Supporting Information of

Excess Relative Risk as an Effect Measure in Case-Control Studies of Rare Diseases

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S7 Exhibit. A proof that a constant excess relative risk (ERR) and a constant risk ratio (RR) models cannot be reconciled except for a weak exposure or when disease risks vary little across strata.

Under a constant ERR model, we have $\mathrm{RR}_s = \frac{\mathrm{Risk}_{s,2} + \mathrm{ER}}{\mathrm{Risk}_{s,2}} = 1 + \frac{\mathrm{Risk}_{E=2} \times \mathrm{ERR}}{\mathrm{Risk}_{s,2}}$.

Therefore,

$$\begin{aligned}\mathrm{Var}\left(\mathrm{RR}_s\right) &= \mathrm{Var}\left(\frac{\mathrm{Risk}_{E=2} \times \mathrm{ERR}}{\mathrm{Risk}_{s,2}}\right) \\ &= \frac{\mathrm{Risk}_{E=2}^2 \times \mathrm{ERR}^2}{\mathrm{Risk}_{E=2}^4} \times \mathrm{Var}\left(\mathrm{Risk}_{s,2}\right) \\ &= \mathrm{ERR}^2 \times \mathrm{CV}^2\left(\mathrm{Risk}_{s,2}\right),\end{aligned}$$

where $\mathrm{CV}\left(\mathrm{Risk}_{s,2}\right) = \frac{\sqrt{\mathrm{Var}\left(\mathrm{Risk}_{s,2}\right)}}{\mathrm{Risk}_{E=2}}$ is the coefficient of variation of the disease risks of the unexposed population across the strata. Under a constant RR model, we have

$\mathrm{ERR}_s = \frac{\mathrm{RR} \times \mathrm{Risk}_{s,2} - \mathrm{Risk}_{s,2}}{\mathrm{Risk}_{E=2}} = \frac{\left(\mathrm{RR} - 1\right)}{\mathrm{Risk}_{E=2}} \times \mathrm{Risk}_{s,2}$. Therefore,

$$\begin{aligned}\mathrm{Var}\left(\mathrm{ERR}_s\right) &= \mathrm{Var}\left[\frac{\left(\mathrm{RR} - 1\right)}{\mathrm{Risk}_{E=2}} \times \mathrm{Risk}_{s,2}\right] \\ &= \frac{\left(\mathrm{RR} - 1\right)^2}{\mathrm{Risk}_{E=2}^2} \times \mathrm{Var}\left(\mathrm{Risk}_{s,2}\right) \\ &= \left(\mathrm{RR} - 1\right)^2 \times \mathrm{CV}^2\left(\mathrm{Risk}_{s,2}\right).\end{aligned}$$