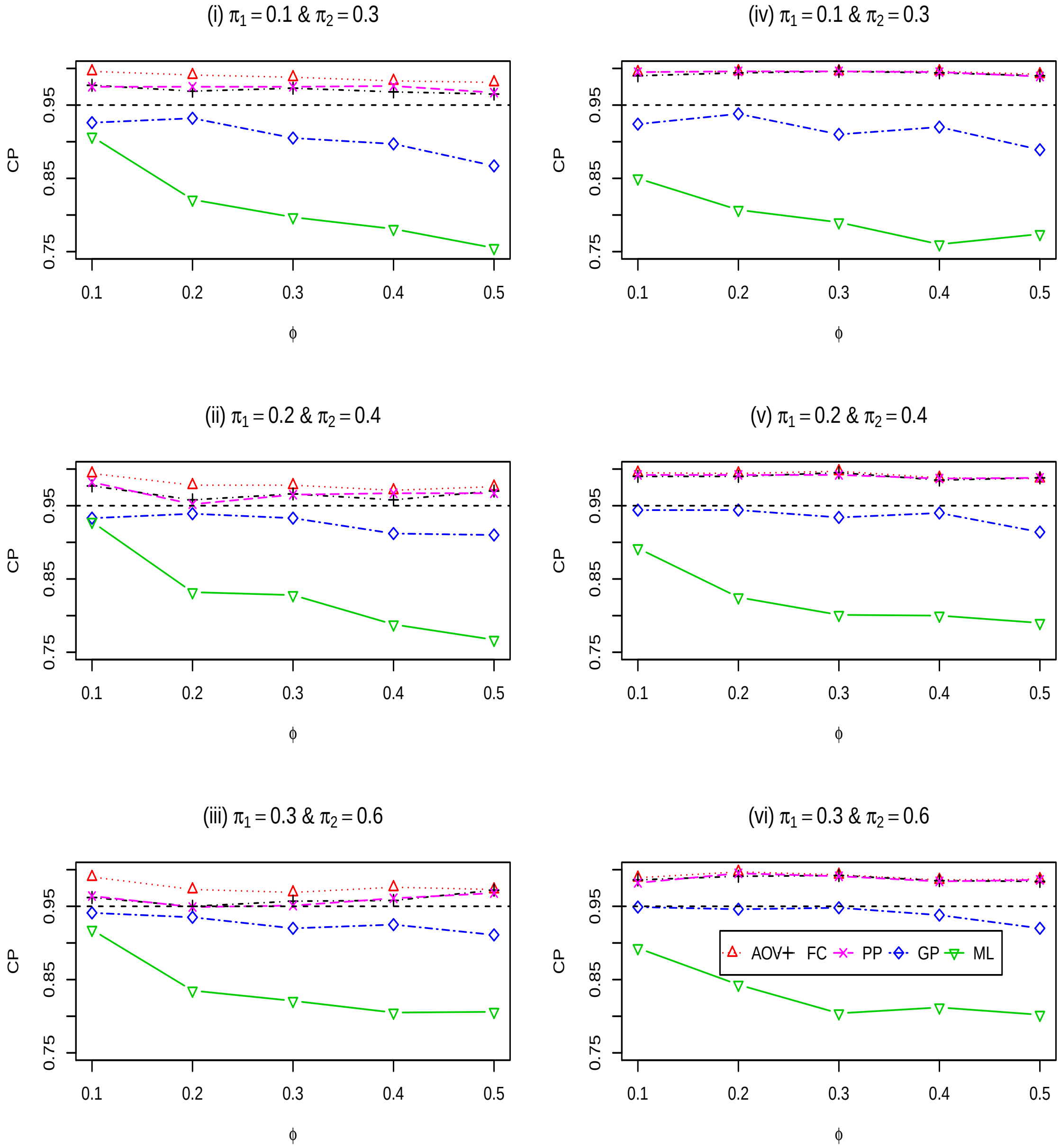

Figure 1: The coverage probability estimates of 95% nominal confidence intervals for the common intraclass correlation ϕ based on the five methods: AOV, FC, PP, GP, and ML.

where

$$\hat{\phi}^p = \frac{\sum_{i=1}^k W_{\hat{\phi}_i^p}\hat{\phi}_i^p}{\sum_{i=1}^k W_{\hat{\phi}_i^p}} \quad \text{with} \quad \hat{\phi}_i^p = \frac{1}{\hat{\mu}_i(1-\hat{\mu}_i)}\left[\frac{\sum_j Y_{ij}(Y_{ij}-1)}{\sum_j n_{ij}(n_{ij}-1)} - \hat{\mu}_i^2\right],$$

$$\text{Var}(\hat{\phi}_i^f) = \frac{1-\phi_i}{[\sum_j n_{ij}(n_{ij}-1)]^2}\left[2\sum_j n_{ij}(n_{ij}-1) + \phi_i\Lambda_{1i} + \phi_i^2\Lambda_{2i}\right].$$

with

$$\hat{\mu}_i = \frac{\sum_j Y_{ij}(n_{ij}-1)}{\sum_j n_{ij}(n_{ij}-1)},$$

$$\Lambda_{1i} = \left\{\frac{1}{\pi_i(1-\pi_i)} - 3\right\}\sum_j n_{ij}^2(n_{ij}-1)^2,$$

$$\Lambda_{2i} = \left\{4 - \frac{1}{\pi_i(1-\pi_i)}\right\}\sum_j n_{ij}(n_{ij}-1)^3.$$

