Confidence interval for odds ratio

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Odds ratio

Odds ratio

Let ξ_A and ξ_B be two independent r.v.'s:

$$\xi_A \sim Bin(n_A, p_A) \qquad \xi_B \sim Bin(n_B, p_B)$$

$$OR = \frac{(p_A/(1-p_A))}{(p_B/(1-p_B))} = \frac{p_A}{(1-p_A)} \cdot \frac{(1-p_B)}{p_B}.$$

Cornfied, J. (1951). A Method of Estimating Comparative Rates from Clinical Data. Applications to Cancer of the Lung, Breast, and Cervix. JNCI: Journal of the National Cancer Institute. 11:1269-1275, DOI: 10.1093/jnci/11.6.1269

Example

	+	−
$Rn-222+$	0.5455	0.4545
$Rn-222-$	0.3451	0.6549

Odds

$$Rn-222+ : 1.2000\ ; \qquad Rn-222- : 0.5269$$

Odds ratio

$$Rn-222+\ \ vs\ Rn-222- : 2.2776$$

Odds ratio

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Problem

Construct confidence interval for odds ratio

Odds ratio

Standard estimator

Let n_{A1} and n_{B1} be observed numbers of successes.

$$\widehat{OR} = \frac{n_{A1}}{n_A - n_{A1}} \cdot \frac{n_B - n_{B1}}{n_{B1}} \qquad (\star)$$

2×2 table

	success	failure	
Group A	n_{A1}	n_{A0}	n_A
Group B	n_{B1}	n_{B0}	n_B
	n_1	n_0	n

Standard estimator

Let n_{A1} and n_{B1} be observed numbers of successes.

$$\widehat{OR} = \frac{n_{A1}}{n_A - n_{A1}} \cdot \frac{n_B - n_{B1}}{n_{B1}} \qquad (\star)$$

Standard (asymptotic) confidence interval

$$\left(\widehat{OR} \cdot \exp\left(u_{\frac{1-\gamma}{2}} \mathcal{S}\right), \widehat{OR} \cdot \exp\left(u_{\frac{1+\gamma}{2}} \mathcal{S}\right)\right)$$

where

$$\mathcal{S} = \sqrt{\frac{1}{n_{A1}} + \frac{1}{n_A - n_{A1}} + \frac{1}{n_{B1}} + \frac{1}{n_B - n_{B1}}}$$

Standard confidence interval - defect #1

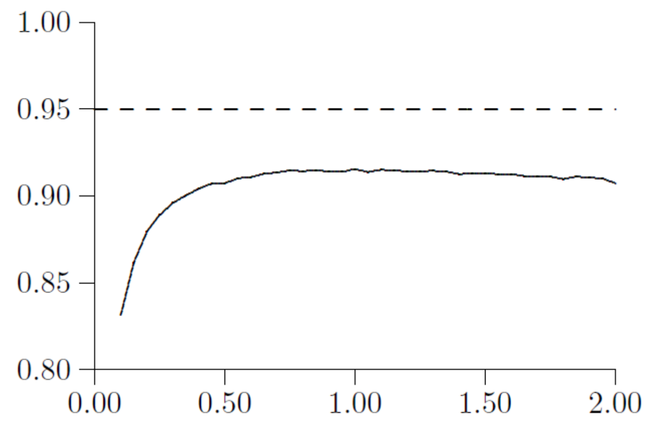
The standard c.i. does not exist if

$$n_{A1} = 0 \text{ or } n_A - n_{A1} = 0 \text{ or } n_{B1} = 0 \text{ or } n_B - n_{B1} = 0$$

http://www.hutchon.net/ConfidOR.htm

Standard confidence interval - defect #2

The probability of coverage is less than the nominal one.
Picture for $n_A = 60$, $n_B = 70$ and $\gamma = 0.95$.



