Table S1 Associational risk ratios in terms of response types

Pooled associational risk ratios among those who do not drop out in observational studies (see Figures 2A and 3)

$$\mathrm{aRR}_{S=1}=\frac{\left(\sum_{\substack{i=1,2\\ j=1,2,3,4,5,6,7,8\\ k=1,2,3,4,5,6,7,8}} P_{C|EiDjSk}P_{EiDjSk}+\sum_{\substack{i=1,3\\ j=1,2,3,4,9,10,11,12\\ k=1,2,3,4,5,6,7,8}} P_{\bar{C}|EiDjSk}P_{EiDjSk}\right)}{\left(\sum_{\substack{i=1,2\\ j=1,2,3,4,5,6,7,8\\ k=1,2,3,4,5,6,7,8}} P_{C|EiDjSk}P_{EiDjSk}+\sum_{\substack{i=1,2\\ j=9,10,11,12,13,14,15,16\\ k=1,2,5,6,9,10,13,14}} P_{C|EiDjSk}P_{EiDjSk}+\sum_{\substack{i=1,3\\ j=1,2,3,4,9,10,11,12\\ k=1,2,3,4,5,6,7,8}} P_{\bar{C}|EiDjSk}P_{EiDjSk}+\sum_{\substack{i=1,3\\ j=5,6,7,8,13,14,15,16\\ k=1,2,5,6,9,10,13,14}} P_{\bar{C}|EiDjSk}P_{EiDjSk}\right)}\Bigg/\frac{\left(\sum_{\substack{i=3,4\\ j=1,2,5,6,9,10,13,14\\ k=1,2,3,4,9,10,11,12}} P_{C|EiDjSk}P_{EiDjSk}+\sum_{\substack{i=2,4\\ j=1,3,5,7,9,11,13,15\\ k=1,2,3,4,9,10,11,12}} P_{\bar{C}|EiDjSk}P_{EiDjSk}\right)}{\left(\sum_{\substack{i=3,4\\ j=1,2,5,6,9,10,13,14\\ k=1,2,3,4,9,10,11,12}} P_{C|EiDjSk}P_{EiDjSk}+\sum_{\substack{i=3,4\\ j=3,4,7,8,11,12,15,16\\ k=1,3,5,7,9,11,13,15}} P_{C|EiDjSk}P_{EiDjSk}+\sum_{\substack{i=2,4\\ j=1,3,5,7,9,11,13,15\\ k=1,2,3,4,9,10,11,12}} P_{\bar{C}|EiDjSk}P_{EiDjSk}+\sum_{\substack{i=2,4\\ j=2,4,6,8,10,12,14,16\\ k=1,3,5,7,9,11,13,15}} P_{\bar{C}|EiDjSk}P_{EiDjSk}\right)} \quad \text{(A1)}$$

Stratum-specific associational risk ratios among those who do not drop out in observational studies (see Figures 2A and 3)

$$\mathrm{aRR}_{C=1,S=1}=\frac{\sum_{\substack{i=1,2\\ j=1,2,3,4,5,6,7,8\\ k=1,2,3,4,5,6,7,8}} P_{C|EiDjSk}P_{EiDjSk}}{\sum_{\substack{i=1,2\\ j=1,2,3,4,5,6,7,8\\ k=1,2,3,4,5,6,7,8}} P_{C|EiDjSk}P_{EiDjSk}+\sum_{\substack{i=1,2\\ j=9,10,11,12,13,14,15,16\\ k=1,2,5,6,9,10,13,14}} P_{C|EiDjSk}P_{EiDjSk}}\Bigg/\frac{\sum_{\substack{i=3,4\\ j=1,2,5,6,9,10,13,14\\ k=1,2,3,4,9,10,11,12}} P_{C|EiDjSk}P_{EiDjSk}}{\sum_{\substack{i=3,4\\ j=1,2,5,6,9,10,13,14\\ k=1,2,3,4,9,10,11,12}} P_{C|EiDjSk}P_{EiDjSk}+\sum_{\substack{i=3,4\\ j=3,4,7,8,11,12,15,16\\ k=1,3,5,7,9,11,13,15}} P_{C|EiDjSk}P_{EiDjSk}} \quad \text{(A2)}$$

