Approximate and Exact Methods for Computing the Confidence Limits for the Common Odds Ratio in a Series of 2×2 Tables

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Summary

For computing the confidence limits of the common odds ratio in K 2×2 tables, Monte Carlo experiments compared respective performances of the original exact method (Gart, 1970, and Zelen, 1971), the mid-P (Lancaster, 1961) modification methods, the ln-method using the conditional maximum likelihood estimate and its variance, or using the Mantel-Haenszel estimate and its asymptotic variance proposed by Robins et al (1986), and the Sato's method (1990) with and without a continuity correction. Approximate methods gave the accurate and symmetric lower and upper percentages when the true common odds ratio was unity, while upper percentages became liberal but lower percentages conservative, reversely, as the true common odds ratio increased, especially in matched designs. The original exact method and the Sato's method with the correction gave conservative results. The mid-P exact method gave the most accurate, symmetric and nearest lower and upper percentages to the nominal size, regardless of the true common odds ratio, the sample size, and the number of strata.

1. Introduction

In the epidemiologic studies, especially in case-control studies, the data are often stratified into a series of 2×2 tables to elucidate a dichotomous risk factor without the influences of the confounding variables. We usually compute the estimate and confidence limits for the common odds ratio, ψ , in K 2×2 independent contingency tables. Several asymptotic methods have been proposed to this problem.

The Mantel-Haenszel (1959) estimate, $\hat{\psi}_{MH}$, is ordinarily used to estimate ψ . To construct the confidence limits for ψ , the asymptotic variance of the Mantel-Haenszel estimator was given by Hauck (1979) based on "large-stratum" sets wherein the number of tables remained fixed but individual cell sizes increased without bound. Breslow (1981) proposed one variance for "sparse-data" settings where the cell sizes remained bounded but the number of tables increased. Robins et al (1986) provided a good asymptotic variance for both sparse-data and large-stratum settings. We may construct an approximate

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confidence interval by the "ln-method" that is based on a normal distribution with a mean of $\log \hat{\psi}_{MH}$ and its asymptotic variance.

Another approximate methods are derived from the test statistics such as the extended Cornfield method by Gart (1970, 1971) that performs well for large-stratum sets but poorly for sparse-data sets, while Sato (1990) proposed a good method for both sparse-data and large-stratum settings based on the estimating function for the common odds ratio.

However, we can also construct an exact confidence interval based on the conditional distribution (Gart, 1970, and Zelen, 1971), which guarantees the desired coverage probability. Though the computational complexity exists in estimating the exact confidence limits, Mehta et al (1985) provided the network algorithm and also Takagi (1990) developed a simple recursive algorithm to overcome the time consumption even for sparse-data settings.

To give the answer what method should be recommended, in this paper, we compare the performances of approximate methods based on the asymptotic distribution of the logarithm of the Mantel-Haenszel estimator and the conditional maximum likelihood estimator, and the estimating function with those of the original exact and mid-P methods through several Monte Carlo experiments.

2. Exact Confidence Limits

Consider K 2×2 tables with pairs of independent binomial observations (x_k, y_k) with denominators (n_k, m_k) and success probabilities (p_{1k}, p_{0k}) for $k = 1, \dots, K$. In case-control studies, x_k and y_k persons are exposed in n_k cases and m_k controls respectively in the k th stratum. To measure the disease-exposure association, the odds ratio $\psi_k = (p_{1k}q_{0k})/(p_{0k}q_{1k})$ is always available, where $q_{1k} = 1 - p_{1k}$ and $q_{0k} = 1 - p_{0k}$ in the k th table. Usually assumed $\psi_k = \psi$ for all k , where ψ is the common odds ratio. The Mantel-Haenszel estimate is obtained as $\hat{\psi}_{MH} = \sum_k [x_k(m_k - y_k)/N_k] / \sum_k [y_k(n_k - x_k)/N_k]$, where $N_k = n_k + m_k$.

The "exact" estimator and confidence limits for ψ are derived from the conditional distribution (Gart, 1970, and Zelen, 1971). Given the table marginals n_k, m_k and $t_k = x_k + y_k$, the conditional distribution is the noncentral hypergeometric distribution for x_k ,

$$f(x_k|t_k, \psi) = \frac{\binom{n_k}{x_k} \binom{m_k}{t_k - x_k} \psi^{x_k}}{\sum_{r_k} \binom{n_k}{r_k} \binom{m_k}{t_k - r_k} \psi^{r_k}}, \quad (1)$$

where $l_k = \max(0, t_k - m_k) \leq r_k \leq \min(n_k, t_k) = u_k$.

