Tests for Homogeneity of Risk Differences in Stratified Design with Correlated Bilateral Data

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SUPPLEMENTARY MATERIALS

Web Appendix

A. Derivation of the score statistic

From Equation (3) in the text, we have the first partial derivatives as follows:

$$\begin{aligned}
\frac{\partial \ell_j(\delta,\lambda_{1j},R_j)}{\partial \delta} &= \frac{2m_{00j}[R_j(\delta+\lambda_{1j})-1]}{1+R_j(\delta+\lambda_{1j})^2-2(\delta+\lambda_{1j})} + \frac{m_{10j}+2m_{20j}}{\delta+\lambda_{1j}} - \frac{m_{10j}R_j}{1-R_j(\delta+\lambda_{1j})} = S_j, \qquad (A.1)\\
\frac{\partial \ell_j(\delta,\lambda_{1j},R_j)}{\partial \lambda_{1j}} &= \frac{\partial \ell_j(\delta,\lambda_{1j},R_j)}{\partial \delta} + \frac{2m_{01j}(R_j\lambda_{1j}-1)}{1+R_j\lambda_{1j}^2-2\lambda_{1j}} + \frac{m_{11j}+2m_{21j}}{\lambda_{1j}} - \frac{m_{11j}R_j}{1-R_j\lambda_{1j}},\\
\frac{\partial \ell_j(\delta,\lambda_{1j},R_j)}{\partial R_j} &= \frac{m_{00j}(\delta+\lambda_{1j})^2}{1+R_j(\delta+\lambda_{1j})^2-2(\delta+\lambda_{1j})} - \frac{m_{10j}(\delta+\lambda_{1j})}{1-R_j(\delta+\lambda_{1j})}\\
&\quad + \frac{m_{20j}+m_{21j}}{R_j} + \frac{m_{01j}\lambda_{1j}^2}{1+R_j\lambda_{1j}^2-2\lambda_{1j}} - \frac{m_{11j}\lambda_{1j}}{1-R_j\lambda_{1j}}.
\end{aligned}$$

The second partial derivatives are given by

$$\begin{aligned}
\frac{\partial^2 \ell_j(\delta,\lambda_{1j},R_j)}{\partial^2 \delta} &= \frac{2m_{00j}\{R_j[1+R_j(\delta+\lambda_{1j})^2-2(\delta+\lambda_{1j})]-2[R_j(\delta+\lambda_{1j})-1]^2\}}{[1+R_j(\delta+\lambda_{1j})^2-2(\delta+\lambda_{1j})]^2}\\
&\quad -\frac{m_{10j}+2m_{20j}}{(\delta+\lambda_{1j})^2} - \frac{m_{10j}R_j^2}{[1-R_j(\delta+\lambda_{1j})]^2},\\
\frac{\partial^2 \ell_j(\delta,\lambda_{1j},R_j)}{\partial\delta\partial\lambda_{1j}} &= \frac{\partial^2 \ell_j(\delta,\lambda_{1j},R_j)}{\partial^2 \delta},\\
\frac{\partial^2 \ell_j(\delta,\lambda_{1j},R_j)}{\partial\delta\partial R_j} &= \frac{2m_{00j}(\delta+\lambda_{1j})[1-(\delta+\lambda_{1j})]}{[1+R_j(\delta+\lambda_{1j})^2-2(\delta+\lambda_{1j})]^2} - \frac{m_{10j}}{[1-R_j(\delta+\lambda_{1j})]^2},\\
\frac{\partial^2 \ell_j(\delta,\lambda_{1j},R_j)}{\partial^2 \lambda_{1j}} &= \frac{\partial^2 \ell_j(\delta,\lambda_{1j},R_j)}{\partial^2 \delta} + \frac{2m_{01j}[R_j(1+R_j\lambda_{1j}^2-2\lambda_{1j})-2(R_j\lambda_{1j}-1)^2]}{(1+R_j\lambda_{1j}^2-2\lambda_{1j})^2}\\
&\quad -\frac{m_{11j}+2m_{21j}}{\lambda_{1j}^2} - \frac{m_{11j}R_j^2}{(1-R_j\lambda_{1j})^2},\\
\frac{\partial^2 \ell_j(\delta,\lambda_{1j},R_j)}{\partial\lambda_{1j}\partial R_j} &= \frac{\partial^2 \ell_j(\delta,\lambda_{1j},R_j)}{\partial\delta\partial R_j} + \frac{2m_{01j}\lambda_{1j}(1-\lambda_{1j})}{(1+R_j\lambda_{1j}^2-2\lambda_{1j})^2} - \frac{m_{11j}}{(1-R_j\lambda_{1j})^2},\\
\frac{\partial^2 \ell_j(\delta,\lambda_{1j},R_j)}{\partial^2 R_j} &= -\frac{m_{00j}(\delta+\lambda_{1j})^4}{[1+R_j(\delta+\lambda_{1j})^2-2(\delta+\lambda_{1j})]^2} - \frac{m_{10j}(\delta+\lambda_{1j})^2}{[1-R_j(\delta+\lambda_{1j})]^2}\\
&\quad -\frac{m_{01j}\lambda_{1j}^4}{[1+R_j\lambda_{1j}^2-2\lambda_{1j}]^2} - \frac{m_{11j}\lambda_{1j}^2}{1-R_j\lambda_{1j}^2} - \frac{m_{20j}+m_{21j}}{R_j^2}.
\end{aligned}$$

