Sufficient cause interactions for categorical and ordinal outcomes

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Supplementary Material

This online supplement examines the more general definitions and theorems of sufficient cause interactions for ordinal and categorical outcomes. The main paper examined ordinal outcomes with three levels, whereas in the online supplement we consider ordinal outcomes with an arbitrary number of levels. Additionally, global conditions for different forms of sufficient cause interactions are presented here. The connection to polytopes to detect different forms of interdependence is explicated at the very end. We also provide the Theorems that proof of the generalized results as well as associated proofs that are presented in the main section.

S1 Proofs

S1.1 Appendix 2: Proofs

The proofs of theorems and corollaries in the main text are collected here. The proof of Theorem 4.1in the main paper collected in Section S4: Appendix 1B, given the need of more general notation. Theorem 4.1 is provided again as Theorem S4.5 in Section S4: Appendix 1B.

Proof of Theorem 2.1. Mirroring the proof of Theorem 1 in VanderWeele and Robins (2008), construct $A_0^L, \ldots, A_8^L$ according to the following 16 rules: (1) If $Y_{x_1x_2}^L(\omega) = 1$ for all $\{x_1, x_2\} \in \{0,1\}$,[2] let $A_0^L(\omega) = 1$ and $A_i^L(\omega) = 0$ for all $i \notin 0$. (2) If $Y_{00}^L(\omega) = 0$ and $Y_{11}^L(\omega) = Y_{10}^L(\omega) = Y_{01}^L(\omega) = 1$, let $A_1^L(\omega) = A_3^L(\omega) = 1$ and $A_i^L(\omega) = 0$ for $i \notin \{1,3\}$. (3) If $Y_{10}^L(\omega) = 0$, and $Y_{00}^L(\omega) = Y_{01}^L(\omega) = Y_{11}^L(\omega) = 1$, let $A_i^L(\omega) = 1$ for $i \in \{2,3\}$ and $A_i^L(\omega) = 0$ for $i \notin \{2,3\}$. (4) If $Y_{00}^L(\omega) = Y_{10}^L(\omega) = 0$ and $Y_{01}^L(\omega) = Y_{11}^L(\omega) = 1$, let $A_3^L(\omega) = 1$ and $A_i^L(\omega) = 0$ for $i \notin \{3\}$. (5) If $Y_{01}^L(\omega) = 0$ and $Y_{00}^L(\omega) = Y_{10}^L(\omega) = Y_{11}^L(\omega) = 1$, let $A_i^L(\omega) = 1$ for $i \in \{1,4\}$ and $A_i^L(\omega) = 0$ for $i \notin \{1,4\}$. (6) If $Y_{00}^L(\omega) = Y_{01}^L(\omega) = 0$ and $Y_{10}^L(\omega) = Y_{11}^L(\omega) = 1$, let $A_1^L(\omega) = 1$ and $A_i^L(\omega) = 0$. (7) If $Y_{01}^L(\omega) = Y_{10}^L(\omega) = 0$ and $Y_{00}^L(\omega) = Y_{11}^L(\omega) = 1$,let $A_i^L(\omega) = 1$ for $i \in \{5,8\}$ and $A_i^L(\omega) = 0$ for $i \notin \{5,8\}$. (8) If $Y_{11}^L(\omega) = 1$ and $Y_{00}^L(\omega) = Y_{01}^L(\omega) = Y_{10}^L(\omega) = 0$, let

$A_5^L(\omega) = 1$ and $A_i^L(\omega) = 0$ for $i \notin \{5\}$. (9) If $Y_{11}^L(\omega) = 0$ and $Y_{00}^L(\omega) = Y_{10}^L(\omega) = Y_{01}^L(\omega) = 1$, let $A_i^L(\omega) = 1$ for $i \in \{2, 4\}$ and $A_i^L(\omega) = 0$ for $i \notin \{2, 4\}$. (10) If $Y_{00}^L(\omega) = Y_{11}^L(\omega) = 0$ and $Y_{01}^L(\omega) = Y_{10}^L(\omega) = 1$, let $A_i(\omega) = 1$ for $i \in \{6, 7\}$ and $A_i^L(\omega) = 0$ for $i \notin \{6, 7\}$. (11) If $Y_{10}^L(\omega) = Y_{11}^L(\omega) = 0$ and $Y_{00}^L(\omega) = Y_{01}^L(\omega) = 1$, let $A_i^L(\omega) = 1$ for $i \in \{2\}$ and $A_i^L(\omega) \notin \{2\}$. (12) If $Y_{11}^L(\omega) = Y_{10}^L(\omega) = Y_{00}^L(\omega) = 0$ and $Y_{01}^L(\omega) = 1$, let $A_i^L(\omega) = 1$ for $i \in \{6\}$ and $A_i^L(\omega) = 0$ for $i \notin \{6\}$. (13) If $Y_{01}^L(\omega) = Y_{11}^L(\omega) = 0$ and $Y_{00}^L(\omega) = Y_{10}^L(\omega) = 1$, let $A_i^L(\omega) = 1$ for $i \in \{4\}$ and $A_i^L(\omega) = 0$ for $i \notin \{4\}$. (14) If $Y_{00}^L(\omega) = Y_{01}^L(\omega) = Y_{11}^L(\omega) = 0$ and $Y_{10}^L(\omega) = 1$, let $A_i^L(\omega) = 1$ for $i \in \{7\}$ and $A_i^L(\omega) = 0$ for $i \notin \{7\}$. (15) If $Y_{01}^L(\omega) = Y_{10}^L(\omega) = Y_{11}^L(\omega) = 0$ and $Y_{00}^L(\omega) = 1$, let $A_i^L(\omega) = 1$ for $i \in \{8\}$ and $A_i^L(\omega) = 0$ for $i \notin \{8\}$. (16) If $Y_{x_1 x_2}^L(\omega) = 0$ for all $\{x_1, x_2\} \in \{0, 1\}^2$, let $A_i^L(\omega) = 0$. $\square$

Proof of Theorem 2.2. We mirror the proof in (VanderWeele and Robins, 2008). We first prove the converse. Suppose $X_1 X_2$ do not display a minimal sufficient cause interaction for a specified outcome Y^L. Consequently, there exists a non-redundant minimal sufficient cause representation in which equations 2.1 and 2.2 hold and $A_5^L(\omega) = 0$ for all $\omega \in \Omega$. Consider an individual ω, for whom $Y_{10}^L(\omega) = Y_{01}^L(\omega) = 0$, by construction of $A_i^L(\omega)$, we have that $A_0^L(\omega) = A_1^L(\omega) = A_2^L(\omega) = A_3^L(\omega) = A_4^L(\omega) = A_6^L(\omega) = A_7^L(\omega) = 0$. Therefore, for such an individual we have, $Y_{11}^L(\omega)$=$A_8^L(1-1)(1-1) = 0$. Consequently, there cannot be an individual for whom $Y_{11}^L(\omega) = 1$ and $Y_{10}^L(\omega) = Y_{01}^L(\omega) = 0$ and $X_1 X_2$ do not display a minimal sufficient cause interaction for specified outcome Y^L.

For the opposite direction, consider the situation where $X_1 X_2$ does display minimal sufficient cause interaction for a ternary outcome under specified outcome Y^L. For every sufficient cause representation for Y^L there exists a conjunction such that $X_1 X_2$ is contained within it. Using the sufficient cause representation that was constructed in Theorem 2.1, we have an individual ω such that $A_5^L(\omega) \neq 0$ if an only if the individual has one of two possible potential outcomes (1) $Y_{01}^L(\omega) = Y_{10}^L(\omega) = 0$ and $Y_{00}^L(\omega) = Y_{11}^L(\omega) = 1$ or (2) $Y_{10}^L(\omega) = Y_{01}^L(\omega) = Y_{00}^L(\omega) = 0$ and $Y_{11}^L(\omega) = 1$. In either situation, $Y_{10}^L(\omega) = Y_{01}^L(\omega) = 0$ and $Y_{11}^L(\omega) = 1$. $\square$

Proof of Theorem 2.3. We prove this result by contradiction. Suppose for outcome under specified condition $L \in \{A, B, C, D, E, F\}$, we have that $X_1 X_2$ does not exhibit sufficient cause interaction. Theorem 2.2 then implies that there is no individual $\omega \in \Omega$

for whom $Y^L_{11}(\omega.) = 1$ and $Y^L_{10}(\omega) = Y^L_{01}(\omega) = 0$. This is equivalent to stating that for all $\omega \in \Omega$, we have that $Y^L_{11}(\omega) - Y^L_{10}(\omega) - Y^L_{01}(\omega) \leq 0$. Therefore, taking expectations on both sides we have $E(Y^L_{11}(\omega) - Y^L_{10}(\omega) - Y^L_{01}(\omega) \mid V = v) \leq 0$.

$$\begin{aligned}
& E(Y^L \mid X_1 = 1, X_2 = 1, V = v) - E(Y^L \mid X_1 = 1, X_2 = 0, V = v) \\
& -E(Y^L \mid X_1 = 0, X_2 = 1, V = v) \\
= \; & E(Y^L_{11}(\omega) \mid X_1 = 1, X_2 = 1, V = v) - E(Y^L_{10}(\omega) \mid X_1 = 1, X_2 = 0, V = v) \\
& -E(Y^L_{01}(\omega) \mid X_1 = 0, X_2 = 1, V = v) \\
= \; & E(Y^L_{11}(\omega) \mid V = v) - E(Y^L_{10}(\omega) \mid V = v) - E(Y^L_{01}(\omega) \mid V = v) \\
= \; & E(Y^L_{11}(\omega) - Y^L_{10}(\omega) - Y^L_{01}(\omega) \mid V = v) \leq 0.
\end{aligned}$$

The first equality stems from the consistency assumption and the second equality stems from the no unmeasured confounding assumption $Y^L_{x_1x_2} \amalg \{X_1, X_2\} \mid V$. This completes our proof. □