The conditional maximum likelihood estimate (CMLE) $\hat{\psi}_c$ can be obtained by the following equation with an iterative method.

$$\sum_{k=1}^K x_k = \sum_{k=1}^K \sum_{r_k=l_k}^{u_k} r_k f(r_k|t_k, \hat{\psi}_c). \quad (2)$$

Recently, according to the developments of computer and algorithm for the calculation, the CMLE can be easily computed without time spending even by 16 bit micro-computer (Satten and Kupper, 1990, and Takagi, 1990).

Let $L = \sum_k l_k$ and $U = \sum_k u_k$, and by using (1), the conditional distribution of $s = \sum_k x_k$ is given (Zelen, 1971) by

$$g(s|\psi) = \frac{C_s \psi^s}{\sum_{r=L}^U C_r \psi^r}, \quad (3)$$

where

$$C_s = \sum_{R(s)} \prod_{k=1}^K \binom{n_k}{r_k} \binom{m_k}{t_k - r_k},$$

and $R(s)$ is the set of all K -fold partitions of all $\sum_k r_k = s$.

Hence, exact $100(1 - \alpha)\%$ confidence limits for ψ are given by $\{\hat{\psi}_L, \hat{\psi}_U\}$ such that

$$\sum_{z=s}^U g(z|\hat{\psi}_L) = \frac{\alpha}{2}, \quad (4)$$

and

$$\sum_{z=L}^s g(z|\hat{\psi}_U) = \frac{\alpha}{2}. \quad (5)$$

Note that $\hat{\psi}_L = 0$ if $s = L$, and $\hat{\psi}_U = \infty$ if $s = U$.

To estimate exact confidence limits, we may use the network algorithm by Mehta et al (1985) or the simple recursive algorithm by Takagi (1990).

Since equations (4) and (5) provide a conservative confidence interval as Mehta et al (1985) pointed out, if liberal confidence limits are preferable, we may modify the original exact method; i.e., the “mid-P” method (Lancaster, 1961, Rothman, 1986, and Vollset and Hirji, 1991) for estimating equations as follows;

$$\frac{1}{2}g(s|\hat{\psi}_L) + \sum_{z=s+1}^U g(z|\hat{\psi}_L) = \frac{\alpha}{2}, \quad (6)$$

and

$$\frac{1}{2}g(s|\hat{\psi}_U) + \sum_{z=L}^{s-1} g(z|\hat{\psi}_U) = \frac{\alpha}{2}. \quad (7)$$

3. Approximate Confidence Limits

To construct the confidence limits for ψ , the asymptotic variance of the Mantel-Haenszel estimator was given by Hauck (1979) based on large-stratum sets. Breslow (1981) proposed one variance for sparse-data settings. Robins et al (1986) provided a good asymptotic variance, V_R , for both sparse-data and large-stratum settings as follows;

$$V_R = \frac{1}{2} \sum_{k=1}^K \left[\frac{P_k R_k}{R_+^2} + \frac{Q_k R_k + P_k S_k}{R_+ S_+} + \frac{Q_k S_k}{S_+^2} \right], \quad (8)$$

where $R_k = x_k(m_k - y_k)/N_k$, $S_k = y_k(n_k - x_k)/N_k$, $P_k = (x_k + m_k - y_k)/N_k$, $Q_k = (y_k + n_k - x_k)/N_k$, $R_+ = \sum_k R_k$, and $S_+ = \sum_k S_k$.

We may construct an approximate confidence interval by the ln-method based on the asymptotic distribution of the logarithm of the Mantel-Haenszel estimator. The approximate $(1 - \alpha)$ confidence limits are given by

$$(\psi_L, \psi_U) = \hat{\psi}_{MH} \exp \left[\pm \chi_\alpha \sqrt{V(\log \hat{\psi}_{MH})} \right], \quad (9)$$

where χ_α^2 is the upper α point of the chi-square distribution with one degree of freedom.

