Additional file 1. Derivations of the bounding formulas.

Let $\text{Rate}^{\text{profile}=x_1,x_2}(t)$ denote the (instantaneous) disease rate at follow-up time t, for people in the population with $\text{profile}=x_1,x_2$. Let $\text{Rate}_{\text{class}=c_1,c_2}(t)$ denote the (instantaneous) arrival rate in the study population for the unknown components for the $\text{class}=c_1,c_2$ sufficient causes at follow-up time t (i.e., the completion rate for a $\text{class}=c_1,c_2$ at the time t). Under the no redundancy assumption, the disease rates and the completion rates are related through the following equations:

$$\text{Rate}^{\text{profile}=i,j}(t)=\text{Rate}_{\text{class}=*,*}(t)+\text{Rate}_{\text{class}=i,*}(t)+\text{Rate}_{\text{class}=*,j}(t)+\text{Rate}_{\text{class}=i,j}(t), \qquad \text{(A1.1)}$$

for $i\in\{1,...,L_1\}$ and $j\in\{1,...,L_2\}$.

Let $\text{Rate}_{\text{class}=\text{int}}(t)$ denote the rate of completion at a time t for any *interaction* class, and $\text{Rate}_{\text{class}=\text{any}}(t)$, the rate of completion at a time t for *any* class (all-unknown, main-effect, or interaction). Under the no redundancy assumption, we have that

$$\text{Rate}_{\text{class}=\text{int}}(t)=\sum_{i=1}^{L_1}\sum_{j=1}^{L_2}\text{Rate}_{\text{class}=i,j}(t) \qquad \text{(A1.2)}$$

and

$$\text{Rate}_{\text{class}=\text{any}}(t)=\text{Rate}_{\text{class}=*,*}(t)+\sum_{i=1}^{L_1}\text{Rate}_{\text{class}=i,*}(t)+\sum_{j=1}^{L_2}\text{Rate}_{\text{class}=*,j}(t)+\text{Rate}_{\text{class}=\text{int}}(t). \qquad \text{(A1.3)}$$

The following derivations make frequent use of the peril index (PLoS ONE 2013;8: e67424). A ‘peril’ is identically a cumulative rate exponentiated, the reciprocal of a cumulative risk complement, and a one plus a cumulative odds, that is,

$$\text{Peril}=\exp\left[\int_0^T \text{Rate}(t)\times dt\right]=\left(1-\text{Risk}\right)^{-1}=1+\text{Odds}, \qquad \text{(A1.4)}$$

and is an index no less than 1.

The cumulative completion risk over (0, T) for a specific $\text{class} = i, j$ sufficient-cause interaction is

$$\text{Risk}_{\text{class}=i,j} = 1 - \text{Peril}_{\text{class}=i,j}^{-1} = 1 - \exp\left[-\int_0^T \text{Rate}_{\text{class}=i,j}(t)dt\right], \quad \text{(A1.5)}$$

for $i \in \{1,...,L_1\}$ and $j \in \{1,...,L_2\}$. The cumulative completion risk over (0, T) for the global sufficient-cause interaction is

$$\text{Risk}_{\text{class}=\text{int}} = 1 - \text{Peril}_{\text{class}=\text{int}}^{-1} = 1 - \exp\left[-\int_0^T \text{Rate}_{\text{class}=\text{int}}(t)dt\right]. \quad \text{(A1.6)}$$

The cumulative completion risk over (0, T) for any class is

$$\text{Risk}_{\text{class}=\text{any}} = 1 - \text{Peril}_{\text{class}=\text{any}}^{-1} = 1 - \exp\left[-\int_0^T \text{Rate}_{\text{class}=\text{any}}(t)dt\right]. \quad \text{(A1.7)}$$

To set a lower bound on $\text{Risk}_{\text{class}=i,j}$ ($i \in \{1,...,L_1\}$, $j \in \{1,...,L_2\}$), we first establish the following inequalities from (A1.1):

$$\begin{aligned}
\text{Peril}_{\text{class}=i,j} &= \exp\left[\int_0^T \text{Rate}_{\text{class}=i,j}(t)dt\right] \\
&\geq \exp\left[\int_0^T \left[\text{Rate}^{\text{profile}=i,j}(t) - \text{Rate}^{\text{profile}=i',j}(t) - \text{Rate}^{\text{profile}=i,j'}(t)\right]dt\right] \\
&= \frac{\exp\left[\int_0^T \text{Rate}^{\text{profile}=i,j}(t)dt\right]}{\exp\left[\int_0^T \text{Rate}^{\text{profile}=i',j}(t)dt\right] \times \exp\left[\int_0^T \text{Rate}^{\text{profile}=i,j'}(t)dt\right]} \\
&= \frac{\text{Peril}^{\text{profile}=i,j}}{\text{Peril}^{\text{profile}=i',j} \times \text{Peril}^{\text{profile}=i,j'}},
\end{aligned} \quad \text{(A1.8)}$$

for any $(i' \neq i) \in \{1,...,L_1\}$ and $(j' \neq j) \in \{1,...,L_2\}$. Therefore