Proof of Theorem 2.4. Suppose $X_1$and X_2 do not display synergism for outcome Y^B. Then, by Theorem 2.3, we have for all $\omega \in \Omega$, $Y^B_{11}(\omega) - Y^B_{10}(\omega) - Y^B_{01}(\omega) \leq 0$. Consider two different cases. Case 1: if $Y_{00}(\omega) = 0$, then $Y^B_{00}(\omega) = 0$ and adding this to $Y^B_{11}(\omega) - Y^B_{10}(\omega) - Y^B_{01}(\omega) \leq 0$, we have $Y^B_{11}(\omega) - Y^B_{10}(\omega) - Y^B_{01}(\omega) + Y^B_{00}(\omega) \leq 0$. Case 2: say $Y_{00}(\omega) = 1$ or $Y_{00}(\omega) = 2$, then in either case $Y^B_{00}(\omega) = 1$ and by our monotonicity constraints $Y^B_{11}(\omega) = Y^B_{01}(\omega) = Y^B_{10}(\omega) = 1$, and as a result $Y^B_{11}(\omega) - Y^B_{10}(\omega) - Y^B_{01}(\omega) + Y^B_{00}(\omega) \leq 0$. So, in both cases, we have that if $X_1$and X_2 do not display synergism for outcome Y^B, then $Y^B_{11}(\omega) - Y^B_{10}(\omega) - Y^B_{01}(\omega) + Y^B_{00}(\omega) \leq 0$. Taking expectations on both sides and following the logic present in the proof of Theorem 2.3, we complete our proof. □

Proof of Theorem 2.5. Similar to the proof of Theorem 2.4, and therefore omitted. □

Proof of Theorem 2.6. Suppose X_1 and X_2 do not display synergism for outcome Y^A. Then, by Theorem 2.2, we have for all $\omega \in \Omega$, $Y^A_{11}(\omega) - Y^A_{10}(\omega) - Y^A_{01}(\omega) \leq 0$. Taking expectations of both sides of this inequality and following logic present in the the proof of Theorem 2.3, we have the condition $p^A_{11v} - p^A_{10v} - p^A_{01v} \leq 0$. For the first inequality. Consider three different cases. Case 1: Suppose $Y_{11}(\omega) = 1$, then $Y^A_{11}(\omega) = 1$, $Y_{01}(\omega) \in \{0, 1\}$, $Y_{10}(\omega) \in \{0, 1\}$, and $Y_{00}(\omega) \in \{0, 1\}$. (Subcase a): If $Y_{00}(\omega) = 1$, then $Y^A_{00}(\omega) = 1$, and $Y_{10}(\omega) = Y_{01}(\omega) = 1$ to satisfy the monotonicity constraints. This implies that $Y^C_{00}(\omega) = Y^C_{01}(\omega) = 0$. This means that $Y^A_{11}(\omega) - Y^A_{10}(\omega) - Y^A_{01}(\omega) + Y^A_{00}(\omega) +$

$Y^C_{00}(\omega) - Y^C_{01}(\omega) \leq 0$. (Subcase b): If $Y_{00}(\omega) = 0$, then $Y^A_{00}(\omega) = Y^C_{00}(\omega) = 0$, and either or both $Y^A_{01}(\omega) = 1$ or $Y^A_{01}(\omega) = 1$ as X_1 and X_2 do not display synergism for Y^A. Therefore $Y^A_{11}(\omega) - Y^A_{10}(\omega) - Y^A_{01}(\omega) + Y^A_{00}(\omega) + Y^C_{00}(\omega) - Y^C_{01}(\omega) \leq 0$. Case 2: $Y_{11}(\omega) = 0$, then $Y_{01}(\omega) = Y_{10}(\omega) = Y_{00}(\omega) = 0$ to satisfy monotonicity constraints. Therefore, $Y^A_{11}(\omega) = Y^A_{10}(\omega) = Y^A_{01}(\omega) = Y^A_{00}(\omega) = Y^C_{00}(\omega) = Y^C_{01}(\omega) = 0$, and consequently $Y^A_{11}(\omega) - Y^A_{10}(\omega) - Y^A_{01}(\omega) + Y^A_{00}(\omega) + Y^C_{00}(\omega) - Y^C_{01}(\omega) \leq 0$. Case 3: $Y_{11}(\omega) = 2$, (Sub case a): Suppose $Y_{00}(\omega) = 2$, then $Y_{11}(\omega) = Y_{10}(\omega) = Y_{01}(\omega) = Y_{00}(\omega) = 2$ to satisfy the monotonicity constraints. This implies that $Y^A_{11}(\omega) = Y^A_{10}(\omega) = Y^A_{01}(\omega) = Y^A_{00}(\omega) = 0$, $Y^C_{00}(\omega) = Y^C_{01}(\omega) = 0$, and $Y^A_{11}(\omega) - Y^A_{10}(\omega) - Y^A_{01}(\omega) + Y^A_{00}(\omega) + Y^C_{00}(\omega) - Y^C_{01}(\omega) \leq 0$. (Subcase b): Suppose $Y_{00}(\omega) = 1$, then to satisfy monotonicity constraints, $Y_{01}(\omega) \in \{1, 2\}$ and $Y_{10}(\omega) \in \{1, 2\}$. This implies that either $Y^C_{01}(\omega) = 1$ or $Y^A_{01}(\omega) = 1$. This means that $Y^A_{11}(\omega) - Y^A_{10}(\omega) - Y^A_{01}(\omega) + Y^A_{00}(\omega) + Y^C_{00}(\omega) - Y^C_{01}(\omega) \leq 0$. Taking expectations on both sides and following the same logic present in the proof of Theorem 2.3, we have the condition, $p^A_{11v} - p^A_{10v} - p^A_{01v} + p^A_{00v} + p^C_{00v} - p^C_{10v} \leq 0$. To prove the second inequality, a similar proof is trivially constructed. □

Proof of Corollary 2.1. We have that

$$\begin{aligned}
2 \cdot p^A_{11v} - p^A_{10v} - p^A_{01v} + p^A_{00v} &> 1, \iff \\
p^A_{11v} - p^D_{11v} - p^C_{11v} - p^A_{10v} - p^A_{01v} + p^A_{00v} &> 0 \iff \\
p^A_{11v} - p^A_{10v} - p^A_{01v} + p^A_{00v} - p^C_{11v} &> p^D_{11v} \implies \\
p^A_{11v} - p^A_{10v} - p^A_{01v} + p^A_{00v} + p^C_{00v} - p^C_{01v} &> 0
\end{aligned}$$

The last line stems from the positive monotonic effect of X_1 and X_2 on $p^C_{11v} \geq p^C_{01v}$. Theorem 2.6 establishes that this a sufficient condition to show that X_1 and X_2 display synergism for outcome $Y^A = I(Y = 1)$.

From Corollary 2.1, we have that

$$\begin{aligned}
&2 \cdot P(Y = 1 \mid X_1 = 1, X_2 = 1, V = v) \\
&\quad -P(Y = 1 \mid X_1 = 1, X_2 = 0, V = v) - P(Y = 1 \mid X_1 = 0, X_2 = 1, V = v) \\
&\quad +P(Y = 1 \mid X_1 = 0, X_2 = 0, V = v) > 1,
\end{aligned}$$

implies that X_1 and X_2 exhibits synergism for outcome $Y^A = I(Y = 1)$. We note that

$\sum_{i=0}^{2} P(Y = i \mid X_1 = 1, X_2 = 1, V = v) = 1$. Substituting this summation into the inequality, and moving terms from the right hand side to the left hand side, it is trivial to show that conditions (2.4.1)-(2.4.3) are equivalent to one another. □

Proof of Theorem 4.2. The contrast

$$
\begin{aligned}
&P\left(Y \in y_a \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_a \mid X_1 = 1, X_2 = 0\right) \\
&- P\left(Y \in y_a \mid X_1 = 0, X_2 = 1\right).
\end{aligned}
$$

is equal to

$$
P\left(Y_{11} \in y_a\right) - P\left(Y_{10} \in y_a\right) - P\left(Y_{01} \in y_a\right),
$$

under $Y_{x_1x_2} \amalg X_1X_2$. Applying the law of total probability, we have

$$
\begin{aligned}
&P\left(Y_{11} \in y_a\right) - P\left(Y_{10} \in y_a\right) - P\left(Y_{01} \in y_a\right) \\
&= P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) + P\left(Y_{11} \in y_a, Y_{10} \notin y_a, Y_{01} \in y_a\right) \\
&\quad + P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \notin y_a\right) + P\left(Y_{11} \in y_a, Y_{10} \notin y_a, Y_{01} \notin y_a\right) \\
&- \{P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) + P\left(Y_{11} \notin y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) \\
&\quad + P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \notin y_a\right) + P\left(Y_{11} \notin y_a, Y_{10} \in y_a, Y_{01} \notin y_a\right)\} \\
&- \{P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) + P\left(Y_{11} \notin y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) \\
&\quad + P\left(Y_{11} \in y_a, Y_{10} \notin y_a, Y_{01} \in y_a\right) + P\left(Y_{11} \notin y_a, Y_{10} \notin y_a, Y_{01} \in y_a\right)\}.
\end{aligned}
$$

Simplifying this equality, we have

$$
\begin{aligned}
&P\left(Y \in y_a \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_a \mid X_1 = 1, X_2 = 0\right) \\
&- P\left(Y \in y_a \mid X_1 = 0, X_2 = 1\right)
\end{aligned}
$$

is equal to

$$
\begin{aligned}
&P\left(Y_{11} \in y_a, Y_{10} \notin y_a, Y_{01} \notin y_a\right) - P\left(Y_{11} \notin y_a, Y_{10} \in y_a, Y_{01} \notin y_a\right) \\
&\quad - P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) - P\left(Y_{11} \notin y_a, Y_{10} \notin y_a, Y_{01} \in y_a\right).
\end{aligned}
$$

□

Proof of Theorem 4.3. The contrast

$$\begin{aligned}&P\left(Y\in y_c\mid X_1=1,X_2=1\right)-P\left(Y\in y_c\mid X_1=1,X_2=0\right)\\&-P\left(Y\in y_c\mid X_1=0,X_2=1\right)+P\left(Y\in y_c\mid X_1=0,X_2=0\right)\end{aligned}$$

is equal to $P\left(Y_{11}\in y_c\right)-P\left(Y_{10}\in y_c\right)-P\left(Y_{01}\in y_c\right)+P\left(Y_{00}\in y_c\right)$, under $Y_{x_1x_2}$ II X_1X_2. Applying the law of total probability, we have the following results:

$$\begin{aligned}&P\left(Y_{11}\in y_c\right)\\&=P\left(Y_{11}\in y_c,Y_{10}\in y_c,Y_{01}\in y_c,Y_{00}\in y_c\right)+P\left(Y_{11}\in y_c,Y_{10}\in y_c,Y_{01}\in y_c,Y_{00}\notin y_c\right)\\&\quad+P\left(Y_{11}\in y_c,Y_{10}\notin y_c,Y_{01}\in y_c,Y_{00}\in y_c\right)+P\left(Y_{11}\in y_c,Y_{10}\notin y_c,Y_{01}\in y_c,Y_{00}\notin y_c\right)\\&\quad+P\left(Y_{11}\in y_c,Y_{10}\in y_c,Y_{01}\notin y_c,Y_{00}\in y_c\right)+P\left(Y_{11}\in y_c,Y_{10}\in y_c,Y_{01}\notin y_c,Y_{00}\notin y_c\right)\\&\quad+P\left(Y_{11}\in y_c,Y_{10}\notin y_c,Y_{01}\notin y_c,Y_{00}\in y_c\right)+P\left(Y_{11}\in y_c,Y_{10}\notin y_c,Y_{01}\notin y_c,Y_{00}\notin y_c\right),\end{aligned}$$

and similar equalities after applying the theorem of total probability are available for $P\left(Y_{10}\in y_c\right)$, $P\left(Y_{01}\in y_c\right)$ and $P\left(Y_{00}\in y_c\right)$.