For constructing the confidence interval by the ln-method, We may use the CMLE ψ_c given by (2) and the asymptotic variance of the logarithm of ψ_c ,

$$V_c = \left[\sum_{k=1}^K \{G_k(x_k^2|t_k, \hat{\psi}_c) - G_k^2(x_k|t_k, \hat{\psi}_c)\} \right]^{-1}, \quad (10)$$

where

$$G_k(x_k^a|t_k, \hat{\psi}_c) = \frac{\sum_{r_k} r_k^a \binom{n_k}{r_k} \binom{m_k}{t_k - r_k} \hat{\psi}_c^{r_k}}{\sum_{r_k} \binom{n_k}{r_k} \binom{m_k}{t_k - r_k} \hat{\psi}_c^{r_k}}.$$

Another approximate methods are derived from the test statistics such as the extended Cornfield method by Gart (1970, 1971) that performs well for large-stratum sets but poorly for sparse-data sets, while Sato (1990) proposed a good method for both sparse-data and large-stratum settings based on the estimating function, $R_k - \psi S_k$. The approximate $(1 - \alpha)$ confidence limits (ψ_L, ψ_U) are the solutions of the quadratic equation

$$\frac{(|R_+ - \psi S_+| - c)^2}{\psi W} = \chi_\alpha^2, \quad (11)$$

where $W = \sum_k [(Q_k + N_k^{-1})R_k + (P_k + N_k^{-1})S_k]$, and $c = (1 + \psi)/4$ when a continuity correction is needed, or $c = 0$, otherwise. Solving (10), Sato(1990) showed the upper and lower limits

$$(\psi_L, \psi_U) = \frac{2R_+S_+ + \chi_\alpha^2 W \pm \sqrt{(4R_+S_+ + \chi_\alpha^2 W)\chi_\alpha^2 W}}{2S_+^2}, \quad (12)$$

without a continuity correction, and when it is needed, change R_+ and S_+ to $R_+ - \frac{1}{4}$ and $S_+ + \frac{1}{4}$ for calculating ψ_L , and to $R_+ + \frac{1}{4}$ and $S_+ - \frac{1}{4}$ for calculating ψ_U .

4. Monte Carlo Experiments

Several Monte Carlo experiments were conducted to compare the performances of the original exact and mid-P methods, equations (4) to (8), with those of the ln-method using the logarithm of the Mantel-Haenszel estimate $\hat{\psi}_{MH}$ and its asymptotic variance V_R , the logarithm of the CMLE $\hat{\psi}_c$ and its variance V_c , and also with those of Sato's equation (12) with and without the continuity correction.

Table 1

Percentage of trials in which ψ fell below the lower or above the upper bound of the 95% confidence interval, $\psi = 1.0$.

n	m	K	Exact method				ln-method				Sato			
			Original		mid-P		ψ_c, V_c		ψ_{MH}, V_R		Without corr.		With corr.	
			L	U	L	U	L	U	L	U	L	U	L	U
1	1	200	2.0	2.0	2.5	2.5	2.4	2.4	2.4	2.4	2.5	2.5	1.9	1.9
		100	1.8	1.8	2.5	2.6	2.2	2.3	2.2	2.3	2.5	2.6	1.7	1.7
	2	100	1.8	1.9	2.4	2.4	2.3	2.4	2.3	2.4	2.4	2.5	1.8	1.8
1	4	50	1.7	1.7	2.4	2.4	2.3	2.4	2.3	2.3	2.5	2.6	1.6	1.6
		50	1.7	1.8	2.4	2.5	2.3	2.5	2.2	2.5	2.4	2.6	1.6	1.8
	8	25	1.5	1.5	2.4	2.3	2.2	2.3	2.1	2.2	2.5	2.5	1.4	1.4
1	8	50	1.8	1.7	2.4	2.4	2.3	2.4	2.3	2.4	2.4	2.5	1.7	1.7
		25	1.4	1.5	2.3	2.3	2.1	2.3	2.0	2.3	2.4	2.6	1.3	1.5
5	5	20	1.7	1.7	2.4	2.3	2.4	2.3	2.4	2.3	2.6	2.5	1.8	1.7
		10	1.4	1.5	2.3	2.3	2.3	2.3	2.3	2.3	2.6	2.6	1.4	1.5
	15	15	2.1	2.0	2.5	2.5	2.5	2.5	2.5	2.5	2.6	2.5	2.1	2.1
15	15	10	1.9	1.8	2.5	2.4	2.5	2.4	2.5	2.4	2.6	2.5	1.9	1.8
		5	1.6	1.6	2.3	2.4	2.3	2.4	2.4	2.4	2.6	2.7	1.6	1.6
	30	30	2.1	2.1	2.5	2.4	2.5	2.4	2.5	2.4	2.5	2.5	2.1	2.1
30	30	10	1.9	2.0	2.4	2.5	2.4	2.5	2.4	2.5	2.5	2.5	1.9	2.0
		5	1.8	1.7	2.4	2.3	2.4	2.4	2.5	2.4	2.6	2.5	1.9	1.8
5	10	20	1.8	1.8	2.4	2.4	2.4	2.4	2.4	2.4	2.5	2.5	1.8	1.8
		10	1.6	1.6	2.3	2.4	2.3	2.4	2.3	2.4	2.6	2.6	1.6	1.6
	15	30	2.0	2.1	2.4	2.6	2.4	2.5	2.4	2.6	2.5	2.6	2.0	2.1
15	30	10	1.9	1.9	2.5	2.4	2.5	2.4	2.5	2.4	2.6	2.5	1.9	1.9
		5	1.7	1.7	2.4	2.4	2.4	2.4	2.4	2.5	2.6	2.6	1.7	1.8
	60	10	2.2	2.0	2.5	2.4	2.5	2.4	2.6	2.4	2.6	2.4	2.2	2.0
30	60	5	1.9	1.9	2.4	2.5	2.4	2.5	2.4	2.5	2.5	2.6	1.9	1.9