$$\mathrm{aRR}_{C=0,S=1}=\frac{\sum_{\substack{i=1,3\\ j=1,2,3,4,9,10,11,12\\ k=1,2,3,4,5,6,7,8}} P_{\bar{C}|EiDjSk}P_{EiDjSk}}{\sum_{\substack{i=1,3\\ j=1,2,3,4,9,10,11,12\\ k=1,2,3,4,5,6,7,8}} P_{\bar{C}|EiDjSk}P_{EiDjSk}+\sum_{\substack{i=1,3\\ j=5,6,7,8,13,14,15,16\\ k=1,2,5,6,9,10,13,14}} P_{\bar{C}|EiDjSk}P_{EiDjSk}}\Bigg/\frac{\sum_{\substack{i=2,4\\ j=1,3,5,7,9,11,13,15\\ k=1,2,3,4,9,10,11,12}} P_{\bar{C}|EiDjSk}P_{EiDjSk}}{\sum_{\substack{i=2,4\\ j=1,3,5,7,9,11,13,15\\ k=1,2,3,4,9,10,11,12}} P_{\bar{C}|EiDjSk}P_{EiDjSk}+\sum_{\substack{i=2,4\\ j=2,4,6,8,10,12,14,16\\ k=1,3,5,7,9,11,13,15}} P_{\bar{C}|EiDjSk}P_{EiDjSk}} \quad \text{(A3)}$$

Pooled associational risk ratios in the total population in observational studies (see Figures 2B and 3)

$$\mathrm{aRR}=\frac{\left(\sum_{\substack{i=1,2\\ j=1,2,3,4,5,6,7,8\\ k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}} P_{C|EiDjSk}P_{EiDjSk}+\sum_{\substack{i=1,3\\ j=1,2,3,4,9,10,11,12\\ k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}} P_{\bar{C}|EiDjSk}P_{EiDjSk}\right)}{\left(\sum_{\substack{i=1,2\\ j=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16\\ k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}} P_{C|EiDjSk}P_{EiDjSk}+\sum_{\substack{i=1,3\\ j=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16\\ k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}} P_{\bar{C}|EiDjSk}P_{EiDjSk}\right)}\Bigg/\frac{\left(\sum_{\substack{i=3,4\\ j=1,2,5,6,9,10,13,14\\ k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}} P_{C|EiDjSk}P_{EiDjSk}+\sum_{\substack{i=2,4\\ j=1,3,5,9,11,13,15\\ k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}} P_{\bar{C}|EiDjSk}P_{EiDjSk}\right)}{\left(\sum_{\substack{i=3,4\\ j=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16\\ k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}} P_{C|EiDjSk}P_{EiDjSk}+\sum_{\substack{i=2,4\\ j=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16\\ k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}} P_{\bar{C}|EiDjSk}P_{EiDjSk}\right)}$$

$$=\frac{\sum_{\substack{i=1,2\\ j=1,2,3,4,5,6,7,8}} P_{C|EiDj}P_{EiDj}+\sum_{\substack{i=1,3\\ j=1,2,3,4,9,10,11,12}} P_{\bar{C}|EiDj}P_{EiDj}}{\sum_{i=1,2} P_{C|Ei}P_{Ei}+\sum_{i=1,3} P_{\bar{C}|Ei}P_{Ei}}\Bigg/\frac{\sum_{\substack{i=3,4\\ j=1,2,5,6,9,10,13,14}} P_{C|EiDj}P_{EiDj}+\sum_{\substack{i=2,4\\ j=1,3,5,9,11,13,15}} P_{\bar{C}|EiDj}P_{EiDj}}{\sum_{i=3,4} P_{C|Ei}P_{Ei}+\sum_{i=2,4} P_{\bar{C}|Ei}P_{Ei}} \quad \text{(A4)}$$

Stratum-specific associational risk ratios in the total population in observational studies (see Figures 2B and 3)

$$\mathrm{aRR}_{C=1}=\frac{\sum_{\substack{i=1,2\\ j=1,2,3,4,5,6,7,8\\ k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}} P_{C|EiDjSk}P_{EiDjSk}}{\sum_{\substack{i=1,2\\ j=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16\\ k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}} P_{C|EiDjSk}P_{EiDjSk}}\Bigg/\frac{\sum_{\substack{i=3,4\\ j=1,2,5,6,9,10,13,14\\ k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}} P_{C|EiDjSk}P_{EiDjSk}}{\sum_{\substack{i=3,4\\ j=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16\\ k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}} P_{C|EiDjSk}P_{EiDjSk}}=\frac{\left(\sum_{\substack{i=1,2\\ j=1,2,3,4,5,6,7,8}} P_{C|EiDj}P_{EiDj}\Big/\sum_{i=1,2} P_{C|Ei}P_{Ei}\right)}{\left(\sum_{\substack{i=3,4\\ j=1,2,5,6,9,10,13,14}} P_{C|EiDj}P_{EiDj}\Big/\sum_{i=3,4} P_{C|Ei}P_{Ei}\right)} \quad \text{(A5)}$$