Simplifying this equality, we have

$$\begin{aligned}&P\left(Y\in y_c\mid X_1=1,X_2=1\right)-P\left(Y\in y_c\mid X_1=1,X_2=0\right)\\&-P\left(Y\in y_c\mid X_1=0,X_2=1\right)+P\left(Y\in y_c\mid X_1=0,X_2=0\right)\end{aligned}$$

is equal to

$$\begin{aligned}&2P\left(Y_{11}\in y_c,Y_{10}\notin y_c,Y_{01}\notin y_c,Y_{00}\in y_c\right)+P\left(Y_{11}\in y_c,Y_{10}\notin y_c,Y_{01}\notin y_c,Y_{00}\notin y_c\right)\\&\quad-P\left(Y_{11}\notin y_c,Y_{10}\in y_c,Y_{01}\in y_c,Y_{00}\notin y_c\right)-P\left(Y_{11}\notin y_c,Y_{10}\in y_c,Y_{01}\notin y_c,Y_{00}\notin y_c\right)\\&\quad-P\left(Y_{11}\in y_c,Y_{10}\in y_c,Y_{01}\in y_c,Y_{00}\notin y_c\right)-P\left(Y_{11}\notin y_c,Y_{10}\in y_c,Y_{01}\in y_c,Y_{00}\in y_c\right)\\&\quad-P\left(Y_{11}\notin y_c,Y_{10}\in y_c,Y_{01}\in y_c,Y_{00}\notin y_c\right)-P\left(Y_{11}\notin y_c,Y_{10}\notin y_c,Y_{01}\in y_c,Y_{00}\notin y_c\right)\\&\quad+P\left(Y_{11}\in y_c,Y_{10}\in y_c,Y_{01}\notin y_c,Y_{00}\in y_c\right)+P\left(Y_{11}\in y_c,Y_{10}\notin y_c,Y_{01}\in y_c,Y_{00}\in y_c\right)\\&\quad+P\left(Y_{11}\notin y_c,Y_{10}\notin y_c,Y_{01}\notin y_c,Y_{00}\in y_c\right).\end{aligned}$$

When X_1 and X_2 have positive monotonic effects on $Y\in y_c$, the contrast

$$\begin{aligned}&P\left(Y\in y_c\mid X_1=1,X_2=1\right)-P\left(Y\in y_c\mid X_1=1,X_2=0\right)\\&-P\left(Y\in y_c\mid X_1=0,X_2=1\right)-P\left(Y\in y_c\mid X_1=0,X_2=0\right)\end{aligned}$$

is equal to $P\left(Y_{11}\in y_c,Y_{10}\notin y_c,Y_{01}\notin y_c,Y_{00}\notin y_c\right)$. $\square$

S2 Continuous Sufficient Cause Interaction

These results can be further generalized for outcomes on $\mathbf{R}^n$. For this section, we allow $(Y_{11}, Y_{10}, Y_{01}, Y_{00})$ to have a distribution function $P(Y_{11} \in y_{11}, Y_{10} \in y_{10}, Y_{01} \in y_{01}, Y_{00} \in y_{00})$, where $y_{11}, y_{10}, y_{01}, y_{00}$ are all subsets of $\mathbf{R}$. We first provide a generalized notion of positive monotonicity for continuous outcomes that will be used in the subsequent theorems.

Definition S2.1 (Generalized Positive Monotonicity)**.** We say that X_1 has a positive monotonic effect on $Y \in y_c$ for any fixed $y_c \subset \mathbf{R}$ if there is no individual $\omega \in \Omega$ such that $Y_{x_1x_2}(\omega) \notin y_c$ and $Y_{x_3x_2}(\omega) \in y_c$ for all $x_1 > x_3$ for any fixed x_2. Similarly, we say that X_2 has a positive monotonic effect on $Y \in y_c$ for some $y_c \subset \mathbf{R}$ if there is no individual $\omega \in \Omega$ such that $Y_{x_1x_2}(\omega) \notin y_c$ and $Y_{x_1x_3}(\omega) \in y_c$ for all $x_2 > x_3$ for any fixed x_1. If X_1 and X_2 each individually have a positive monotonic effect on $Y \in y_c$ for any fixed $y_c \subset \mathbf{R}$ then we say that X_1 and X_2 have positive monotonic effects on $Y \in y_c$.

Theorem S2.1. *Suppose $Y_{x_1x_2} \amalg X_1X_2$. Here, y_a is any subset of $\mathbf{R}$. The contrast*

$$\begin{aligned}&P\left(Y \in y_a \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_a \mid X_1 = 1, X_2 = 0\right)\\&- P\left(Y \in y_a \mid X_1 = 0, X_2 = 1\right)\end{aligned}$$

is equal to

$$\begin{aligned}&P\left(Y_{11} \in y_a, Y_{10} \notin y_a, Y_{01} \notin y_a\right) - P\left(Y_{11} \notin y_a, Y_{10} \in y_a, Y_{01} \notin y_a\right)\\&\quad - P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) - P\left(Y_{11} \notin y_a, Y_{10} \notin y_a, Y_{01} \in y_a\right).\end{aligned}$$

Proof of Theorem S2.1. The contrast

$$\begin{aligned}&P\left(Y \in y_a \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_a \mid X_1 = 1, X_2 = 0\right)\\&- P\left(Y \in y_a \mid X_1 = 0, X_2 = 1\right)\end{aligned}$$

is equal to $P\left(Y_{11} \in y_a\right) - P\left(Y_{10} \in y_a\right) - P\left(Y_{01} \in y_a\right)$, under $Y_{x_1x_2} \amalg X_1X_2$. Applying the law of total probability, we have

$$
\begin{aligned}
&P\left(Y_{11} \in y_a\right) - P\left(Y_{10} \in y_a\right) - P\left(Y_{01} \in y_a\right) \\
&= P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) + P\left(Y_{11} \in y_a, Y_{10} \notin y_a, Y_{01} \in y_a\right) \\
&\quad + P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \notin y_a\right) + P\left(Y_{11} \in y_a, Y_{10} \notin y_a, Y_{01} \notin y_a\right) \\
&\quad - \{P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) + P\left(Y_{11} \notin y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) \\
&\quad + P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \notin y_a\right) + P\left(Y_{11} \notin y_a, Y_{10} \in y_a, Y_{01} \notin y_a\right)\} \\
&\quad - \{P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) + P\left(Y_{11} \notin y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) \\
&\quad + P\left(Y_{11} \in y_a, Y_{10} \notin y_a, Y_{01} \in y_a\right) + P\left(Y_{11} \notin y_a, Y_{10} \notin y_a, Y_{01} \in y_a\right)\}.
\end{aligned}
$$

Simplifying this equality, we have

$$
\begin{aligned}
&P\left(Y \in y_a \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_a \mid X_1 = 1, X_2 = 0\right) \\
&- P\left(Y \in y_a \mid X_1 = 0, X_2 = 1\right)
\end{aligned}
$$

is equal to

$$
\begin{aligned}
&P\left(Y_{11} \in y_a, Y_{10} \notin y_a, Y_{01} \notin y_a\right) - P\left(Y_{11} \notin y_a, Y_{10} \in y_a, Y_{01} \notin y_a\right) \\
&\quad - P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) - P\left(Y_{11} \notin y_a, Y_{10} \notin y_a, Y_{01} \in y_a\right).
\end{aligned}
$$

$\square$

Theorem S2.2. *Suppose* $Y_{x_1 x_2} \amalg X_1 X_2$ *and suppose* X_1 *and* X_2 *have positive monotonic effects on* $Y \in y_c$. *For any* y_c *that is a subset of* $\mathbf{R}$, *the contrast*

$$
\begin{aligned}
&P\left(Y \in y_c \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_c \mid X_1 = 1, X_2 = 0\right) \\
&\quad - P\left(Y \in y_c \mid X_1 = 0, X_2 = 1\right) + P\left(Y \in y_c \mid X_1 = 0, X_2 = 0\right)
\end{aligned}
$$

is equal to $P\left(Y_{11} \in y_c, Y_{10} \notin y_c, Y_{01} \notin y_c, Y_{00} \notin y_c\right)$.

