2014

Comparison of Confidence Intervals of Intracluster Correlation Coefficient Estimates for Binary Variables

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COMPARISON OF CONFIDENCE INTERVALS OF INTRACLUSTER CORRELATION COEFFICIENT ESTIMATES FOR BINARY VARIABLES

by

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Bachelor of Technology
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Submitted in Partial Fulfillment of the Requirements

For the Degree of Master of Science in Public Health in

Biostatistics

The Norman J. Arnold School of Public Health

University of South Carolina

2014

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Dedication

I dedicate my thesis to my family and friends who believed in me and supported me both morally and financially from the start of my career in the United States. The encouragement that I got from my father, Venkateswara Raju , Mother, Durga Bhavani and my brother, Rama Krishna Raju is enormous, when I decided to pursue my masters.

I also dedicate this thesis to all my friends back in India and the friends that I made in the United States. I would like to thank all my friends who supported me, which includes Nitin, Sanjeev, Eshwar, Rajiv, Subash, Narasimha, Hareesh, Srikar, Arun and Abhilash.

I also dedicate my thesis to all the professors who helped me in my career. I would like to specially mention Dr. Pruss Gail, Research professor of Biological sciences, who advised me to go for Biostatistics.

Acknowledgements

I would like to acknowledge all my friends and professors who helped me throughout my masters program. I would like to thank Dr. James Hussey, one of the committee members, who accepted me into the Biostatistics program and supported me. I would like to thank my other committee member Dr. Bob Moran for his help and advice. I would like to thank Dr. Hongmei Zhang, who supported me and motivated me towards research. Finally I would like to thank Dr. Hrishikesh Chakraborty, thesis director, for his enormous encouragement and guidance in completing my thesis.

ABSTRACT

The present study evaluates the length of the confidence interval and the percentage of time the true parameter is captured by the confidence interval for four intracluster correlation estimators. These are the ANOVA estimator, the Pearson pairwise estimator with constant weights (PEQ), the kappa type estimator called FC, and an estimator using a Resampling method (RM) for binary data. We compared these different estimates by using a large simulation study. The data we simulated is correlated binary data, which assumes an exchangeable correlation structure. We also included different variations of the number of clusters, cluster size, cluster size variation, event rate, event rate variation and the population intracluster correlation coefficients.

The results showed that, among all the confidence limits for the 4 estimators, the confidence limits by the PEQ estimator performs best and it is the ideal one to use in most situations, but if the cluster size is very small, the confidence limits by the FC estimator performs best and is the ideal one to use. Finally, if the number of clusters is very small, the confidence limits obtained by the RM estimator performs best and this is the ideal one to use.

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CHAPTER 1

INTRODUCTION

1.1 BACKGROUND

A simple randomized trial is one in which an individual is the unit of randomization, but in a cluster randomized trial (CRT), a group is the unit of randomization (Donner and Klar 2000). CRTs, also known as group randomized trials, randomize groups such as hospitals, worksites, medical practices, schools, households, or communities. For example, we might randomize the whole village if there is a spread of endemic disease in a rural area to have the intervention or not, rather than any individual. Here we say that the unit of randomization is the village. Cluster randomized trials are accepted as the gold standard for the evaluation of many health interventions such as episiotomy rate, neonatal mortality rate, and post hemorrhage rate (Hayes and Bennett 1999).

There are many reasons for adopting cluster randomized trials as identified by Hayes and Bennett (Hayes and Bennett 1999). One of the reasons is that many intervention trials, like hospital intervention trials and educational intervention trials should be implemented at the cluster level to avoid resentment or contamination that could occur if some individuals in a cluster received the intervention but others did not (Chakraborty 2007). Another situation where CRTs are preferred is when we want to

capture the main effect of disease on vast size of community members, like providing advanced training to birth attendants in a rural setting for reduction of neonatal mortality. Other main reasons for adopting CRTs are to increase administrative efficiency, to provide less intrusive randomization, to control costs, and to eliminate potential ethical problems (Biswas, Datta et al. 2007).

The main disadvantage of cluster randomized trials is that the participants within a given cluster tend to behave or respond similarly, and hence we cannot assume that the subjects are independent of one another. We have two types of correlation: between and within clusters. Between-cluster (intercluster) correlation measures the variation in outcomes across clusters. Within-cluster (intracluster) correlation measures the variation in outcomes within the cluster and is influenced by common factors, such as age, race, gender, geographic, socioeconomic, and political factors (Chuang, Hripcsak et al. 2002, Killip, Mahfoud et al. 2004).

The unit of inference in cluster randomized trials can be directed either at the individual level or at the cluster level. The unit of analysis should always be same as the unit of randomization. This unit selection of analysis is based on the theory developed by Sir Ronald Fisher (Fisher 1935), who assumed that the experimental unit which is randomized is also the unit of analysis. We may use standard methods to perform the analysis for either a dichotomous outcome or a continuous outcome, but two major limitations arise from this approach: Since the number of clusters may not be large, we end up with fewer data points and thus have a lower statistical power for data analysis;

the number of subjects in each cluster may not be the same, and thus cluster-level analyses providing equal weight to all the clusters prove to be imprecise (Chakraborty 2007).

On the other hand, we will experience statistical challenges and complications if we draw individual-level references for cluster randomized trials, since the randomization is at the cluster level. Cornfield (Cornfield 1978) made it clear from a statistical sense that such allocation schemes are less efficient than designs which randomize individuals to intervention group. The loss of efficiency is because the responses of individuals in a cluster tend to be more similar or more highly correlated than responses of individuals from different clusters.

The term “Unit of analysis error” is often used to denote incorrect analysis where some of the studies have incorrectly analyzed trial data as though the unit of allocation had been the individual participant because the unit of analysis is different from the unit of allocation (Whiting-O'Keefe, Henke et al. 1984). If we ignore the clustering and analyze CRTs as though individuals had been randomized, we get small p values, resulting in false-positive conclusions that the intervention had an effect.

Many studies have reported that cluster randomized trials routinely fail to take between-cluster variation into account in both the design and analysis phase. Brown et al (J Trig Brown MD and Frazier 1992) found that 70% out of 54 published papers used the wrong unit of analysis. Only four statistically significant analyses were found after reanalyzing the data. Simpson et al. (Simpson, Klar et al. 1995) showed that out of 21

primary prevention trials using cluster randomized trial, only 4 studies (19%) took into account between-cluster variation for sample size and power calculations and 12 (57%) took into account between-cluster variation for analysis. We found similar results from several other reviewers (Butler and Bachmann 1996, Rooney and Murray 1996).

We need to take into account the within- and between-cluster correlation if we randomize by cluster and draw the inference at individual level. The Intracluster/Intraclass correlation coefficient (ICC) typically measures the degree of similarity among responses within a cluster. This parameter, denoted by ρ, is also interpreted as the standard Pearson correlation coefficient between any two responses in the same cluster.

The intracluster correlation coefficient plays a major role in the design and analysis of cluster randomized trials. The ICC will nullify the standard approaches to both the estimation of sample size and the analysis of clinical trial data. The standard formulas for estimation of sample size and analysis mainly lead to underpowered studies, which may be inconclusive. Also application of these standard methods for statistical analysis leads to lower p-values, leading to false statistical significance. Ignoring this correlation leads to smaller standard errors and narrower confidence intervals (Biswas, Datta et al. 2007).

Although the ICC could be negative in theory, this almost never occurs in practice. If it becomes negative, the ICC is set to zero and analysis will be done using simple randomized trials. In almost all human studies, ICC values are between 0 and 1

(Baskerville, Hogg et al. 2001, Killip, Mahfoud et al. 2004). Small values of ρ in combination with large cluster sizes, can yield large design effects and have a notable impact on data analysis. Hence, assuming the existence of intracluster correlation has been proposed for analysis of CRTs (Donner and Klar 2000).

The ICC can be calculated with different methods, and different ICC results are provided by different software packages. Many estimators of ICC have been reviewed by Ridout (Ridout, Demetrio et al. 1999), Paul (Paul, Saha et al. 2003) and Gao (Gao 2012). These include the most widely used analysis of variance (ANOVA) estimators, the quasi-likelihood estimator, estimators with a direct probabilistic interpretation, maximum likelihood estimators for beta-binomial data, estimators based on direct calculation of correlation within each group, moment estimators, extended quasi-likelihood and pseudo-likelihood estimators, and estimators using a resampling method.

Although inference procedures are well developed for ICC under the assumption of multivariate normality for the case of continuous data (Donner 1986), techniques for binary data have been less well developed, with the emphasis mainly on point estimation (Ridout, Demetrio et al. 1999). The two most popular approaches for ICC inference are generalized estimating equations (GEE) and the beta-binomial (BB) distribution (Lui, Cumberland et al. 1996). But the GEE approach was not designed for inference concerning the ICC and may result in considerable below nominal confidence interval coverage (Evans, Feng et al. 2001). A disadvantage of the BB model is that it

assumes that “the binary observations within a cluster are assumed to be a finite subset of an infinite exchangeable sequence of random variables” (Bowman 2001).

“A confidence interval is defined as the range of values for a variable of interest constructed so that this range has a specified probability of including the true value of the variable. The specified probability is called the confidence level, and the end points of the confidence interval are called the confidence limits” (Gupta 2012). The confidence level is often set at 95%, which means that the confidence interval covers the true value in 95 out of 100 studies performed (Greenfield, Kuhn et al. 1998). A 99% confidence interval is wider than a 95% confidence interval. As the probability of covering the true value increases, the confidence interval becomes wider.

Although the best approximation to the true value is provided by the point estimate, details about how precise they are is not provided. This is achieved by confidence intervals. Though it is very difficult to make any precise statement about the size of the difference between the estimated parameters for the sample and the true value for the population, one would like to have some confidence that the point estimate is in the vicinity of the true value. Confidence intervals can be used to describe the probability that the true value is within a given range. The upper and lower limits of the interval give us information on how big or small the true effect might plausibly be, and the width of the confidence interval also gives us useful information (Gupta 2012).

The paper from Zou and Donner (Zou and Donner 2004) provides an extensive review of earlier work on the estimation of confidence intervals for intraclass

correlation and conducted simulation studies to compare the percent capture of true ICC value by the confidence limits and width of confidence interval of different ICC estimators. A common correlation model was adopted (Madsen 1993) to derive explicit variance formulae for three estimators of the ICC previously found to perform well in terms of mean square error and bias by Ridout et al. (Ridout, Demetrio et al. 1999). They performed simulations by generating variable cluster sizes from a truncated negative binomial distribution with mean 3.12 and variance 4.52.

The simulation technique for the present study is different from that performed by Zou and Donner (Zou and Donner 2004), since we do not make a distributional assumption for the group total Y_i. A simple and efficient simulation method which was reported by Lunn (Lunn and Davies 1998) was adopted by our study to generate the clustered binary outcome data.

1.2 PREVIOUS STUDIES

The role of ICC in both the design and analysis phase for cluster randomized trials is very important and has been widely accepted. An important aspect of CRT is calculating and reporting ICC and its confidence intervals, as different estimation methods are available to compute the ICC. Several authors have proposed and redefined different approaches to estimate the ICC for binary data (Ridout, Demetrio et al. 1999, Paul, Saha et al. 2003, Gao 2012). Ridout et al. (1999) found 3 estimators to perform well in terms of mean square error and bias. A study by Gao (Gao 2012)

showed that 11 out of the 14 estimators had less bias and smaller standard deviations when varying the values of all variables consistently. Only one author has proposed an approach to estimate the confidence interval of ICC for binary data (Zou and Donner 2004).

Zou and Donner (Zou and Donner 2004) estimated the confidence intervals for 3 Intracluster correlation coefficients for binary outcome. Among these, the confidence intervals based on $\hat{\rho}_{\mathrm{FC}}$ (Fleiss-Cuzick estimator) performs better than $\hat{\rho}_{\mathrm{PEQ}}$ (Pearson pairwise estimator) which is better than $\hat{\rho}_{\mathrm{AOV}}$ (ANOVA estimator).

1.3 SPECIFIC AIM

The value of ICC estimators depend on the values of event rate, event rate variability between clusters, cluster size, cluster size variability, number of clusters and the true value of ICC assumed in a dataset (Chakraborty, Moore et al. 2009). For this study we varied all of these parameters at different levels and tested their effects on the 3 ICC estimators that are found to perform well by Ridout et al. (1999) as well as an estimator based on a resampling method proposed by Chakraborty, and calculated their confidence intervals. We compared the different ICC estimators and their confidence intervals for each combination number of clusters, overall event rate, event rate variation between clusters, cluster size and cluster size variation. The better confidence interval estimators will have lower confidence interval lengths and percentage coverage of the true ICC value should be closer to 95%.

CHAPTER 2

COMPARISON OF CONFIDENCE INTERVALS FOR INTRACLUSTER CORRELATION COEFFICIENT ESTIMATES USING DIFFERENT CALCULATION METHODS

2.1 METHODS

2.1.1 The underlying model

Suppose we have k clusters in a clinical trial, and that there are n_i individuals in the i^{th} cluster, with each subject having a binary response X_{ij} (i=1…,k; j=1…, n_i). The two possible values of X_{ij} are coded as one and zero for success and failure respectively. Let $Y_i = \sum_{j=1}^{n} X_{ij}$ denote the total number of successes in the *ith* group. The probability of success, irrespective of the individuals group, is assumed to be the same for all individuals. $P(X_{ij}=1)=\pi$ for all i,j. Also, the responses of individuals from different clusters are assumed to be independent. The responses within each group are correlated and the correlation between any pair (X_{ij}, X_{il}) ($j \neq l$) is the intra cluster correlation coefficient, denoted as *ρ.* This model is therefore a common-correlated model and the correlation is assumed not to vary with group size (Ridout, Demetrio et al. 1999). A simple estimator for π is given by $\hat{\pi} = \frac{1}{N}\sum_{i=1}^{k} Y_i$ Where $N= \sum_{i=1}^{k} n_i$ is the total number of observations in the study.

2.1.2 Estimators of Intra cluster correlation

The Analysis of variance Estimator (ANOVA)

A sample estimate of ρ may be obtained by performing a standard one-way analysis of variance (ANOVA) among and within clusters. Consider that there are k clusters each with a sample size n_i . Let us say that MSB and MSW denote mean square error between and within clusters respectively. Then the analysis of variance (ANOVA) estimator for ρ given by Ridout et al (Ridout, Demetrio et al. 1999) is

$$\hat{\rho}_{AOV} = \frac{MSB - MSW}{MSB + (n_0 - 1)MSW}, \text{ where } n_0 = \frac{1}{k-1}\left[N - \frac{1}{N}\sum_{i=1}^{k} \mathrm{n}_\mathrm{i}^2\right].$$

Previously, this estimator of the intraclass correlation was proposed for continuous outcome variables, but it has been used later for binary outcome variables by some of the researchers (Elston 1977, Fleiss and Cuzick 1979, Ridout, Demetrio et al. 1999). For binary data, MSB and MSW are defined as

$$MSB = \frac{1}{k-1}\left[\sum_{i=1}^{k} \frac{Y_i^2}{n_i} - \frac{1}{N}\left(\sum_{i=1}^{k} Y_i\right)^2\right], MSW = \frac{1}{N-k}\left[\sum_{i=1}^{k} Y_i - \sum_{i=1}^{k}\left(\frac{y_i^2}{n_i}\right)\right]$$

Variance of ANOVA estimator

A consistent variance estimator for $\hat{\rho}_{AOV}$ given by Zou and Donner (Zou and Donner 2004) is

$$V(\hat{\rho}_{AOV}) = \frac{\{(k-1)n_0N(N-k)\}^2}{\lambda^4}\left[2k + \left(\frac{1}{\pi(1-\pi)} - 6\right)\sum n_i^{-1} + \left[\left(\frac{1}{\pi(1-\pi)} - 6\right)\right]\sum n_i^{-1} - 2N + 7k - \frac{8k^2}{N} - \frac{2k\left(1-\frac{k}{N}\right)}{\pi(1-\pi)} + \left(\frac{1}{\pi(1-\pi)} - 6\right)\sum n_0^2\right]\rho + \left[\frac{N^2-k^2}{\pi(1-\pi)} - 2N - k + \frac{4k^2}{N} + \left(7 - \frac{8k}{N} - \frac{2\left(1-\frac{k}{N}\right)}{\pi(1-\pi)}\right)\sum n_0^2\right]\rho^2 + \left(\frac{1}{\pi(1-\pi)} - 4\right)\left(\frac{N-k}{N}\right)^2 \left(\sum n_0^2 - N\right)\rho^3$$

Where $\lambda = (N-k)\,[N-1-n_0(k-1)]\,\rho + N\,(k-1)(n_0-1)$

Confidence Interval for ANOVA estimator

The confidence interval for ρ_{AOV} is given by $\hat{\rho}_{AOV} \pm Z_{\alpha/2}\sqrt{\text{var}(\hat{\rho}_{AOV})}$

The 95% confidence interval for ρ_{AOV} is given by $\hat{\rho}_{AOV} \pm 1.96\sqrt{\text{var}(\hat{\rho}_{AOV})}$

Kappa Type Estimator (FC estimator)

Let us say that α is the probability that two individuals having the same outcome coming from the same group and β, the probability that it comes from different group. Then $\alpha = 1 - 2\pi(1-\pi)(1-\rho)$, $\beta = 1 - 2\pi(1-\pi)$, and hence $\rho = \frac{\alpha-\beta}{1-\beta}$.

Fleiss and Cuzick (Fleiss and Cuzick 1979) estimated α as a weighted average of these within-group estimators, with weights proportional to $n_i - 1$. Then they estimated β by $1 - 2\hat{\pi}(1-\hat{\pi})$ where $\hat{\pi} = \frac{1}{N}\sum_{i=1}^{k} Y_i$ is the overall proportion of success in the sample data. The estimator derived can be written as $\hat{\rho}_{FC}$ (FC),

$$\hat{\rho}_{FC} = 1 - \frac{1}{(N-k)\hat{\pi}(1-\hat{\pi})}\sum_{i=1}^{k}\frac{Y_i(n_i-Y_i)}{n_i}$$

Variance of FC estimator

A consistent variance estimator of $\hat{\rho}_{\mathrm{FC}}$ given by Zou and Donner (Zou and Donner 2004) is

$$V(\hat{\rho}_{FC}) = (1-\rho)\left[\left(\frac{1}{\pi(1-\pi)} - 6\right)\sum\frac{n_0^{-1}}{(N-k)^2} + \left(2N + 4k - \frac{k}{\pi(1-\pi)}\right)\frac{k}{N(N-k)^2} + \left[\frac{\sum n_0^2}{N^2\pi(1-\pi)} - \frac{(3N-2k)(N-2k)\sum n_0^2}{N^2(N-k)^2} - \frac{2N-k}{(N-k)^2}\right]\rho + \left(4 - \frac{1}{\pi(1-\pi)}\right)\left(\frac{\sum n_0^2 - N}{N^2}\right)\rho^2\right]$$

Confidence Interval for FC estimator

The confidence interval for estimate ρ_{FC} is given by $\hat{\rho}_{\mathrm{FC}} \pm \mathrm{Z}_{\alpha/2}\sqrt{\mathrm{var}(\hat{\rho}_{\mathrm{FC}})}$

The 95% confidence interval for estimate ρ_{FC} is given by $\hat{\rho}_{\mathrm{FC}} \pm 1.96\sqrt{\mathrm{var}(\hat{\rho}_{\mathrm{FC}})}$

Pearson pairwise Estimator (PEQ estimator)

The Pearson pairwise estimator with constant weights given by Ridout et al (Ridout, Demetrio et al. 1999) is

$$\hat{\rho}_{PEQ} = \frac{1}{\hat{\mu}_{PEQ}(1-\hat{\mu}_{PEQ})}\left[\sum_{i=1}^{k}\frac{Y_i(1-Y_i)}{n_i(n_i-1)} - \hat{\mu}_{PEQ}^2\right], \text{ where } \hat{\mu}_{PEQ} = \sum_{i=1}^{k}\frac{Y_i(n_i-1)}{n_i(n_i-1)}$$

Variance of PEQ estimator

A consistent variance estimator for $\hat{\rho}_{\mathrm{PEQ}}$ given by Zou and Donner (Zou and Donner 2004) is

$$V(\hat{\rho}_{PEQ}) = \frac{(1-\rho)}{[\sum n_0(n_0-1)]^2}\left[2\sum n_0(n_0-1) + \sum n_0^2(n_0-1)^2\left[\frac{1}{\pi(1-\pi)}\right]\rho + \sum n_0(n_0-1)^3\left(4-\frac{1}{\pi(1-\pi)}\right)\rho^2\right]$$

Confidence Interval for PEQ estimator

The confidence interval for estimate ρ_{PEQ} is given by $\hat{\rho}_{\mathrm{PEQ}} \pm \mathrm{Z}_{\alpha/2}\sqrt{\mathrm{var}(\hat{\rho}_{\mathrm{PEQ}})}$

The 95% confidence interval for estimate ρ_{PEQ} is given by $\hat{\rho}_{\mathrm{PEQ}} \pm 1.96\sqrt{\mathrm{var}(\hat{\rho}_{\mathrm{PEQ}})}$

Estimator using a Resampling method (RM estimator)

A resampling method has been proposed by Chakraborty (Chakraborty and Sen) to estimate ICC for clustered binary data. The overall probability of success is estimated by a U-statistic of $U_1 = \frac{1}{n}\sum_{i=1}^{k}\sum_{j=1}^{n_i} I(x_{ij}=1)$, where *I* define the indicator function. The mean of U_1 is $E(U_1) = E\left[\frac{1}{n}\sum_{i=1}^{k}\sum_{j=1}^{n_i} I(x_{ij}=1)\right] = \alpha = \theta_1$ and the variance of U_1 is

$$V(U_1) = V\left[\frac{1}{n}\sum_{i=1}^{k}\sum_{j=1}^{n_i} I(x_{ij}=1)\right] = \alpha(1-\alpha)\left[\frac{1}{n} + \frac{\rho}{n^2}\sum_{i=1}^{k} n_i(n_i-1)\right].$$

A U-statistic of T_W is defined as the overall within cluster pair probability, when two samples are drawn from a same cluster with replacement.

$$T_w = \left[\sum_{i=1}^{k} n_i(n_i-1)\right]^{-1}\left[\sum_{i=1}^{k}\sum_{j,j'=1;j\neq j'}^{n_i} I\left(x_{ij}=1 \; and \; x_{ij'}=1\right) + \sum_{i=1}^{k}\sum_{j,j'=1;j\neq j'}^{n_i} I\left(x_{ij}=0 \; and \; x_{ij'}=0\right) - \sum_{i=1}^{k}\sum_{j,j'=1;j\neq j'}^{n_i} I\left(x_{ij}=1 \; and \; x_{ij'}=0\right) - \sum_{i=1}^{k}\sum_{j,j'=1;j\neq j'}^{n_i} I\left(x_{ij}=0 \; and \; x_{ij'}=1\right)\right]$$

The expected value of T_W is

$$E(T_w) = \alpha^2 + (1-\alpha)^2 - 2\alpha(1-\alpha) + 4\rho\alpha(1-\alpha) = \theta_2$$

and the variance of T_W is

$$V(T_w) = \frac{\alpha(1-\alpha)}{\sum_{i=1}^{k} n_i^2 - n}[(1+\alpha-\rho\alpha)\{\alpha+\rho(1-\alpha)\} + (1-\alpha+\rho\alpha)\{2-\alpha-\rho\,(1-\alpha)\} + 2(1+\rho)\{1-\alpha(1-\alpha)(1+\rho)\}]$$

A U-statistic of T_B is defined as the overall between cluster pair probability, when two samples are drawn from two different clusters with replacement.

$$T_B = \left[n(n-1) - \sum_{i=1}^{k} n_i(n_i-1)\right]^{-1}\left[\sum_{i,i'=1;i\neq i'}^{k}\sum_{j,j'=1}^{n_i} I\left(x_{ij}=1 \; and \; x_{i'j'}=1\right) + \sum_{i,i'=1;i\neq i'}^{k}\sum_{j,j'=1}^{n_i} I\left(x_{ij}=0 \; and \; x_{i'j'}=0\right) - \sum_{i,i'=1;i\neq i'}^{k}\sum_{j,j'=1}^{n_i} I\left(x_{ij}=1 \; and \; x_{i'j'}=0\right) - \sum_{i,i'=1;i\neq i'}^{k}\sum_{j,j'=1}^{n_i} I\left(x_{ij}=0 \; and \; x_{i'j'}=1\right)\right]$$

The expected value of T_B is $E(T_B) = \alpha^2 + (1-\alpha)^2 - 2\alpha(1-\alpha) = \theta_3$

and the variance of T_B is $V(T_B) = \frac{1}{n^2 - \sum_{i=1}^{k} n_i^2} + [2\alpha(1-\alpha)+1]^2$

The estimate of ICC is denoted as $\hat{\rho}_{RM} = \frac{T_W - T_B}{4U_1(1-U_1)}$, which is an unbiased estimator of ρ.