Let $\boldsymbol{I}^{(j)} = (I_{kl}^{(j)})$ be the 3×3 symmetrical Fisher information matrix for the jth stratum, whose elements are given by

$$\begin{aligned}
I_{11}^{(j)} &= E(-\tfrac{\partial^2\ell_j(\delta,\lambda_{1j},R_j)}{\partial^2\delta}) \\
&= 2m_{+0j}\{\tfrac{[R_j(\delta+\lambda_{1j})-1]^2+(1-R_j)}{1+R_j(\delta+\lambda_{1j})^2-2(\delta+\lambda_{1j})}+\tfrac{1}{\delta+\lambda_{1j}}+\tfrac{R_j^2(\delta+\lambda_{1j})}{1-R_j(\delta+\lambda_{1j})}\}, \\
I_{12}^{(j)} &= E(-\tfrac{\partial^2\ell_j(\delta,\lambda_{1j},R_j)}{\partial\delta\partial\lambda_{1j}}) = I_{11}^{(j)}, \\
I_{13}^{(j)} &= E(-\tfrac{\partial^2\ell_j(\delta,\lambda_{1j},R_j)}{\partial\delta\partial R_j}) = 2m_{+0j}(\delta+\lambda_{1j})\{\tfrac{1}{1-R_j(\delta+\lambda_{1j})}-\tfrac{[1-(\delta+\lambda_{1j})]}{1+R_j(\delta+\lambda_{1j})^2-2(\delta+\lambda_{1j})}\}, \\
I_{22}^{(j)} &= E(-\tfrac{\partial^2\ell_j(\delta,\lambda_{1j},R_j)}{\partial^2\lambda_{1j}}) \\
&= I_{11}^{(j)}+2m_{+1j}[\tfrac{(R_j\lambda_{1j}-1)^2+1-R_j}{1+R_j\lambda_{1j}^2-2\lambda_{1j}}+\tfrac{1}{\lambda_{1j}}+\tfrac{\lambda_{1j}R_j^2}{1-R_j\lambda_{1j}}], \\
I_{23}^{(j)} &= E(-\tfrac{\partial^2\ell_j(\delta,\lambda_{1j},R_j)}{\partial\lambda_{1j}\partial R_j}) \\
&= I_{13}^{(j)}+2m_{+1j}\lambda_{1j}[\tfrac{1}{1-R_j\lambda_{1j}}-\tfrac{1-\lambda_{1j}}{1+R_j\lambda_{1j}^2-2\lambda_{1j}}], \\
I_{33}^{(j)} &= E(-\tfrac{\partial^2\ell_j(\delta,\lambda_{1j},R_j)}{\partial^2 R_j}) \\
&= m_{+0j}(\delta+\lambda_{1j})^2[\tfrac{(\delta+\lambda_{1j})^2}{1+R_j(\delta+\lambda_{1j})^2-2(\delta+\lambda_{1j})}+\tfrac{2(\delta+\lambda_{1j})}{1-R_j(\delta+\lambda_{1j})}+\tfrac{1}{R_j}]+ \\
&\quad m_{+1j}\lambda_{1j}^2[\tfrac{\lambda_{1j}^2}{1+R_j\lambda_{1j}^2-2\lambda_{1j}}+\tfrac{2\lambda_{1j}}{1-R_j\lambda_{1j}}+\tfrac{1}{R_j}],
\end{aligned}$$