3. Simulations

This section reports on a simulation study conducted to investigate the small and moderate sample behavior of the five interval procedures ML, GP, AOV, FC, and PP in terms of observed coverage probability and average interval length using the pre-assigned confidence level of 95%. For simplicity, we consider k=2 groups and the number of clusters for k=2 groups are chosen as (i) m_1=19 and m_2=27 and (ii) m_1=73 and m_2=87. In this study, we consider the cluster sizes for case (i) from the low dose treatment group (m_1=19) and the control group (m_2=27) of the data in Table 1 of Paul (1982) and for case (ii), the cluster sizes are the same as those of the Dose 0 group (m_1=73) and Dose 30 group (m_2=87) for the data in Table 4. The true values of the proportion parameters (π_1, π_2) and the intraclass correlation parameters (ϕ_1, ϕ_2) we considered for this simulation were (π_1, π_2) = (0.1, 0.3), (0.2, 0.4), (0.3, 0.6) and $\phi_1 = \phi_2$ = 0.1,0.2, 0.3, 0.4, 0.5. All results are obtained using FORTRAN 90 code. We generate data from the beta-binomial distribution using the IMSL random number generators RNBET and RNBIN. We compute the observed coverage probability for the intraclass correlation by the relative frequency out of 1000 intervals that contained the true value. The average interval length is the mean of the lengths computed on the basis of 1000 intervals. The results are reported in Tables 1-2 and Figure 1 from which we make the following observations:

- The CP results between small and moderate number of clustered sizes for all five methods are in remarkable agreement irrespective of the proportion parameter combinations. Specifically, the CPs for all five methods are virtually the same across all combinations of π and ϕ.
- The ML method shows severe under-coverage across the board, and it becomes very severe under-coverage for larger values of ϕ for all combinations of the proportion parameters.
- The AOV, FC, and PP methods show severe over-coverage across the board; however, the CPs for these methods are slightly improved for larger values of ϕ particularly for the small number of clusters.
- The GP method produces better coverage compared to the other four methods, especially for small values of ϕ and for larger proportion parameter combinations when the number of clustered sizes is large.

- For all five methods, the ELs increase as the true intraclass correlation ϕ increases; the ELs decrease as the number of clustered sizes increases; and also the ELs decrease as the value of the proportion parameters (π_1, ϕ_2) increases.
- The AOV, FC, and PP methods tend to have similar ELs which are larger than the ELs of the ML and GP methods.
- The ML method has among the lowest ELs which in many situations is at the expense of severe under-coverage, whereas good coverage properties of the GP method tends to have larger ELs compared to the ML method, but smaller ELs compared to the AOV, FC, and PP methods.

4. Example: Solar Protection Study

This study was an educational intervention program on behavior change with regard to solar protection. In this study, there were 29 classes (clusters) in each group with sizes (number of children in each class) ranging from 1 to 6 in the intervention group and from 1 to 4 in the control groups. Below are summary statistics of this study.

Table 3: Summary statistics for the data set in a solar protection study

Study Arm	# of subjects	# of clusters	mean cluster size	success prob
Control	68	29	2.345	0.618
Intervention	64	29	2.07	0.422

The distributions of cluster-level proportions for control and treatment groups are shown below:

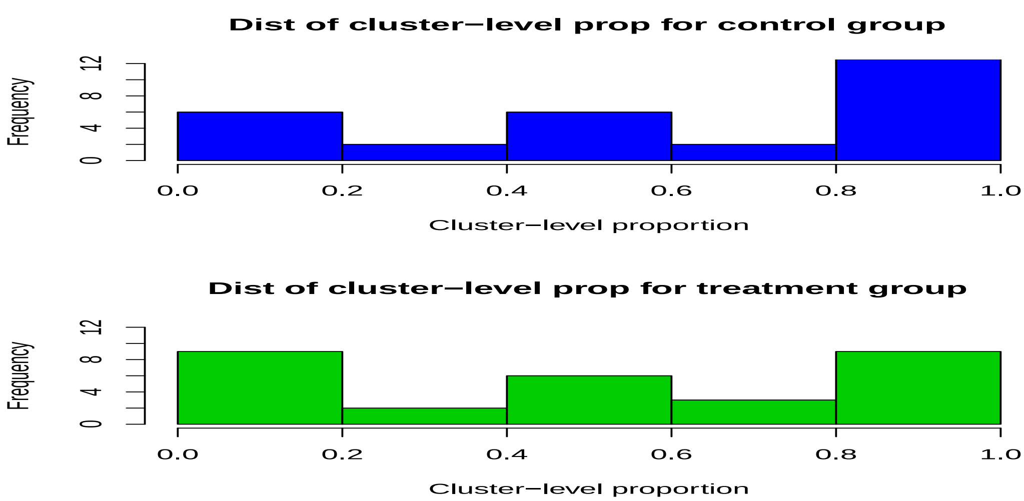

Figure 2: The distributions of cluster-level proportions for control and treatment groups in a solar production study.

The estimated success probability and the estimated intraclass correlation for both study arms and the estimated common intraclass correlation are provided below:

Table 4: The point estimates of the parameters obtained based on the four different methods for the data set in a solar protection study.

Methods	π_1	π_2	ϕ_1	ϕ_2	ϕ
ML1	0.621	0.462	0.324	0.249	0.286
AOV1	0.618	0.422	0.337	0.266	0.301
FC1	0.618	0.422	0.321	0.248	0.287
PP1	0.618	0.422	0.382	0.265	0.331

Then, the 95% confidence intervals for a common intraclass correlation ϕ obtained using the ML, GP, AOV, FC, and PP methods are given below:

Table 5: The 95% confidence intervals for a common intraclass correlation ϕ obtained using the ML, GP, AOV, FC, and PP methods.

Method	Lower Limit	Upper Limit	Length	Length Comparison ind/ML
ML	0.124	0.449	0.325	1.000
GP	0.030	0.502	0.472	1.451
AOV	0.108	0.493	0.385	1.184
FC	0.057	0.516	0.459	1.410
PP	0.078	0.583	0.505	1.554

5. Conclusion

In this article, we applied the generalized pivot as the analogy of formulas for continuous data to binary data to construct a new CI for a common intraclass correlation using the weighted average of the generalized pivots. The proposed CI works satisfactory in term of coverage probabilities when a common intraclass correlation is smaller than 0.4, in particular for the moderate number of clusters. For a larger common intraclass correlation, this proposed CI could be somewhat anti-conservative. We also developed four other asymptotic confidence intervals, which were compared with the proposed method. The asymptotic CIs based on AOV, PP, and FC showed very conservative behaviors, whereas the asymptotic CI based on ML showed severe anti-conservative behavior. Beside the ML method, the GP based CI showed a shorter expected length compared to the other three asymptotic CIs.

Acknowledgements

This paper was supported in part by a CSU-AAUP University research grant.

REFERENCES

Kupper, L.L. and Haseman, J.K. (1978), ”The Use of a Correlated Binomial Model for the Analysis of Certain Toxicological Experiments. *Biometrics*, **34**, 69-76.

Lee, Y. (2004), ”Estimating Intraclass Correlation for Binary Data using Extended Quasilikelihood”. *Statistical Modelling*, **4**, 113-126.

Lui, K-J, Cumberland, W.G., and Kuo, L. (1996), ”An Interval Estimate for the Intraclass Correlation in Beta-Binomial Sampling”. *Biometrics*, **52**, 412-425.

Paul, S.R. (1982), ”Analysis of Proportions of Affected Foetuses in Teratological Experiments,” *Biometrics*, **38**, 361-370.

Paul, S.R. and Islam, A.S. (1998), ”Joint Estimation of the Mean and Dispersion Parameters in the Analysis of Proportions: A Comparison of Efficiency and Bias”. *The Canadian Journal of Statistics*, **26**, 83-94.

Paul, S.R., Saha, K.K., and Balasooriya, U. (2003), ”An Empirical Investigation of Different Operating Characteristics of Several Estimators of the Intraclass Correlation in the Analysis of Binary Data”. *Journal of Statistical Computation and Simulation*, **73**, 507-523.

Ridout, M.S., Demetrio, C.G.B, and Firth, D. (1999), ”Estimating Intraclass Correlation for Binary Data”. *Biometrics*, **55**, 137-148.

Saha, K.K. (2012), ”Profile Likelihood-Based Confidence Intervals of the Intraclass Correlation for Binary Outcome Data Sampled from Clusters”. *Statistics in Medicine*, **31**, 3982-4002.

Saha, K.K. and Paul, S.R. (2005), ”Bias-Corrected Maximum Likelihood Estimator of the Intrclass Correlation Parameter for Binary Data”. *Statistics in Medicine*, **24**, 3497-3512.

Zou, G. and Donner, A. (2004), ”Confidence Interval Estimation of the Intraclass Correlation Coefficient for Binary Outcome Data”. *Biometrics*, **60**, 807-811.