L and U stand for Lower and Upper noncoverage rates, respectively, and corr. for the continuity correction.

We performed several Monte Carlo experiments, using an experiment protocol nearly identical to those reported in Sato (1990), namely $p_{1k} = .3 + .5(k - 1)/(K - 1)$ for $K \in \{200, 100, 50, 25\}$, $k = 1, \dots, K$, and $n_k = 1$ and $m_k = 1, 2, 4, 8$ in matched designs. The experiments in balanced designs used $p_{1k} = .05 + .8(k - 1)/(K - 1)$ for $K \in \{20, 10, 5\}$, $k = 1, \dots, K$, $n_k = m_k = 5, 15, 30$, and experiments in inbalanced designs used the same levels of p_{1K} , K and n_k except $m_k = 2n_k = 10, 30, 60$. All experiments used $\psi = 1, 3.5, 6.5$, and 10000 trials per experiment in order to estimate the actual noncoverage rate of nominal 95% confidence interval.

Binomial random variables were generated using the random number generator by a physical process on a HITAC-M682H in the Institute of Statistical Mathematics. When $R_+ = 0$ or $S_+ = 0$ in a given trial, we ignored the trial for comparability because V_R is undefined.

For each trial we computed six nominal 95% confidence limits (ψ_L, ψ_U) , and cumulated the number of times that the true common odds ratio fell below the lower ($\psi < \psi_L$) or above the upper ($\psi > \psi_U$) limit.

Table 2
Percentage of trials in which ψ fell below the lower or above the upper bound of the 95% confidence interval, $\psi = 3.5$.

n	m	K	Exact method				ln-method				Sato			
			Original		mid-P		ψ_c, V_c		ψ_{MH}, V_R		Without corr.		With corr.	
			L	U	L	U	L	U	L	U	L	U	L	U
1	1	200	1.8	2.0	2.4	2.4	1.9	2.7	1.9	2.7	2.0	2.8	1.5	2.2
		100	1.5	1.7	2.4	2.3	1.4	2.9	1.4	2.9	2.1	2.9	1.2	2.1
1	2	100	1.7	1.8	2.4	2.4	1.9	2.6	2.0	2.6	2.1	2.8	1.3	2.0
		50	1.5	1.7	2.4	2.4	1.6	2.7	1.7	2.7	2.0	3.1	1.0	1.9
1	4	50	1.6	1.7	2.3	2.4	2.0	2.5	2.0	2.6	2.0	2.9	1.1	1.8
		25	1.3	1.5	2.2	2.3	1.4	2.5	1.5	2.5	1.7	3.1	.6	1.7
1	8	50	1.7	1.8	2.4	2.4	2.2	2.5	2.1	2.5	2.1	2.8	1.2	1.8
		25	1.5	1.4	2.4	2.2	2.0	2.3	2.0	2.3	2.0	2.8	.8	1.5
5	5	20	1.6	1.7	2.3	2.4	2.0	2.7	2.1	2.6	2.2	2.8	1.3	1.9
		10	1.3	1.5	2.1	2.3	1.5	2.7	1.6	2.6	2.0	3.1	.8	1.8
15	15	20	1.9	2.0	2.4	2.4	2.3	2.6	2.3	2.5	2.3	2.6	1.7	2.0
		10	1.7	1.9	2.4	2.4	2.2	2.6	2.3	2.6	2.4	2.7	1.5	1.9
30	30	5	1.4	1.6	2.2	2.4	1.9	2.6	2.0	2.6	2.3	2.8	1.1	1.6
		20	2.1	2.1	2.5	2.5	2.4	2.6	2.5	2.5	2.5	2.6	2.0	2.1
		10	1.9	2.0	2.4	2.5	2.3	2.6	2.4	2.6	2.4	2.6	1.8	2.0
		5	1.7	1.8	2.4	2.4	2.2	2.6	2.2	2.6	2.4	2.7	1.5	1.8
5	10	20	1.7	1.8	2.4	2.4	2.2	2.6	2.3	2.5	2.4	2.7	1.5	1.8
		10	1.5	1.6	2.3	2.3	2.0	2.6	2.1	2.5	2.4	2.8	1.1	1.6
15	30	20	2.1	2.2	2.5	2.6	2.4	2.7	2.5	2.6	2.5	2.7	1.9	2.1
		10	1.8	1.9	2.4	2.4	2.3	2.5	2.4	2.5	2.4	2.6	1.6	1.9
30	60	5	1.5	1.7	2.3	2.4	2.0	2.6	2.1	2.5	2.3	2.7	1.2	1.7
		10	2.0	2.0	2.5	2.4	2.4	2.5	2.4	2.5	2.5	2.5	1.9	2.0
		5	1.8	1.9	2.5	2.4	2.3	2.6	2.4	2.5	2.5	2.6	1.6	1.9