Proof of Theorem S2.2. The contrast

$$
\begin{aligned}
&P\left(Y \in y_c \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_c \mid X_1 = 1, X_2 = 0\right) \\
&- P\left(Y \in y_c \mid X_1 = 0, X_2 = 1\right) + P\left(Y \in y_c \mid X_1 = 0, X_2 = 0\right)
\end{aligned}
$$

is equal to $P(Y_{11} \in y_c) - P(Y_{10} \in y_c) - P(Y_{01} \in y_c) + P(Y_{00} \in y_c)$, under $Y_{x_1x_2} \amalg X_1X_2$. Applying the law of total probability, we have the following results:

$$
\begin{aligned}
&P(Y_{11} \in y_c) \\
&= P(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_c) + P(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \notin y_c) \\
&\quad + P(Y_{11} \in y_c, Y_{10} \notin y_c, Y_{01} \in y_c, Y_{00} \in y_c) + P(Y_{11} \in y_c, Y_{10} \notin y_c, Y_{01} \in y_c, Y_{00} \notin y_c) \\
&\quad + P(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \notin y_c, Y_{00} \in y_c) + P(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \notin y_c, Y_{00} \notin y_c) \\
&\quad + P(Y_{11} \in y_c, Y_{10} \notin y_c, Y_{01} \notin y_c, Y_{00} \in y_c) + P(Y_{11} \in y_c, Y_{10} \notin y_c, Y_{01} \notin y_c, Y_{00} \notin y_c),
\end{aligned}
$$

and similar equalities after applying the theorem of total probability are available for $P(Y_{10} \in y_c)$, $P(Y_{01} \in y_c)$ and $P(Y_{00} \in y_c)$.

Simplifying this equality, we have

$$
\begin{aligned}
&P(Y \in y_c \mid X_1 = 1, X_2 = 1) - P(Y \in y_c \mid X_1 = 1, X_2 = 0) \\
&- P(Y \in y_c \mid X_1 = 0, X_2 = 1) + P(Y \in y_c \mid X_1 = 0, X_2 = 0)
\end{aligned}
$$

is equal to

$$
\begin{aligned}
&2P(Y_{11} \in y_c, Y_{10} \notin y_c, Y_{01} \notin y_c, Y_{00} \in y_c) + P(Y_{11} \in y_c, Y_{10} \notin y_c, Y_{01} \notin y_c, Y_{00} \notin y_c) \\
&\quad - P(Y_{11} \notin y_c, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \notin y_c) - P(Y_{11} \notin y_c, Y_{10} \in y_c, Y_{01} \notin y_c, Y_{00} \notin y_c) \\
&\quad - P(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \notin y_c) - P(Y_{11} \notin y_c, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_c) \\
&\quad - P(Y_{11} \notin y_c, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \notin y_c) - P(Y_{11} \notin y_c, Y_{10} \notin y_c, Y_{01} \in y_c, Y_{00} \notin y_c) \\
&\quad + P(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \notin y_c, Y_{00} \in y_c) + P(Y_{11} \in y_c, Y_{10} \notin y_c, Y_{01} \in y_c, Y_{00} \in y_c) \\
&\quad + P(Y_{11} \notin y_c, Y_{10} \notin y_c, Y_{01} \notin y_c, Y_{00} \in y_c).
\end{aligned}
$$

When X_1 and X_2 have positive monotonic effects on $Y \in y_c$, the contrast

$$
\begin{aligned}
&P(Y \in y_c \mid X_1 = 1, X_2 = 1) - P(Y \in y_c \mid X_1 = 1, X_2 = 0) \\
&- P(Y \in y_c \mid X_1 = 0, X_2 = 1) - P(Y \in y_c \mid X_1 = 0, X_2 = 0)
\end{aligned}
$$

is equal to $P(Y_{11} \in y_c, Y_{10} \notin y_c, Y_{01} \notin y_c, Y_{00} \notin y_c)$. □

S3 Global Interaction Tests for an Ordinal Outcome with Three Levels

The notation here follows the main text. Previous sections examined how to test for the presence of sufficient cause interaction for an ordinal outcome under one specified condition. Theorems 2.3-2.6 in the main text used counterfactual conditions to derive empirical conditions for such sufficient cause interaction for ordinal outcomes, which generalizes the results of VanderWeele and Robins (2008). Here, we attempt to examine what occurs if we test for the presence of sufficient cause interaction for an ordinal outcome at different specified conditions simultaneously. We first examine the case where we have positive monotonicity constraints on both X_1 and X_2, and then we present the situation where there are no monotonicity constraints.

Earlier, in Theorem 2.1 in the main text, we had provided a sufficient cause representation for an outcome under a specified condition. We had specifically examined the situation, where one is testing the presence of only one type of sufficient cause interaction at a specified condition. Now, one might be interested in testing if there evidence for sufficient cause interaction for at least one of the specified conditions of the outcome. For example, we might be interested if our study population displays X_1X_2 sufficient cause interaction for the outcome $Z^A = I(Z = 1)$, $Z^C = I(Z = 2)$, or $Z^D = I(Z = 0)$. One could simply test the different conditions separately. We first provide the case where one assumes that X_1 and X_2 both have positive monotonic effects on Z, and then examine the case when we relax the monotonicity assumption.

Theorem S3.1. *Global Tests for Sufficient Cause Interaction for an outcome under multiple specified conditions under monotonic constraints Suppose X_1 and X_2 both have positive monotonic effects on ordinal outcome Z, and that $Z_{x_1x_2} \amalg \{X_1, X_2\} \mid V$. If for* *some value $v \in V$ we have that at least one of the following inequalities is satisfied*

$$
\begin{aligned}
p_{11v}^{A} - p_{10v}^{A} - p_{01v}^{A} + p_{00v}^{A} + p_{00}^{C} - p_{01}^{C} &> 0, & \text{(S3.1)}\\
p_{11v}^{A} - p_{10v}^{A} - p_{01v}^{A} &> 0 & \text{(S3.2)}\\
p_{11v}^{A} - p_{10v}^{A} - p_{01v}^{A} + p_{00v}^{A} + p_{00}^{C} - p_{01}^{C} &> 0 & \text{(S3.3)}\\
p_{11v}^{B} - p_{10v}^{B} - p_{01v}^{B} + p_{00v}^{B} &> 0 & \text{(S3.4)}\\
p_{11v}^{C} - p_{10}^{C} - p_{01}^{C} + p_{00}^{C} &> 0, & \text{(S3.5)}
\end{aligned}
$$

then X_1 and X_2 display synergism for at least one of the following outcomes $Z^A = I(Z = 1)$, $Z^B = I(Z \geq 1)$, or $Z^C = I(Z = 2)$.

Proof. If any of inequalities S3.1, S3.2, S3.3, S3.4, or S3.5 are met than by Theorems 2.2-2.6 in the main text there is X_1 and X_2 synergism for the respective outcome under specified condition. This completes our proof. □

Theorem S3.2. *Global Tests for Sufficient Cause Interaction for an outcome under multiple specified considtions Suppose that $Z_{x_1 x_2} \amalg \{X_1, X_2\} \mid V$. If for some value $v \in V$, we have at least one of the following inequalities is satisfied*

$$
\begin{aligned}
p_{11}^{D} - p_{01}^{D} - p_{10}^{D} &> 0 & \text{(S3.6)}\\
p_{11}^{D} - p_{10}^{D} - p_{01}^{D} &< -1 & \text{(S3.7)}\\
p_{11v}^{A} - p_{10v}^{A} - p_{01v}^{A} &> 0 & \text{(S3.8)}\\
p_{11v}^{A} - p_{10v}^{A} - p_{01v}^{A} &< -1 & \text{(S3.9)}\\
p_{11v}^{B} - p_{10v}^{B} - p_{01v}^{B} &> 0 & \text{(S3.10)}\\
p_{11v}^{B} - p_{10v}^{B} - p_{01v}^{B} &< -1 & \text{(S3.11)}\\
p_{11v}^{C} - p_{10}^{C} - p_{01}^{C} &> 0 & \text{(S3.12)}\\
p_{11v}^{C} - p_{10}^{C} - p_{01}^{C} &< -1 & \text{(S3.13)}
\end{aligned}
$$

then X_1 and X_2 display synergism for at least one of the following outcomes $Z^A = I(Z = 1)$, $Z^B = I(Z \geq 1)$, $Z^C = I(Z = 2)$, or $Z^D = I(Z = 0)$.

Proof. If any of the odd inequalities are met then by Theorem 2.2-2.6 in the main paper there is X_1 and X_2 synergism for the respective outcome under specified condition. If any of the even inequalities is met, then this implies that at least one of the odd inequalities is also met. Applying Theorems 2.2-2.6, we again have that X_1 and X_2

display synergism for at least one of the outcomes $Z^A = I(Z = 1)$, $Z^B = I(Z \geq 1)$, $Z^C = I(Z = 2)$, or $Z^D = I(Z = 0)$. $\square$

S4 Appendix 1B

The notation here departs from the main text to cover ordinal outcomes with n levels. Theorem 4.1 is provided again as Theorem S4.5.

Notation: Y is an ordinal variable that takes values $Y \in \{0, \ldots, n\} = Y$. We denote singleton value y, which can take a value within the interval $0 < y \leq n$. We also denote S to be a particular subset of values of $Y : S$ can be any subset of $\{1, \ldots, n-1\}$ and S must be an arithmetic sequence with common difference of one. We also use the shorthand notation $p^L_{x_1x_2}$ to denote $E(Y^L \mid X_1 = x_1, X_2 = x_2)$ and $p^L_{x_1x_2v}$ to denote $E(Y^L \mid X_1 = x_1, X_2 = x_2, V = v)$.

The potential outcome or counterfactual value of an individual ω had X_1 been set to x_1 and X_2 been set to x_2 is denoted $Y_{x_1,x_2}(\omega)$; more generally, we write the potential outcome $Y_{x_1,\ldots,x_s}(\omega)$ of Y for individual ω if for $j = 1, \ldots, s$ each putative cause $X_j \in \{X_1, \ldots, X_s\}$ were set x_j. An indicator function denoted $Y^S = I(Y \in S)$ or $Y^y = I(Y \geq y)$ is used to denote a new random variables constructed from Y which takes value 1 if $S \subset Y$ or singleton $y > Y$ respectively, 0 otherwise. Potential outcome versions of Y^S or Y^y are defined as $Y^S_{x_1,\ldots,x_s}(\omega) = I(Y_{x_1,\ldots,x_s}(\omega) \in S)$ or $Y^y_{x_1,\ldots,x_s}(\omega) = I(Y_{x_1,\ldots,x_s}(\omega) = y)$. Also, denote $Y^{S+}_{x_1,\ldots,x_s}(\omega) = I(Y_{x_1,\ldots,x_s}(\omega) > \max(S))$.