Variance of RM estimator

$\hat{\rho}$ is a function of U_1, T_W, and T_B and the function can be defined as

$$\hat{\rho} = g(U_1, T_W, T_B) = g\left(\theta_1 + \frac{Z_1}{\sqrt{n}}, \theta_2 + \frac{Z_2}{\sqrt{n}}, \theta_3 + \frac{Z_3}{\sqrt{n}}\right).$$

If $\underset{\sim}{a}$ is the coefficient matrix and

$$\underset{\sim}{Z} = \begin{bmatrix} Z_1 \\ Z_2 \\ Z_3 \end{bmatrix} \xrightarrow{d} N_3\left[\begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix}, \begin{Bmatrix} V(Z_1) & Cov(Z_1, Z_2) & Cov(Z_1, Z_3) \\ Cov(Z_1, Z_2) & V(Z_2) & Cov(Z_2, Z_3) \\ Cov(Z_1, Z_3) & Cov(Z_2, Z_3) & V(Z_3) \end{Bmatrix}\right],$$

then Taylor series expansion of the function $g(U_1, T_W, T_B)$ about the values of

$\{E(U_1), E(T_W), E(T_B)\}$ is

$$\hat{\rho} = \rho + \frac{Z_1}{\sqrt{n}} \frac{1}{4\theta_1(1-\theta_1)} - \frac{Z_2}{\sqrt{n}} \frac{1}{4\theta_1(1-\theta_1)} + \frac{Z_3}{\sqrt{n}} \frac{(\theta_2 - \theta_3)(2\theta_1 - 1)}{4\{\theta_1(1-\theta_1)\}^2} + O_p(n^{-1}) = \rho + \underset{\sim}{a}' \underset{\sim}{Z} + O_p(n^{-1})$$

Second order derivative of $\hat{\rho}$ gives us its variance.

After we ignore the higher order terms,

$$V(\hat{\rho}) = \frac{1}{16nU_1^2(1-U_1)^2}V(T_W) + \frac{1}{16nU_1^2(1-U_1)^2}V(T_B) + \frac{(T_W - T_B)^2(1-2U_1)^2}{16n\{U_1(1-U_1)\}^4}V(U_1)$$

The variance of resampling method given by Chakraborty (Chakraborty and Sen) is

$$V(\hat{\rho}_{RM}) = \frac{1}{16nU_1^2(1-U_1^2)}\left[\frac{1}{n^2-\sum_{i=1}^{k} n_i^2} + \{2\alpha(1-\alpha)+1\}^2 + \frac{\alpha(1-\alpha)}{\sum_{i=1}^{k} n_i^2}[(1+\alpha-\rho\alpha)\{\alpha + \rho(1-\alpha)\} + (1-\alpha+\rho\alpha)\{2-\alpha-\rho\,(1-\alpha)\} + 2(1+\rho)\{1-\alpha(1-\alpha)(1+\rho)\}] + \frac{\alpha(1-\alpha)(T_W-T_B)^2(1-2U_1)^2}{\{U_1(1-U_1)\}^2}\left[\frac{1}{n} + \frac{\rho}{n^2}\sum_{i=1}^{k} n_i(n_i-1)\right]\right]$$

Confidence Interval for RM estimator

The confidence interval for estimate ρ_{RM} is given by $\hat{\rho}_{\mathrm{RM}} \pm \mathrm{Z}_{\alpha/2}\sqrt{\mathrm{var}(\hat{\rho}_{\mathrm{RM}})}$

The 95% confidence interval for estimate ρ_{RM} is given by $\hat{\rho}_{\mathrm{RM}} \pm 1.96\sqrt{\mathrm{var}(\hat{\rho}_{\mathrm{RM}})}$

2.1.3 Monte Carlo simulation and clustered binary data generation

We adopted a simple and efficient method of generating correlated binary variables reported by Lunn in the present study. Fast and efficient simulations to generate clustered data with exchangeable correlation structures are allowed by this method. Using this method we can generate a large number of Monte Carlo samples for ICC estimation since we assumed a fixed correlation between pair responses within a cluster for all the groups. Also, we can use the simulated data to estimate the sample

size during the design phase of a clinical trial and in a parametric bootstrap (Lunn and Davies 1998). An exchangeable correlation matrix Λ is frequently used for correlated data, where $\Lambda_{jl} = \rho$, for all $j \neq l$. The present study generated k clusters of binary variables with exchangeable correlation ρ within each cluster using Monte Carlo simulations (Lunn and Davies 1998)

Based on this method, we simulated the dichotomous outcome data integrating several variations for the different variables we were interested in. The variations include the overall event rate (0.2, 0.4), event rate variation (10%, 50%) between clusters, number of clusters (5, 10, 30), cluster size (10, 25, 50), cluster size variation (10%, 50%) across clusters, and the population intraclass correlation coefficient (0.05, 0.2, 0.4). A fully factorial combination of these six factors was used, giving a total of 216 scenarios. For example one scenario has 30 clusters, event rate of 0.4 with 50% event rate variation clusters, a cluster size of 10 for each cluster with 50% cluster size variation between clusters, and a population intracluster correlation of 0.2. For each unique combination of these variables, we performed 2000 simulations.

CHAPTER 3

RESULTS

Tables 3.1 to 3.12 gives the specific values of mean ICC estimates, length of the confidence interval and the percentage captured of the ICC estimate by their confidence intervals for the 4 ICC estimates for different variations of number of clusters (50, 10, 30), cluster sizes (10, 25, 50), cluster size variations (10%, 50%), event rates (0.2, 0.4), event rate variation (10%, 50%), and population ICC coefficients (0.05, 0.2, 0.4).

Figures 3.1 to 3.10 summarizes the percent coverage and length of confidence interval of the 4 ICC estimators when the assumed population ICC is 0.05, Figures 3.11 to 3.20 summarizes the percent coverage and length of confidence interval of the 4 ICC estimators when the assumed population ICC is 0.2, Figures 3.21 to 3.30 summarizes the percent coverage and length of confidence interval of the 4 ICC estimators when the assumed population ICC is 0.4, Figures 3.31 to 3.42 summarizes the percent coverage and length of confidence intervals for different population ICC estimates, event rates, event rate variations, cluster sizes, cluster size variations and number of clusters and Figures 3.43 and 3.44 shows the overall percent coverage and length of confidence interval for all the 216 scenarios.

Figure 3.1 and 3.2 display the percentage of the true ICC covered by the confidence limits and length of confidence interval for the overall event rate of 0.2 and 0.4 when the population ICC is 0.05. The confidence intervals by FC estimator and PEQ estimator captured the true ICC value 100% of the time for an event rate of 0.2 and 0.4. The confidence intervals by ANOVA estimator which captured the true ICC value 96% of the time when the event rate is 0.2, decreased to 54% when vent rate is 0.4. The confidence intervals by RM estimator captured the true ICC value 98% of the time when event rate is 0.2, which further decreased to 94% as the event rate increases to 0.4. The length of the confidence intervals decreases with an increase in event rate from 0.2 to 0.4 for all the ICC estimators. Also the length of the confidence interval is smaller for the FC estimator compared to the remaining 3 estimators when the event rate is 0.2 and small for the ANOVA method when the event rate is 0.4.

Figure 3.3 and 3.4 display the percentage of the true ICC covered by the confidence limits and length of confidence interval for the overall event rate variation of 10% and 50% when the population ICC is 0.05. The confidence limits by ANOVA estimator captured the true ICC less often, while the confidence limits by remaining 3 estimators captured the true ICC value nearly 100% of the time when the event rate variation is 10%. Also as the event rate variation increases from 10% to 50%, we see a decrease in capture for the confidence limits by the ANOVA and RM estimators. The length of the confidence interval increases with an increase in event rate variation from 10% to 50% except for PEQ method. Also, the length of the confidence interval is

smaller for the ANOVA method compared to remaining 3 estimators when event rate variation is 10% and smaller for the PEQ method when the event rate variation is 50%.

Figure 3.5 and 3.6 display the percentage of the true ICC covered by the confidence limits and length of confidence interval for the overall cluster size of 10, 25, and 50 when the population ICC is 0.05. Except the confidence limits by the ANOVA estimator, all the confidence limits by the 3 estimators captured the true ICC value nearly 100% of the time when the cluster size is 10. As the cluster size increases, the percentage capture of both the confidence limits by the ANOVA and RM estimators decreased. The length of the confidence interval is smaller for ANOVA compared to the remaining 3 estimators for all the three cluster sizes.

Figures 3.7 and 3.8 display the percentage of the true ICC covered by the confidence limits and length of confidence interval for the overall cluster size variation of 10% and 50%, when the population ICC is 0.05. The percentage captured is smallest for the confidence limits by the ANOVA estimate, while intervals captured the true ICC value more than 95% of the time for the 3 remaining estimates. As the CSV increases from 10% to 50%, the percentage captured remained nearly the same. The length of the confidence interval is smaller for ANOVA estimate compared to remaining 3 estimators. The length remained the same even after the increase of cluster size variation from 10% to 50%.

Figures 3.9 and 3.10 display the percentage of the true ICC covered by the confidence limits and length of confidence interval for the overall number of clusters of

5, 10, and 30 when the population ICC is 0.05. When the number of clusters is 5, the percent coverage for the confidence limits by ANOVA estimator is considerably smaller than the others, where the confidence limits by 3 estimators captured the true ICC value nearly 100% of the time. As the number of clusters increases from 5 to 10 to 30, the percent captured of the confidence limits by the ANOVA estimator increased, while percent captured of the confidence limits by the RM estimate decreased. The length of the confidence interval is smaller for the ANOVA estimator compared to remaining 3 estimators when number of clusters is 5 and 10, and is smaller for the PEQ estimate compared to remaining 3 estimators when the number of clusters is 30.

Figures 3.11 to 3.30, where the population ICC is 0.2 and 0.4, display that the confidence limits by the ANOVA estimator captured the true ICC value 100% of time while the confidence limits by the PEQ and FC estimator captured the true ICC value more than 95% of the time in many cases. Also the length of the confidence limits is smaller for the RM estimator compared to remaining 3 estimators.

Figures 3.31 and 3.32 display the percentage of the true ICC covered by the confidence limits and length of confidence interval for the population ICC values of 0.05, 0.2 and 0.4. When the population ICC value is 0.05, the percent coverage for the confidence limits by the ANOVA estimator is much less than for the other three. The remaining confidence limits by the 3 estimators captured the true ICC value more than 95% of the time, with the confidence limits by FC method capturing the true ICC value 100% of the time. As the population ICC value increases from 0.05 to 0.2 to 0.4, the

percent captured by the ANOVA estimator increased, while the percent captured of the confidence limits by the remaining 3 estimators decreased. The length of the confidence interval is smaller for the ANOVA estimator compared to remaining 3 estimators when the population ICC value is 0.05, and is smaller for the RM estimator compared to remaining 3 estimators when the population ICC value is 0.2 and 0.4.

Figure 3.33 and 3.34 display the percentage of the true ICC covered by the confidence limits and length of confidence interval when event rate is 0.2 and 0.4. The confidence intervals by the ANOVA estimator and FC estimator captured the true ICC value nearly 100% of the time for event rate of 0.2 and 0.4 respectively. The length of the confidence intervals decreases with an increase in the event rate from 0.2 to 0.4 for all the ICC estimators except PEQ estimator. Also the length of the confidence interval is smaller for the FC method for both the event rates of 0.2 and 0.4 compared to remaining 3 estimators.

Figure 3.35 and 3.36 display, the percentage of the true ICC covered by the confidence limits and length of confidence interval for the overall event rate variation of 10% and 50%. The confidence limits by the FC estimator captured the true ICC value 97% of the time, while the confidence limits by remaining 3 estimators captured the true ICC value less than 95% of the time when the event rate variation is 10%. Also as event rate variation increases from 10% to 50%, we do not see any change in percent capture by the confidence limits except for the RM estimator, which captures less often. The length of the confidence interval does not change with increase in event rate

variation from 10% to 50%. Also the length of the confidence interval is smaller for the RM estimator for both the event rate variations of 10% and 50%, compared to remaining 3 estimators.

Figures 3.37 and 3.38 display the percentage of the true ICC covered by the confidence limits and length of confidence interval for the overall cluster size of 10, 25, and 50. The confidence limits by the RM estimator captured the true ICC value 97% of the time while the confidence limits by remaining 3 estimators captured the true ICC value less than 95% of the time when the cluster size is 10. As the cluster size increases, the percentage capture of the confidence limits by the RM estimator decreased, while the percent capture of the confidence limits by remaining 3 estimators remained the same. The length of the confidence interval is smaller for the PEQ estimator compared to remaining 3 estimators when the cluster size is 10, and is smaller for the RM estimator compared to remaining 3 estimators when the cluster size is 25 and 50.

Figure 3.39 and 3.40 display the percentage of the true ICC covered by the confidence limits and length of confidence interval for the overall cluster size variation of 10% and 50%. The confidence limits by the ANOVA estimator captured the true ICC value 96% of the time, while it captured the true ICC value less than 95% for the confidence limits by the 3 remaining estimators. As the CSV increases from 10% to 50%, the percentage captured remained nearly the same. The length of the confidence interval is smaller for the RM estimator compared to remaining 3 estimators. The length remained the same even after the increase of cluster size variation from 10% to 50%.

Figure 3.41 and 3.42 display the percentage of the true ICC covered by the confidence limits and length of confidence interval for the overall number of clusters of 5, 10, and 30. When the number of clusters is 5, the percent coverage for the confidence limits by the ANOVA estimator is much less than for the others, while the confidence limits by the PEQ estimator captured the true ICC value nearly 100% of the time. As the number of clusters increases from 5 to 10 to 30, the percent captured of the confidence limits by the ANOVA estimator and the FC estimator increased, while the percent captured of the confidence limits by the PEQ estimator and the RM estimator decreased. The length of the confidence interval is smaller for the RM estimator compared to remaining 3 estimators for all the number of clusters. Also, as number of clusters increases, the length of the confidence limits for all the estimators decreases, except for the ANOVA method, where we see an increase.

Table 3.1 Mean ICC estimate, length of confidence interval and percentage of true ICC captured by its confidence interval with overall event rate of 0.2, population ICC value of 0.05 and event rate variation of 10%

TC	CS	CSV	AOV			FC			PEQ			RM		
			Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured
5	10	10%	0.060	0.400	87.80	0.041	0.339	99.40	0.025	0.398	100	0.077	0.630	99.85
		50%	0.063	0.413	87	0.042	0.350	99.70	0.024	0.439	99.95	0.086	0.631	99.50
	25	10%	0.049	0.352	90.75	0.036	0.348	100	0.021	0.376	100	0.061	0.410	99.70
		50%	0.050	0.361	89.60	0.035	0.357	100	0.020	0.415	100	0.068	0.422	99.60
	50	10%	0.048	0.344	94.25	0.037	0.355	100	0.022	0.371	100	0.055	0.298	99.60
		50%	0.048	0.345	91.60	0.036	0.363	100	0.020	0.404	100	0.059	0.302	99.10
10	10	10%	0.054	0.362	99.65	0.043	0.261	99.50	0.027	0.286	100	0.070	0.458	99.85
		50%	0.056	0.366	99.50	0.045	0.269	99.65	0.027	0.314	100	0.073	0.454	99.35
	25	10%	0.050	0.334	100	0.043	0.266	100	0.026	0.274	100	0.058	0.300	99.45
		50%	0.049	0.336	100	0.041	0.273	100	0.025	0.303	100	0.060	0.302	99.40
	50	10%	0.050	0.327	100	0.044	0.270	100	0.027	0.272	100	0.054	0.224	99.20
		50%	0.048	0.327	100	0.041	0.275	100	0.025	0.297	100	0.056	0.225	98.25
30	10	10%	0.052	0.335	100	0.048	0.178	99.85	0.030	0.180	100	0.056	0.279	99.75
		50%	0.052	0.336	100	0.048	0.183	99.65	0.030	0.197	100	0.058	0.279	99.80
	25	10%	0.051	0.314	100	0.048	0.178	100	0.030	0.172	100	0.052	0.194	99.65
		50%	0.050	0.314	100	0.047	0.182	100	0.029	0.188	100	0.053	0.195	99.40
	50	10%	0.050	0.308	100	0.048	0.179	100	0.031	0.170	100	0.051	0.150	98.35
		50%	0.050	0.309	100	0.048	0.184	100	0.030	0.187	100	0.052	0.150	97.20

Note: TC: total clusters; CS: Cluster sizes; CSV: Cluster size variation

Table 3.2 Mean ICC estimate, length of confidence interval and percentage of true ICC captured by its confidence interval with overall event rate of 0.2, population ICC value of 0.05 and event rate variation of 50%

TC	CS	CSV	AOV			FC			PEQ			RM		
			Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured
5	10	10%	0.074	0.416	86.65	0.051	0.353	99.40	0.031	0.410	100	0.096	0.655	99.50
		50%	0.074	0.423	84.50	0.051	0.360	99.40	0.029	0.448	99.90	0.109	0.656	99.35
	25	10%	0.065	0.368	89.50	0.048	0.361	99.90	0.029	0.387	100	0.085	0.442	98.95
		50%	0.064	0.376	86.80	0.046	0.370	100	0.026	0.426	100	0.094	0.452	97.95
	50	10%	0.063	0.356	89.80	0.048	0.367	100	0.029	0.382	100	0.079	0.324	96.85
		50%	0.064	0.364	89.50	0.048	0.377	100	0.028	0.417	100	0.085	0.329	95.75
10	10	10%	0.069	0.380	99.05	0.057	0.277	99.60	0.035	0.297	100	0.090	0.484	99.15
		50%	0.069	0.382	99.05	0.056	0.284	99.45	0.034	0.324	100	0.094	0.485	98.95
	25	10%	0.066	0.350	99.95	0.057	0.281	99.95	0.035	0.284	100	0.083	0.329	98.40
		50%	0.064	0.353	99.85	0.055	0.287	100	0.033	0.313	100	0.087	0.332	97.60
	50	10%	0.065	0.343	100	0.058	0.284	100	0.036	0.281	100	0.080	0.248	96.25
		50%	0.065	0.346	99.95	0.057	0.291	100	0.034	0.308	100	0.082	0.247	93.10
30	10	10%	0.068	0.352	100	0.063	0.193	99	0.040	0.190	100	0.080	0.307	99.20
		50%	0.068	0.353	100	0.063	0.198	99.45	0.039	0.208	100	0.083	0.307	98.50
	25	10%	0.067	0.331	100	0.064	0.194	100	0.041	0.182	100	0.077	0.218	97.35
		50%	0.066	0.331	100	0.063	0.198	100	0.039	0.199	100	0.079	0.220	96.55
	50	10%	0.067	0.325	100	0.064	0.195	100	0.041	0.181	100	0.079	0.171	91.95
		50%	0.068	0.327	100	0.065	0.200	100	0.041	0.198	100	0.081	0.170	88.50

Note: TC: total clusters; CS: Cluster sizes; CSV: Cluster size variation

Table 3.3 Mean ICC estimate, length of confidence interval and percentage of true ICC captured by its confidence interval with overall event rate of 0.2, population ICC value of 0.2 and event rate variation of 10%

TC	CS	CSV	AOV			FC			PEQ			RM		
			Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured
		10%	0.173	0.990	99.90	0.138	0.602	94.60	0.079	0.734	99.90	0.175	0.750	98.85
	10	50%	0.171	0.987	99.90	0.135	0.606	94.30	0.073	0.790	99.90	0.182	0.743	98.40
		10%	0.170	0.992	100	0.140	0.645	98.25	0.080	0.728	100	0.162	0.533	96.60
5	25	50%	0.167	0.991	100	0.136	0.657	98.15	0.073	0.784	100	0.172	0.545	95.75
		10%	0.172	0.993	100	0.143	0.669	99.85	0.082	0.720	100	0.156	0.392	88.35
	50	50%	0.169	0.990	100	0.139	0.679	100	0.075	0.774	100	0.165	0.40	87.55
		10%	0.187	1	100	0.166	0.520	98.45	0.102	0.556	100	0.186	0.591	98.25
	10	50%	0.184	1	100	0.163	0.528	98.65	0.096	0.608	100	0.184	0.587	97.80
		10%	0.187	1	100	0.170	0.545	99.80	0.104	0.546	100	0.177	0.408	93.20
10	25	50%	0.186	1	100	0.167	0.555	99.60	0.098	0.596	100	0.180	0.412	92.50
		10%	0.188	1	100	0.172	0.554	100	0.105	0.541	100	0.178	0.306	81.90
	50	50%	0.183	0.999	100	0.167	0.560	100	0.097	0.585	100	0.178	0.307	81.45
		10%	0.198	1	100	0.191	0.387	99.40	0.120	0.374	100	0.190	0.399	97.10
	10	50%	0.196	1	100	0.188	0.395	99.55	0.117	0.404	100	0.190	0.398	96.55
		10%	0.199	1	100	0.193	0.408	100	0.121	0.368	100	0.189	0.276	90.15
30	25	50%	0.196	1	100	0.190	0.415	99.85	0.118	0.396	100	0.192	0.278	89.95
		10%	0.198	1	100	0.192	0.414	99.90	0.121	0.365	100	0.192	0.203	79.20
	50	50%	0.197	1	100	0.191	0.421	99.95	0.119	0.393	100	0.191	0.203	77.85

Note: TC: total clusters; CS: Cluster sizes; CSV: Cluster size variation

Table 3.4 Mean ICC estimate, length of confidence interval and percentage of true ICC captured by its confidence interval with overall event rate of 0.2, population ICC value of 0.2 and event rate variation of 50%

TC	CS	CSV	AOV			FC			PEQ			RM		
			Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured
		10%	0.186	0.989	99.80	0.150	0.611	93.55	0.086	0.740	99.80	0.189	0.759	98
	10	50%	0.180	0.985	99.65	0.142	0.611	93.40	0.077	0.791	99.65	0.200	0.755	98.10
		10%	0.183	0.993	100	0.151	0.655	97.95	0.087	0.734	100	0.182	0.553	95
5	25	50%	0.180	0.991	100	0.146	0.663	97.65	0.079	0.788	100	0.195	0.562	93.55
		10%	0.181	0.992	100	0.151	0.672	99.30	0.087	0.730	100	0.178	0.407	86.05
	50	50%	0.183	0.991	100	0.151	0.688	99.45	0.082	0.782	100	0.188	0.414	84.30
		10%	0.204	1	100	0.182	0.536	98.55	0.111	0.566	100	0.205	0.608	97.75
	10	50%	0.197	1	100	0.175	0.538	98	0.103	0.617	100	0.202	0.603	97.15
		10%	0.201	1	100	0.183	0.558	99.80	0.112	0.555	100	0.201	0.424	91.30
10	25	50%	0.198	1	100	0.179	0.566	99.65	0.105	0.606	100	0.206	0.429	90.55
		10%	0.201	1	100	0.184	0.565	99.95	0.112	0.550	100	0.202	0.316	79.10
	50	50%	0.198	1	100	0.181	0.573	100	0.106	0.596	100	0.202	0.314	78.40
		10%	0.212	1	100	0.205	0.395	99.45	0.129	0.383	100	0.213	0.413	95.90
	10	50%	0.209	1	100	0.201	0.403	99.50	0.126	0.413	100	0.212	0.409	94.75
		10%	0.213	1	100	0.207	0.416	100	0.130	0.376	100	0.213	0.282	87.75
30	25	50%	0.210	1	100	0.203	0.424	99.90	0.126	0.405	100	0.215	0.284	87.45
		10%	0.211	1	100	0.205	0.423	99.85	0.129	0.374	100	0.216	0.206	75.90
	50	50%	0.212	1	100	0.206	0.432	99.95	0.128	0.403	100	0.218	0.205	73.55

Note: TC: total clusters; CS: Cluster sizes; CSV: Cluster size variation

Table 3.5 Mean ICC estimate, length of confidence interval and percentage of true ICC captured by its confidence interval with overall event rate of 0.2, population ICC value of 0.4 and event rate variation of 10%

TC	CS	CSV	AOV			FC			PEQ			RM		
			Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured
5	10	10%	0.314	0.994	99.40	0.273	0.633	69.25	0.152	0.865	99.40	0.307	0.830	96.70
		50%	0.306	0.989	98.95	0.263	0.616	67	0.139	0.889	98.95	0.339	0.830	95.55
	25	10%	0.314	1	100	0.275	0.667	68.50	0.151	0.870	100	0.301	0.639	87.70
		50%	0.313	1	100	0.271	0.654	67.55	0.143	0.904	100	0.321	0.646	87.35
	50	10%	0.321	1	100	0.283	0.683	69.20	0.156	0.874	100	0.290	0.467	73.95
		50%	0.314	1	100	0.274	0.666	67.95	0.144	0.900	100	0.309	0.474	71.40
10	10	10%	0.365	0.999	99.95	0.340	0.626	83.80	0.207	0.735	99.90	0.354	0.694	93.35
		50%	0.358	1	100	0.332	0.628	82.40	0.194	0.786	100	0.359	0.702	93.55
	25	10%	0.363	1	100	0.34	0.685	87.95	0.205	0.722	99.85	0.350	0.483	81.65
		50%	0.366	1	100	0.341	0.692	86.30	0.200	0.779	99.90	0.353	0.491	80.65
	50	10%	0.368	1	100	0.345	0.710	90.10	0.209	0.720	99.95	0.349	0.348	64.90
		50%	0.358	1	100	0.334	0.701	86.45	0.194	0.768	99.90	0.353	0.353	63.90
30	10	10%	0.391	1	100	0.382	0.443	94.20	0.242	0.523	98.20	0.387	0.464	91
		50%	0.391	1	100	0.382	0.46	94.55	0.239	0.563	99.65	0.378	0.466	90.85
	25	10%	0.393	1	100	0.384	0.475	96.35	0.242	0.517	98.95	0.382	0.300	78.90
		50%	0.393	1	100	0.384	0.489	96.25	0.240	0.556	99.65	0.382	0.302	76.70
	50	10%	0.392	1	100	0.384	0.482	96.40	0.242	0.516	99.15	0.385	0.213	63.70
		50%	0.392	1	100	0.383	0.495	96.70	0.239	0.551	99.45	0.387	0.214	63.55

Note: TC: total clusters; CS: Cluster sizes; CSV: Cluster size variation

Table 3.6 Mean ICC estimate, length of confidence interval and percentage of true ICC captured by its confidence interval with overall event rate of 0.2, population ICC value of 0.4 and event rate variation of 50%