The first main-diagonal element of the inverse of the Fisher information matrix for the jth stratum is given by

$$\begin{aligned}
I_j(1,1) &= \left[I_{11}^{(j)}-(I_{12}^{(j)},I_{13}^{(j)})\begin{pmatrix} I_{22}^{(j)} & I_{23}^{(j)} \\ I_{23}^{(j)} & I_{33}^{(j)}\end{pmatrix}^{-1}\begin{pmatrix} I_{12}^{(j)} \\ I_{13}^{(j)}\end{pmatrix}\right]^{-1}, \\
&= \tfrac{I_{22}^{(j)}I_{33}^{(j)}-(I_{23}^{(j)})^2}{2I_{12}^{(j)}I_{13}^{(j)}I_{23}^{(j)}+I_{11}^{(j)}I_{22}^{(j)}I_{33}^{(j)}-I_{11}^{(j)}(I_{23}^{(j)})^2-I_{22}^{(j)}(I_{13}^{(j)})^2-I_{33}^{(j)}(I_{12}^{(j)})^2}.
\end{aligned} \qquad (A.2)$$

Therefore, the homogeneity score test for testing $H_0 : \delta_j = \delta$ for all $j \in \{1, 2, \cdots, J\}$ can be given by

$$T_{sc} = \sum_{j=1}^{J} S_j^2 \cdot I_j(1,1)|_{\delta=\tilde{\delta},\lambda_{1j}=\tilde{\lambda}_{1j},R_j=\tilde{R}_j},$$

where $\tilde{\delta}$, $\tilde{\lambda}_{1j}$ and $\tilde{R}_j$ are the constrained MLEs of δ, λ_{1j} and R_j.

Therefore, the modified score test statistic is given by

$$T_{sc}^* = \{\sum_{j=1}^{J} S_j^2 \cdot I_j(1,1) - (\sum_{j=1}^{J} S_j)^2/\sum_{j=1}^{J}[I_j(1,1)]^{-1}\}|_{\delta=\tilde{\delta}^*,\lambda_{1j}=\tilde{\lambda}_{1j}^*,R_j=\tilde{R}_j^*}.$$

B. Derivation of sample size formulas

(i) Derivation of sample size formulae based on T_{wls}

Under the alternative hypothesis H_1, T_{wls} is asymptotically distributed as non-central chi-square distribution with $J-1$ degrees of freedom and non-central parameter τ_1. From Equation (6) in the text, we have

$$\begin{aligned}
\tau_1 + J - 1 &= E(T_{wls}|H_1) = E[\sum_{j=1}^{J}\hat{w}_j(\hat{\delta}_j-\sum_{j=1}^{J}\hat{w}_j\hat{\delta}_j/\sum_{j=1}^{J}\hat{w}_j)^2|H_1] \\
&\approx \sum_{j=1}^{J}E[(\hat{\delta}_j-\sum_{j=1}^{J}\hat{w}_j\hat{\delta}_j/\sum_{j=1}^{J}\hat{w}_j)^2|H_1]\cdot m_{+1}W_{1j},
\end{aligned} \qquad (B.1)$$

where $m_{+1}W_{1j}$ is the value of $\hat{w}_j$ with all observed frequencies being substituted by with their expected frequencies, and W_{1j} is given by

$$\begin{aligned} W_{1j} &= 4\kappa r_j/\{(p_{10j}+2p_{20j})(p_{00j}-p_{20j})+\kappa(p_{11j}+2p_{21j})(p_{01j}-p_{21j})+2(1+\kappa)(\kappa p_{20j}+p_{21j}) \\ &\quad \cdot[(p_{10j}+2p_{20j})^2+\kappa(p_{11j}+2p_{21j})^2]/[\kappa(p_{10j}+2p_{20j})+(p_{11j}+2p_{21j})]^2\}. \qquad (B.2) \end{aligned}$$

Since

$$E\{[\hat{\delta}_j-\sum_{j=1}^{J}\hat{w}_j\hat{\delta}_j/\sum_{j=1}^{J}\hat{w}_j]|H_1\}=\delta_j-\sum_{j=1}^{J}W_{1j}\delta_j/\sum_{j=1}^{J}W_{1j},$$

and

$$\mathrm{Var}\{[\hat{\delta}_j-\sum_{j=1}^{J}\hat{w}_j\hat{\delta}_j/\sum_{j=1}^{J}\hat{w}_j]|H_1\}=(1/W_{1j}-1/\sum_{j=1}^{J}W_{1j})/m_{+1},$$

then

$$E\{[\hat{\delta}_j-\sum_{j=1}^{J}\hat{w}_j\hat{\delta}_j/\sum_{j=1}^{J}\hat{w}_j]^2|H_1\}=(\delta_j-\sum_{j=1}^{J}W_{1j}\delta_j/\sum_{j=1}^{J}W_{1j})^2+(1/W_{1j}-1/\sum_{j=1}^{J}W_{1j})/m_{+1}.$$