Definition S4.1 (Sufficient cause for a specified outcome)**.** We say that putative binary causes $X_1, \ldots, X_n$ are called sufficient causes for Y^L where $L \in \{S\}$, if for all values of $x_1, \ldots, x_n \in X^n$ such that $x_1 \cdots x_n = 1$ we have that $Y^L_{x_1 \cdots x_n}(\omega) = 1$ for all $\omega \in \Omega$.

Definition S4.2 (Minimal sufficient cause for a specified outcome)**.** We say that putative binary causes $X_1, \ldots, X_n$ form a minimal sufficient cause for Y^L where $L \in \{S\}$, if $X_1, \ldots, X_n$ are a sufficient causes for Y^L and no proper subset of $\{X_1, \ldots, X_n\}$ is also a sufficient cause for Y^L.

Definition S4.3 (Determinative sufficient causes for a specified outcome)**.** A set of sufficient causes $M^L_1, \ldots, M^L_n$ each of which are composed of a product of binary causes for an outcome under a specified condition Y^L, where $L \in \{S\}$, is defined to be determinative for Y^L if for all $\omega \in \Omega$, $Y^L_{x_1 \cdots x_s}(\omega) = 1$ if and only if $M_1^L \vee M_2^L \vee \ldots \vee M_n^L = 1$.

Definition S4.4 (Non-redundant sufficient causes for a specified outcome)**.** A set of determinative sufficient causes $M_1^L, \ldots, M_n^L$ for Y^L, where $L \in \{S, y\}$, is called a non-redundant determinative set of minimal sufficient causes if there is no proper subset of $M_1^L, \ldots, M_n^L$ that is also a determinative set of minimal sufficient causes for Y^L.

Theorem S4.1. *Sufficient cause representation for a specified outcome For putative binary causes X_1 and X_2 of outcome under specified condition Y^L, where $L \in \{S\}$, we say that there exists binary variables*

$$A_0(\omega), A_1(\omega), A_2(\omega), A_3(\omega), A_4(\omega), A_5(\omega), A_6(\omega), A_7(\omega), A_8(\omega),$$

which are functions of the counterfactuals $\{Y^L_{11}(\omega), Y^L_{10}(\omega), Y^L_{01}(\omega), Y^L_{00}(\omega)\}$ such that

$$Y^L = A_0 \vee A_1 X_1 \vee A_2 \bar{X}_1 \vee A_3 X_2 \vee A_4 \bar{X}_2 \vee A_5 X_1 X_2 \vee A_6 \bar{X}_1 X_2 \vee A_7 X_1 \bar{X}_2 \vee A_8 \bar{X}_1 \bar{X}_2, \tag{S4.1}$$

and such that

$$\begin{aligned} Y^L_{x_1 x_2} \quad = \quad & A_0 \vee A_1 x_1 \vee A_2(1-x_1) \vee A_3 x_2 \vee A_4(1-x_2) \vee A_5 x_1 x_2 \\ & \vee A_6(1-x_1)x_2 \vee A_7 x_1(1-x_2) \vee A_8(1-x_1)(1-x_2) \end{aligned} \tag{S4.2}$$

Proof. Mirroring the proof of Theorem 1 in VanderWeele and Robins (2008), construct $A_0, \ldots, A_8$ according to the following 16 rules: (1) If $Y^L_{x_1x_2}(\omega) = 1$ for all $\{x_1, x_2\} \in \{0,1\}$,[2] let $A_0(\omega) = 1$ and $A_i(\omega) = 0$ for all $i \notin 0$. (2) If $Y^L_{00}(\omega) = 0$ and $Y^L_{11}(\omega) = Y^L_{10}(\omega) = Y^L_{01}(\omega) = 1$, let $A_1(\omega) = A_3(\omega) = 1$ and $A_i(\omega) = 0$ for $i \notin \{1,3\}$. (3) If $Y^L_{10}(\omega) = 0$, and $Y^L_{00}(\omega) = Y^L_{01}(\omega) = Y^L_{11}(\omega) = 1$, let $A_i(\omega) = 1$ for $i \in \{2,3\}$ and $A_i(\omega) = 0$ for $i \notin \{2,3\}$. (4) If $Y^L_{00}(\omega) = Y^L_{10}(\omega) = 0$ and $Y^L_{01}(\omega) = Y^L_{11}(\omega) = 1$, let $A_3(\omega) = 1$ and $A_i(\omega) = 0$ for $i \notin \{3\}$. (5) If $Y^L_{01}(\omega) = 0$ and $Y^L_{00}(\omega) = Y^L_{10}(\omega) = Y^L_{11}(\omega) = 1$, let $A_i(\omega) = 1$ for $i \in \{1,4\}$ and $A_i(\omega) = 0$ for $i \notin \{1,4\}$. (6) If $Y^L_{00}(\omega) = Y^L_{01}(\omega) = 0$ and $Y^L_{10}(\omega) = Y^L_{11}(\omega) = 1$, let $A_1(\omega) = 1$ and $A_i(\omega) = 0$. (7) If $Y^L_{01}(\omega) = Y^L_{10}(\omega) = 0$ and $Y^L_{00}(\omega) = Y^L_{11}(\omega) = 1$,let $A_i(\omega) = 1$ for $i \in \{5,8\}$ and $A_i(\omega) = 0$ for $i \notin \{5,8\}$. (8) If $Y^L_{11}(\omega) = 1$ and $Y^L_{00}(\omega) = Y^L_{01}(\omega) = Y^L_{10}(\omega) = 0$, let $A_5(\omega) = 1$ and $A_i(\omega) = 0$ for $i \notin \{5\}$. (9) If $Y^L_{11}(\omega) = 0$ and $Y^L_{00}(\omega) = Y^L_{10}(\omega) = Y^L_{01}(\omega) = 1$, let $A_i(\omega) = 1$ for $i \in \{2,4\}$ and $A_i(\omega) = 0$ for $i \notin \{2,4\}$. (10) If $Y^L_{00}(\omega) = Y^L_{11}(\omega) = 0$ and $Y^L_{01}(\omega) = Y^L_{10}(\omega) = 1$, let $A_i(\omega) = 1$ for $i \in \{6,7\}$ and $A_i(\omega) = 0$ for $i \notin \{6,7\}$. (11) If $Y^L_{10}(\omega) = Y^L_{11}(\omega) = 0$ and $Y^L_{00}(\omega) = Y^L_{01}(\omega) = 1$, let $A_i(\omega) = 1$ for $i \in \{2\}$ and $A_i(\omega) \notin \{2\}$. (12) If $Y^L_{11}(\omega) =$

$Y^L_{10}(\omega) = Y^L_{00}(\omega) = 0$ and $Y_{01}(\omega) = 1$, let $A_i(\omega) = 1$ for $i \in \{6\}$ and $A_i(\omega) = 0$ for $i \notin \{6\}$. (13) If $Y^L_{01}(\omega) = Y^L_{11}(\omega) = 0$ and $Y^L_{00}(\omega) = Y^L_{10}(\omega) = 1$, let $A_i(\omega) = 1$ for $i \in \{4\}$ and $A_i(\omega) = 0$ for $i \notin \{4\}$. (14) If $Y^L_{00}(\omega) = Y^L_{01}(\omega) = Y^L_{11}(\omega) = 0$ and $Y^L_{10}(\omega) = 1$, let $A_i(\omega) = 1$ for $i \notin \{7\}$ and $A_i(\omega) = 0$ for $i \notin \{7\}$. (15) If $Y^L_{01}(\omega) = Y^L_{10}(\omega) = Y^L_{11}(\omega) = 0$ and $Y^L_{00}(\omega) = 1$, let $A_i(\omega) = 1$ for $i \in \{8\}$ and $A_i(\omega) = 0$ for $i \notin \{8\}$. (16) If $Y^L_{x_1x_2}(\omega) = 0$ for all $\{x_1, x_2\} \in \{0, 1\}^2$, let $A_i(\omega) = 0$. □

Sufficient cause interaction for ordinal outcomes

Theorem S4.2. *Suppose $L \in \{S, y\}$. There exists an individual $\omega \in \Omega$ for whom $Y^L_{11}(\omega) = 1$ and $Y^L_{10}(\omega) = Y^L_{01}(\omega) = 0$ if and only if the conjunction X_1X_2 exhibits sufficient cause interaction for an outcome under specified condition: Y^L.*

Proof. Similar to Theorem 2.2 in main article therefore omitted.

□

Theorem S4.3. *Suppose V is a set of variables that are enough to control for the confounding of the variables of X_1 and X_2 on Y^L, where $L \in \{S, y\}$, ie such that $Y^L_{x_1x_2} \amalg \{X_1, X_2\} \mid V$. We can say that X_1X_2 exhibit sufficient cause interaction if for some value v of V, the following inequality holds:*

$$\begin{aligned} 0 \quad < \quad & E(Y^L \mid X_1 = 1, X_2 = 1, V = v) - E(Y^L \mid X_1 = 0, X_2 = 1, V = v) \\ & - E(Y^L \mid X_1 = 0, X_2 = 0, V = v) \end{aligned}$$

Proof. We prove this result by contradiction. Suppose for outcome under specified condition $L \in \{S, y\}$, we have that X_1X_2 does not exhibit sufficient cause interaction. Theorem S4.2 then implies that there is no individual $\omega \in \Omega$ for whom $Y^L_{11}(\omega.) = 1$ and $Y^L_{10}(\omega) = Y^L_{01}(\omega) = 0$. This is equivalent to stating that for all $\omega \in \Omega$, we have that $Y^L_{11}(\omega) - Y^L_{10}(\omega) - Y^L_{01}(\omega) \leq 0$. Therefore, taking expectations on both sides we have

$E(Y_{11}^L(\omega) - Y_{10}^L(\omega) - Y_{01}^L(\omega)) \leq 0$.

$$\begin{aligned}
& E(Y^L \mid X_1 = 1, X_2 = 1, V = v) - E(Y^L \mid X_1 = 1, X_2 = 0, V = v) \\
& -E(Y^L \mid X_1 = 0, X_2 = 1, V = v) \\
= \quad & E(Y_{11}^L \mid X_1 = 1, X_2 = 1, V = v) - E(Y_{10}^L \mid X_1 = 1, X_2 = 0, V = v) \\
& -E(Y_{01}^L \mid X_1 = 0, X_2 = 1, V = v) \\
= \quad & E(Y_{11}^L \mid V = v) - E(Y_{10}^L \mid V = v) - E(Y_{01}^L \mid V = v) \\
= \quad & E(Y_{11}^L(\omega) - Y_{10}^L(\omega) - Y_{01}^L(\omega)) \leq 0.
\end{aligned}$$