TC	CS	CSV	AOV			FC			PEQ			RM		
			Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured
5	10	10%	0.322	0.994	99.40	0.281	0.633	69	0.157	0.867	99.40	0.321	0.831	95.60
		50%	0.310	0.990	99	0.267	0.615	66.90	0.141	0.892	99	0.351	0.832	94.80
	25	10%	0.325	1	100	0.285	0.674	69.05	0.157	0.872	100	0.318	0.644	87.05
		50%	0.321	1	100	0.279	0.656	67.85	0.147	0.905	100	0.338	0.648	85.40
	50	10%	0.325	1	100	0.286	0.675	68	0.157	0.874	100	0.311	0.475	71.15
		50%	0.325	1	100	0.283	0.674	68.65	0.151	0.903	100	0.327	0.482	69.95
10	10	10%	0.375	1	100	0.350	0.629	83.80	0.214	0.741	99.80	0.369	0.698	92.70
		50%	0.366	0.999	99.95	0.339	0.631	82.35	0.198	0.789	99.95	0.370	0.708	93.10
	25	10%	0.372	1	100	0.349	0.688	88.10	0.210	0.727	99.80	0.368	0.488	80.60
		50%	0.373	1	100	0.348	0.689	85.50	0.204	0.785	99.90	0.371	0.499	79.30
	50	10%	0.377	1	100	0.354	0.713	89.65	0.214	0.726	99.90	0.370	0.355	65.45
		50%	0.371	1	100	0.347	0.706	86.45	0.202	0.776	99.80	0.373	0.356	62.90
30	10	10%	0.402	1	100	0.393	0.444	94.85	0.249	0.527	98.35	0.406	0.467	90.45
		50%	0.401	1	100	0.391	0.459	94.80	0.245	0.570	99.60	0.397	0.469	89.85
	25	10%	0.404	1	100	0.396	0.475	97	0.249	0.521	99.20	0.401	0.301	78.70
		50%	0.403	1	100	0.394	0.487	96.65	0.247	0.564	99.50	0.399	0.303	73.15
	50	10%	0.403	1	100	0.395	0.482	97.20	0.248	0.521	99.15	0.403	0.215	62.75
		50%	0.403	1	100	0.394	0.494	96.75	0.246	0.558	99.60	0.407	0.216	60.25

Note: TC: total clusters; CS: Cluster sizes; CSV: Cluster size variation

Table 3.7 Mean ICC estimate, length of confidence interval and percentage of true ICC captured by its confidence interval with overall event rate of 0.4, population ICC value of 0.05 and event rate variation of 10%

TC	CS	CSV	AOV			FC			PEQ			RM		
			Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured
5	10	10%	0.064	0.020	8.05	0.043	0.350	99.80	0.015	0.260	100	0.054	0.464	99.60
		50%	0.067	0.021	7.65	0.044	0.362	99.80	0.015	0.282	100	0.057	0.471	99.60
	25	10%	0.052	0.004	2.40	0.037	0.358	100	0.013	0.231	100	0.045	0.312	99.95
		50%	0.054	0.004	2.25	0.038	0.369	100	0.013	0.254	100	0.047	0.317	99.90
	50	10%	0.052	0.001	1.15	0.039	0.365	100	0.014	0.227	100	0.043	0.233	100
		50%	0.052	0.001	1.10	0.038	0.374	100	0.013	0.247	100	0.045	0.237	99.85
10	10	10%	0.058	0.135	81.45	0.046	0.270	99.95	0.016	0.189	100	0.054	0.348	99.85
		50%	0.060	0.097	56.20	0.048	0.280	100	0.017	0.205	100	0.051	0.347	100
	25	10%	0.052	0.091	69.90	0.044	0.273	100	0.016	0.168	100	0.048	0.238	99.95
		50%	0.052	0.062	47.95	0.043	0.281	100	0.015	0.186	100	0.047	0.238	99.95
	50	10%	0.052	0.094	77.85	0.045	0.277	100	0.016	0.165	100	0.048	0.183	100
		50%	0.051	0.059	50.90	0.044	0.283	100	0.015	0.181	100	0.047	0.183	99.95
30	10	10%	0.053	0.246	100	0.049	0.182	99.95	0.018	0.117	100	0.051	0.223	99.95
		50%	0.054	0.244	100	0.049	0.187	100	0.018	0.127	100	0.049	0.221	100
	25	10%	0.052	0.231	100	0.049	0.182	100	0.018	0.105	100	0.051	0.161	100
		50%	0.052	0.228	100	0.049	0.186	100	0.017	0.115	100	0.050	0.160	100
	50	10%	0.052	0.227	100	0.050	0.183	100	0.018	0.103	100	0.051	0.129	100
		50%	0.052	0.225	100	0.050	0.188	100	0.018	0.113	100	0.050	0.128	99.95

Note: TC: total clusters; CS: Cluster sizes; CSV: Cluster size variation

Table 3.8 Mean ICC estimate, length of confidence interval and percentage of true ICC captured by its confidence interval with overall event rate of 0.4, population ICC value of 0.05 and event rate variation of 50%

TC	CS	CSV	AOV			FC			PEQ			RM		
			Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured
5	10	10%	0.098	0.034	10.95	0.071	0.384	99.50	0.026	0.276	100	0.116	0.540	98.35
		50%	0.102	0.033	11.15	0.073	0.396	99.50	0.025	0.298	100	0.114	0.543	98.45
	25	10%	0.095	0.014	5.65	0.072	0.395	100	0.026	0.248	100	0.110	0.380	97.25
		50%	0.097	0.015	6.20	0.073	0.406	100	0.025	0.272	100	0.111	0.382	95.85
	50	10%	0.094	0.011	5.45	0.074	0.400	100	0.026	0.243	100	0.108	0.292	93.20
		50%	0.094	0.009	4.50	0.073	0.409	100	0.025	0.264	100	0.112	0.295	90.65
10	10	10%	0.096	0.159	69.40	0.081	0.309	99.05	0.029	0.204	100	0.123	0.423	98.20
		50%	0.099	0.115	48.90	0.083	0.318	99.05	0.029	0.220	100	0.116	0.417	97.95
	25	10%	0.096	0.108	51.55	0.084	0.314	99.90	0.030	0.184	100	0.121	0.308	95.70
		50%	0.097	0.078	37.60	0.084	0.322	99.90	0.030	0.202	100	0.116	0.302	94.60
	50	10%	0.096	0.109	53.55	0.086	0.317	100	0.031	0.181	100	0.120	0.240	87.25
		50%	0.095	0.078	38.95	0.085	0.323	100	0.030	0.197	100	0.117	0.237	85.95
30	10	10%	0.096	0.289	99.85	0.090	0.221	97.80	0.032	0.133	100	0.126	0.296	96.30
		50%	0.098	0.289	99.85	0.092	0.227	97.45	0.033	0.143	100	0.122	0.291	95.85
	25	10%	0.096	0.275	100	0.092	0.223	99.70	0.033	0.121	100	0.127	0.213	82.30
		50%	0.097	0.273	100	0.092	0.229	100	0.033	0.131	100	0.126	0.211	81.80
	50	10%	0.096	0.272	100	0.093	0.226	100	0.033	0.119	100	0.127	0.155	52.05
		50%	0.097	0.270	100	0.093	0.231	100	0.033	0.129	100	0.127	0.155	52.60

Note: TC: total clusters; CS: Cluster sizes; CSV: Cluster size variation

Table 3.9 Mean ICC estimate, length of confidence interval and percentage of true ICC captured by its confidence interval with overall event rate of 0.4, population ICC value of 0.2 and event rate variation of 10%

TC	CS	CSV	AOV			FC			PEQ			RM		
			Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured
5	10	10%	0.199	0.899	100	0.157	0.711	100	0.055	0.481	100	0.168	0.598	99.20
		50%	0.196	0.890	100	0.153	0.723	100	0.052	0.528	100	0.166	0.599	99.20
	25	10%	0.196	0.889	100	0.159	0.742	100	0.056	0.462	100	0.166	0.432	99.45
		50%	0.195	0.877	100	0.156	0.758	100	0.052	0.506	100	0.173	0.441	98.60
	50	10%	0.197	0.886	100	0.163	0.754	100	0.057	0.458	100	0.168	0.337	95.25
		50%	0.198	0.872	100	0.161	0.770	100	0.053	0.495	100	0.173	0.341	94.50
10	10	10%	0.201	0.973	100	0.179	0.578	100	0.064	0.354	100	0.184	0.483	99.50
		50%	0.202	0.971	100	0.178	0.591	99.95	0.063	0.388	100	0.181	0.480	99.50
	25	10%	0.201	0.963	100	0.182	0.597	100	0.065	0.343	100	0.185	0.352	98.45
		50%	0.198	0.959	100	0.178	0.608	100	0.062	0.375	100	0.184	0.353	98.45
	50	10%	0.201	0.958	100	0.183	0.603	100	0.065	0.340	100	0.187	0.264	95.25
		50%	0.199	0.953	100	0.180	0.614	100	0.063	0.369	100	0.184	0.265	94.95
30	10	10%	0.202	0.998	100	0.194	0.419	100	0.070	0.233	92.60	0.194	0.335	99.55
		50%	0.202	0.998	100	0.194	0.429	100	0.069	0.253	99.15	0.192	0.333	99.55
	25	10%	0.203	0.994	100	0.196	0.435	100	0.070	0.227	92.20	0.196	0.221	99
		50%	0.200	0.993	100	0.194	0.443	100	0.069	0.246	99.55	0.195	0.221	98.90
	50	10%	0.202	0.991	100	0.196	0.439	100	0.070	0.226	94.10	0.198	0.157	97.90
		50%	0.202	0.991	100	0.196	0.448	100	0.070	0.243	99.35	0.195	0.157	97.30

Note: TC: total clusters; CS: Cluster sizes; CSV: Cluster size variation

Table 3.10 Mean ICC estimate, length of confidence interval and percentage of true ICC captured by its confidence interval with overall event rate of 0.4 population ICC value of 0.2 and event rate variation of 50%

TC	CS	CSV	AOV			FC			PEQ			RM		
			Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured
5	10	10%	0.229	0.919	100	0.185	0.736	100	0.065	0.499	100	0.228	0.650	97.30
		50%	0.231	0.910	100	0.184	0.752	99.95	0.062	0.545	100	0.224	0.649	96.65
	25	10%	0.230	0.916	100	0.190	0.771	100	0.067	0.481	100	0.227	0.471	94.45
		50%	0.231	0.907	100	0.189	0.787	100	0.064	0.526	100	0.230	0.473	92.25
	50	10%	0.228	0.914	100	0.190	0.780	100	0.067	0.477	100	0.223	0.355	86.45
		50%	0.229	0.905	100	0.189	0.796	100	0.064	0.515	100	0.233	0.359	84.80
10	10	10%	0.236	0.983	100	0.212	0.609	100	0.076	0.368	100	0.250	0.530	97.60
		50%	0.237	0.982	100	0.212	0.624	99.95	0.075	0.403	100	0.240	0.524	97.10
	25	10%	0.237	0.979	100	0.216	0.631	100	0.078	0.358	100	0.252	0.372	92.80
		50%	0.238	0.977	100	0.216	0.646	100	0.076	0.391	100	0.242	0.370	91.90
	50	10%	0.238	0.977	100	0.218	0.638	100	0.078	0.356	100	0.247	0.270	83.40
		50%	0.236	0.975	100	0.215	0.649	100	0.076	0.385	100	0.245	0.272	82.45
30	10	10%	0.238	0.999	100	0.230	0.440	99.85	0.083	0.247	96.80	0.261	0.348	94.65
		50%	0.240	0.999	100	0.232	0.453	99.90	0.083	0.268	99.90	0.254	0.346	95.25
	25	10%	0.238	0.999	100	0.231	0.460	100	0.083	0.240	97.30	0.263	0.222	83.20
		50%	0.239	0.999	100	0.232	0.473	100	0.083	0.260	99.85	0.260	0.222	83
	50	10%	0.239	0.998	100	0.233	0.468	100	0.084	0.239	98.25	0.261	0.157	65.50
		50%	0.239	0.998	100	0.232	0.478	100	0.083	0.257	99.90	0.260	0.157	63.10

Note: TC: total clusters; CS: Cluster sizes; CSV: Cluster size variation

Table 3.11 Mean ICC estimate, length of confidence interval and percentage of true ICC captured by its confidence interval with overall event rate of 0.4 population ICC value of 0.4 and event rate variation of 10%

TC	CS	CSV	AOV			FC			PEQ			RM		
			Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured
5	10	10%	0.386	1	100	0.333	0.902	96.95	0.117	0.639	100	0.340	0.728	96.90
		50%	0.376	1	100	0.320	0.900	97.05	0.109	0.693	100	0.354	0.737	96.75
	25	10%	0.384	1	100	0.334	0.942	98.60	0.116	0.624	100	0.344	0.525	88.90
		50%	0.385	1	100	0.331	0.938	97.60	0.111	0.679	100	0.360	0.534	88.20
	50	10%	0.385	1	100	0.335	0.947	98.60	0.117	0.624	100	0.340	0.380	77.90
		50%	0.388	1	100	0.335	0.955	99.10	0.114	0.670	100	0.355	0.385	77.05
10	10	10%	0.400	1	100	0.372	0.832	99.60	0.133	0.483	86.30	0.378	0.592	97.40
		50%	0.395	1	100	0.365	0.841	99.60	0.131	0.525	97.40	0.377	0.592	96.55
	25	10%	0.396	1	100	0.370	0.865	99.35	0.132	0.473	84.60	0.375	0.388	92.85
		50%	0.395	1	100	0.367	0.878	99.20	0.129	0.515	97.40	0.374	0.392	92.50
	50	10%	0.397	1	100	0.372	0.876	99.15	0.134	0.473	84.90	0.377	0.277	86.40
		50%	0.395	1	100	0.368	0.888	99.50	0.130	0.507	97.05	0.376	0.279	85.15
30	10	10%	0.402	1	100	0.392	0.555	100	0.141	0.335	6.95	0.393	0.352	98.20
		50%	0.400	1	100	0.390	0.576	100	0.141	0.361	18.70	0.389	0.352	97.85
	25	10%	0.400	1	100	0.391	0.583	100	0.140	0.329	3.35	0.393	0.223	96.55
		50%	0.401	1	100	0.392	0.604	100	0.140	0.354	13.40	0.391	0.223	94.80
	50	10%	0.400	1	100	0.392	0.590	100	0.141	0.330	2.35	0.395	0.158	92.95
		50%	0.400	1	100	0.391	0.611	100	0.140	0.351	9.65	0.393	0.158	90.75

Note: TC: total clusters; CS: Cluster sizes; CSV: Cluster size variation

Table 3.12 Mean ICC estimate, length of confidence interval and percentage of true ICC captured by its confidence interval with overall event rate of 0.4 population ICC value of 0.4 and event rate variation of 50%.

TC	CS	CSV	AOV			FC			PEQ			RM		
			Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured	Mean	Length	Percent captured
5	10	10%	0.404	1	100	0.351	0.899	96.15	0.122	0.650	100	0.389	0.746	95.45
		50%	0.399	1	100	0.343	0.900	95.80	0.118	0.708	100	0.398	0.745	95.20
	25	10%	0.403	1	100	0.352	0.935	97	0.124	0.643	100	0.390	0.533	86.15
		50%	0.405	1	100	0.351	0.934	97.10	0.120	0.697	100	0.398	0.539	84.90
	50	10%	0.402	1	100	0.353	0.937	97.25	0.123	0.639	100	0.383	0.386	72.90
		50%	0.408	1	100	0.356	0.942	97.30	0.120	0.686	100	0.406	0.391	69.15
10	10	10%	0.423	1	100	0.395	0.843	99.40	0.142	0.494	88.70	0.431	0.602	95.70
		50%	0.421	1	100	0.391	0.855	99.30	0.142	0.540	98.05	0.420	0.599	95.15
	25	10%	0.422	1	100	0.396	0.885	99.70	0.143	0.487	87.20	0.429	0.393	89.15
		50%	0.425	1	100	0.397	0.902	99.40	0.142	0.527	98.05	0.420	0.395	87.40
	50	10%	0.425	1	100	0.399	0.899	99.55	0.144	0.484	87.70	0.424	0.278	78
		50%	0.424	1	100	0.397	0.911	99.45	0.142	0.522	98.25	0.422	0.281	77.30
30	10	10%	0.429	1	100	0.419	0.555	100	0.151	0.345	12.35	0.445	0.353	95
		50%	0.427	1	100	0.417	0.576	100	0.152	0.372	27.10	0.438	0.353	94.60
	25	10%	0.426	1	100	0.417	0.582	100	0.150	0.340	7.05	0.444	0.223	87.85
		50%	0.429	1	100	0.420	0.604	100	0.150	0.364	22.15	0.440	0.223	86.60
	50	10%	0.427	1	100	0.419	0.590	100	0.151	0.340	5.90	0.443	0.158	73.75
		50%	0.429	1	100	0.420	0.610	100	0.151	0.362	18.65	0.443	0.158	70.55

Note: TC: total clusters; CS: Cluster sizes; CSV: Cluster size variation

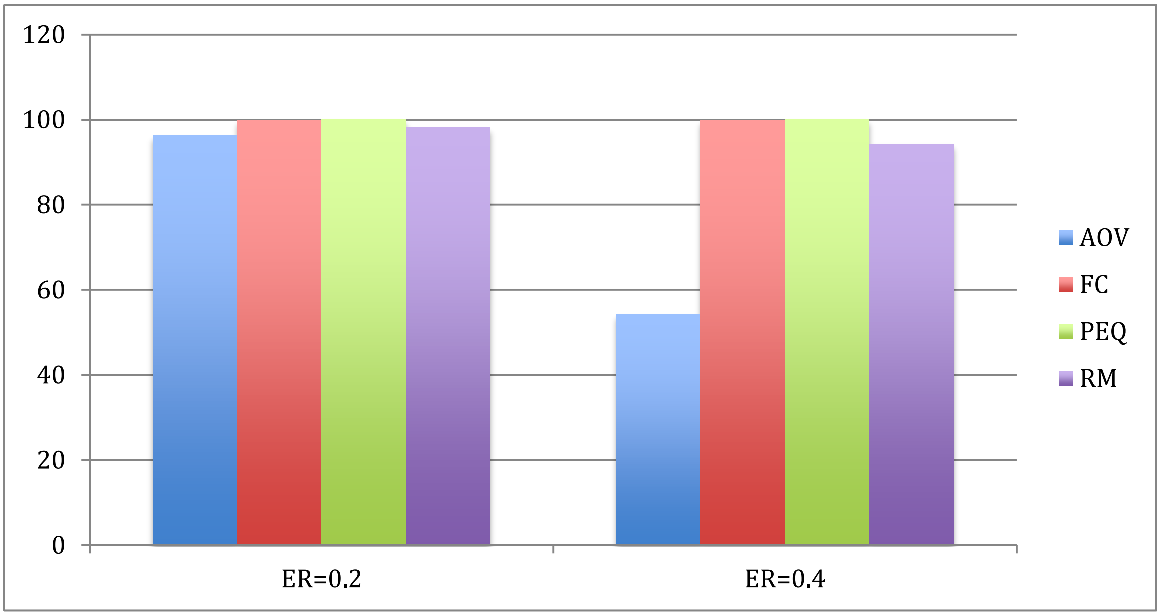

Figure 3.1 Percent coverage of confidence interval for ICC with event rate of 0.2 and 0.4, assuming the population ICC value of 0.05

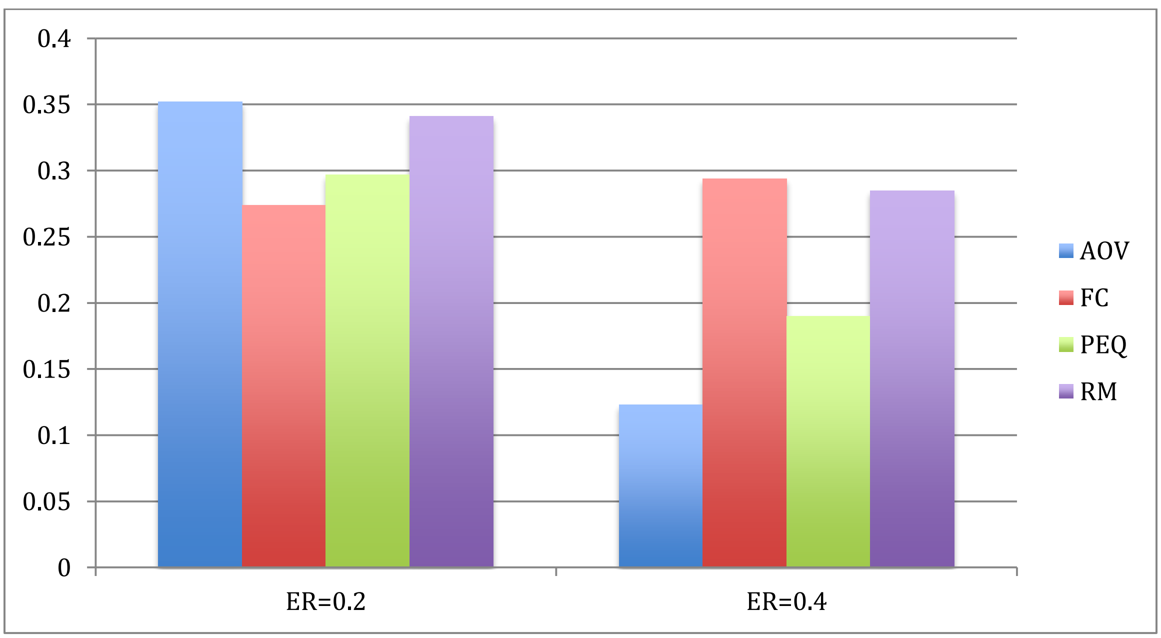

Figure 3.2 length of confidence interval for ICC with event rate of 0.2 and 0.4, assuming the population ICC value of 0.05

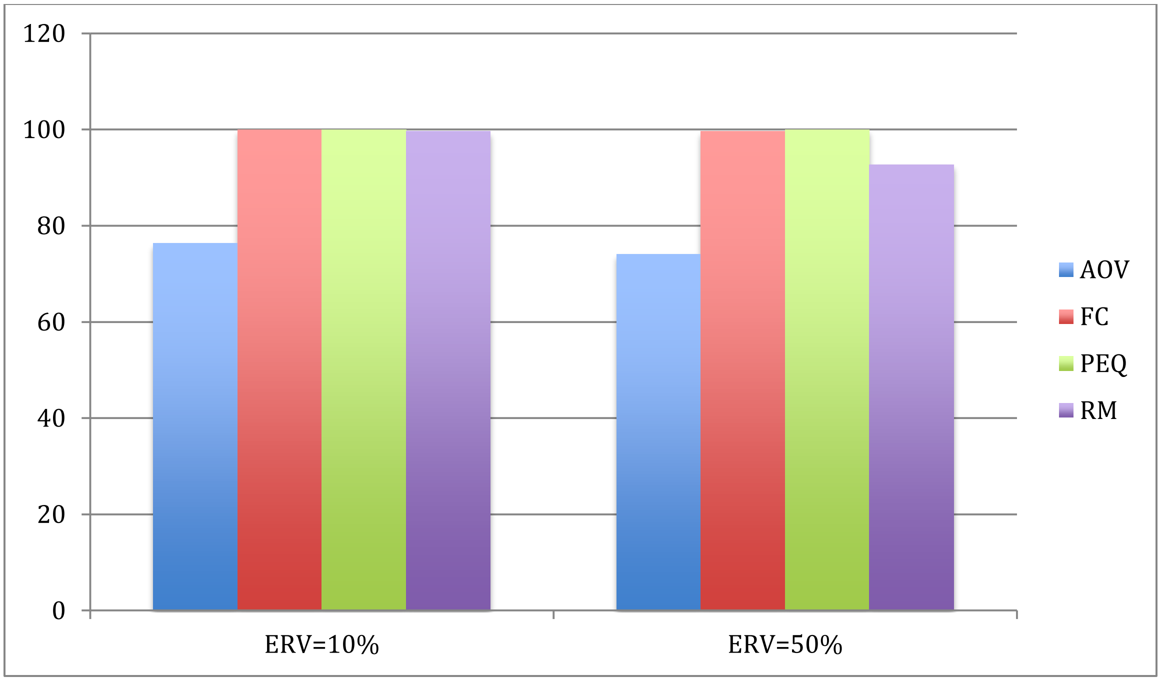

Figure 3.3 percent coverage of confidence interval for ICC with event rate variation of 10% and 50%, assuming the population ICC value of 0.05