To obtain the sample size for achieving the power of $1-\beta$ at the significance level α, we can solve the equation $\chi^2_{J-1,1-\beta}(\tau_1)=\chi^2_{J-1,1-\alpha}$ to obtain the non-central parameter τ_1, then the sample size formulae based on WLS statistic can be given by

$$n_{wls}=m_{+1}=\frac{\tau_1}{\sum_{j=1}^{J}W_{1j}[\delta_j-\sum_{j=1}^{J}W_{1j}\delta_j/\sum_{j=1}^{J}W_{1j}]^2}.$$

(ii) Derivation of sample size formulae based on T_{mh}

Under the alternative hypothesis H_1, T_{mh} is asymptotically distributed as non-central chi-square distribution with $J-1$ degrees of freedom and non-central parameter τ_2. From Equation (8) in the text, we have

$$\tau_2+J-1=E(T_{mh}|H_1)=E[\sum_{j=1}^{J}\bar{w}_j(\hat{\delta}_j-\bar{\delta}_{wls})^2|H_1]\approx\sum_{j=1}^{J}E[(\hat{\delta}_j-\bar{\delta}_{wls})^2|H_1]\cdot m_{+1}W_{2j}, \qquad (B.3)$$

where $m_{+1}W_{2j}$ is the value of $\bar{w}_j$ with all observed frequencies being substituted by with their expected frequencies, and W_{2j} is given by

$$\begin{aligned} W_{2j} &= 4r_j/\Big\{[(1+\kappa)(p_{11j}+2p_{21j})+\sum_{j=1}^{J}r_j(p_{10j}+2p_{20j}-p_{11j}-2p_{21j})]/\kappa \\ &\quad +\Big[(p_{11j}+2p_{21j})^2+[p_{11j}+2p_{21j}+\sum_{j=1}^{J}r_j(p_{10j}+2p_{20j}-p_{11j}-2p_{21j})]^2/\kappa\Big]\cdot \\ &\quad \Big[2(1+\kappa)(\kappa p_{20j}+p_{21j})/[\kappa(p_{10j}+2p_{20j})+(p_{11j}+2p_{21j})]^2-1\Big]\Big\}. \qquad (B.4) \end{aligned}$$

Similarly, we have

$$\begin{aligned} E(\hat{\delta}_j - \bar{\delta}_{wls}|H_1) &\approx \delta_j - \frac{\sum_{j=1}^J W_{2j}\delta_j}{\sum_{j=1}^J W_{2j}} \quad \text{and} \\ \mathrm{Var}(\hat{\delta}_j - \bar{\delta}_{wls}|H_1) &= \mathrm{Var}(\hat{\delta}_j|H_1) + \mathrm{Var}(\bar{\delta}_{wls}|H_1) - 2\mathrm{Cov}(\hat{\delta}_j, \bar{\delta}_{wls}|H_1) \\ &\approx \frac{1}{m_{+1}}[\frac{1}{W_{3j}} + \frac{\sum_{j=1}^J (W_{2j}^2/W_{3j})}{(\sum_{j=1}^J W_{2j})^2} - \frac{2(W_{2j}/W_{3j})}{\sum_{j=1}^J W_{2j}}]. \end{aligned}$$

where W_{3j} can be expressed as

$$W_{3j} = \frac{4r_j}{\frac{p_{10j}+4p_{20j}-(p_{10j}+2p_{20j})^2}{\kappa} + p_{11j}+4p_{21j}-(p_{11j}+2p_{21j})^2}. \qquad (B.5)$$

Therefore,

$$\begin{aligned} E[(\hat{\delta}_j - \bar{\delta}_{wls})^2|H_1] &= E(\hat{\delta}_j - \bar{\delta}_{wls}|H_1)^2 + \mathrm{Var}(\hat{\delta}_j - \bar{\delta}_{wls}|H_1) \\ &= (\delta_j - \frac{\sum_{j=1}^J W_{2j}\delta_j}{\sum_{j=1}^J W_{2j}})^2 + \frac{1}{m_{+1}}[\frac{1}{W_{3j}} + \frac{\sum_{j=1}^J (W_{2j}^2/W_{3j})}{(\sum_{j=1}^J W_{2j})^2} - \frac{2(W_{2j}/W_{3j})}{\sum_{j=1}^J W_{2j}}]. \end{aligned}$$

and (B.3) becomes

$$\tau_2 + J - 1 = m_{+1}\sum_{j=1}^J(\delta_j - \frac{\sum_{j=1}^J W_{2j}\delta_j}{\sum_{j=1}^J W_{2j}})^2 W_{2j} + \sum_{j=1}^J(\frac{W_{2j}}{W_{3j}}) - \frac{\sum_{j=1}^J (W_{2j}^2/W_{3j})}{\sum_{j=1}^J W_{2j}}.$$