The first equality stems from the consistency assumption and the second equality stems from the no unseen confounding assumption $Y_{x_1 x_2}^L \amalg \{X_1, X_2\} \mid V$. This completes our proof. $\square$

Theorem S4.4. *Suppose X_1 and X_2 both have positive monotonic effects on ordinal variable Y, and that $Y_{x_1 x_2}^y \amalg \{X_1, X_2\} \mid V$. If for some value $v \in V$, we have*

$$p_{11v}^y - p_{10v}^y - p_{01v}^y + p_{00v}^y > 0,$$

Proof. Suppose $X_1$and X_2 do not display synergism for outcome Y^y. Then, by Theorem S4.2, we have for all $\omega \in \Omega$, $Y_{11}^B(\omega) - Y_{10}^B(\omega) - Y_{01}^B(\omega) \leq 0$. Consider two different cases. Case 1: if $Y_{00}(\omega) < y$, then $Y_{00}^y(\omega) = 0$ and adding this to $Y_{11}^B(\omega) - Y_{10}^B(\omega) - Y_{01}^B(\omega) \leq 0$, we have $Y_{11}^B(\omega) - Y_{10}^B(\omega) - Y_{01}^B(\omega) + Y_{00}^B(\omega) \leq 0$. Case 2: say $Y_{00}^y(\omega) \geq y$ then $Y_{00}^y(\omega) = 1$ and by our monotonicity constraints $Y_{11}^y(\omega) = Y_{01}^y(\omega) = Y_{10}^y(\omega) = 1$, and as a result $Y_{11}^y(\omega) - Y_{10}^y(\omega) - Y_{01}^y(\omega) + Y_{00}^y(\omega) \leq 0$. So, in both cases, we have that if $X_1$and X_2 do not display synergism for outcome Y^y, then $Y_{11}^y(\omega) - Y_{10}^y(\omega) - Y_{01}^y(\omega) + Y_{00}^y(\omega) \leq 0$. Taking expectations on both sides and following the logic present in the proof of Theorem 3.3, we complete our proof.

$\square$

Theorem S4.5. *Suppose X_1 and X_2 both have positive monotonic effects on ordinal variable Y, and that $Y_{x_1 x_2}^S \amalg \{X_1, X_2\} \mid V$. If for some value $v \in V$, we have*

$$\begin{aligned}
p_{11v}^S - p_{10v}^S - p_{01v}^S + p_{00v}^S + p_{00}^{S+} - p_{01}^{S+} &> 0, \quad \textit{or} \\
p_{11v}^S - p_{10v}^S - p_{01v}^S + p_{00v}^S + p_{00}^{S+} - p_{01}^{S+} &> 0, \quad \textit{or} \\
p_{11v}^S - p_{10v}^S - p_{01v}^S &> 0
\end{aligned}$$

then X_1 and X_2 display synergism for outcome $Y^S = I(Y \in S)$.

Proof. Suppose $X_1$and X_2 do not display synergism for outcome Y^S. Then, by Theorem S4.2, we have for all $\omega \in \Omega$, $Y^S_{11}(\omega) - Y^S_{10}(\omega) - Y^S_{01}(\omega) \leq 0$. Taking expectations of both sides of this inequality and following logic present in the the proof of Theorem S4.3, we have the condition $p^S_{11v} - p^S_{10v} - p^S_{01v} \leq 0$.

Denote S^- to be the set of numbers in Y that are all less than the least number in S, and denote S^+ to be the set of numbers in Y that are greater than the largest number in S. Denote $s_i \in S$, $s_i^- \in S^-$, and $s_i^+ \in S^+$ for $i \in \{1, \dots, 8\}$. Consider three different cases to prove the other inequality: $p^S_{11v} - p^S_{10v} - p^S_{01v} + p^S_{00v} + p^{S+}_{00v} - p^{S+}_{01} > 0$. Case 1: Suppose $Y_{00}(\omega)$ is equal to $a^- \in S^-$. Then $Y^S_{00}(\omega) = 0$, $Y^{S+}_{00}(\omega) = 0$,$Y_{01}(\omega) \in \{s_1^-, s_1, s_1^+\}$, $Y_{10}(\omega) \in \{s_2^-, s_2, s_2^+\}$, and $Y_{11}(\omega) \in \{s_3^-, s_3, s_3^+\}$. (Sub-case a): If $Y_{11}(\omega) = s_3$, then either $Y_{10}(\omega) \in S$ or $Y_{01}(\omega) \in S$ because X_1 and X_2 do not display synergism for Y^S and therefore $Y^S_{11}(\omega) - Y^S_{10}(\omega) - Y^S_{01}(\omega) + Y^S_{00} + Y^{S+}_{00} - Y^{S+}_{01}(\omega) \leq 0$. (Sub-case b): If $Y_{11}(\omega) \in S^+$, then $Y^S_{11}(\omega) = 0$, and we still have the inequality $Y^S_{11}(\omega) - Y^S_{10}(\omega) - Y^S_{01}(\omega) + Y^S_{00} + Y^{S+}_{00} - Y^{S+}_{01}(\omega) \leq 0$. Case 2: if $Y_{00}(\omega) \in S$, then $Y_{11}(\omega) \in \{s_4, s_4^+\}$, $Y_{01}(\omega) \in \{s_5, s_5^+\}$, $Y_{10} \in \{s_6, s_6^+\}$. Regardless of which $Y_{11}(\omega), Y_{10}(\omega), Y_{01}(\omega)$ we pick satisfying the monotonicity constraints and ensuring that we do not have X_1 and X_2 do not display synergism for Y^S, we have that $Y^S_{11}(\omega) - Y^S_{10}(\omega) - Y^S_{01}(\omega) + Y^S_{00} + Y^{S+}_{00} - Y^{S+}_{01}(\omega) \leq 0$. Case 3: if $Y_{00}(\omega) \in S^+$, then $Y^S_{00}(\omega) = Y^S_{11}(\omega) = Y^S_{01}(\omega) = Y^S_{10}(\omega) = 0$, and $Y^S_{11}(\omega) - Y^S_{10}(\omega) - Y^S_{01}(\omega) + Y^S_{00} + Y^{S+}_{00} - Y^{S+}_{01}(\omega) \leq 0$. Taking expectations on both sides and following the same logic present in the proof of Theorem S4.3, we complete our proof. To prove the first inequality. The result follows flowing the same logic as presented above. □

S5 Connection to Polytopes

Following Ramsahai (2013), polytopes can be used to detect different interdependence patterns for ordinal and categorical outcome. With deterministic counterfactuals or potential outcomes, one defines the set of vertices associated with the counterfactuals are of interest. Let Ψ_r denote the total set of response types associated with the vector $\mathbf{Y}(\omega) = (Y_{11}(\omega), Y_{10}(\omega), Y_{01}(\omega), Y_{00}(\omega))$. In the case of ordinal Y that takes values in $Y \in \{0, 1, 2\}$, Ψ_r has 81 rows representing the different response types associated with this vector of length four $\mathbf{Y}(\omega)$. For an ordinal Y that can take values in $Y \in \{0, \ldots, n\}$, the Ψ_r has $(n+1)^4$ rows, representing the total number of response types. After consulting scientific collaborators, write down the interdependence patterns of interest. For example, the response patterns $Y_{11}(\omega) = 2$, $Y_{10}(\omega) \in \{0, 1\}$, $Y_{01}(\omega) \in \{0, 1\}$, and $Y_{00}(\omega) \in \{0, 1\}$ might be of interest. To construct the associated polytope to detect these response types consider the following procedure: (1) list all the potential outcomes that are possible $\mathbf{Y}(\omega)$=$(Y_{11}(\omega), Y_{10}(\omega), Y_{01}(\omega), Y_{00}(\omega))$, which is denoted Ψ_r; (2) construct a new list through dichotomizing each vector $\mathbf{Y}(\omega)$ at each of the outcome levels of the ordinal outcome, e.g. let $\mathbf{Y}^y(\omega) = (I(Y_{11}(\omega) = y), I(Y_{10}(\omega) = y), I(Y_{01}(\omega) = y), I(Y_{00}(\omega) = y))$, where $y \in Y$; (3) define the full set of response types as Ψ, where each row is equal to $(\mathbf{Y}^0(\omega), \mathbf{Y}^1(\omega), \ldots, \mathbf{Y}^n(\omega))$; here Ψ will still have $(n+1)^4$ rows, but will now have $4(n+1)$ columns; (4) remove the rows associated with the response types of interest, and denote this new set of vertices Ψ^p.

Computational software, such as rcdd, can be used to compute the half-space representation of the polytope associated with Ψ^p. The half-space representation $\mathcal{H}(\Psi^p)$ can be used to construct empirical conditions to detect the interdependence of interest. First construct the polytope associated with the monotonicity constraints denoted Ψ^m, and use the half space representation $\mathcal{H}(\Psi^m)$ see which empirical conditions are associated solely with the monotonicity constraints. Then, construct the relevant polytope Ψ^p that removes vertices that do not follow the monotonic constraints and the interdependence patterns of interest. Then check which empirical conditions associated with the half-space representation of the polytope $\mathcal{H}(\Psi^p)$ are not present in the half-space representation of the polytope associated with the monotonicity constraints $\mathcal{H}(\Psi^m)$. Use the empirical conditions that are only associated with $\mathcal{H}(\Psi^p)$ and not $\mathcal{H}(\Psi^m)$ to construct empirical tests of the interdependence patterns of interest.