$$\mathrm{aRR}_{C=0}=\frac{\sum_{\substack{i=1,3\\ j=1,2,3,4,9,10,11,12\\ k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}} P_{\bar{C}|EiDjSk}P_{EiDjSk}}{\sum_{\substack{i=1,3\\ j=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16\\ k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}} P_{\bar{C}|EiDjSk}P_{EiDjSk}}\Bigg/\frac{\sum_{\substack{i=2,4\\ j=1,3,5,9,11,13,15\\ k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}} P_{\bar{C}|EiDjSk}P_{EiDjSk}}{\sum_{\substack{i=2,4\\ j=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16\\ k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}} P_{\bar{C}|EiDjSk}P_{EiDjSk}}=\frac{\left(\sum_{\substack{i=1,3\\ j=1,2,3,4,9,10,11,12}} P_{\bar{C}|EiDj}P_{EiDj}\Big/\sum_{i=1,3} P_{\bar{C}|Ei}P_{Ei}\right)}{\left(\sum_{\substack{i=2,4\\ j=1,3,5,9,11,13,15}} P_{\bar{C}|EiDj}P_{EiDj}\Big/\sum_{i=2,4} P_{\bar{C}|Ei}P_{Ei}\right)} \quad \text{(A6)}$$

Abbreviation: aRR, associational risk ratio.

For the definitions of notations, see Figure 3.

Table S2 Causal risk ratios in terms of response types

Pooled causal risk ratios among those who do not drop out in randomized controlled trials (see Figures 2C and 4)

$$\mathrm{cRR}_{S=1}=\frac{\left(\dfrac{\sum_{\substack{j=1,2,3,4,5,6,7,8\\k=1,2,3,4,5,6,7,8}}P_{C|DjSk}P_{DjSk}+\sum_{\substack{j=1,2,3,4,9,10,11,12\\k=1,2,3,4,5,6,7,8}}P_{\bar{C}|DjSk}P_{DjSk}}{\sum_{\substack{j=1,2,3,4,5,6,7,8\\k=1,2,3,4,5,6,7,8}}P_{C|DjSk}P_{DjSk}+\sum_{\substack{j=9,10,11,12,13,14,15,16\\k=1,2,5,6,9,10,13,14}}P_{C|DjSk}P_{DjSk}+\sum_{\substack{j=1,2,3,4,9,10,11,12\\k=1,2,3,4,5,6,7,8}}P_{\bar{C}|DjSk}P_{DjSk}+\sum_{\substack{j=5,6,7,8,13,14,15,16\\k=1,2,5,6,9,10,13,14}}P_{\bar{C}|DjSk}P_{DjSk}}\right)}{\left(\dfrac{\sum_{\substack{j=1,2,5,6,9,10,13,14\\k=1,2,3,4,9,10,11,12}}P_{C|DjSk}P_{DjSk}+\sum_{\substack{j=1,3,5,7,9,11,13,15\\k=1,2,3,4,9,10,11,12}}P_{\bar{C}|DjSk}P_{DjSk}}{\sum_{\substack{j=1,2,5,6,9,10,13,14\\k=1,2,3,4,9,10,11,12}}P_{C|DjSk}P_{DjSk}+\sum_{\substack{j=3,4,7,8,11,12,15,16\\k=1,3,5,7,9,11,13,15}}P_{C|DjSk}P_{DjSk}+\sum_{\substack{j=1,3,5,7,9,11,13,15\\k=1,2,3,4,9,10,11,12}}P_{\bar{C}|DjSk}P_{DjSk}+\sum_{\substack{j=2,4,6,8,10,12,14,16\\k=1,3,5,7,9,11,13,15}}P_{\bar{C}|DjSk}P_{DjSk}}\right)} \quad \text{(A7)}$$

Stratum-specific causal risk ratios among those who do not drop out in randomized controlled trials (see Figures 2C and 4)

$$\mathrm{cRR}_{C=1,S=1}=\frac{\sum_{\substack{j=1,2,3,4,5,6,7,8\\k=1,2,3,4,5,6,7,8}}P_{C|DjSk}P_{DjSk}}{\sum_{\substack{j=1,2,3,4,5,6,7,8\\k=1,2,3,4,5,6,7,8}}P_{C|DjSk}P_{DjSk}+\sum_{\substack{j=9,10,11,12,13,14,15,16\\k=1,2,5,6,9,10,13,14}}P_{C|DjSk}P_{DjSk}}\Bigg/\frac{\sum_{\substack{j=1,2,5,6,9,10,13,14\\k=1,2,3,4,9,10,11,12}}P_{C|DjSk}P_{DjSk}}{\sum_{\substack{j=1,2,5,6,9,10,13,14\\k=1,2,3,4,9,10,11,12}}P_{C|DjSk}P_{DjSk}+\sum_{\substack{j=3,4,7,8,11,12,15,16\\k=1,3,5,7,9,11,13,15}}P_{C|DjSk}P_{DjSk}} \quad \text{(A8)}$$