L and U stand for Lower and Upper noncoverage rates, respectively.
 and corr. for the continuity correction.

Results, presented in Table 1 for $\psi = 1.0$, show that the original exact method, using (4) and (5), were extremely conservative, and the Sato's method, using (12) with the continuity correction, gave the almost same percentages. The mid-P method, the ln-method, using (8) or (10), and the Sato's method without the correction gave the very accurate and similar lower and upper percentages in all designs, though the ln-method were slightly conservative in the lower tail when $n = 1$, $m = 8$, and $K = 25$.

Results for $\psi = 3.5$ (Table 2) show that the mid-P method were the most accurate and gave the nearest percentages to the nominal size 2.5%. For the mid-P method, none out of 46 lower and upper percentages fell outside the interval (2, 3), while 7 and 5 out of 46 fell outside that interval for the ln-method using V_c and V_R , respectively, and most of lower percentages were smaller than the upper percentage. For the original exact method, results show the almost symmetric but conservative. For the Sato's method, the continuity correction gave conservative results and more asymmetry than the exact method, while only 4 out of 46 lower and upper percentages fell outside the interval (2, 3)

Table 3

Percentage of trials in which ψ fell below the lower or above the upper bound of the 95% confidence interval, $\psi = 6.5$.

n	m	K	Exact method				ln-method				Sato			
			Original		mid-P		ψ_c, V_c		ψ_{MH}, V_R		Without corr.		With corr.	
			L	U	L	U	L	U	L	U	L	U	L	U
1	1	200	1.6	2.0	2.3	2.4	1.5	2.9	1.5	2.9	1.7	3.2	1.1	2.4
		100	1.2	1.7	2.1	2.3	.4	3.0	.4	3.0	1.4	3.2	.6	2.2
1	2	100	1.5	1.9	2.3	2.5	1.5	2.9	1.6	2.9	1.7	3.2	.9	2.1
		50	1.2	1.7	2.1	2.4	.4	2.9	.5	3.0	1.4	3.4	.4	2.0
1	4	50	1.5	1.7	2.4	2.4	1.7	2.7	1.7	2.7	1.7	3.1	.7	1.8
		25	.8	1.4	1.8	2.2	.3	2.6	.3	2.7	1.1	3.4	.1	1.5
1	8	50	1.6	1.7	2.4	2.4	2.1	2.5	2.0	2.6	1.9	2.9	.8	1.6
		25	1.4	1.5	2.2	2.3	1.6	2.5	1.5	2.6	1.6	3.2	.4	1.5
5	5	20	1.4	1.6	2.3	2.4	1.7	2.8	1.7	2.7	1.9	3.0	.8	1.8
		10	.8	1.4	1.7	2.3	.6	2.8	.7	2.7	1.3	3.2	.2	1.6
15	15	20	1.9	1.9	2.4	2.4	2.2	2.6	2.3	2.6	2.3	2.6	1.5	1.9
		10	1.7	1.7	2.4	2.4	2.0	2.7	2.1	2.6	2.2	2.7	1.2	1.8
30	30	5	1.3	1.5	2.2	2.3	1.5	2.8	1.6	2.7	1.9	3.0	.7	1.6
		20	2.1	2.2	2.5	2.6	2.3	2.7	2.3	2.7	2.3	2.7	1.8	2.1
		10	2.0	1.9	2.6	2.5	2.3	2.7	2.4	2.6	2.5	2.7	1.6	1.9
		5	1.6	1.7	2.3	2.3	2.0	2.7	2.0	2.5	2.2	2.7	1.1	1.7
5	10	20	1.7	1.8	2.4	2.4	2.1	2.7	2.1	2.7	2.2	2.9	1.1	1.8
		10	1.3	1.6	2.2	2.3	1.6	2.7	1.8	2.6	2.1	2.9	.6	1.5
15	30	20	2.0	2.1	2.5	2.5	2.4	2.6	2.4	2.6	2.5	2.6	1.7	2.0
		10	1.8	1.8	2.4	2.3	2.2	2.6	2.3	2.5	2.4	2.6	1.4	1.6
30	60	5	1.5	1.7	2.3	2.4	1.9	2.8	2.0	2.7	2.2	2.9	1.0	1.6
		10	2.1	2.0	2.5	2.4	2.4	2.6	2.4	2.5	2.4	2.6	1.7	1.9
		5	1.8	1.9	2.4	2.4	2.1	2.7	2.2	2.6	2.3	2.7	1.3	1.8