Departing from previous notation slightly, let $p^{\{S\}}_{x_1,x_2} = P(Y \in S \mid x_1, x_2)$ for some set $S \in \{0,1,2\}$, $x_1 \in \{0,1\}$ and $x_2 \in \{0,1\}$. Here, we consider one example. Suppose $Y \in \{0,1,2\}$. As before suppose scientific collaborators were interested in knowing whether an individual in the population displayed at least one of the following response patterns: $Y_{11}(\omega) = 2$, $Y_{10}(\omega) \in \{0,1\}$, $Y_{01}(\omega) \in \{0,1\}$, and $Y_{00}(\omega) \in \{0,1\}$. If $p^{\{2\}}_{11v} - p^{\{2\}}_{10v} - p^{\{2\}}_{01v} - p^{\{2\}}_{00v} > 0$ assuming no confounding, we have that there exists and individual who displays one of the following response profile: $Y_{11}(\omega) = 2$, $Y_{10}(\omega) \in \{0,1\}$, $Y_{01}(\omega) \in \{0,1\}$, and $Y_{00}(\omega) \in \{0,1\}$. Under monotonic constraints, if $p^{\{2\}}_{11v} - p^{\{2\}}_{10v} - p^{\{2\}}_{01v} + p^{\{2\}}_{00v} > 0$ assuming no confounding, we have that there exists and individual who displays the following response profile: $Y_{11}(\omega) = 2$, $Y_{10}(\omega) \in \{0,1\}$, $Y_{01}(\omega) \in \{0,1\}$, and $Y_{00}(\omega) \in \{0,1\}$.

Consider a second example, suppose we are interested in the response type $Y_{11}(\omega) = 2, Y_{10}(\omega) = 1, Y_{01}(\omega) = 1$ and $Y_{00}(\omega) = 1$. Then assuming no confounding, if $p^{\{2\}}_{11v} + p^{\{1\}}_{10v} + p^{\{1\}}_{01v} + p^{\{1\}}_{00v} > 3$, then we have that there exists an individual who displays the following response profile: $Y_{11}(\omega) = 2, Y_{10}(\omega) = 1, Y_{01}(\omega) = 1$ and $Y_{00}(\omega) = 1$. If we are willing to assume monotonicity constraints, then if $p^{\{2\}}_{11v} + p^{\{0\}}_{11v} - p^{\{2\}}_{10v} - p^{\{2\}}_{01v} + p^{\{2\}}_{00v} - p^{\{2\}}_{00v} > 0$, then there exists and individual with response profile $Y_{11}(\omega) = 2, Y_{10}(\omega) = 1, Y_{01}(\omega) = 1$ and $Y_{00}(\omega) = 1$.

The connection to polytopes can also be used to construct partial converses to detecting sufficient cause interaction. If one believed that everyone in the population displayed the response type $Y_{11}(\omega) = 2, Y_{10}(\omega) = 1, Y_{01}(\omega) = 1$ and $Y_{00}(\omega) = 1$ in our population, then a valid null hypothesis is that $H_0 : \quad p^{\{2\}}_{11} = p^{\{1\}}_{10} = p^{\{1\}}_{01} = p^{\{1\}}_{00} = 1$ vs H_1 : at least one of the qualities does not hold true to detect an individual that did not display $Y_{11}(\omega) = 2, Y_{10}(\omega) = 1, Y_{01}(\omega) = 1$ and $Y_{00}(\omega) = 1$.

S6 Generalized Stochastic Counterfactuals and Continuous Outcomes

As before, we allow $(Y_{11}, Y_{10}, Y_{01}, Y_{00})$ to have a distribution function $P(Y_{11} \in y_{11}, Y_{10} \in y_{10}, Y_{01} \in y_{01}, Y_{00} \in y_{00})$, where $y_{11}, y_{10}, y_{01}, y_{00}$ are all subsets of $\mathbf{R}$.

Here, our results are derived with the randomization assumption $Y_{x_1x_2} \amalg X_1X_2$.

Similar results are easy to derive with the no unobserved confounding assumption $Y_{x_1x_2} \amalg X_1X_2 \mid V$. Out of space constraints, we choose to present results only using the randomization assumption $Y_{x_1x_2} \amalg X_1X_2$.

Definition S6.1. Generalized Positive Monotonicity We say that X_1 has a positive monotonic effect on $Y \in y_c$ for any fixed $y_c \subset \mathbf{R}$ if there is no individual $\omega \in \Omega$ such that $Y_{x_1x_2}(\omega) \notin y_c$ and $Y_{x_3x_2}(\omega) \in y_c$ for all $x_1 > x_3$ for any fixed x_2. Similarly, we say that X_2 has a positive monotonic effect on $Y \in y_c$ for some $y_c \subset \mathbf{R}$ if there is no individual $\omega \in \Omega$ such that $Y_{x_1x_2}(\omega) \notin y_c$ and $Y_{x_1x_3}(\omega) \in y_c$ for all $x_2 > x_3$ for any fixed x_1. If X_1 and X_2 each individually have a positive monotonic effect on $Y \in y_c$ for any $y_c \subset \mathbf{R}$ then we say that x_1 and x_2 have positive monotonic effects on $Y \in y_c$.

Theorem S6.1. *Suppose $Y_{x_1x_2} \amalg X_1X_2$. Here, y_a is any subset of $\mathbf{R}$. The contrast*

$$\begin{aligned}
&P\left(Y \in y_a \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_a \mid X_1 = 1, X_2 = 0\right) \\
&- P\left(Y \in y_a \mid X_1 = 0, X_2 = 1\right)
\end{aligned}$$

is equal to

$$\begin{aligned}
&P\left(Y_{11} \in y_a, Y_{10} \notin y_a, Y_{01} \notin y_a\right) - P\left(Y_{11} \notin y_a, Y_{10} \in y_a, Y_{01} \notin y_a\right) \\
&\quad - P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) - P\left(Y_{11} \notin y_a, Y_{10} \notin y_a, Y_{01} \in y_a\right),
\end{aligned}$$

as well as

$$\begin{aligned}
&P\left(Y_{11} \in y_a, Y_{10} \notin y_a, Y_{01} \notin y_a, Y_{00} \in y_a\right) + P\left(Y_{11} \in y_a, Y_{10} \notin y_a, Y_{01} \notin y_a, Y_{00} \notin y_a\right) \\
&\quad - P\left(Y_{11} \notin y_a, Y_{10} \in y_a, Y_{01} \notin y_a, Y_{00} \in y_a\right) - P\left(Y_{11} \notin y_a, Y_{10} \in y_a, Y_{01} \notin y_a, Y_{00} \notin y_a\right) \\
&\quad - P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \notin y_a\right) \\
&\quad - P\left(Y_{11} \notin y_a, Y_{10} \notin y_a, Y_{01} \in y_a, Y_{00} \in y_a\right) - P\left(Y_{11} \notin y_a, Y_{10} \notin y_a, Y_{01} \in y_a, Y_{00} \notin y_a\right).
\end{aligned}$$

Consequently, if

$$\begin{aligned}
&P\left(Y \in y_a \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_a \mid X_1 = 1, X_2 = 0\right) \\
&- P\left(Y \in y_a \mid X_1 = 0, X_2 = 1\right) > 0,
\end{aligned}$$

then there must exist an individual $\omega \in \Omega$ such that $Y_{11}(\omega) \in y_a$, $Y_{10}(\omega) \notin y_a$, and $Y_{01}(\omega) \notin y_a$.

Theorem S6.2. *Suppose $Y_{x_1x_2} \amalg X_1X_2$, and X_1 and X_2 have positive monotonic effects on $Y \in y_c$, where y_c that is a subset of $\mathbf{R}$. The contrast*

$$
\begin{aligned}
&P\left(Y \in y_c \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_c \mid X_1 = 1, X_2 = 0\right) \\
&\quad - P\left(Y \in y_c \mid X_1 = 0, X_2 = 1\right) + P\left(Y \in y_c \mid X_1 = 0, X_2 = 0\right)
\end{aligned}
$$

is equal to

$$
P\left(Y_{11} \in y_c, Y_{10} \notin y_c, Y_{01} \notin y_c, Y_{00} \notin y_c\right),
$$

and consequently when

$$
\begin{aligned}
&P\left(Y \in y_c \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_c \mid X_1 = 1, X_2 = 0\right) \\
&\quad - P\left(Y \in y_c \mid X_1 = 0, X_2 = 1\right) + P\left(Y \in y_c \mid X_1 = 0, X_2 = 0\right) > 0,
\end{aligned}
$$

then there must exist an individual $\omega \in \Omega$ such that $Y_{11}(\omega) \in y_c$, $Y_{10}(\omega) \notin y_c$, $Y_{01}(\omega) \notin y_c$, and $Y_{00}(\omega) \notin y_c$.

Theorem S6.3. *Suppose $Y_{x_1x_2} \amalg X_1X_2$. Suppose X_1 and X_2 have positive monotonic effects on $Y \in y_c$, where y_c is any subset of $\mathbf{R}$. Let $y_a \subset \mathbf{R}$, $y_b \subset \mathbf{R}$, $y_c \subset \mathbf{R}$, where $\max y_a < \min y_b$ and $\max y_b < \min y_c$, and $y_a \cup y_b \cup y_c = \mathbf{R}$, $y_a \cap y_b = \varnothing$, $y_b \cap y_c = \varnothing$, $y_b \cap y_c = \varnothing$, and $y_a \cap y_b \cap y_c = \varnothing$. The contrast*

$$
\begin{aligned}
&P\left(Y \in y_b \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_b \mid X_1 = 1, X_2 = 0\right) \\
&\quad - P\left(Y \in y_b \mid X_1 = 0, X_2 = 1\right) + P\left(Y \in y_b \mid X_1 = 0, X_2 = 0\right) \\
&\quad + P\left(Y \in y_c \mid X_1 = 0, X_2 = 0\right) - P\left(Y \in y_c \mid X_1 = 1, X_2 = 0\right)
\end{aligned}
$$

is equal to

$$
\begin{aligned}
&P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_a, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_c, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_a, Y_{01} \in y_b, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_b, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_b\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_a, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_b\right) - P\left(Y_{11} \in y_a, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_b\right) \\
&\quad - P\left(Y_{11} \in y_a, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_c\right).
\end{aligned}
$$

Consequently, when the above monotonicity conditions hold and

$$
\begin{aligned}
&P\left(Y \in y_b \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_b \mid X_1 = 1, X_2 = 0\right) \\
&\quad - P\left(Y \in y_b \mid X_1 = 0, X_2 = 1\right) + P\left(Y \in y_b \mid X_1 = 0, X_2 = 0\right) \\
&\quad + P\left(Y \in y_c \mid X_1 = 0, X_2 = 0\right) - P\left(Y \in y_c \mid X_1 = 1, X_2 = 0\right) > 0
\end{aligned}
$$

then there must exist an individual $\omega \in \Omega$ *such that* $Y_{11}(\omega) \in y_a$, $Y_{10}(\omega) \notin y_a$, $Y_{01}(\omega) \notin y_a$, *and* $Y_{00}(\omega) \notin y_a$.

