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Laud, P.J. orcid.org/0000-0002-3766-7090 (2025) Comments on "New confidence intervals for relative risk of two correlated proportions" by DelRocco N, Wang Y, Wu D, Yang Y and Shan G (2023). Statistics in Biosciences. ISSN 1867-1764

https://doi.org/10.1007/s12561-025-09479-4

Statistics in Biosciences
https://doi.org/10.1007/s12561-025-09479-4

COMMENTARY

Comments on "New Confidence Intervals for Relative Risk of Two Correlated Proportions" by DelRocco N, Wang Y, Wu D, Yang Y and Shan G (2023)

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Received: 28 December 2024 / Revised: 16 February 2025 / Accepted: 21 February 2025

In their recent article for Statistics in Biosciences, DelRocco et al. presented a summary of methods for producing a confidence interval (CI) for relative risk (θ_{RR}) from paired data, including a demonstration of the equivalence of the two established asymptotic score methods [1]. I congratulate the authors on deriving the closed-form solution to the asymptotic score method, with an optional continuity correction, and thank them for including clear details of the algebraic method in their Appendix. However, I would like to highlight a defect in the proposed continuity-corrected method, and provide an improved solution, followed by some additional comments about MOVER intervals.

Unfortunately, the proposed continuity correction does not satisfy the equivariance property [2, 3], which in this context requires that the lower and upper limits for an estimate of $\theta_{RR} = p_1/p_2$ are the reciprocals of the upper and lower limits, respectively, of the estimate of $\theta'_{RR} = p_2/p_1$. For example, the data for the first case study (AHR pre- and post-SCT study) produces an asymptotic score interval of (0.0653, 0.9069), and if the columns and rows of the table are transposed, the result is (1.1027, 15.3188) = (1/0.9069, 1/0.0653). For the ASCC-H method however, the interval from transposed data is (1.0918, 15.357) which does not equal the reciprocal of the results in Table 3 (1/0.9461, 1/0.0555).

To obtain an equivariant continuity-corrected interval, a modified correction term can be applied to the test statistic, using $\left(1+\theta_0\right)$ in place of $(1/n)\left(x_{11}+x_{21}\right)$

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Published online: 12 March 2025

in Eq. (9). A closed-form solution is derived by adapting the algebraic solution in Appendix 3 as follows, with $z = z_{1-\alpha/2}$, first for θ_L:

$$
\begin{aligned}
a &= \left(x_{\bullet 1} + \gamma\right)^4 + z^2 x_{\bullet 1}\left(x_{\bullet 1} + \gamma\right)^2 \\
b &= -\left[2\left(x_{\bullet 1} + \gamma\right)^2 + z^2 x_{\bullet 1}\right]\left[2\left(x_{\bullet 1} + \gamma\right)\left(x_{1\bullet} - \gamma\right) + z^2\left(x_{11} + x_{12} + x_{21}\right)\right] \\
c &= 6\left(x_{\bullet 1} + \gamma\right)^2\left(x_{1\bullet} - \gamma\right)^2 + z^4\left(x_{1\bullet} + x_{\bullet 1}\right)\left(x_{11} + x_{12} + x_{21}\right) \\
&\quad + z^2\left[x_{\bullet 1}\left(x_{1\bullet} - \gamma\right)^2 + 4\left(x_{11} + x_{12} + x_{21}\right)\left(x_{1\bullet} - \gamma\right)\left(x_{\bullet 1} + \gamma\right) + x_{1\bullet}\left(x_{\bullet 1} + \gamma\right)^2\right] \\
d &= -\left[2\left(x_{1\bullet} - \gamma\right)^2 + z^2 x_{1\bullet}\right]\left[2\left(x_{\bullet 1} + \gamma\right)\left(x_{1\bullet} - \gamma\right) + z^2\left(x_{11} + x_{12} + x_{21}\right)\right] \\
e &= \left(x_{1\bullet} - \gamma\right)^4 + z^2 x_{1\bullet}\left(x_{1\bullet} - \gamma\right)^2
\end{aligned}
$$

where the continuity correction γ is a constant between 0 and 0.5.