$$\begin{aligned}
\text{Risk}_{\text{class}=i,j}^{\text{LB}} &= 1 - \max_{\substack{(i'\neq i)\in\{1,...,L_1\} \\ (j'\neq j)\in\{1,...,L_2\}}}^{-1} \left\{\frac{\text{Peril}^{\text{profile}=i,j}}{\text{Peril}^{\text{profile}=i',j} \times \text{Peril}^{\text{profile}=i,j'}}, 1\right\} \\
&= 1 - \min_{\substack{(i'\neq i)\in\{1,...,L_1\} \\ (j'\neq j)\in\{1,...,L_2\}}} \left\{\frac{1 - \text{Risk}^{\text{profile}=i,j}}{\left(1 - \text{Risk}^{\text{profile}=i',j}\right) \times \left(1 - \text{Risk}^{\text{profile}=i,j'}\right)}, 1\right\}.
\end{aligned} \quad \text{(A1.9)}$$

To set an upper bound on $\text{Risk}_{\text{class}=i,j}$ ($i \in \{1,...,L_1\}$, $j \in \{1,...,L_2\}$), Again from (A1.1), we have

$$\text{Rate}_{\text{class}=i,j}(t) \leq \text{Rate}^{\text{profile}=i,j}(t) \quad \text{(A1.10)}$$

for all t in (0, T), which implies $\text{Peril}_{\text{class}=i,j} \le \text{Peril}^{\text{profile}=i,j}$. Therefore

$$\text{Risk}^{\text{UB}}_{\text{class}=i,j} = \text{Risk}^{\text{profile}=i,j}. \tag{A1.11}$$

To set a lower bound on $\text{Risk}_{\text{class}=\text{int}}$, we first establish the following inequalities with the use of contrast coefficients described in the text. Again from (A1.1), we have

$$\begin{aligned}
\text{Peril}_{\text{class}=\text{int}} &= \exp\left\{\int_0^T \left[\sum_{i=1}^{L_1}\sum_{j=1}^{L_2} \text{Rate}_{\text{class}=i,j}(t)\right]dt\right\} \\
&\ge \exp\left\{\int_0^T \left[\sum_{i=1}^{L_1}\sum_{j=1}^{L_2} u_i \times v_j \times \text{Rate}_{\text{class}=i,j}(t)\right]dt\right\} \\
&= \exp\left\{\int_0^T \left[\sum_{i=1}^{L_1}\sum_{j=1}^{L_2} u_i \times v_j \times \text{Rate}^{\text{profile}=i,j}(t)\right]dt\right\} \\
&= \prod_{i=1}^{L_1}\prod_{j=1}^{L_2}\left(\text{Peril}^{\text{profile}=i,j}\right)^{u_i \times v_j},
\end{aligned} \tag{A1.12}$$

for any legitimate contrast coefficients $(u_1,...,u_{L_1})$ and $(v_1,...,v_{L_2})$. Therefore,

$$\begin{aligned}
\text{Risk}^{\text{LB}}_{\text{class}=\text{int}} &= 1 - \max_{\substack{\text{permutations of } (u_1,...,u_{L_1}) \\ \text{and permutations of } (v_1,...,v_{L_2})}}{}^{-1} \left\{\prod_{i=1}^{L_1}\prod_{j=1}^{L_2}\left(\text{Peril}^{\text{profile}=i,j}\right)^{u_i \times v_j},\ 1\right\} \\
&= 1 - \min_{\substack{\text{permutations of } (u_1,...,u_{L_1}) \\ \text{and permutations of } (v_1,...,v_{L_2})}} \left\{\prod_{i=1}^{L_1}\prod_{j=1}^{L_2}\left(1-\text{Risk}^{\text{profile}=i,j}\right)^{u_i \times v_j},\ 1\right\}.
\end{aligned} \tag{A1.13}$$

To set an upper bound on $\text{Risk}_{\text{class}=\text{int}}$, from (A1.1)~(A1.3) we have

$$\text{Rate}_{\text{class}=\text{int}}(t) \le \text{Rate}_{\text{class}=\text{any}}(t) \le \sum_{i=1}^{L_1}\sum_{j=1}^{L_2} \text{Rate}^{\text{profile}=i,j}(t) \tag{A1.14}$$

for all t in (0, T), which implies $\text{Peril}_{\text{class}=\text{int}} \le \text{Peril}_{\text{class}=\text{any}} \le \prod_{i=1}^{L_1}\prod_{j=1}^{L_2} \text{Peril}^{\text{profile}=i,j}$. Therefore

$$\text{Risk}^{\text{UB}}_{\text{class}=\text{int}} = 1 - \left(\prod_{i=1}^{L_1}\prod_{j=1}^{L_2} \text{Peril}^{\text{profile}=i,j}\right)^{-1} = 1 - \prod_{i=1}^{L_1}\prod_{j=1}^{L_2}\left(1-\text{Risk}^{\text{profile}=i,j}\right). \tag{A1.15}$$

Finally, the bounds on the relative prevalence of sufficient-cause interactions are functions of the above bounds on the cumulative completion risks, as presented in the text.