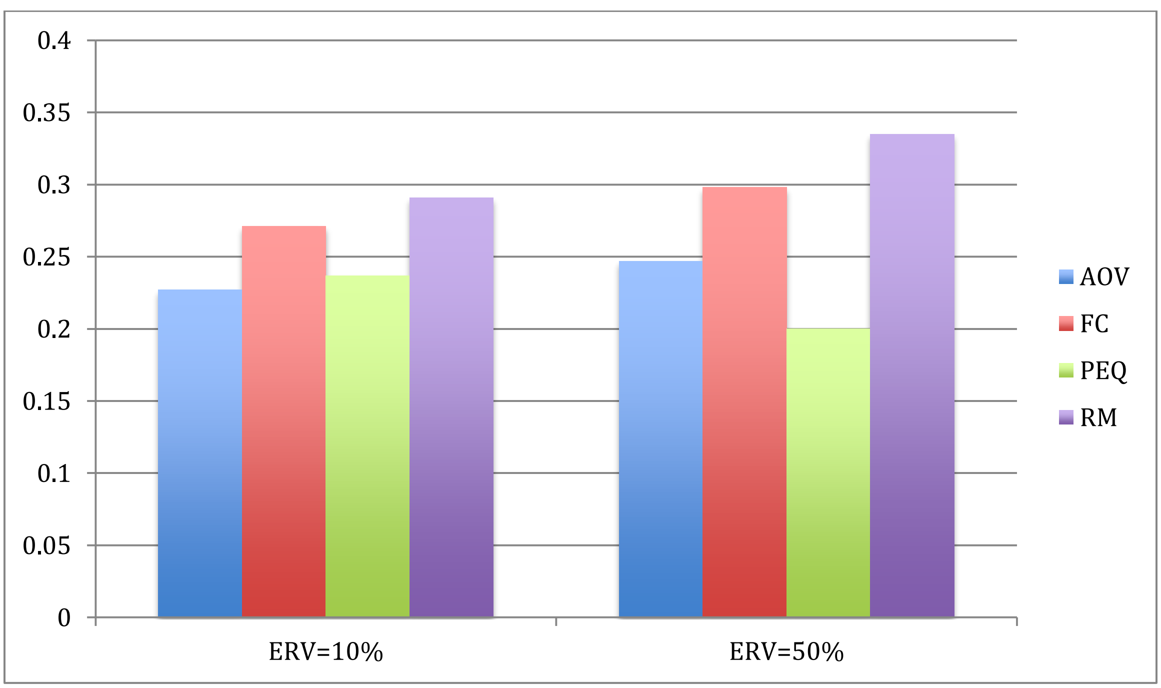

Figure 3.4 length of confidence interval for ICC with event rate variation of 10% and 50%, assuming the population ICC value of 0.05

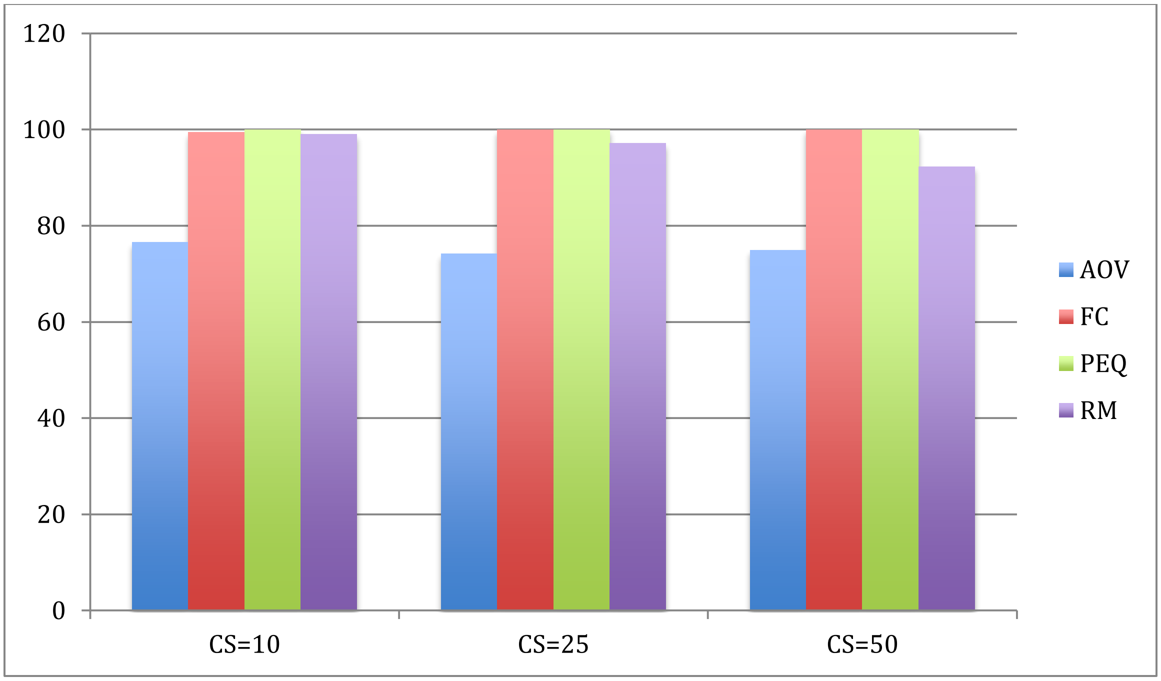

Figure 3.5 percent coverage of confidence interval for ICC with cluster size of 10, 25 and 50,, assuming the population ICC value of 0.05

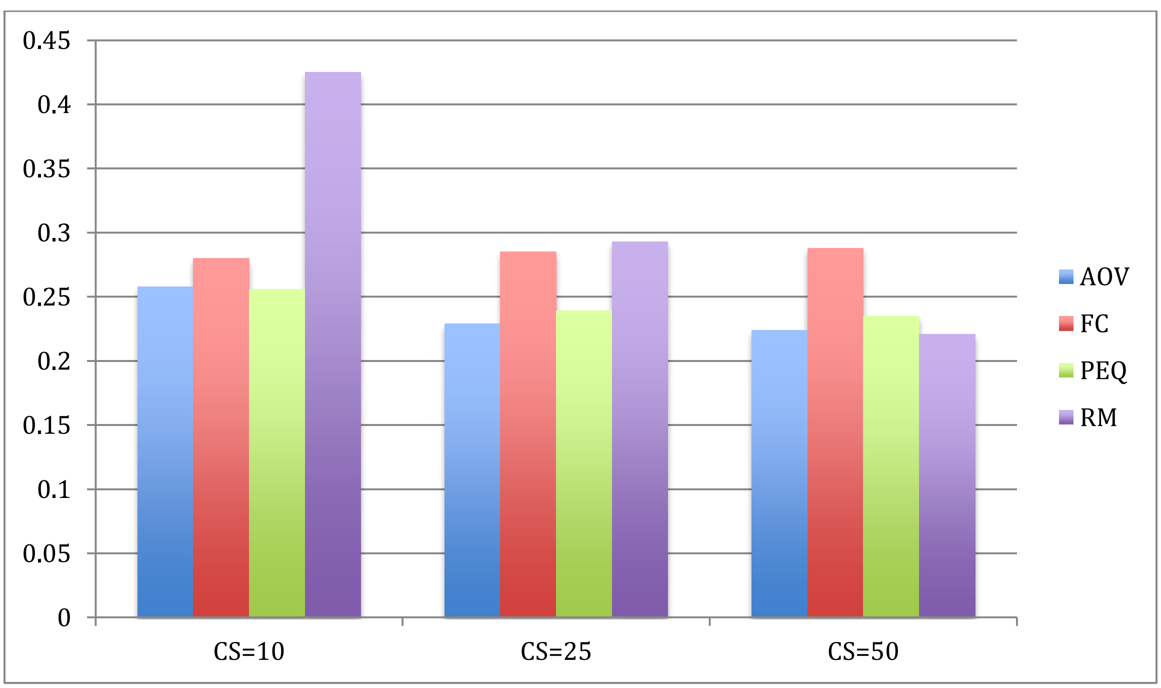

Figure 3.6 length of confidence interval for ICC with cluster size of 10, 25 and 50, assuming the population ICC value of 0.05

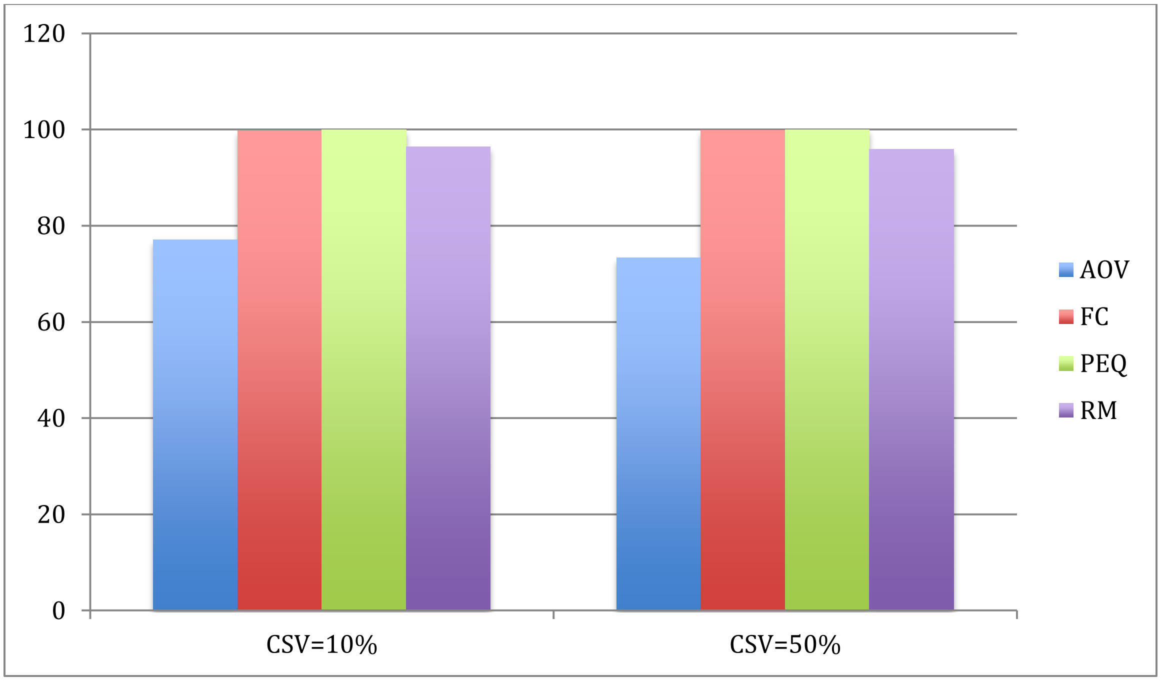

Figure 3.7 percent coverage of confidence interval for ICC with cluster size variation of 10% and 50%, assuming the population ICC value of 0.05

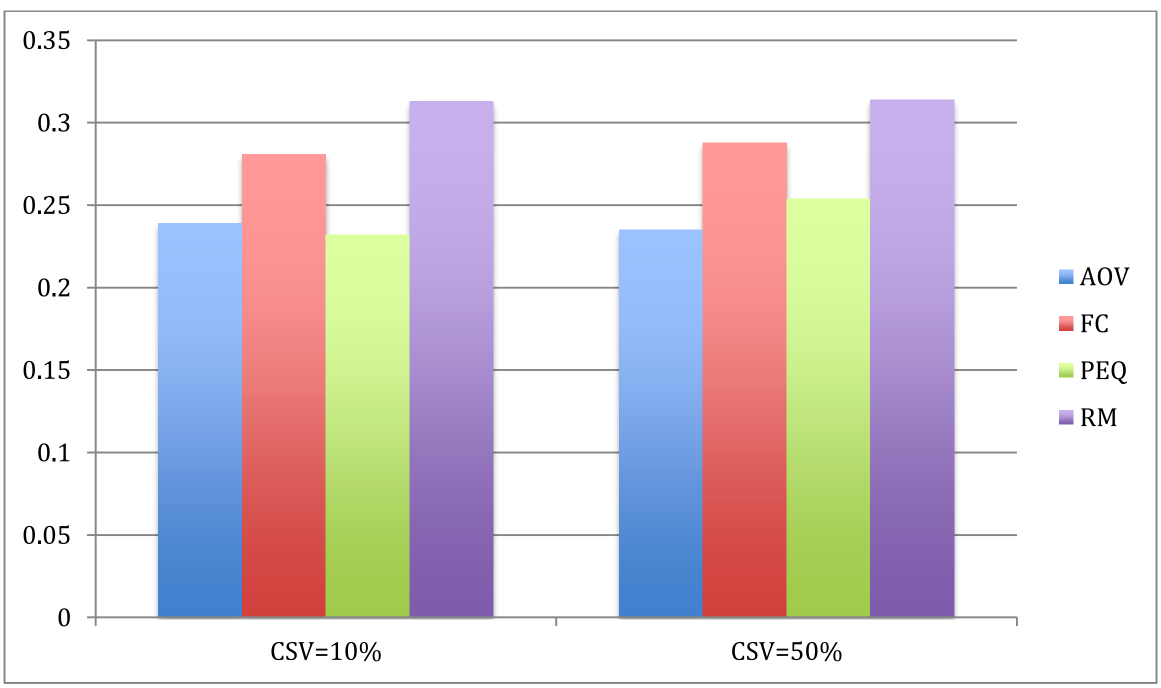

Figure 3.8 length of confidence interval for ICC with cluster size variation of 10% and 50%, assuming the population ICC value of 0.05

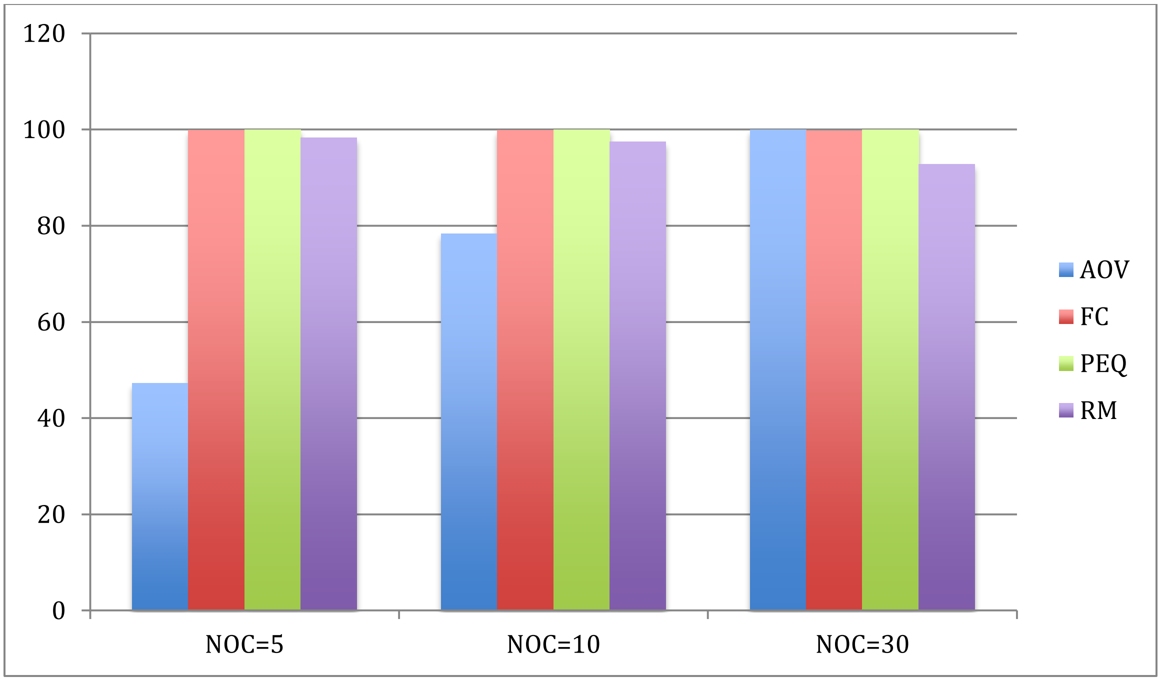

Figure 3.9 percent coverage of confidence interval for ICC with total clusters of 5, 10 and 30, assuming the population ICC value of 0.05

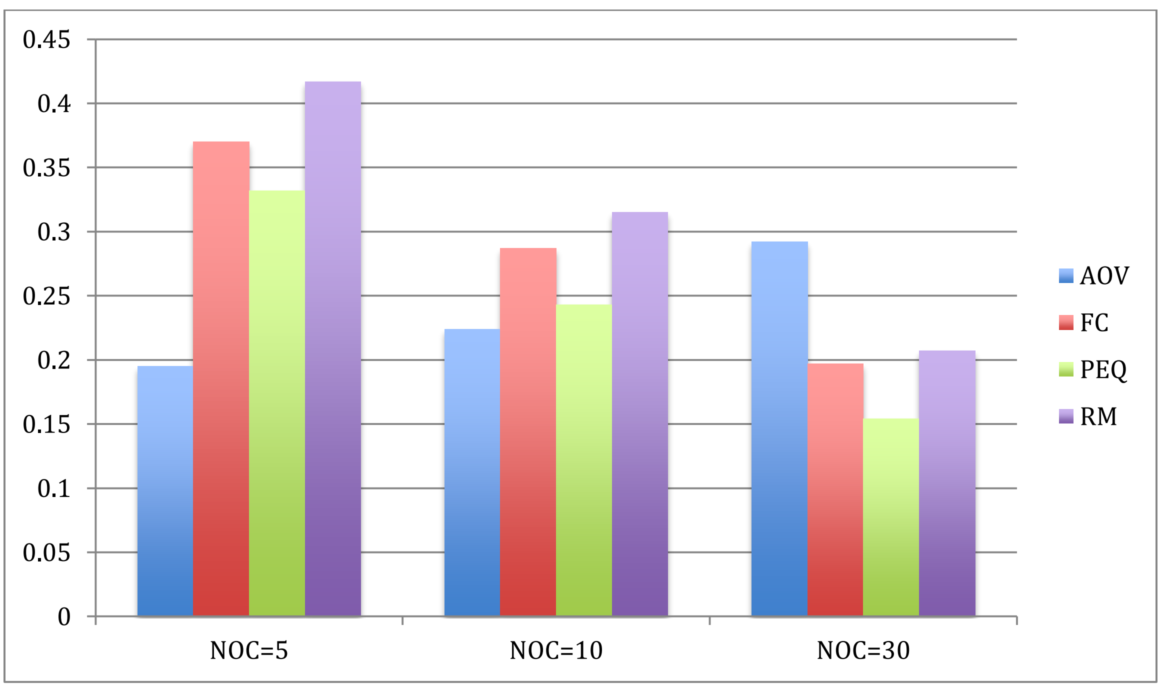

Figure 3.10 length of confidence interval for ICC with total clusters of 5, 10 and 30, assuming the population ICC value of 0.05

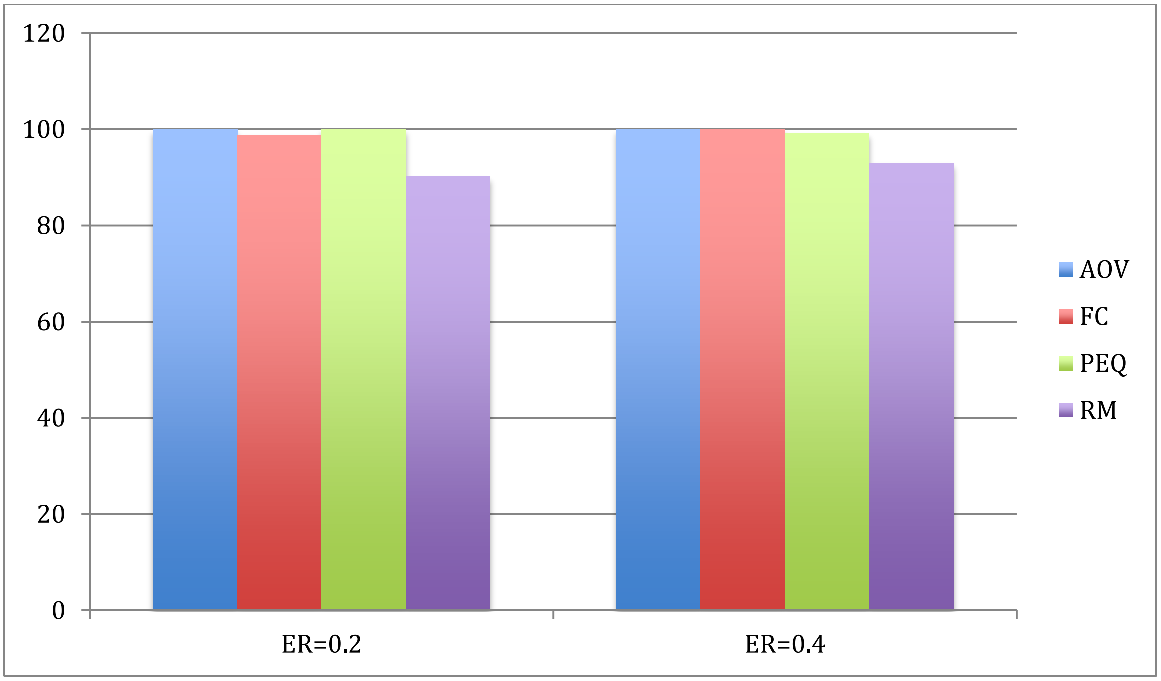

Figure 3.11 Percent coverage of confidence interval for ICC with event rate of 0.2 and 0.4, assuming the population ICC value of 0.2

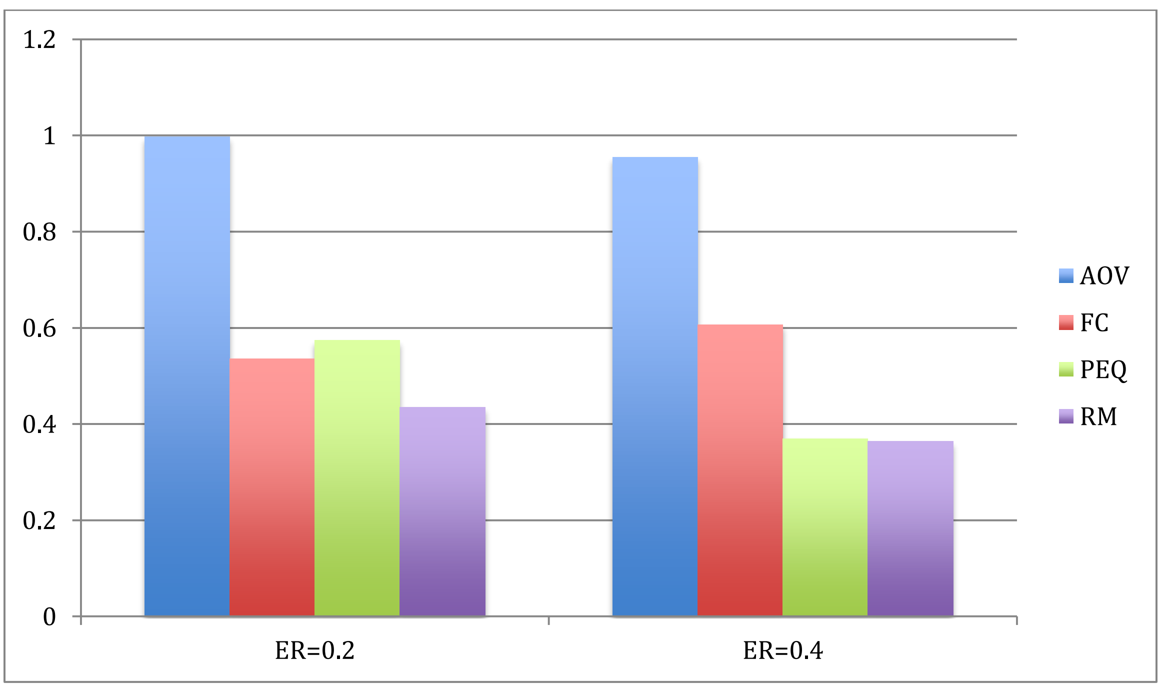

Figure 3.12 length of confidence interval for ICC with event rate of 0.2 and 0.4, assuming the population ICC value of 0.2

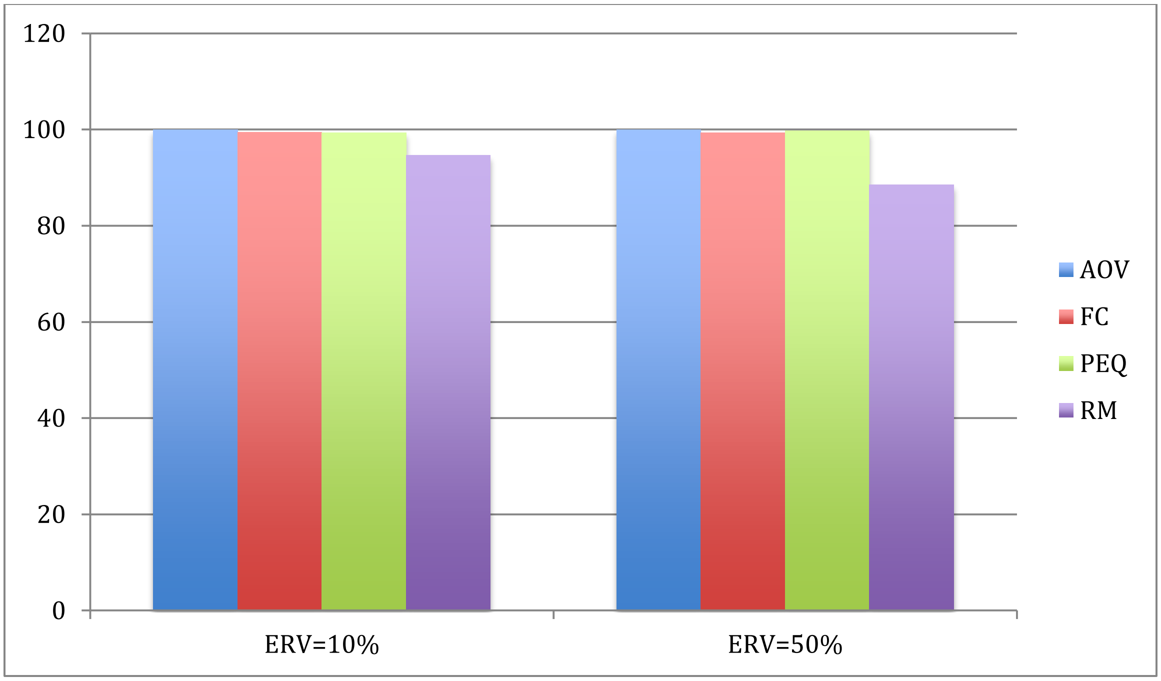

Figure 3.13 percent coverage of confidence interval for ICC with event rate variation of 10% and 50%, assuming the population ICC value of 0.2