Since the non-central parameter τ_2 is obtained by solving the equation $\chi^2_{J-1,1-\beta}(\tau_2) = \chi^2_{J-1,1-\alpha}$, then the approximate sample size based on Mantel-Haenszel-estimate-based statistic is given by

$$n_{mh} = m_{+1} = \frac{\tau_2 + (J-1) - \sum_{j=1}^J (W_{2j}/W_{3j}) + \sum_{j=1}^J (W_{2j}^2/W_{3j})/\sum_{j=1}^J W_{2j}}{\sum_{j=1}^J W_{2j}(\delta_j - \sum_{j=1}^J W_{2j}\delta_j/\sum_{j=1}^J W_{2j})^2}.$$

(iii) Derivation of sample size formulae based on T_{twls}

Under the alternative hypothesis H_1, T_{twls} is asymptotically distributed as non-central chi-square distribution with $J-1$ degrees of freedom and non-central parameter τ_3. From Equation (9) in the text, we have

$$\begin{aligned} \tau_3 + J - 1 &= E(T_{twls}|H_1) = E[\sum_{j=1}^J \tilde{w}_j(\tanh^{-1}(\hat{\delta}_j) - \sum_{j=1}^J \tilde{w}_j \tanh^{-1}(\hat{\delta}_j)/\sum_{j=1}^J \tilde{w}_j)^2|H_1] \\ &\approx \sum_{j=1}^J E[(\tanh^{-1}(\hat{\delta}_j) - \sum_{j=1}^J \tilde{w}_j \tanh^{-1}(\hat{\delta}_j)/\sum_{j=1}^J \tilde{w}_j)^2|H_1] \cdot m_{+1}W_{4j}, \qquad (B.6) \end{aligned}$$

where $m_{+1}W_{4j}$ is the value of $\tilde{w}_j$ with all observed frequencies being substituted by with their expected frequencies, and W_{4j} is given by

$$\begin{aligned} W_{4j} &= 4kr_j[1-(p_{10j}+2p_{20j}-p_{11j}-2p_{21j})^2/4]^2/\{(p_{10j}+2p_{20j})(p_{00j}-p_{20j}) \\ &\quad +\kappa(p_{11j}+2p_{21j})(p_{01j}-p_{21j})+2(1+\kappa)(\kappa p_{20j}+p_{21j}) \\ &\quad \cdot[(p_{10j}+2p_{20j})^2+\kappa(p_{11j}+2p_{21j})^2]/[\kappa(p_{10j}+2p_{20j})+p_{11j}+2p_{21j}]^2\}. \qquad (B.7) \end{aligned}$$

Thus,

$$E\{[\tanh^{-1}(\hat{\delta}_j)-\sum_{j=1}^{J}\tilde{w}_j\tanh^{-1}(\hat{\delta}_j)/\sum_{j=1}^{J}\tilde{w}_j]|H_1\}=\tanh^{-1}(\delta_j)-\sum_{j=1}^{J}W_{4j}\tanh^{-1}(\delta_j)/\sum_{j=1}^{J}W_{4j},$$

and

$$\mathrm{Var}\{[\tanh^{-1}(\hat{\delta}_j)-\sum_{j=1}^{J}\tilde{w}_j\tanh^{-1}(\hat{\delta}_j)/\sum_{j=1}^{J}\tilde{w}_j]|H_1\}=(1/W_{4j}-1/\sum_{j=1}^{J}W_{4j})/m_{+1}.$$

To obtain the sample size for achieving the power of $1-\beta$ at the significance level α, we can solve the equation $\chi^2_{J-1,1-\beta}(\tau_3)=\chi^2_{J-1,1-\alpha}$ to obtain the non-central parameter τ_3, then the sample size formulae based on WLS statistic with inverse hyperbolic tangent transformation can be given by

$$n_{twls}=m_{+1}=\frac{\tau_3}{\sum_{j=1}^{J}W_{4j}[\tanh^{-1}(\delta_j)-\sum_{j=1}^{J}W_{4j}\tanh^{-1}(\delta_j)/\sum_{j=1}^{J}W_{4j}]^2}.$$