$$\mathrm{cRR}_{C=0,S=1}=\frac{\sum_{\substack{j=1,2,3,4,9,10,11,12\\k=1,2,3,4,5,6,7,8}}P_{\bar{C}|DjSk}P_{DjSk}}{\sum_{\substack{j=1,2,3,4,9,10,11,12\\k=1,2,3,4,5,6,7,8}}P_{\bar{C}|DjSk}P_{DjSk}+\sum_{\substack{j=5,6,7,8,13,14,15,16\\k=1,2,5,6,9,10,13,14}}P_{\bar{C}|DjSk}P_{DjSk}}\Bigg/\frac{\sum_{\substack{j=1,3,5,7,9,11,13,15\\k=1,2,3,4,9,10,11,12}}P_{\bar{C}|DjSk}P_{DjSk}}{\sum_{\substack{j=1,3,5,7,9,11,13,15\\k=1,2,3,4,9,10,11,12}}P_{\bar{C}|DjSk}P_{DjSk}+\sum_{\substack{j=2,4,6,8,10,12,14,16\\k=1,3,5,7,9,11,13,15}}P_{\bar{C}|DjSk}P_{DjSk}} \quad \text{(A9)}$$

Pooled causal risk ratios in the total population in ideal randomized controlled trials (see Figures 2D and 4)

$$\mathrm{cRR}=\frac{\left(\dfrac{\sum_{\substack{j=1,2,3,4,5,6,7,8\\k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}}P_{C|DjSk}P_{DjSk}+\sum_{\substack{j=1,2,3,4,9,10,11,12\\k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}}P_{\bar{C}|DjSk}P_{DjSk}}{\sum_{\substack{j=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16\\k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}}P_{DjSk}}\right)}{\left(\dfrac{\sum_{\substack{j=1,2,5,6,9,10,13,14\\k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}}P_{C|DjSk}P_{DjSk}+\sum_{\substack{j=1,3,5,9,11,13,15\\k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}}P_{\bar{C}|DjSk}P_{DjSk}}{\sum_{\substack{j=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16\\k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}}P_{DjSk}}\right)}$$

$$=\frac{\sum_{j=1,2,3,4,5,6,7,8}P_{C|Dj}P_{Dj}+\sum_{j=1,2,3,4,9,10,11,12}P_{\bar{C}|Dj}P_{Dj}}{\sum_{j=1,2,5,6,9,10,13,14}P_{C|Dj}P_{Dj}+\sum_{j=1,3,5,9,11,13,15}P_{\bar{C}|Dj}P_{Dj}} \quad \text{(A10)}$$

Stratum-specific causal risk ratios in the total population in ideal randomized controlled trials (see Figures 2D and 4)

$$\mathrm{cRR}_{C=1}=\frac{\sum_{\substack{j=1,2,3,4,5,6,7,8\\k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}}P_{C|DjSk}P_{DjSk}}{\sum_{\substack{j=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16\\k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}}P_{C|DjSk}P_{DjSk}}\Bigg/\frac{\sum_{\substack{j=1,2,5,6,9,10,13,14\\k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}}P_{C|DjSk}P_{DjSk}}{\sum_{\substack{j=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16\\k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}}P_{C|DjSk}P_{DjSk}}=\frac{\sum_{j=1,2,3,4,5,6,7,8}P_{C|Dj}P_{Dj}}{\sum_{j=1,2,5,6,9,10,13,14}P_{C|Dj}P_{Dj}} \quad \text{(A11)}$$

$$\mathrm{cRR}_{C=0}=\frac{\sum_{\substack{j=1,2,3,4,9,10,11,12\\k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}}P_{\bar{C}|DjSk}P_{DjSk}}{\sum_{\substack{j=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16\\k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}}P_{\bar{C}|DjSk}P_{DjSk}}\Bigg/\frac{\sum_{\substack{j=1,3,5,9,11,13,15\\k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}}P_{\bar{C}|DjSk}P_{DjSk}}{\sum_{\substack{j=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16\\k=1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16}}P_{\bar{C}|DjSk}P_{DjSk}}=\frac{\sum_{j=1,2,3,4,9,10,11,12}P_{\bar{C}|Dj}P_{Dj}}{\sum_{j=1,3,5,9,11,13,15}P_{\bar{C}|Dj}P_{Dj}} \quad \text{(A12)}$$

Abbreviation: cRR, causal risk ratio.

For the definitions of notations, see Figure 4.