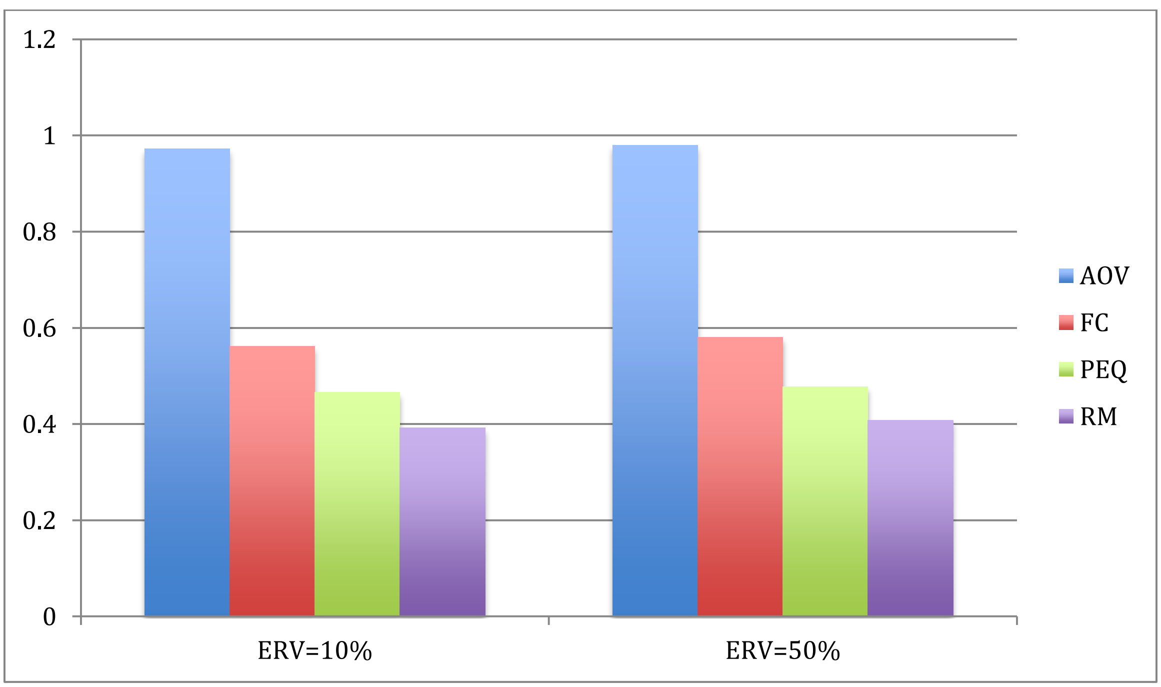

Figure 3.14 length of confidence interval for ICC with event rate variation of 10% and 50%, assuming the population ICC value of 0.2

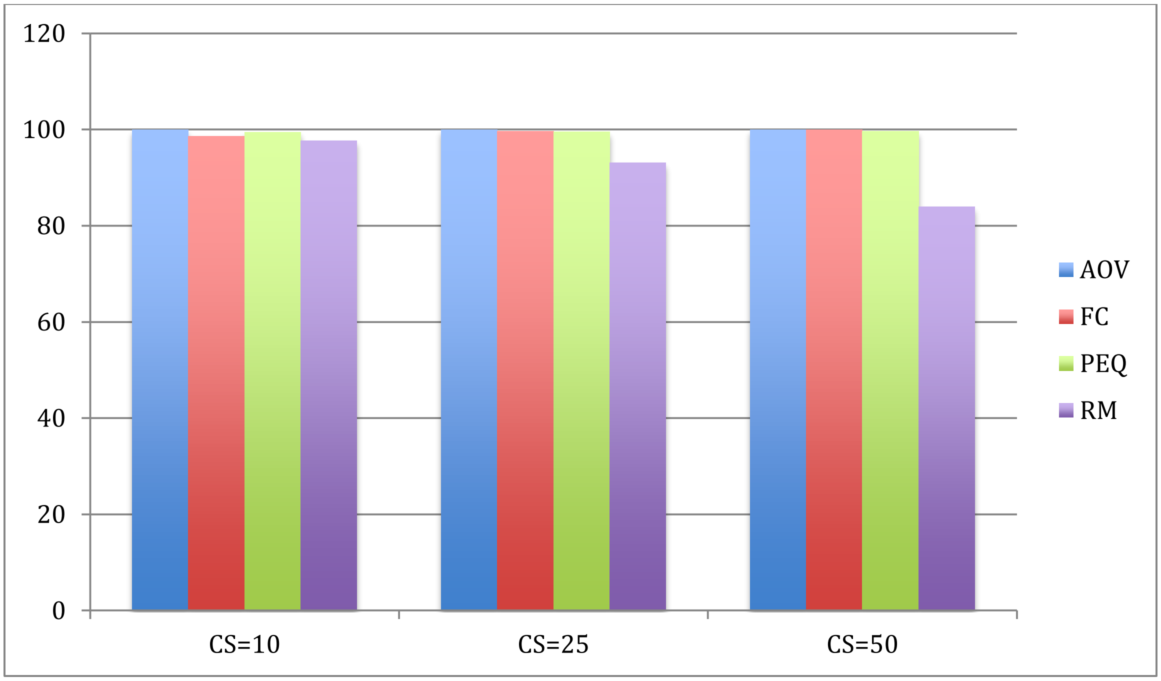

Figure 3.15 percent coverage of confidence interval for ICC with cluster size of 10, 25 and 50, assuming the population ICC value of 0.2

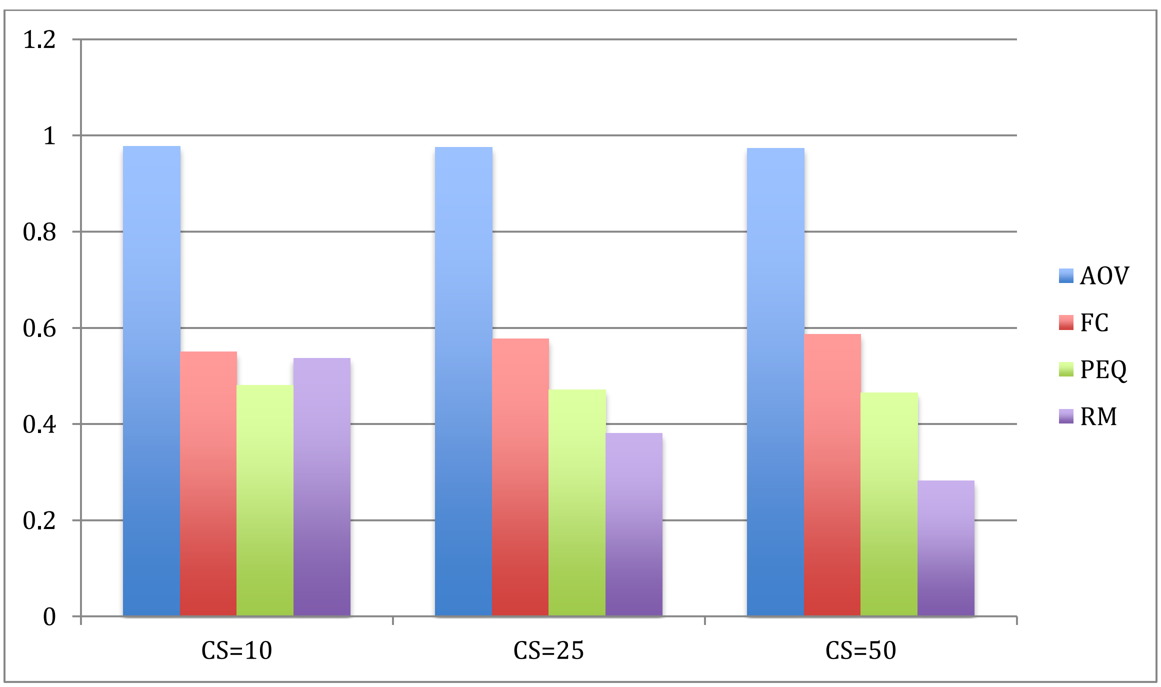

Figure 3.16 length of confidence interval for ICC with cluster size of 10, 25 and 50, assuming the population ICC value of 0.2

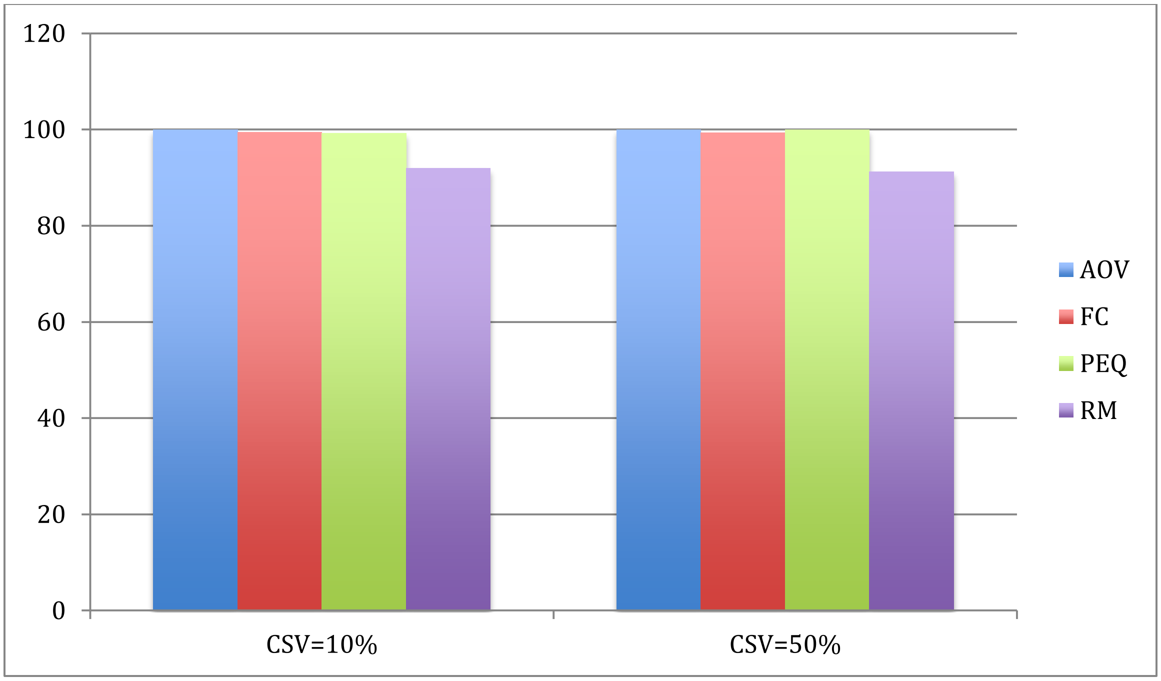

Figure 3.17 percent coverage of confidence interval for ICC with cluster size variation of 10% and 50%, assuming the population ICC value of 0.2

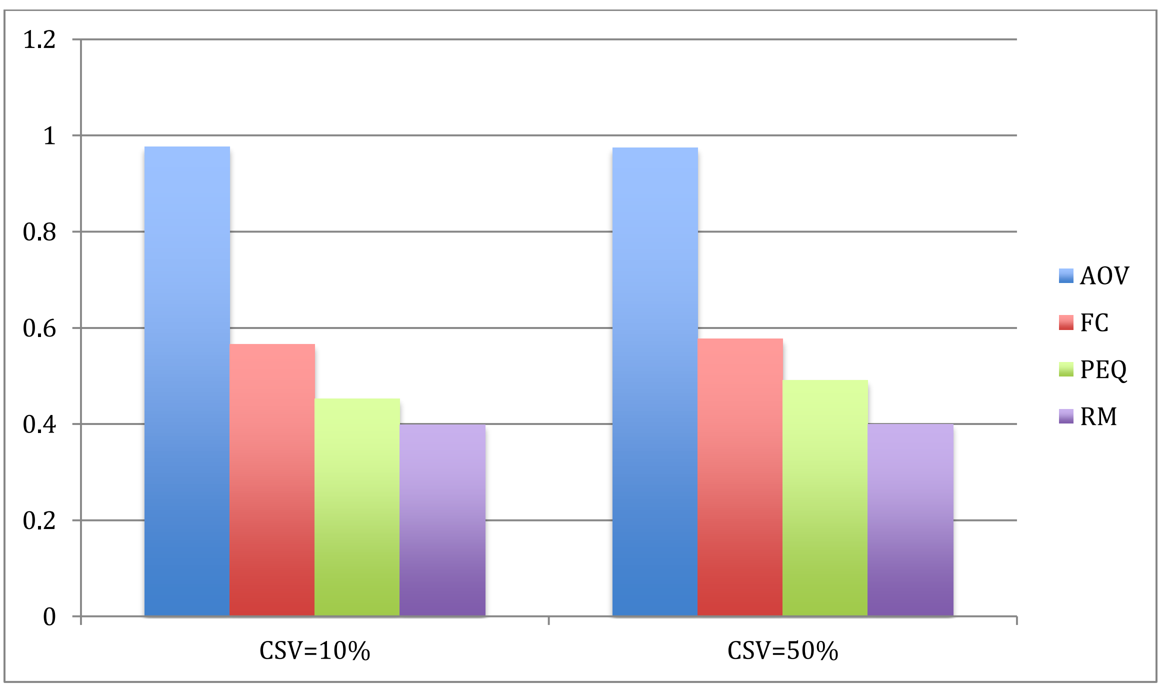

Figure 3.18 length of confidence interval for ICC with cluster size variation of 10% and 50%, assuming the population ICC value of 0.2

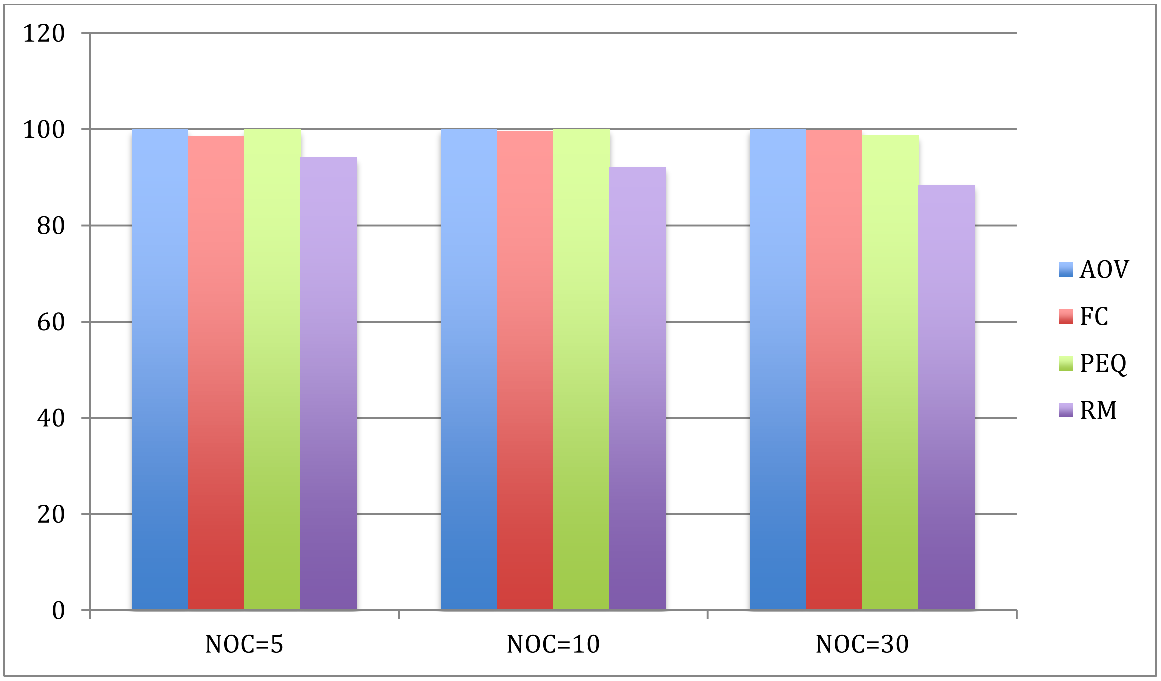

Figure 3.19 percent coverage of confidence interval for ICC with total clusters of 5, 10 and 30, assuming the population ICC value of 0.2

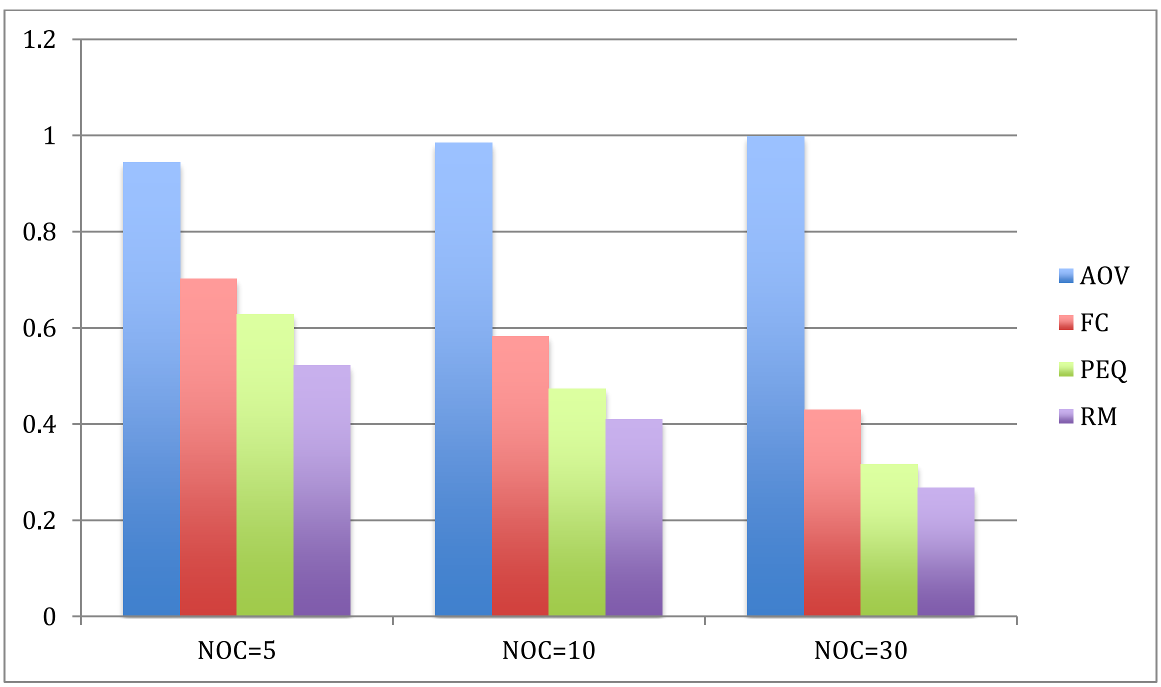

Figure 3.20 length of confidence interval for ICC with total clusters of 5, 10 and 30, assuming the population ICC value of 0.2

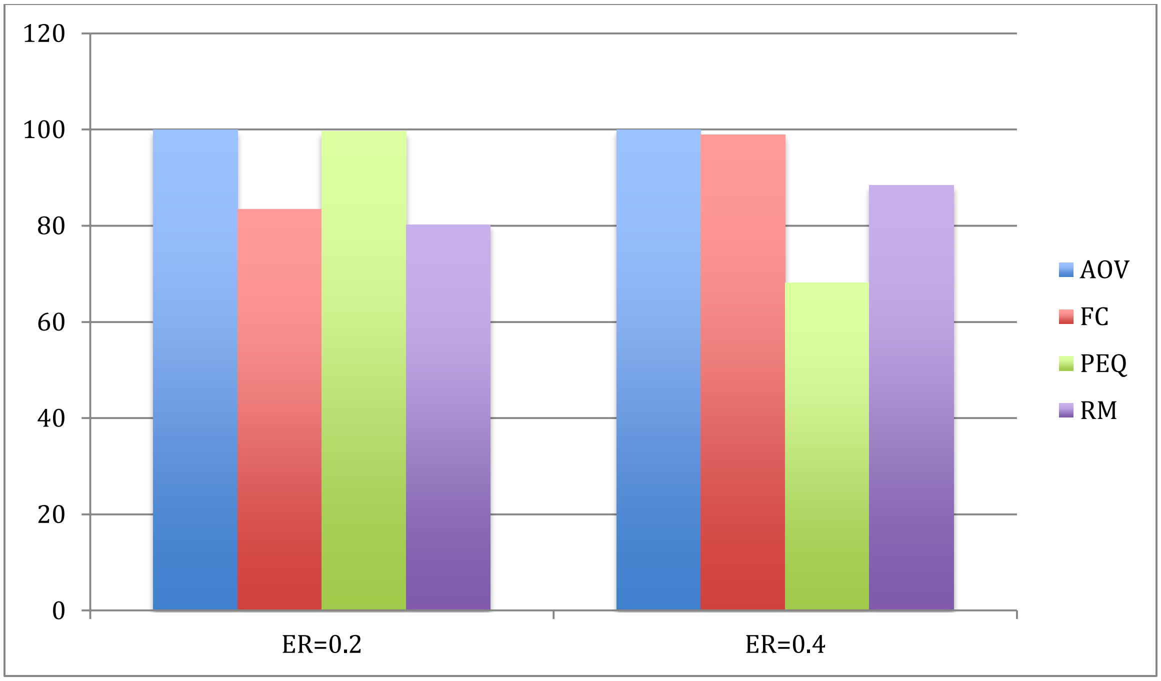

Figure 3.21 Percent coverage of confidence interval for ICC with event rate of 0.2 and 0.4, assuming the population ICC value of 0.4

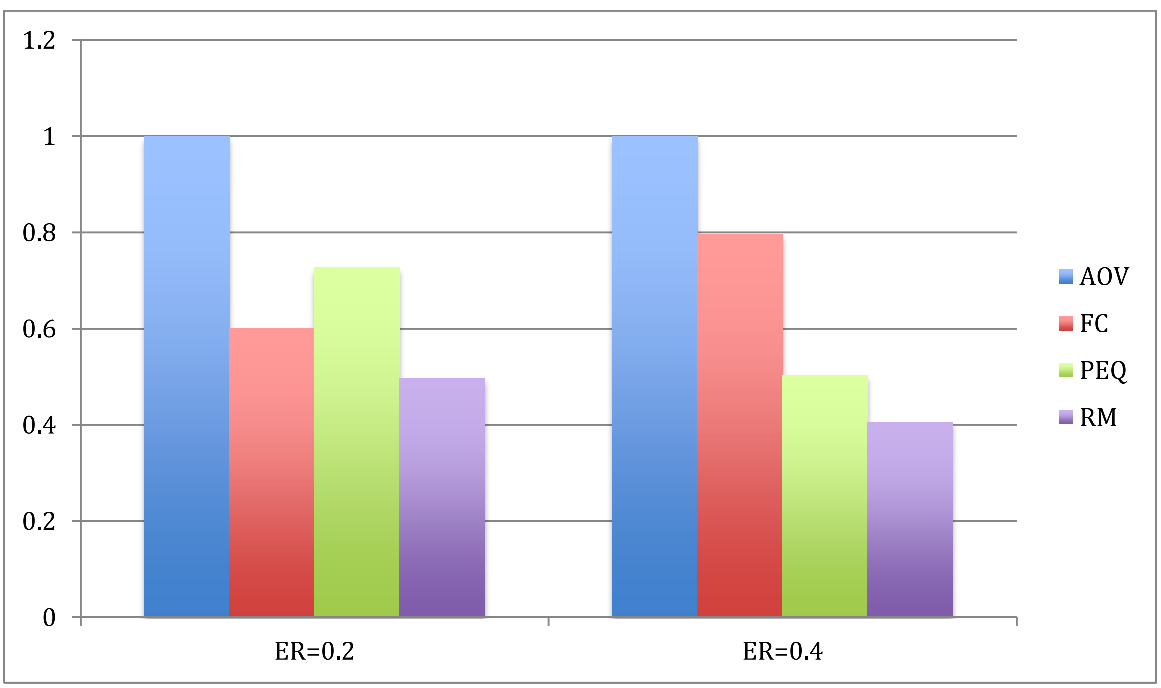

Figure 3.22 length of confidence interval for ICC with event rate of 0.2 and 0.4, assuming the population ICC value of 0.4

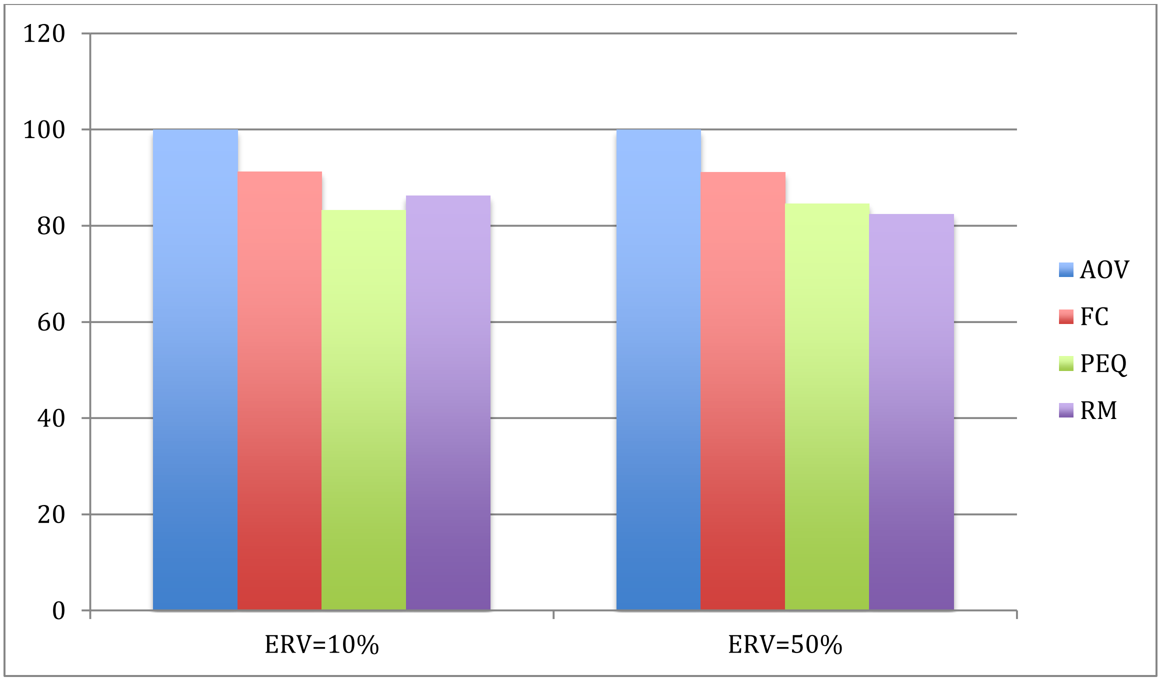

Figure 3.23 percent coverage of confidence interval for ICC with event rate variation of 10% and 50%, assuming the population ICC value of 0.4