L and U stand for Lower and Upper noncoverage rates, respectively.
and corr. for the continuity correction.

without the correction. However, most of lower percentages were smaller than the upper percentage for the Sato's method with or without the correction. Results for $\psi = 6.5$ (Table 3) show that the original exact method gave conservative percentages, especially lower percentages in matched designs, and that the mid-P method gave the most accurate and nearest percentages to the nominal size 2.5%, and only 2 out of 46 lower and upper percentages fell outside the interval (2, 3). For the ln-method, both using V_c or V_R , 7 out of 8 lower percentages fell outside the interval (2, 3) and were quite conservative when the total sample size was small in matched designs, but 3 out of 8 fell outside that interval, respectively, in balanced designs, and only 2 and 1 out of 7 fell outside that interval for using V_c and V_R , respectively, in inbalanced designs, while none out of 46 upper percentages fell outside that interval. The Sato's method with the continuity correction gave more conservative lower percentages than those of the original exact method, while upper percentages were conservative but similar to those of the original exact method in all designs. For the Sato's method without the correction, upper percentages were liberal

in all designs but near to the nominal size 2.5% in balanced and imbalanced designs, while lower percentages in matched designs were conservative but 3 out of 8 and none out of 7 lower percentages fell outside the interval (2, 3) in balanced and imbalanced designs, respectively. In all designs, the Sato's method without the correction gave the nearest two-tailed percentages to the nominal size 5%, regardless of the sample size, the number of strata, and the true common odds ratio.

5. Discussion

For computing the confidence limits of the common odds ratio in a series of 2×2 tables, We compared respective results of the original exact method, the mid-P modification method, the ln-method using the conditional maximum likelihood estimate $\hat{\psi}_c$ and its variance V_c , or using the Mantel-Haenszel estimate $\hat{\psi}_{MH}$ and its asymptotic variance V_R proposed by Robins et al (1986), and the Sato's method (1990) with and without the continuity correction, through Monte Carlo experiments.

Two methods for the ln-method, using $\hat{\psi}_c$ and V_c , and using $\hat{\psi}_{MH}$ and V_R , gave the similar results. In general, all of the approximate methods gave the accurate and symmetric lower and upper percentages when the true common odds ratio was unity, while upper percentages became liberal but lower percentages conservative, reversely, as the true common odds ratio increased, especially in matched designs. Though the Sato's method without the continuity correction gave the nearest two-tailed percentages to the nominal size 5% in all designs, asymmetric results were found in matched designs as well.

In all designs including both sparse-data settings and large-stratum settings, the mid-P exact method gave the most accurate and nearest lower and upper percentages to the nominal size 2.5%, regardless of the true common odds ratio. According to the results, we should recommend the mid-P exact method to construct the confidence interval for the common odds ratio. However, for the mid-P method, 5 out of 138 percentages exceeded to the nominal size 2.5%. Therefore, if it is thought that the actual percentage must be smaller than the nominal size, the original exact method is favor as well as the Sato's method with the continuity correction that gave conservative results in all designs.

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