Then for θ_U:

$$
\begin{aligned}
a &= \left(x_{\bullet 1} - \gamma\right)^4 + z^2 x_{\bullet 1}\left(x_{\bullet 1} - \gamma\right)^2 \\
b &= -\left[2\left(x_{\bullet 1} - \gamma\right)^2 + z^2 x_{\bullet 1}\right]\left[2\left(x_{\bullet 1} - \gamma\right)\left(x_{1\bullet} + \gamma\right) + z^2\left(x_{11} + x_{12} + x_{21}\right)\right] \\
c &= 6\left(x_{\bullet 1} - \gamma\right)^2\left(x_{1\bullet} + \gamma\right)^2 + z^4\left(x_{1\bullet} + x_{\bullet 1}\right)\left(x_{11} + x_{12} + x_{21}\right) \\
&\quad + z^2\left[x_{\bullet 1}\left(x_{1\bullet} + \gamma\right)^2 + 4\left(x_{11} + x_{12} + x_{21}\right)\left(x_{1\bullet} + \gamma\right)\left(x_{\bullet 1} - \gamma\right) + x_{1\bullet}\left(x_{\bullet 1} - \gamma\right)^2\right] \\
d &= -\left[2\left(x_{1\bullet} + \gamma\right)^2 + z^2 x_{1\bullet}\right]\left[2\left(x_{\bullet 1} - \gamma\right)\left(x_{1\bullet} + \gamma\right) + z^2\left(x_{11} + x_{12} + x_{21}\right)\right] \\
e &= \left(x_{1\bullet} + \gamma\right)^4 + z^2 x_{1\bullet}\left(x_{1\bullet} + \gamma\right)^2
\end{aligned}
$$

For simplicity of programming, I prefer to scale the correction using a parameter γ instead of $1/\delta$, (e.g. $\gamma=0.5$ in place of $\delta=2$) so that the uncorrected method is obtained within the same code by setting $\gamma=0$. Using the above correction with $\gamma=0.5$, an interval is obtained which is consistent with the continuity-corrected McNemar test. (For example, using the AHR pre- and post-SCT study data in Table 2 of DelRocco et al., the p-value from a continuity-corrected McNemar test is $p=0.0771$, and the corresponding $100\times(1-0.771)\%$ confidence interval with $\gamma=0.5$ is (0.024, 1.000)). The same is not the case for DelRocco et al.'s 'ASCC-H' method. Although there might be some users who require an interval to agree with the standard continuity-corrected test in such a way (and thus emulate an exact interval achieving the minimum coverage criterion), corrections of such a magnitude are usually excessively conservative. Therefore, smaller values of γ (such as 0.25 or 0.125) allow intermediate "compromise" corrections of varying strength.

Note that the MOVER intervals may also be adapted to incorporate a continuity correction (again, with scope for varying the strength of the correction), by applying continuity-corrected methods to the intervals for the individual proportions p_1 and p_2 [4]. Selecting an equal-tailed method such as Jeffreys, SCAS [4], or mid-p [5], is likely to result in improved location properties compared with the Wilson interval, which has been shown to have a systematic bias in one-sided coverage [6].

Table 1 Illustrative 95% CIs for θ_{RR} for the AHR pre- and post- SCT study

Method	Lower limit	Upper limit	Log width
Asymptotic score	0.0653	0.9069	2.63
ASCC ($\gamma = 0.125$)	0.0584	0.9571	2.80
ASCC ($\gamma = 0.5$)	0.0398	1.1195	3.34
'ASCC-H' (DelRocco)	0.0555	0.9461	2.84
MOVER Wilson ($\hat{\phi}$ uncorrected)	0.0686	0.8695	2.54
MOVER Wilson ($\hat{\phi}$ corrected)	0.0660	0.9048	2.62
MOVER Jeffreys ($\hat{\phi}$ corrected)	0.0513	0.8731	2.83
MOVER-cc Jeffreys ($\gamma = 0.125$)	0.0456	0.9072	2.99

Furthermore, a correction to the correlation estimate $\hat{\phi}$ within the MOVER calculations has also been suggested by Newcombe [2], and labelled as "continuity corrected $\hat{\phi}$"—somewhat confusingly, since its effect is quite different from other continuity corrections. Fagerland et al. [7] included this correction in their evaluation of MOVER intervals for the risk difference, but not for the ratio. As both methods use the same correlation estimate, I see no reason to omit the correlation correction in the estimation of θ_{RR}.

For software validation purposes, example confidence intervals for the above methods are displayed in Table 1, using the AHR case study data for reference against Table 3 of the original article. These are not intended for any formal comparative purpose, other than to illustrate the relative width increase induced by each of the various continuity corrections, and the shift in location for the MOVER Jeffreys method. I include log width, for comparison with the results in Fagerland et al., but in my view interval location is more important than width. As such, the fact that the MOVER Wilson intervals for this example dataset are less wide than MOVER Jeffreys or SCAS does not necessarily mean they are superior. Full evaluation of the merits of these methods requires inspection of their coverage and location properties, which is a subject of further research.

All of the above proposed methods are included in a planned update to the *ratesci* package for R [8].

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