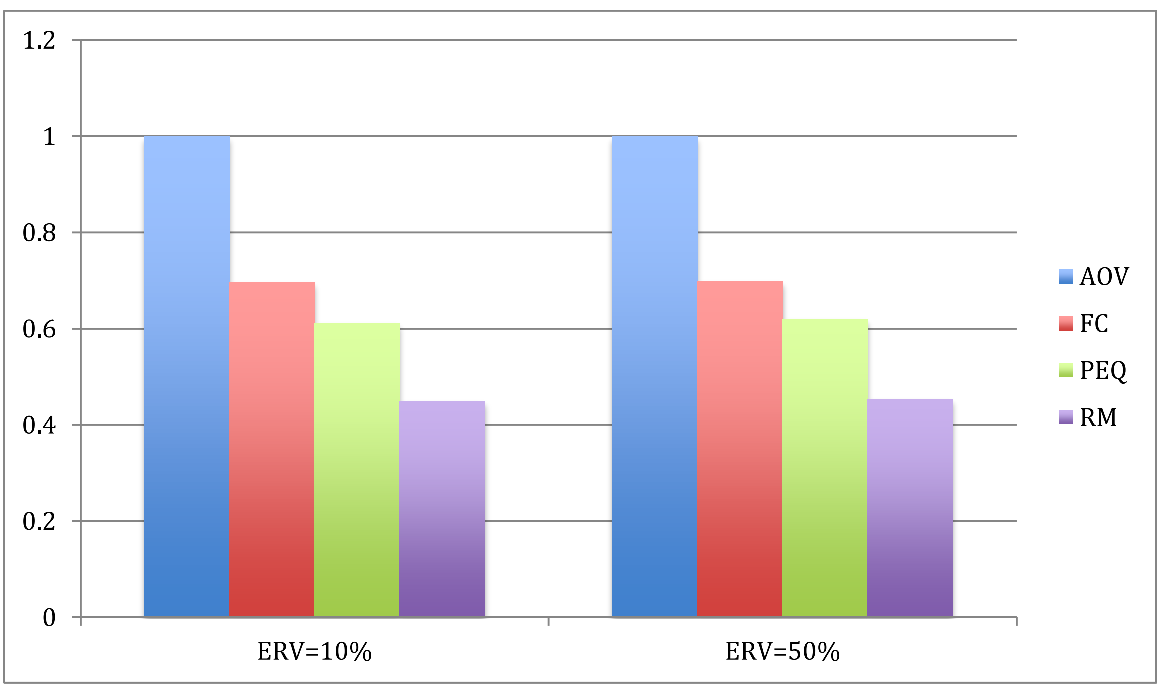

Figure 3.24 length of confidence interval for ICC with event rate variation of 10% and 50%, assuming the population ICC value of 0.4

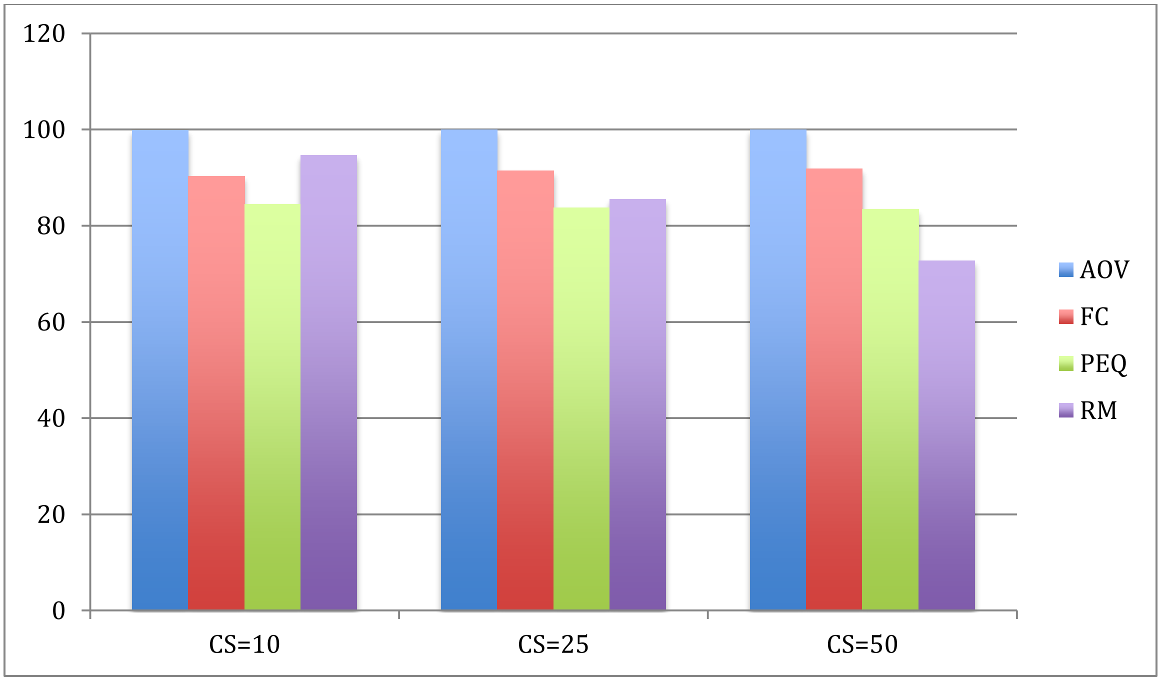

Figure 3.25 percent coverage of confidence interval for ICC with cluster size of 10, 25 and 50, assuming the population ICC value of 0.4

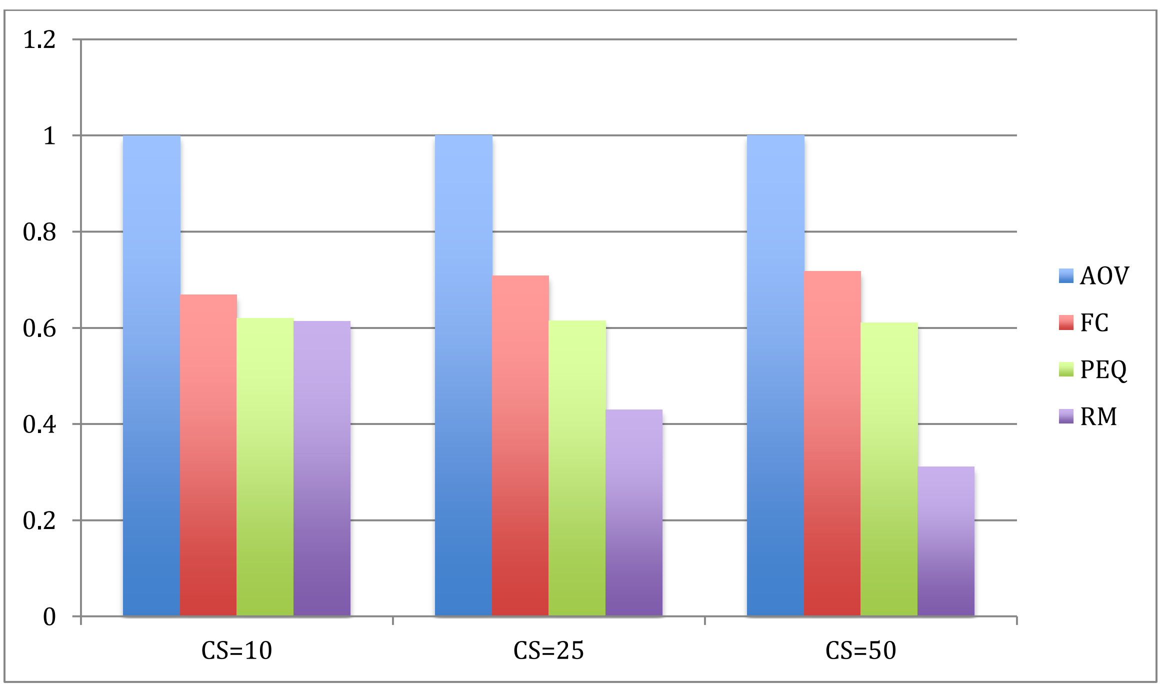

Figure 3.26 length of confidence interval for ICC with cluster size of 10, 25 and 50, assuming the population ICC value of 0.4

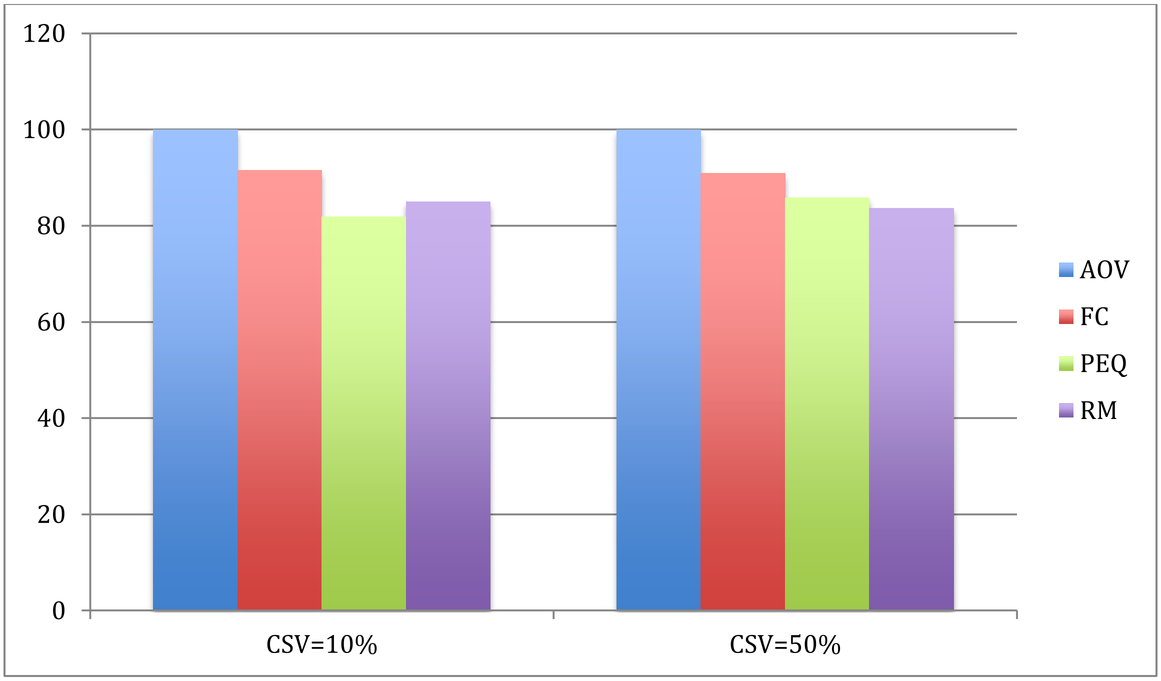

Figure 3.27 percent coverage of confidence interval for ICC with cluster size variation of 10% and 50%, assuming the population ICC value of 0.4

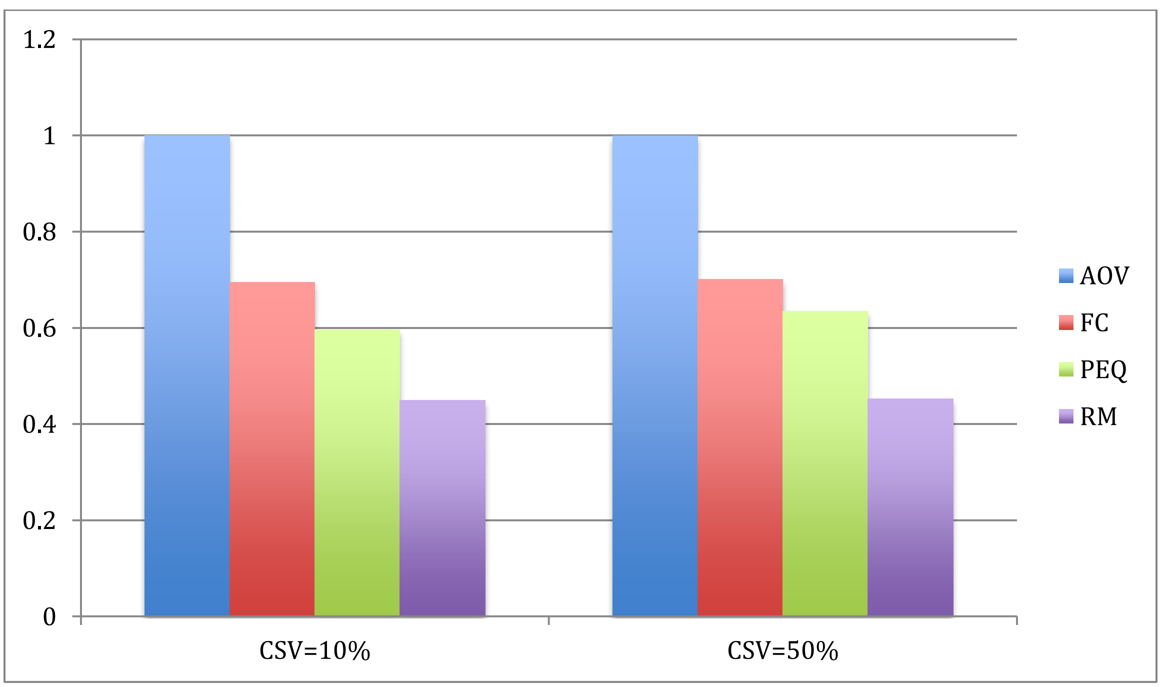

Figure 3.28 length of confidence interval for ICC with cluster size variation of 10% and 50%, assuming the population ICC value of 0.4

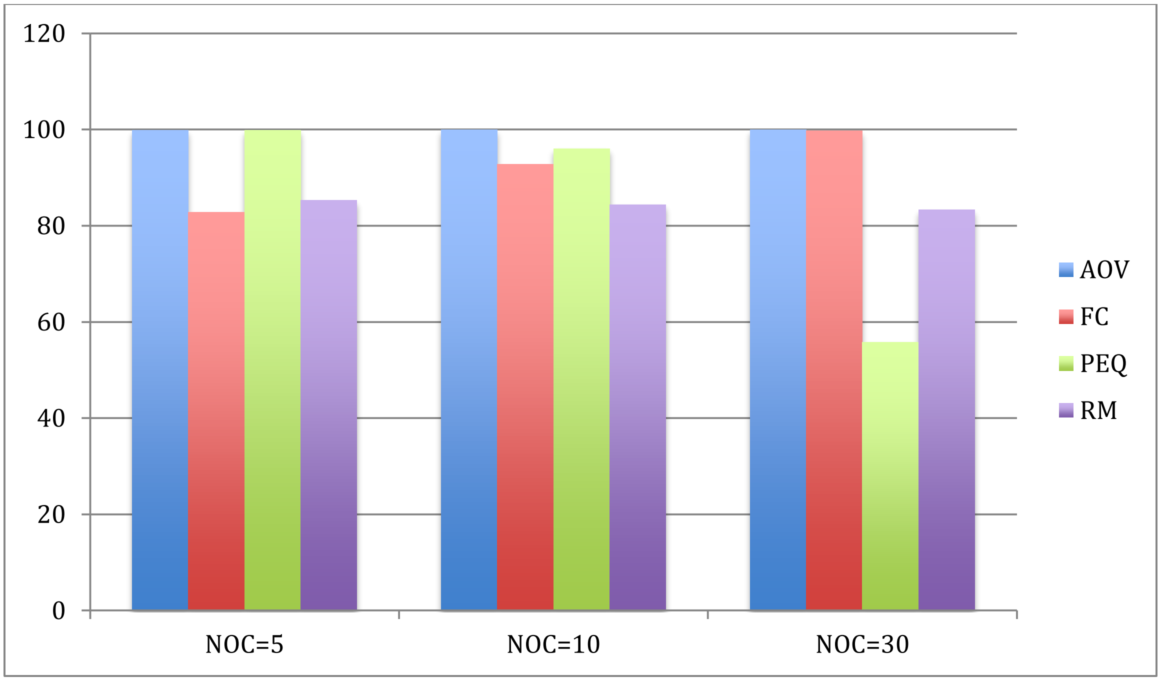

Figure 3.29 percent coverage of confidence interval for ICC with total clusters of 5, 10 and 30, assuming the population ICC value of 0.4

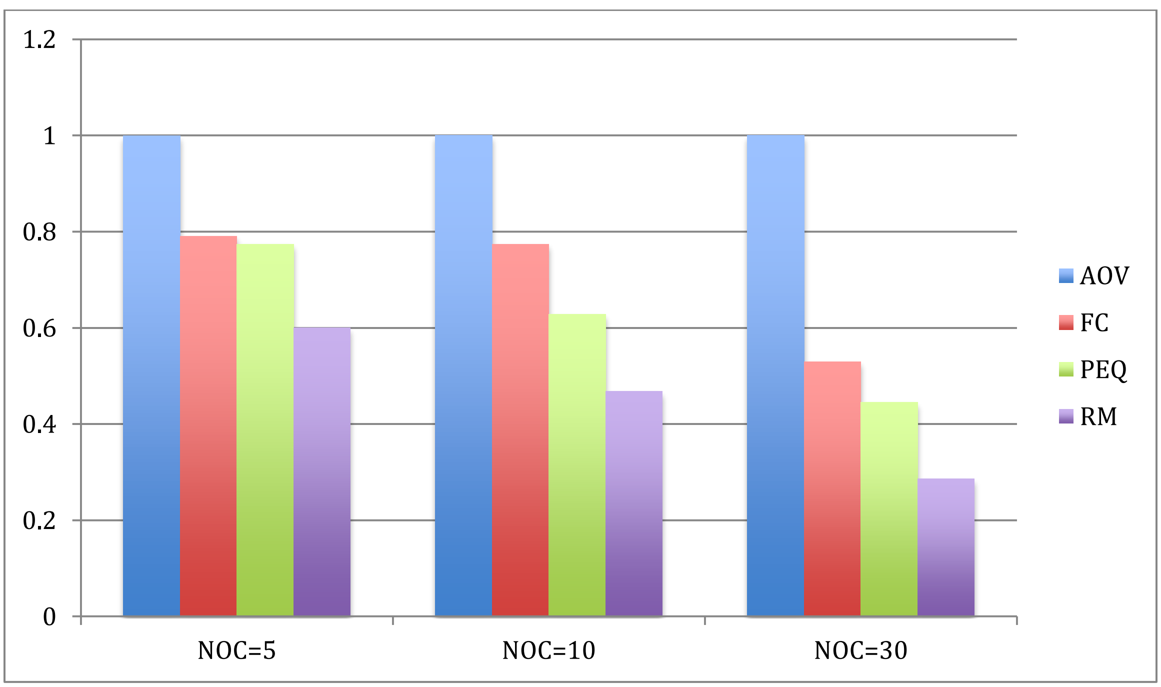

Figure 3.30 length of confidence interval for ICC with total clusters of 5, 10 and 30, assuming the population ICC value of 0.4

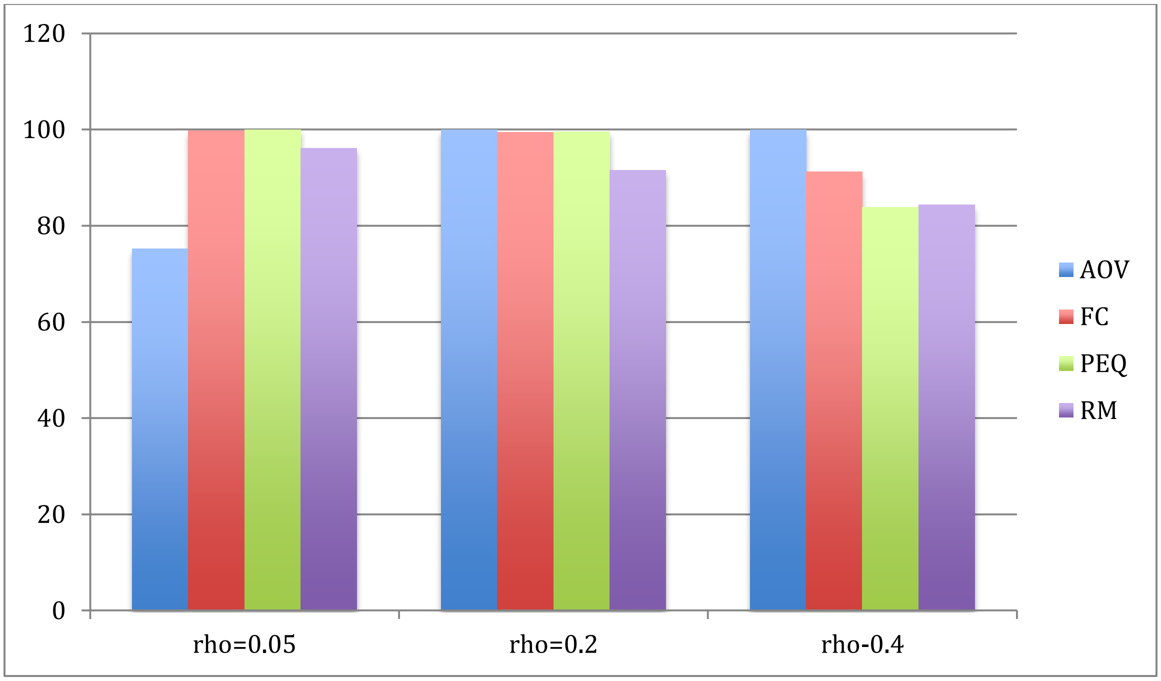

Figure 3.31 percent coverage of confidence interval for ICC with the population ICC value of 0.05, 0.2 and 0.4

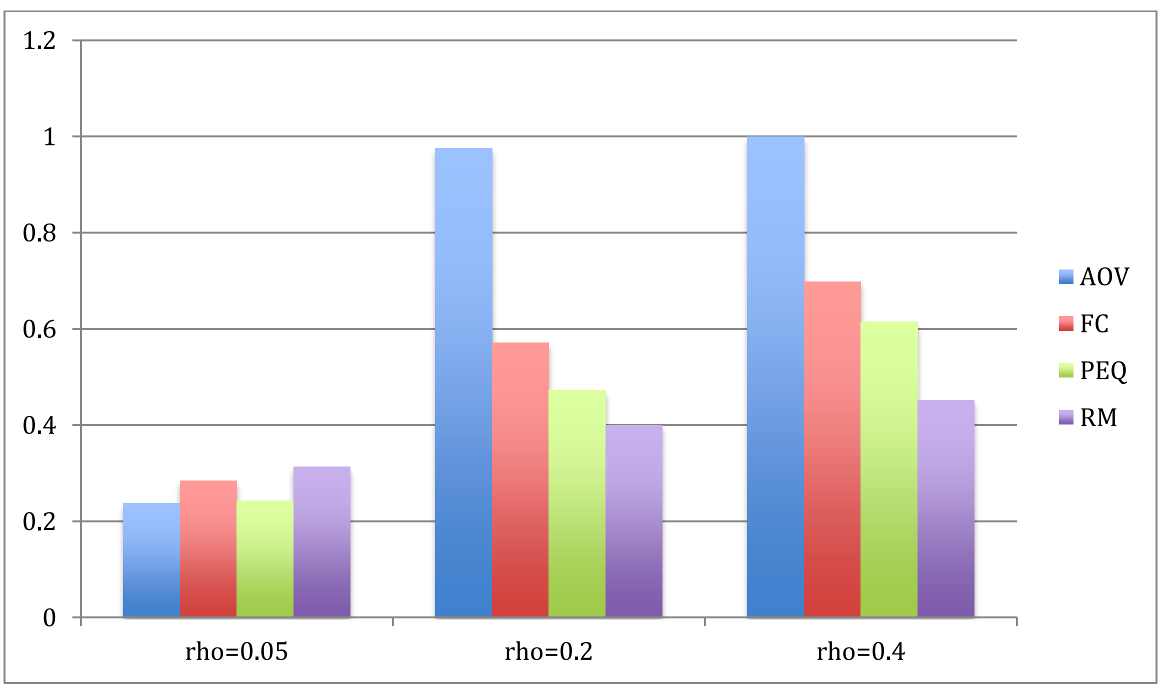

Figure 3.32 length of confidence interval for ICC with the population ICC value of 0.05, 0.2 and 0.4