Standard confidence interval - defect #3

Results of few experiments ($n_1 = 60$, $n_2 = 70$)

n_{A1}	n_{B1}	$\widehat{OR}$	$left$	$right$
6	14	0.4444	0.1592	1.2410
8	18	0.4444	0.1776	1.1122
15	30	0.4444	0.2095	0.9428
24	42	0.4444	0.2199	0.8985
36	54	0.4444	0.2078	0.9506
48	63	0.4444	0.1627	1.2141

Statistical model

Standard

$$\left(\mathcal{X}, \{Bin(n_A, p_A) \cdot Bin(n_B, p_B), (p_A, p_B) \in [0,1] \times [0,1]\}\right),$$

$$\mathcal{X} = \{0, 1, \ldots, n_A\} \times \{0, 1, \ldots, n_B\}.$$

New

$$\left(\mathcal{X}, \{\mathcal{P}(n_A, n_B, r), 0 \le r \le +\infty\}\right),$$

$$\mathcal{X} = \left\{\frac{n_{A1}}{n_A - n_{A1}} \cdot \frac{n_B - n_{B1}}{n_{B1}} : n_{A1} \in \{0, 1, \ldots, n_A\}, n_{B1} \in \{0, 1, \ldots, n_B\}\right\}.$$

Extension

$$\widehat{OR} =$$

$$\begin{cases} 0, & \text{for } (n_{A1} = 0, n_{B1} \geq 1) \text{ or } (n_{A1} \geq 1, n_{B1} = n_B) \\ +\infty, & \text{for } (n_{A1} = n_A, n_{B1} \geq 1) \text{ or } (n_{A1} \leq n_A - 1, n_{B1} = 0) \\ 1, & \text{for } (n_{A1} = 0, n_{B1} = 0) \text{ or } (n_{A1} = n_A, n_{B1} = n_B) \\ (\star), & \text{elsewhere} \end{cases}$$

Distribution of $\widehat{OR}$

For given $OR = r > 0$

$$p_B = \frac{p_A}{p_A + r(1-p_A)};\ 1 - p_B = \frac{r(1-p_A)}{p_A + r(1-p_A)}.$$

$$P_{p_A,p_B}\{n_{A1}, n_{B1}\} = \binom{n_A}{n_{A1}} p_A^{n_{A1}} (1-p_A)^{n_A - n_{A1}} \binom{n_B}{n_{B1}} p_B^{n_{B1}} (1-p_B)^{n_B - n_{B1}}.$$

Distribution of $\widehat{OR}$

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$$P_{r,p_A}\{n_{A1}, n_{B1}\} = r^{n_B - n_{B1}} \binom{n_A}{n_{A1}} \binom{n_B}{n_{B1}} \frac{p_A^{n_{A1}+n_{B1}} (1-p_A)^{n_A+n_B-n_{A1}-n_{B1}}}{(p_A + r(1-p_A))^{n_B}}.$$

Probability p_A is eliminated

$$P_r\{n_{A1}, n_{B1}\} = \int_0^1 P_{r,p_A}\{n_{A1}, n_{B1}\}\, dp_A$$
$$= n! \frac{\binom{n_A}{n_{A1}}\binom{n_B}{n_{B1}}}{\binom{n}{n_1}} \left(\frac{1}{r}\right)^{n_{B1}} {}_2F_1\left[n_B, n_1+1; n+2; 1-\frac{1}{r}\right],$$

where

$${}_2F_1[x, y; z; t] =$$
$$\frac{1}{\Gamma(z-x)\Gamma(x)} \int_0^1 t^{x-1}(1-t)^{z-x-1}(1-zt)^{-y} dt \text{ (for } z > x > 0)$$

Distribution of $\widehat{OR}$

CDF for $\widehat{OR}$

For $t \geq 0$

$$F_r(t) = \sum_{n_{A1}=0}^{n_A} \sum_{n_{B1}=0}^{n_B} P_r \left\{n_{A1}, n_{B1}\right\} \mathbf{1}_{\left\{\widehat{OR}(n_{A1}, n_{B1}) \leq t\right\}} \left(n_{A1}, n_{B1}\right).$$

