Supporting Information of

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

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S3 Exhibit. Estimation of population attributable fraction (PAF) and attributable fraction among the exposed population (AFE) under heterogeneity.

Under heterogeneity,

\[
\text{AFE}_{\text{het}} = \frac{\hat{\text{Risk}}_{E=1} - \sum_{s=1}^{L} \hat{\Pr}(S = s | E = 1) \times \hat{\text{Risk}}_{s,2}}{\hat{\text{Risk}}_{E=1}}
\]

\[
f \times \frac{\text{CS}_{s,1}}{\text{CN}_{s,1}} - \sum_{s=1}^{L} \frac{\text{CN}_{s,1}}{\text{CN}_{s,2}} \times f \times \frac{\text{CS}_{s,2}}{\text{CN}_{s,2}}
\]

\[
= \left( \text{CS}_{s,1} - \sum_{s=1}^{L} \frac{\text{CS}_{s,2} \times \text{CN}_{s,1}}{\text{CN}_{s,2}} \right) \text{CN}_{s,1}
\]

\[
= \sum_{s=1}^{L} \frac{\text{CN}_{s,1}}{\text{CN}_{r,1}} \times \left( \frac{\text{CS}_{s,1}}{\text{CN}_{s,1}} - \frac{\text{CS}_{s,2}}{\text{CN}_{s,2}} \right) \frac{\text{CN}_{r,1}}{\text{CS}_{r,1}}
\]

\[
= \sum_{s=1}^{L} \frac{\text{CN}_{s,1}}{\text{CN}_{r,1}} \times \phi_{s}.
\]

Using Miettinen’s case-based formula (see Miettinen OS. Proportion of disease caused or prevented by a given exposure, trait or intervention. Am J Epidemiol. 1974;99:325–332),

\[
\text{PAF}_{\text{het}} = (\text{exposure prevalence among cases}) \times \text{AFE}_{\text{het}}
\]

\[
= \frac{\text{CS}_{r,1}}{n_{1}} \times \sum_{s=1}^{L} \frac{\text{CN}_{s,1}}{\text{CN}_{r,1}} \times \left( \frac{\text{CS}_{s,1}}{\text{CN}_{s,1}} - \frac{\text{CS}_{s,2}}{\text{CN}_{s,2}} \right) \times \frac{\text{CN}_{r,1}}{\text{CS}_{r,1}}
\]

\[
= \sum_{s=1}^{L} \frac{\text{CN}_{s,1}}{\text{CN}_{r,1}} \times \left( \frac{\text{CS}_{s,1}}{\text{CN}_{s,1}} - \frac{\text{CS}_{s,2}}{\text{CN}_{s,2}} \right) \times \frac{\text{CN}_{r,1}}{n_{1}}
\]

\[
= \sum_{s=1}^{L} \frac{\text{CN}_{s,1}}{\text{CN}_{r,1}} \times \psi_{s}.
\]