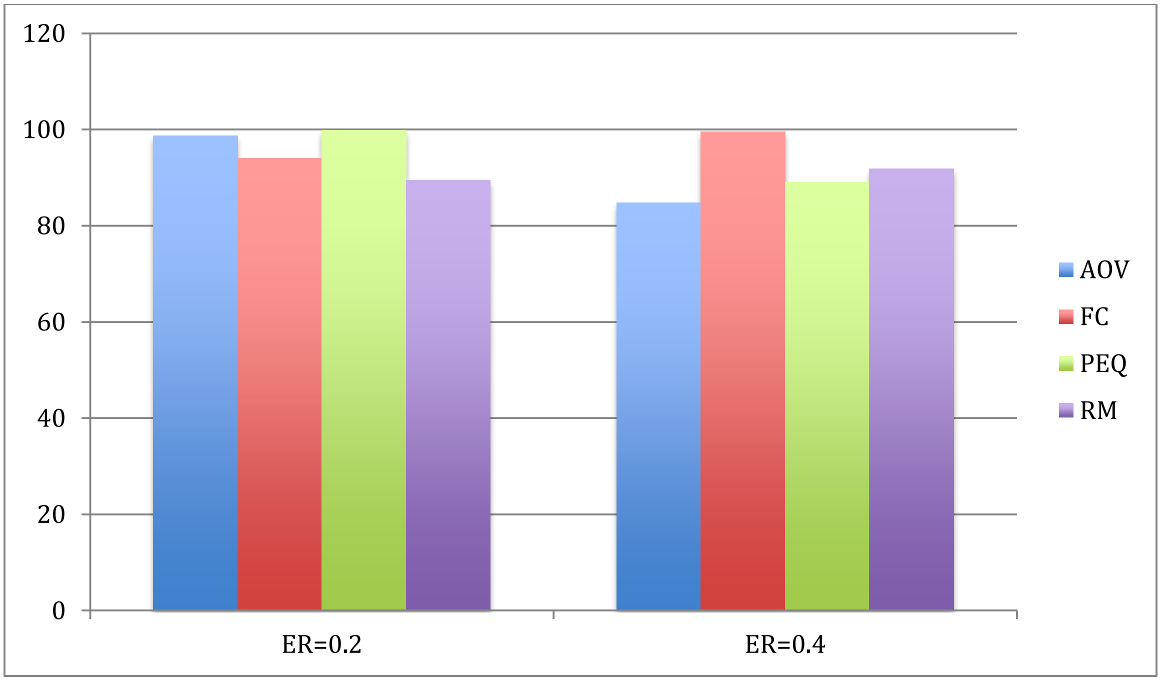

Figure 3.33 Percent coverage of confidence interval for ICC with event rate of 0.2 and 0.4

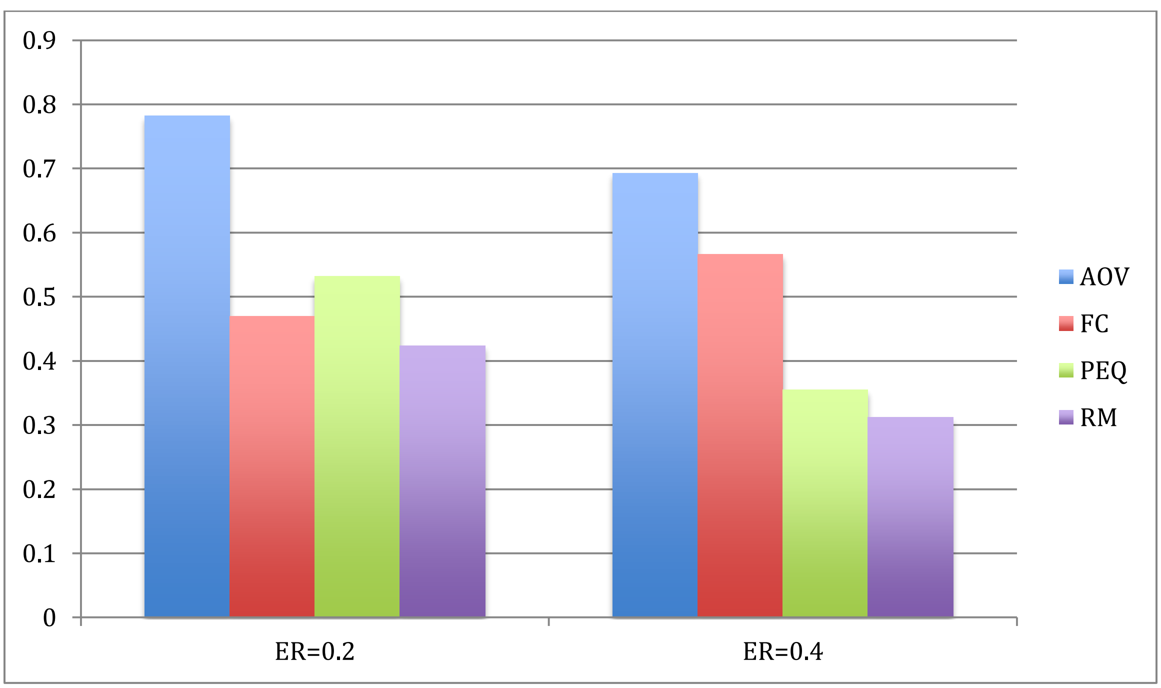

Figure 3.34 Length of confidence interval for ICC with event rate of 0.2 and 0.4

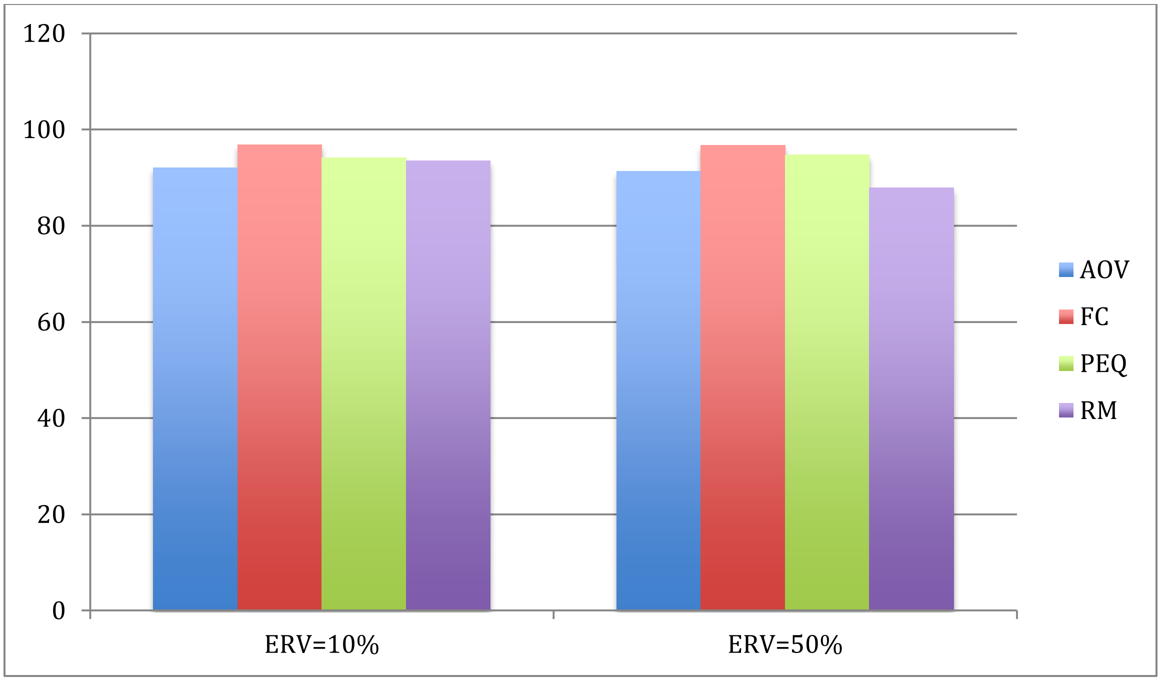

Figure 3.35 percent coverage of confidence interval for ICC with event rate variation of 10% and 50%.

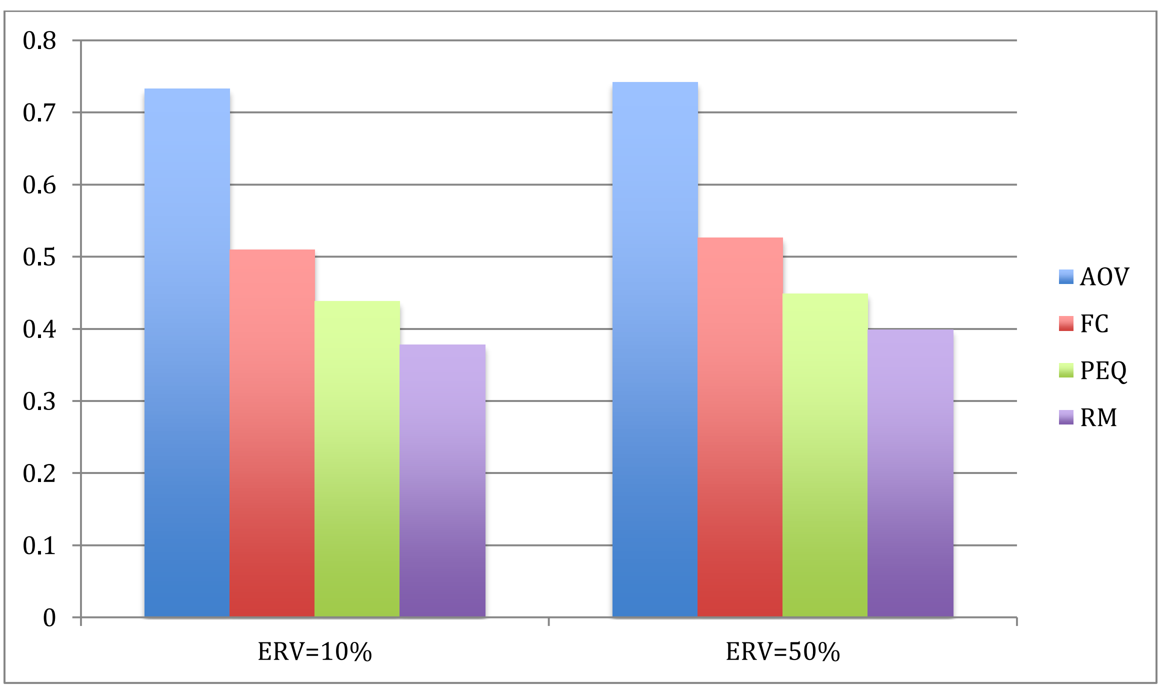

Figure 3.36 Length of confidence interval for ICC with event rate variation of 10% and 50%

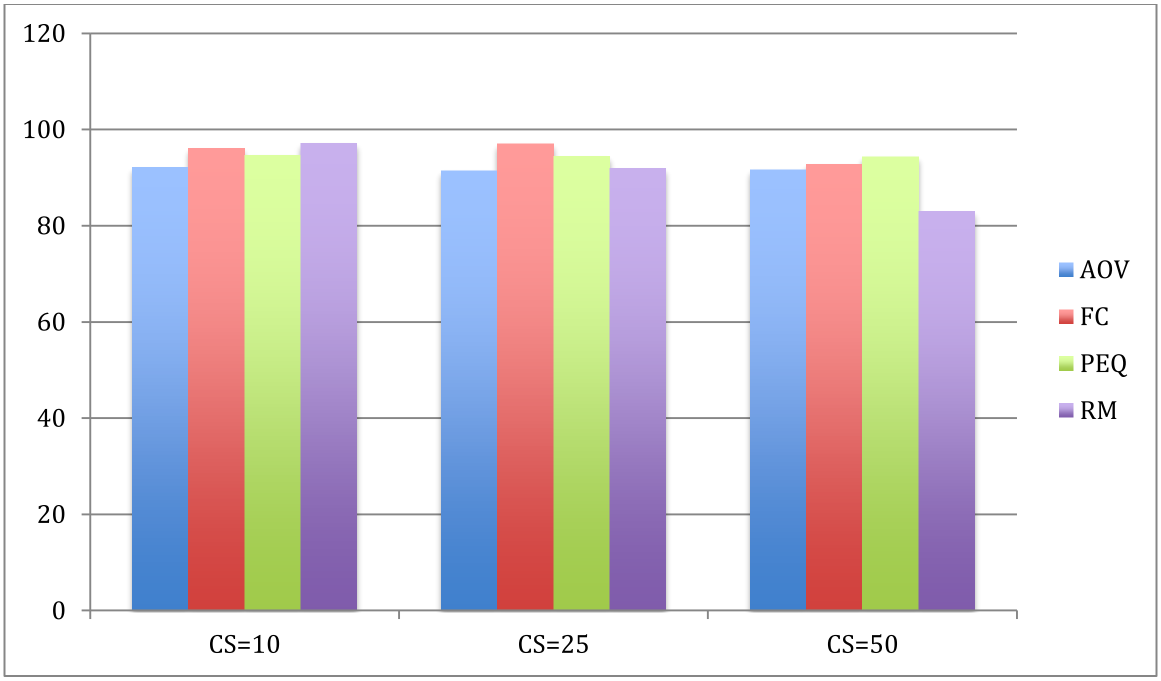

Figure 3.37 percent coverage of confidence interval for ICC with cluster size of 10, 25 and 50.

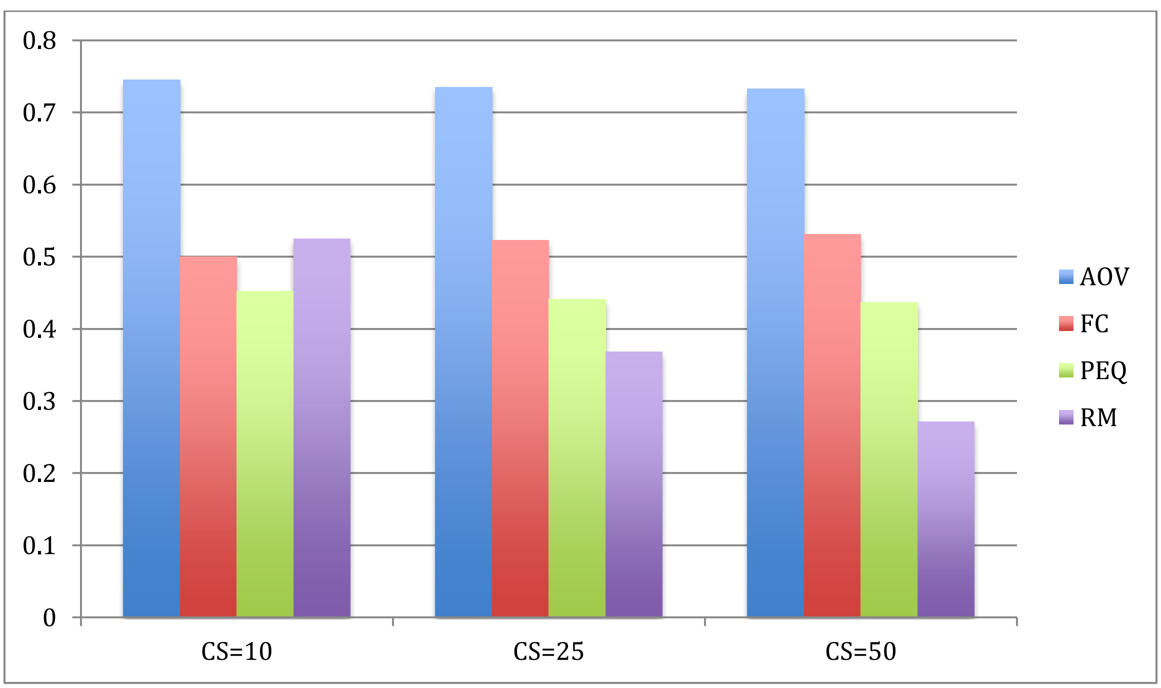

Figure 3.38 length of confidence interval for ICC with cluster size of 10, 25 and 50.

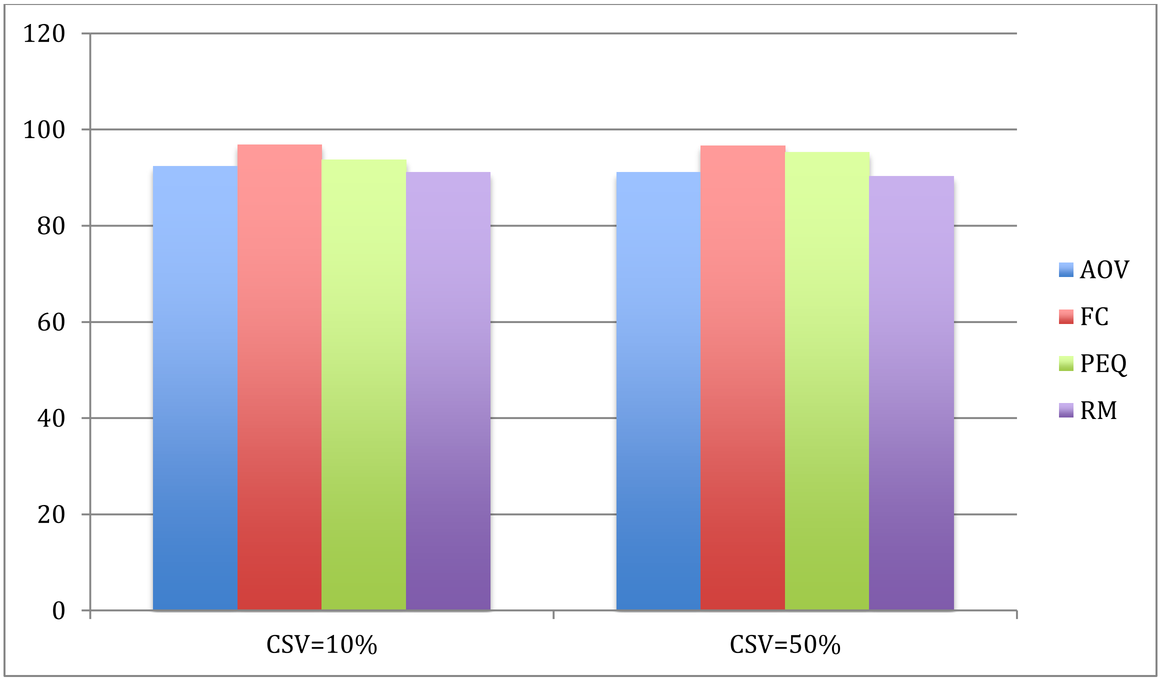

Figure 3.39 percent coverage of confidence interval for ICC with cluster size variation of 10% and 50%.

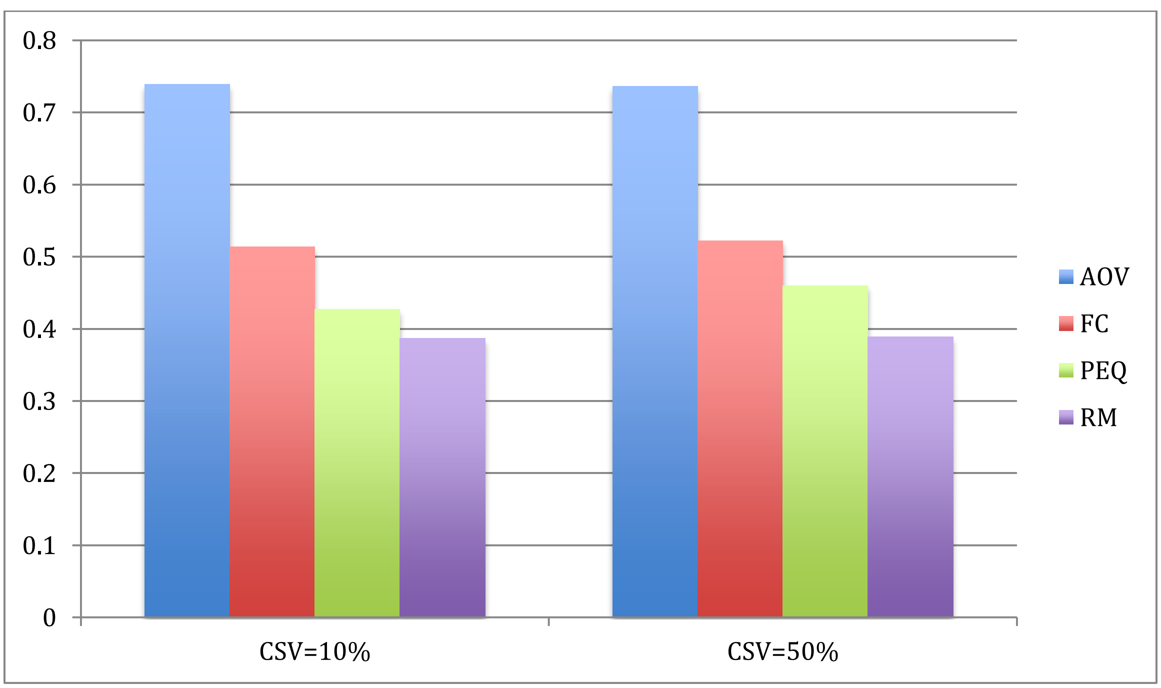

Figure 3.40 length of confidence interval for ICC with cluster size variation of 10% and 50%.

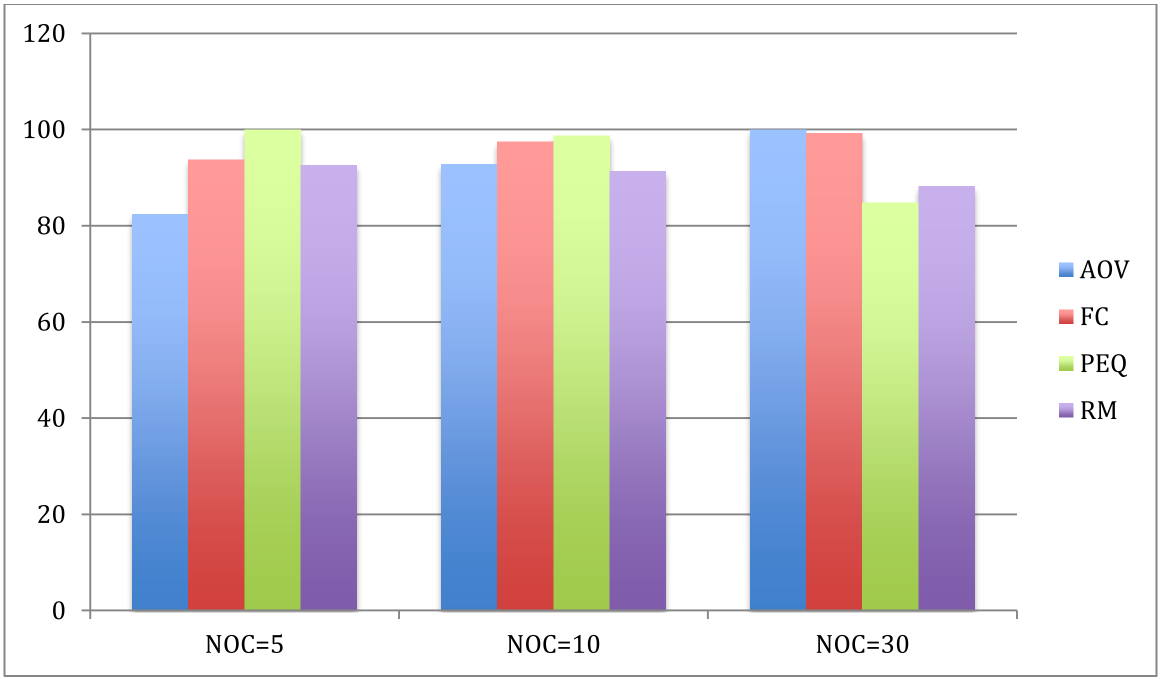

Figure 3.41 percent coverage of confidence interval for ICC with total clusters of 5, 10 and 30.

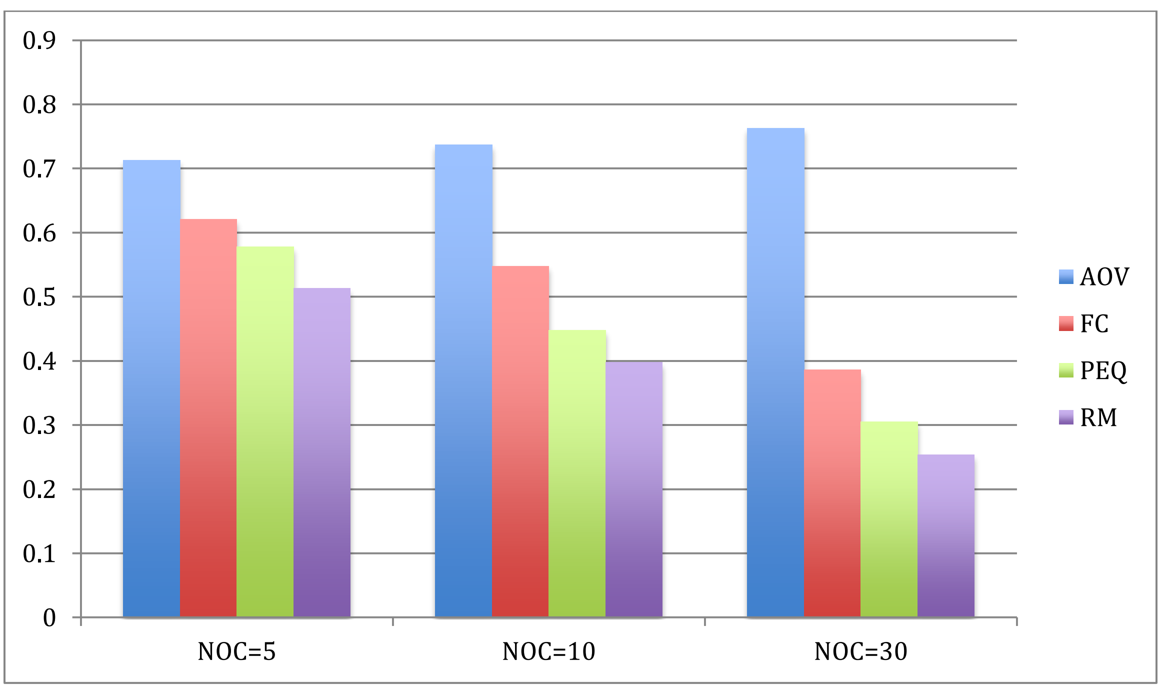

Figure 3.42 length of confidence interval for ICC with total clusters of 5, 10 and 30.