CDF for $\widehat{OR}$

The family $\{F_r, r \geq 0\}$ is stochastically ordered:

$$F_{r_1}(t) \geq F_{r_2}(t) \text{ for } r_1 \leq r_2.$$

$$G_r(t) = P_r\left\{\widehat{OR} < t\right\}$$

$\hat{r}$ is observed odds ratio

Confidence interval for r:

$$(Left\,(\hat{r})\,,\ Right\,(\hat{r})) \qquad (M)$$

$$Left\,(\hat{r}) = \begin{cases} 0, & \hat{r} = 0, \\ 0, & \text{if } \lim_{r\to 0} G_r\,(\hat{r}) < (1+\gamma)/2, \\ r_*, & r_* = \max\{r : G_r\,(\hat{r})\} = (1+\gamma)/2, \end{cases}$$

$$Right\,(\hat{r}) = \begin{cases} \infty, & \hat{r} = \infty, \\ \infty, & \text{if } \lim_{r\to \infty} F_r\,(\hat{r}) > (1-\gamma)/2, \\ r^*, & r^* = \min\{r : F_r\,(\hat{r})\} = (1-\gamma)/2. \end{cases}$$

Theorem

For $n_A > \frac{2}{1-\gamma} - 1$ confidence interval for r is two-sided. Otherwise confidence interval is one-sided.

Remark 1

For $1 \le n_{A1} \le n_A - 1$ and $1 \le n_{B1} \le n_B - 1$

$$P_r\left\{n_{A1}, n_{B1}\right\} \to \begin{cases} 0, & r \to 0 \\ 0, & r \to +\infty \end{cases}$$

Remark 2

$$P_r\{\widehat{OR} = 0\} \to \begin{cases} \frac{n_A}{n_A+1}, & r \to 0 \\ 0, & r \to +\infty \end{cases}$$

Remark 3

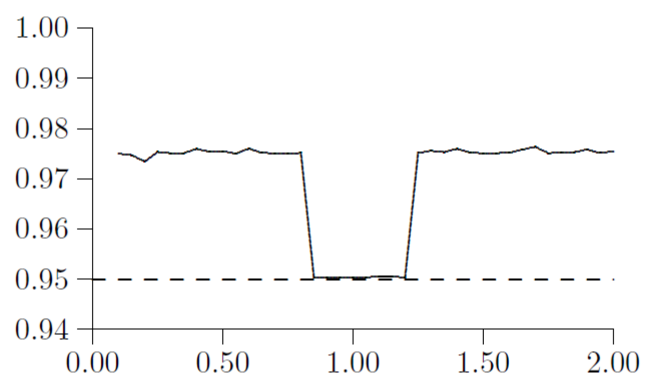
$$P_r\{\widehat{OR} = 1\} \to \begin{cases} \frac{1}{n_A+1}, & r \to 0 \\ \frac{1}{n_A+1}, & r \to +\infty \end{cases}$$

Minimal sample size

γ	0.9	0.95	0.99	0.999
n_A	20	40	200	2000

Confidence interval

Coverage probability



For observed $\hat{r}$ confidence interval for r:

$$\text{if } \hat{r} \in [0,1) : \begin{cases} (0, r^*), & \text{for } n_A \le \frac{2}{1-\gamma} - 1, \\ (r_*, r^*), & \text{for } n_A > \frac{2}{1-\gamma} - 1, \end{cases}$$

$$\text{if } \hat{r} \in [1,+\infty) : \begin{cases} (r_*, +\infty), & \text{for } n_A \le \frac{2}{1-\gamma} - 1, \\ (r_*, r^*), & \text{for } n_A > \frac{2}{1-\gamma} - 1, \end{cases}$$

where r_* and r^* are given by (M).

Confidence interval

$$OR(A \text{ vs } B) = \frac{1}{OR(B \text{ vs } A)}$$

$$Left(A \text{ vs } B) = \frac{1}{Right(B \text{ vs } A)}$$

$$Right(A \text{ vs } B) = \frac{1}{Left(B \text{ vs } A)}$$

Conclusions

- The new confidence interval is based on the exact distribution of the sample odds ratio. Its coverage probability is at least the nominal confidence level
- Closed formulae are not available but the ends may be easily numerically computed with the aid of the standard software.
- The confidence interval may be applied for small as well as for large sample sizes.