CHAPTER 4

Discussion

There is no single estimator that gives us the best confidence intervals in all the cases. Table 4.1 shows which confidence limit estimator performs best in each of the 216 scenarios, considering both the percent coverage of the true ICC value and the length of confidence intervals. Of the 216 scenarios, the confidence limits by the RM estimator performs better in 103 scenarios, the confidence limits by the PEQ estimator performs better in 64 scenarios, the confidence limits by the FC estimator performs better in 45 scenarios, and the confidence limits by the ANOVA estimator performs better in 4 scenarios.

The performance of confidence intervals by the RM estimator is best when the true population ICC is 0.05 and 0.2. When true population ICC is 0.4, the performance of confidence interval by the FC estimator is best.

The confidence limits by the FC estimator perform better than the remaining estimators when the event rate is 0.2. When the event rate is 0.4, the performance of confidence intervals by the RM estimator is better than remaining estimators.

The confidence limits by the RM estimator perform better than remaining estimators when the event rate variation is 10%. When the event rate variation is 50%, the performance of confidence intervals by the PEQ estimator is best.

The performance of confidence limits by the PEQ estimator is best when the cluster size is 10, 25 and 50.

The confidence limits by the PEQ estimator perform better than remaining estimators when the cluster size variation is both 10% and 50%.

The performance of confidence limits by the RM estimator is best when the number of clusters is 5 and 10. When the number of clusters is 30, the confidence limits by the FC estimator perform better than remaining estimators.

When the event rate is 0.2 and the cluster size is 10, the performance of confidence limits by the RM estimator is best. When the event rate is 0.2 and the cluster size is 25 or 50, then the confidence limits by the FC estimator perform better than remaining estimators. When the event rate is 0.4 and the cluster size is 10 or 25, then the confidence limits by the RM estimator performs best. When the event rate is 0.4 and the cluster size is 50, then the confidence limits by the FC estimator perform better than remaining estimators.

When the event rate is 0.2 and the number of clusters is 5, the performance of confidence limits by the RM estimator is best. When the event rate is 0.2 and the number of clusters is 10 or 30, then the confidence limits by the FC estimator perform better than remaining estimators. When the event rate is 0.4 and the number of clusters is 5 or 10, then the confidence limits by the RM estimator performs best. When the event rate is 0.4 and the number of clusters is 30, then the confidence limits by the FC estimator perform better than remaining estimators.

When the cluster size is 10 and the number of clusters is 5 or 10, the performance of confidence limits by the FC estimator is best. When the cluster size is 10 and the number of clusters is 30, the performance of confidence limits by the RM estimator is best. When the cluster size is 25 and the number of clusters is 5 or 10 or 30, the performance of confidence limits by the RM estimator is best. When the cluster size is 50 and the number of clusters is 5 or 30, the performance of confidence limits by the FC estimator is best. When the cluster size is 50 and the number of clusters is 10, the performance of confidence limits by the PEQ estimator is best.

When the event rate is 0.2, cluster size is 10 and the number of clusters is 5, the performance of confidence limits by the ANOVA estimator is best. When the event rate is 0.2, cluster size is 10 and the number of clusters is 10 or 30, the performance of confidence limits by the RM estimator is best. When the event rate is 0.2, cluster size is 25 and the number of clusters is 5, the performance of confidence limits by the RM estimator is best. When the event rate is 0.2, cluster size is 25 and the number of clusters is 10 or 30, the performance of confidence limits by the FC estimator is best. When the event rate is 0.2, cluster size is 50 and the number of clusters is 5, the performance of confidence limits by the ANOVA estimator is best. When the event rate is 0.2, cluster size is 50 and the number of clusters is 10 or 30, the performance of confidence limits by the FC estimator is best.

When the event rate is 0.4, cluster size is 10 and the number of clusters is 5 or 30, the performance of confidence limits by the RM estimator is best. When the event rate

is 0.4, cluster size is 10 and the number of clusters is 10, the performance of confidence limits by the PEQ estimator is best. When the event rate is 0.4, cluster size is 25 and the number of clusters is 5 or 10 or 30, the performance of confidence limits by the RM estimator is best. When the event rate is 0.4, cluster size is 50 and the number of clusters is 5 or 30, the performance of confidence limits by the FC estimator is best. When the event rate is 0.4, cluster size is 50 and the number of clusters is 10, the performance of confidence limits by the PEQ estimator is best.

When the true population ICC is 0.05 and cluster size is 10, then the performance of confidence limits by the PEQ estimator is best. When the true population ICC is 0.05 and cluster size is 25 or 50, then the performance of confidence limits by the RM estimator is best. When the true population ICC is 0.2 and cluster size is 10 or 25, then the performance of confidence limits by the RM estimator is best. When the true population ICC is 0.2 and cluster size is 50, then the performance of confidence limits by the PEQ estimator is best. When the true population ICC is 0.4 and cluster size is 10, then the performance of confidence limits by the RM estimator is best. When the true population ICC is 0.4 and cluster size is 25 or 50, then the performance of confidence limits by the FC estimator is best.

When the true population ICC is 0.05 and number of clusters is 5 or 10 or 30, the performance of confidence limits by the RM estimator is best. When the true population ICC is 0.2 and number of clusters is 5 or 10, then the performance of confidence limits by the RM estimator is best. When the true population ICC is 0.2 and number of clusters

is 30, then the performance of confidence limits by the PEQ estimator is best. When the true population ICC is 0.4 and number of clusters is 5 or 10, then the performance of confidence limits by the PEQ estimator is best. When the true population ICC is 0.4 and number of clusters is 30, then the performance of confidence limits by the FC estimator is best.

When the true population ICC is 0.05 cluster size is 10 and the number of clusters is 5, the performance of confidence limits by the PEQ estimator is best. When the true population ICC is 0.05 cluster size is 10 and the number of clusters is 10, the performance of confidence limits by the FC estimator is best. When the true population ICC is 0.05 cluster size is 10 and the number of clusters is 30, the performance of confidence limits by the RM estimator is best. When the true population ICC is 0.05 cluster size is 25 and the number of clusters is 5 or 10 or 30, the performance of confidence limits by the RM estimator is best. When the true population ICC is 0.05 cluster size is 50 and the number of clusters is 5 or 10, the performance of confidence limits by the RM estimator is best. When the true population ICC is 0.05 cluster size is 50 and the number of clusters is 30, the performance of confidence limits by the PEQ estimator is best.

When the event rate is 0.2 and event rate variation is 10% or 50%, the performance of confidence intervals by the FC estimator is best. When the event rate is 0.4 and event rate variation is 10%, the performance of confidence intervals by the RM

estimator is best. When the event rate is 0.4 and event rate variation is 50%, the performance of confidence intervals by the RM estimator is best.

When cluster size is 10 and cluster size variation is 10%, the performance of confidence intervals by the FC estimator is best. When cluster size is 10 and cluster size variation is 50%, the performance of confidence intervals by the PEQ estimator is best. When cluster size is 25 or 50 and cluster size variation is 10% or 50%, the performance of confidence intervals by the PEQ estimator is best.

When cluster size variation is 10% and event rate variation is 10% or 50%, the performance of confidence intervals by the RM estimator is best. When cluster size variation is 50% and event rate variation is 10% or 50%, the performance of confidence intervals by the PEQ estimator is best.

When the event rate is 0.2 and true population ICC is 0.05, the performance of confidence intervals by the ANOVA estimator is best. When the event rate is 0.2 and true population ICC is 0.2, the performance of confidence intervals by the FC estimator is best. When the event rate is 0.2 and true population ICC is 0.4, the performance of confidence intervals by the PEQ estimator is best. When the event rate is 0.4 and true population ICC is 0.05 or 0.2, the performance of confidence intervals by the RM estimator is best. When the event rate is 0.4 and true population ICC is 0.4, the performance of confidence intervals by the FC estimator is best.

When the event rate is 0.2, population ICC is 0.05 and cluster size is 10 or 25, the performance of confidence intervals by the ANOVA estimator is best. When the event

rate is 0.2, population ICC is 0.05 and cluster size is 50, the performance of confidence intervals by the RM estimator is best. When the event rate is 0.2, population ICC is 0.2 and cluster size is 10 or 50, the performance of confidence intervals by the FC estimator is best. When the event rate is 0.2, population ICC is 0.2 and cluster size is 25, the performance of confidence intervals by the RM estimator is best. When the event rate is 0.2, population ICC is 0.4 and cluster size is 10, the performance of confidence intervals by the RM estimator is best. When the event rate is 0.2, population ICC is 0.4 and cluster size is 25 or 50, the performance of confidence intervals by the PEQ estimator is best.

When the event rate is 0.4, population ICC is 0.05 and cluster size is 10 or 25, the performance of confidence intervals by the RM estimator is best. When the event rate is 0.4, population ICC is 0.05 and cluster size is 50, the performance of confidence intervals by the PEQ estimator is best. When the event rate is 0.4, population ICC is 0.2 and cluster size is 10 or 25, the performance of confidence intervals by the RM estimator is best. When the event rate is 0.4, population ICC is 0.2 and cluster size is 50, the performance of confidence intervals by the PEQ estimator is best. When the event rate is 0.4, population ICC is 0.4 and cluster size is 10, the performance of confidence intervals by the RM estimator is best. When the event rate is 0.4, population ICC is 0.4 and cluster size is 25 or 50, the performance of confidence intervals by the FC estimator is best.

When the event rate is 0.2, population ICC is 0.05 and number of clusters is 5 or 10 or 30, the performance of confidence intervals by the RM estimator is best. When

the event rate is 0.2, population ICC is 0.2 and number of clusters is 5, the performance of confidence intervals by the RM estimator is best. When the event rate is 0.2, population ICC is 0.2 and number of clusters is 10 or 30, the performance of confidence intervals by the FC estimator is best. When the event rate is 0.2, population ICC is 0.4 and number of clusters is 5 or 10, the performance of confidence intervals by the PEQ estimator is best. When the event rate is 0.2, population ICC is 0.4 and number of clusters is 30, the performance of confidence intervals by the FC estimator is best.

When the event rate is 0.4, population ICC is 0.05 and number of clusters is 5 or 10, the performance of confidence intervals by the RM estimator is best. When the event rate is 0.4, population ICC is 0.05 and number of clusters is 30, the performance of confidence intervals by the FC estimator is best. When the event rate is 0.4, population ICC is 0.2 and number of clusters is 5 or 10, the performance of confidence intervals by the RM estimator is best. When the event rate is 0.4, population ICC is 0.2 and number of clusters is 30, the performance of confidence intervals by the PEQ estimator is best. When the event rate is 0.4, population ICC is 0.4 and number of clusters is 5 or 30, the performance of confidence intervals by the FC estimator is best. When the event rate is 0.4, population ICC is 0.4 and number of clusters is 10, the performance of confidence intervals by the PEQ estimator is best.

4.1 CONCLUSIONS

In conclusion, when using the present simulation method to generate correlated binary data, our study showed that among all the confidence limits for the 4 estimators, the confidence limits by the RM estimator performs better in many cases. If the population ICC is small or if the event rate is large or if the event rate variation is small or if the number of clusters is very small, the confidence limits by the RM estimator performs best and is the ideal one to use. If the true ICC population is large or if the event rate is small, or if the number of clusters is large, the confidence limits by the FC estimator perform best and is the ideal one to use. If the event rate variation is large or for different cluster sizes, and different cluster size variations, the confidence limit by the PEQ estimator is best and is the ideal one to use.

4.2 LIMITATIONS

The present study has many limitations. We did not consider large cluster sizes and large number of clusters. Including the large cluster sizes and large number of clusters can be done in the future. We only did 2000 simulations per each scenario due to time constraints. In the future, we can include 5000 simulations. Also the computing time for RM estimator is very large, which limited the number of simulations used for each scenario.

Table 4.1 Performance of Confidence Intervals based on the confidence length and the percentage the true parameter is captured by its confidence limits

Event	Population ICC	Event rate variation	No of clusters	Cluster size	Cluster size variation	Best CI estimator
0.2	0.05	0.1	5	10	0.1	FC
0.2	0.05	0.1	5	10	0.5	FC
0.2	0.05	0.1	5	25	0.1	ANOVA
0.2	0.05	0.1	5	25	0.5	ANOVA
0.2	0.05	0.1	5	50	0.1	ANOVA
0.2	0.05	0.1	5	50	0.5	ANOVA
0.2	0.05	0.1	10	10	0.1	FC
0.2	0.05	0.1	10	10	0.5	FC
0.2	0.05	0.1	10	25	0.1	RM
0.2	0.05	0.1	10	25	0.5	RM
0.2	0.05	0.1	10	50	0.1	RM
0.2	0.05	0.1	10	50	0.5	RM
0.2	0.05	0.1	30	10	0.1	FC
0.2	0.05	0.1	30	10	0.5	FC
0.2	0.05	0.1	30	25	0.1	RM
0.2	0.05	0.1	30	25	0.5	RM
0.2	0.05	0.1	30	50	0.1	RM
0.2	0.05	0.1	30	50	0.5	RM
0.2	0.05	0.5	5	10	0.1	FC
0.2	0.05	0.5	5	10	0.5	FC
0.2	0.05	0.5	5	25	0.1	RM
0.2	0.05	0.5	5	25	0.5	RM
0.2	0.05	0.5	5	50	0.1	RM
0.2	0.05	0.5	5	50	0.5	RM
0.2	0.05	0.5	10	10	0.1	FC
0.2	0.05	0.5	10	10	0.5	FC
0.2	0.05	0.5	10	25	0.1	RM
0.2	0.05	0.5	10	25	0.5	RM
0.2	0.05	0.5	10	50	0.1	RM
0.2	0.05	0.5	10	50	0.5	RM
0.2	0.05	0.5	30	10	0.1	FC
0.2	0.05	0.5	30	10	0.5	FC
0.2	0.05	0.5	30	25	0.1	RM
0.2	0.05	0.5	30	25	0.5	RM
0.2	0.05	0.5	30	50	0.1	RM
0.2	0.05	0.5	30	50	0.5	RM

Table 4.1 Performance of Confidence Intervals based on the confidence length and the percentage the true parameter is captured by its confidence limits (continued)

Event	Population ICC	Event rate variation	No of clusters	Cluster size	Cluster size variation	Best CI estimator
0.2	0.2	0.1	5	10	0.1	FC
0.2	0.2	0.1	5	10	0.5	FC
0.2	0.2	0.1	5	25	0.1	RM
0.2	0.2	0.1	5	25	0.5	RM
0.2	0.2	0.1	5	50	0.1	RM
0.2	0.2	0.1	5	50	0.5	RM
0.2	0.2	0.1	10	10	0.1	RM
0.2	0.2	0.1	10	10	0.5	RM
0.2	0.2	0.1	10	25	0.1	RM
0.2	0.2	0.1	10	25	0.5	RM
0.2	0.2	0.1	10	50	0.1	PEQ
0.2	0.2	0.1	10	50	0.5	PEQ
0.2	0.2	0.1	30	10	0.1	RM
0.2	0.2	0.1	30	10	0.5	RM
0.2	0.2	0.1	30	25	0.1	RM
0.2	0.2	0.1	30	25	0.5	RM
0.2	0.2	0.1	30	50	0.1	PEQ
0.2	0.2	0.1	30	50	0.5	PEQ
0.2	0.2	0.5	5	10	0.1	FC
0.2	0.2	0.5	5	10	0.5	FC
0.2	0.2	0.5	5	25	0.1	RM
0.2	0.2	0.5	5	25	0.5	RM
0.2	0.2	0.5	5	50	0.1	FC
0.2	0.2	0.5	5	50	0.5	FC
0.2	0.2	0.5	10	10	0.1	RM
0.2	0.2	0.5	10	10	0.5	RM
0.2	0.2	0.5	10	25	0.1	RM
0.2	0.2	0.5	10	25	0.5	RM
0.2	0.2	0.5	10	50	0.1	FC
0.2	0.2	0.5	10	50	0.5	FC
0.2	0.2	0.5	30	10	0.1	RM
0.2	0.2	0.5	30	10	0.5	RM
0.2	0.2	0.5	30	25	0.1	PEQ
0.2	0.2	0.5	30	25	0.5	PEQ
0.2	0.2	0.5	30	50	0.1	PEQ
0.2	0.2	0.5	30	50	0.5	PEQ

Table 4.1 Performance of Confidence Intervals based on the confidence length and the percentage the true parameter is captured by its confidence limits (continued)

Event	Population ICC	Event rate variation	No of clusters	Cluster size	Cluster size variation	Best CI estimator
0.2	0.4	0.1	5	10	0.1	RM
0.2	0.4	0.1	5	10	0.5	RM
0.2	0.4	0.1	5	25	0.1	RM
0.2	0.4	0.1	5	25	0.5	RM
0.2	0.4	0.1	5	50	0.1	PEQ
0.2	0.4	0.1	5	50	0.5	PEQ
0.2	0.4	0.1	10	10	0.1	RM
0.2	0.4	0.1	10	10	0.5	RM
0.2	0.4	0.1	10	25	0.1	PEQ
0.2	0.4	0.1	10	25	0.5	PEQ
0.2	0.4	0.1	10	50	0.1	PEQ
0.2	0.4	0.1	10	50	0.5	PEQ
0.2	0.4	0.1	30	10	0.1	FC
0.2	0.4	0.1	30	10	0.5	FC
0.2	0.4	0.1	30	25	0.1	FC
0.2	0.4	0.1	30	25	0.5	FC
0.2	0.4	0.1	30	50	0.1	FC
0.2	0.4	0.1	30	50	0.5	FC
0.2	0.4	0.5	5	10	0.1	RM
0.2	0.4	0.5	5	10	0.5	RM
0.2	0.4	0.5	5	25	0.1	PEQ
0.2	0.4	0.5	5	25	0.5	PEQ
0.2	0.4	0.5	5	50	0.1	PEQ
0.2	0.4	0.5	5	50	0.5	PEQ
0.2	0.4	0.5	10	10	0.1	RM
0.2	0.4	0.5	10	10	0.5	RM
0.2	0.4	0.5	10	25	0.1	PEQ
0.2	0.4	0.5	10	25	0.5	PEQ
0.2	0.4	0.5	10	50	0.1	PEQ
0.2	0.4	0.5	10	50	0.5	PEQ
0.2	0.4	0.5	30	10	0.1	FC
0.2	0.4	0.5	30	10	0.5	FC
0.2	0.4	0.5	30	25	0.1	FC
0.2	0.4	0.5	30	25	0.5	FC
0.2	0.4	0.5	30	50	0.1	FC
0.2	0.4	0.5	30	50	0.5	FC

Table 4.1 Performance of Confidence Intervals based on the confidence length and the percentage the true parameter is captured by its confidence limits (continued)

Event	Population ICC	Event rate variation	No of clusters	Cluster size	Cluster size variation	Best CI estimator
0.4	0.05	0.1	5	10	0.1	PEQ
0.4	0.05	0.1	5	10	0.5	PEQ
0.4	0.05	0.1	5	25	0.1	PEQ
0.4	0.05	0.1	5	25	0.5	PEQ
0.4	0.05	0.1	5	50	0.1	PEQ
0.4	0.05	0.1	5	50	0.5	RM
0.4	0.05	0.1	10	10	0.1	PEQ
0.4	0.05	0.1	10	10	0.5	PEQ
0.4	0.05	0.1	10	25	0.1	PEQ
0.4	0.05	0.1	10	25	0.5	PEQ
0.4	0.05	0.1	10	50	0.1	PEQ
0.4	0.05	0.1	10	50	0.5	PEQ
0.4	0.05	0.1	30	10	0.1	PEQ
0.4	0.05	0.1	30	10	0.5	PEQ
0.4	0.05	0.1	30	25	0.1	PEQ
0.4	0.05	0.1	30	25	0.5	PEQ
0.4	0.05	0.1	30	50	0.1	PEQ
0.4	0.05	0.1	30	50	0.5	PEQ
0.4	0.05	0.5	5	10	0.1	RM
0.4	0.05	0.5	5	10	0.5	RM
0.4	0.05	0.5	5	25	0.1	RM
0.4	0.05	0.5	5	25	0.5	RM
0.4	0.05	0.5	5	50	0.1	RM
0.4	0.05	0.5	5	50	0.5	RM
0.4	0.05	0.5	10	10	0.1	RM
0.4	0.05	0.5	10	10	0.5	RM
0.4	0.05	0.5	10	25	0.1	RM
0.4	0.05	0.5	10	25	0.5	RM
0.4	0.05	0.5	10	50	0.1	PEQ
0.4	0.05	0.5	10	50	0.5	PEQ
0.4	0.05	0.5	30	10	0.1	RM
0.4	0.05	0.5	30	10	0.5	RM
0.4	0.05	0.5	30	25	0.1	PEQ
0.4	0.05	0.5	30	25	0.5	PEQ
0.4	0.05	0.5	30	50	0.1	PEQ
0.4	0.05	0.5	30	50	0.5	PEQ

Table 4.1 Performance of Confidence Intervals based on the confidence length and the percentage the true parameter is captured by its confidence limits (continued)

Event	Population ICC	Event rate variation	No of clusters	Cluster size	Cluster size variation	Best CI estimator
0.4	0.2	0.1	5	10	0.1	PEQ
0.4	0.2	0.1	5	10	0.5	PEQ
0.4	0.2	0.1	5	25	0.1	RM
0.4	0.2	0.1	5	25	0.5	RM
0.4	0.2	0.1	5	50	0.1	RM
0.4	0.2	0.1	5	50	0.5	RM
0.4	0.2	0.1	10	10	0.1	PEQ
0.4	0.2	0.1	10	10	0.5	PEQ
0.4	0.2	0.1	10	25	0.1	RM
0.4	0.2	0.1	10	25	0.5	RM
0.4	0.2	0.1	10	50	0.1	RM
0.4	0.2	0.1	10	50	0.5	RM
0.4	0.2	0.1	30	10	0.1	PEQ
0.4	0.2	0.1	30	10	0.5	PEQ
0.4	0.2	0.1	30	25	0.1	PEQ
0.4	0.2	0.1	30	25	0.5	RM
0.4	0.2	0.1	30	50	0.1	PEQ
0.4	0.2	0.1	30	50	0.5	RM
0.4	0.2	0.5	5	10	0.1	RM
0.4	0.2	0.5	5	10	0.5	RM
0.4	0.2	0.5	5	25	0.1	RM
0.4	0.2	0.5	5	25	0.5	RM
0.4	0.2	0.5	5	50	0.1	PEQ
0.4	0.2	0.5	5	50	0.5	PEQ
0.4	0.2	0.5	10	10	0.1	RM
0.4	0.2	0.5	10	10	0.5	RM
0.4	0.2	0.5	10	25	0.1	RM
0.4	0.2	0.5	10	25	0.5	RM
0.4	0.2	0.5	10	50	0.1	PEQ
0.4	0.2	0.5	10	50	0.5	PEQ
0.4	0.2	0.5	30	10	0.1	RM
0.4	0.2	0.5	30	10	0.5	RM
0.4	0.2	0.5	30	25	0.1	PEQ
0.4	0.2	0.5	30	25	0.5	PEQ
0.4	0.2	0.5	30	50	0.1	PEQ
0.4	0.2	0.5	30	50	0.5	PEQ

Table 4.1 Performance of Confidence Intervals based on the confidence length and the percentage the true parameter is captured by its confidence limits (continued)

Event	Population ICC	Event rate variation	No of clusters	Cluster size	Cluster size variation	Best CI estimator
0.4	0.4	0.1	5	10	0.1	RM
0.4	0.4	0.1	5	10	0.5	RM
0.4	0.4	0.1	5	25	0.1	FC
0.4	0.4	0.1	5	25	0.5	FC
0.4	0.4	0.1	5	50	0.1	FC
0.4	0.4	0.1	5	50	0.5	FC
0.4	0.4	0.1	10	10	0.1	RM
0.4	0.4	0.1	10	10	0.5	RM
0.4	0.4	0.1	10	25	0.1	RM
0.4	0.4	0.1	10	25	0.5	RM
0.4	0.4	0.1	10	50	0.1	FC
0.4	0.4	0.1	10	50	0.5	PEQ
0.4	0.4	0.1	30	10	0.1	RM
0.4	0.4	0.1	30	10	0.5	RM
0.4	0.4	0.1	30	25	0.1	RM
0.4	0.4	0.1	30	25	0.5	RM
0.4	0.4	0.1	30	50	0.1	RM
0.4	0.4	0.1	30	50	0.5	RM
0.4	0.4	0.5	5	10	0.1	RM
0.4	0.4	0.5	5	10	0.5	RM
0.4	0.4	0.5	5	25	0.1	FC
0.4	0.4	0.5	5	25	0.5	FC
0.4	0.4	0.5	5	50	0.1	FC
0.4	0.4	0.5	5	50	0.5	FC
0.4	0.4	0.5	10	10	0.1	RM
0.4	0.4	0.5	10	10	0.5	RM
0.4	0.4	0.5	10	25	0.1	RM
0.4	0.4	0.5	10	25	0.5	RM
0.4	0.4	0.5	10	50	0.1	PEQ
0.4	0.4	0.5	10	50	0.5	PEQ
0.4	0.4	0.5	30	10	0.1	RM
0.4	0.4	0.5	30	10	0.5	RM
0.4	0.4	0.5	30	25	0.1	FC
0.4	0.4	0.5	30	25	0.5	FC
0.4	0.4	0.5	30	50	0.1	FC
0.4	0.4	0.5	30	50	0.5	FC

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