Similarly, the contrast

$$
\begin{aligned}
&P\left(Y \in y_b \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_b \mid X_1 = 1, X_2 = 0\right) \\
&\quad - P\left(Y \in y_b \mid X_1 = 0, X_2 = 1\right) + P\left(Y \in y_b \mid X_1 = 0, X_2 = 0\right) \\
&\quad + P\left(Y \in y_c \mid X_1 = 0, X_2 = 0\right) - P\left(Y \in y_c \mid X_1 = 0, X_2 = 1\right)
\end{aligned}
$$

is equal to

$$
\begin{aligned}
&P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_a, Y_{01} \in y_b, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_a, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_b, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_c, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_b\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_a, Y_{01} \in y_c, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_a, Y_{01} \in y_c, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_c, Y_{00} \in y_b\right) - P\left(Y_{11} \in y_a, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_b\right). \\
&\quad - P\left(Y_{11} \in y_a, Y_{10} \in y_b, Y_{01} \in y_c, Y_{00} \in y_c\right),
\end{aligned}
$$

when both X_1 and $X2$ have positive monotonic effects on $Y \in y_c$.

Proof of Theorem S6.1. The contrast

$$
\begin{aligned}
&P\left(Y \in y_a \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_a \mid X_1 = 1, X_2 = 0\right) \\
&- P\left(Y \in y_a \mid X_1 = 0, X_2 = 1\right).
\end{aligned}
$$

is equal to

$$
P\left(Y_{11} \in y_a\right) - P\left(Y_{10} \in y_a\right) - P\left(Y_{01} \in y_a\right),
$$

under $Y_{x_1x_2} \amalg X_1X_2$. Applying the law of total probability, we have

$$
\begin{aligned}
&P\left(Y_{11} \in y_a\right) - P\left(Y_{10} \in y_a\right) - P\left(Y_{01} \in y_a\right) \\
&= P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) + P\left(Y_{11} \in y_a, Y_{10} \notin y_a, Y_{01} \in y_a\right) \\
&\quad + P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \notin y_a\right) + P\left(Y_{11} \in y_a, Y_{10} \notin y_a, Y_{01} \notin y_a\right) \\
&- \{P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) + P\left(Y_{11} \notin y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) \\
&\quad + P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \notin y_a\right) + P\left(Y_{11} \notin y_a, Y_{10} \in y_a, Y_{01} \notin y_a\right)\} \\
&- \{P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) + P\left(Y_{11} \notin y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) \\
&\quad + P\left(Y_{11} \in y_a, Y_{10} \notin y_a, Y_{01} \in y_a\right) + P\left(Y_{11} \notin y_a, Y_{10} \notin y_a, Y_{01} \in y_a\right)\}.
\end{aligned}
$$

Simplifying this equality, we have

$$
\begin{aligned}
&P\left(Y \in y_a \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_a \mid X_1 = 1, X_2 = 0\right) \\
&- P\left(Y \in y_a \mid X_1 = 0, X_2 = 1\right)
\end{aligned}
$$

is equal to

$$
\begin{aligned}
&P\left(Y_{11} \in y_a, Y_{10} \notin y_a, Y_{01} \notin y_a\right) - P\left(Y_{11} \notin y_a, Y_{10} \in y_a, Y_{01} \notin y_a\right) \\
&\quad - P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_a\right) - P\left(Y_{11} \notin y_a, Y_{10} \notin y_a, Y_{01} \in y_a\right).
\end{aligned}
$$

□

Proof of Theorem S6.2. The contrast

$$
\begin{aligned}
&P\left(Y \in y_c \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_c \mid X_1 = 1, X_2 = 0\right) \\
&- P\left(Y \in y_c \mid X_1 = 0, X_2 = 1\right) + P\left(Y \in y_c \mid X_1 = 0, X_2 = 0\right)
\end{aligned}
$$

is equal to

$$
P\left(Y_{11} \in y_c\right) - P\left(Y_{10} \in y_c\right) - P\left(Y_{01} \in y_c\right) + P\left(Y_{00} \in y_c\right)
$$

under $Y_{x_1x_2} \amalg X_1X_2$. Applying the law of total probability, we have the following results:

$$
\begin{aligned}
&P\left(Y_{11} \in y_c\right) \\
&= P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_c\right) + P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \notin y_c\right) \\
&\quad + P\left(Y_{11} \in y_c, Y_{10} \notin y_c, Y_{01} \in y_c, Y_{00} \in y_c\right) + P\left(Y_{11} \in y_c, Y_{10} \notin y_c, Y_{01} \in y_c, Y_{00} \notin y_c\right) \\
&\quad + P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \notin y_c, Y_{00} \in y_c\right) + P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \notin y_c, Y_{00} \notin y_c\right) \\
&\quad + P\left(Y_{11} \in y_c, Y_{10} \notin y_c, Y_{01} \notin y_c, Y_{00} \in y_c\right) + P\left(Y_{11} \in y_c, Y_{10} \notin y_c, Y_{01} \notin y_c, Y_{00} \notin y_c\right),
\end{aligned}
$$

$$
\begin{aligned}
&P\left(Y_{10} \in y_c\right) \\
&= P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_c\right) + P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \notin y_c\right) \\
&\quad + P\left(Y_{11} \notin y_c, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_c\right) + P\left(Y_{11} \notin y_c, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \notin y_c\right) \\
&\quad + P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \notin y_c, Y_{00} \in y_c\right) + P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \notin y_c, Y_{00} \notin y_c\right) \\
&\quad + P\left(Y_{11} \notin y_c, Y_{10} \in y_c, Y_{01} \notin y_c, Y_{00} \in y_c\right) + P\left(Y_{11} \notin y_c, Y_{10} \in y_c, Y_{01} \notin y_c, Y_{00} \notin y_c\right),
\end{aligned}
$$

$$
\begin{aligned}
&P\left(Y_{01}\in y_c\right)\\
&=P\left(Y_{11}\in y_c,Y_{10}\in y_c,Y_{01}\in y_c,Y_{00}\in y_c\right)+P\left(Y_{11}\in y_c,Y_{10}\in y_c,Y_{01}\in y_c,Y_{00}\notin y_c\right)\\
&\quad+P\left(Y_{11}\notin y_c,Y_{10}\in y_c,Y_{01}\in y_c,Y_{00}\in y_c\right)+P\left(Y_{11}\notin y_c,Y_{10}\in y_c,Y_{01}\in y_c,Y_{00}\notin y_c\right)\\
&\quad+P\left(Y_{11}\in y_c,Y_{10}\notin y_c,Y_{01}\in y_c,Y_{00}\in y_c\right)+P\left(Y_{11}\in y_c,Y_{10}\notin y_c,Y_{01}\in y_c,Y_{00}\notin y_c\right)\\
&\quad+P\left(Y_{11}\notin y_c,Y_{10}\notin y_c,Y_{01}\in y_c,Y_{00}\in y_c\right)+P\left(Y_{11}\notin y_c,Y_{10}\notin y_c,Y_{01}\in y_c,Y_{00}\notin y_c\right),
\end{aligned}
$$

$$
\begin{aligned}
&P\left(Y_{00}\in y_c\right)\\
&=P\left(Y_{11}\in y_c,Y_{10}\in y_c,Y_{01}\in y_c,Y_{00}\in y_c\right)+P\left(Y_{11}\in y_c,Y_{10}\in y_c,Y_{01}\notin y_c,Y_{00}\in y_c\right)\\
&\quad+P\left(Y_{11}\notin y_c,Y_{10}\in y_c,Y_{01}\in y_c,Y_{00}\in y_c\right)+P\left(Y_{11}\notin y_c,Y_{10}\in y_c,Y_{01}\notin y_c,Y_{00}\in y_c\right)\\
&\quad+P\left(Y_{11}\in y_c,Y_{10}\notin y_c,Y_{01}\in y_c,Y_{00}\in y_c\right)+P\left(Y_{11}\in y_c,Y_{10}\notin y_c,Y_{01}\notin y_c,Y_{00}\in y_c\right)\\
&\quad+P\left(Y_{11}\notin y_c,Y_{10}\notin y_c,Y_{01}\in y_c,Y_{00}\in y_c\right)+P\left(Y_{11}\notin y_c,Y_{10}\notin y_c,Y_{01}\notin y_c,Y_{00}\in y_c\right).
\end{aligned}
$$

Simplifying this equality, we have

$$
\begin{aligned}
&P\left(Y\in y_c\mid X_1=1,X_2=1\right)-P\left(Y\in y_c\mid X_1=1,X_2=0\right)\\
&-P\left(Y\in y_c\mid X_1=0,X_2=1\right)+P\left(Y\in y_c\mid X_1=0,X_2=0\right)
\end{aligned}
$$

is equal to

$$
\begin{aligned}
&2P\left(Y_{11}\in y_c,Y_{10}\notin y_c,Y_{01}\notin y_c,Y_{00}\in y_c\right)+P\left(Y_{11}\in y_c,Y_{10}\notin y_c,Y_{01}\notin y_c,Y_{00}\notin y_c\right)\\
&\quad-P\left(Y_{11}\notin y_c,Y_{10}\in y_c,Y_{01}\in y_c,Y_{00}\notin y_c\right)-P\left(Y_{11}\notin y_c,Y_{10}\in y_c,Y_{01}\notin y_c,Y_{00}\notin y_c\right)\\
&\quad-P\left(Y_{11}\in y_c,Y_{10}\in y_c,Y_{01}\in y_c,Y_{00}\notin y_c\right)-P\left(Y_{11}\notin y_c,Y_{10}\in y_c,Y_{01}\in y_c,Y_{00}\in y_c\right)\\
&\quad-P\left(Y_{11}\notin y_c,Y_{10}\in y_c,Y_{01}\in y_c,Y_{00}\notin y_c\right)-P\left(Y_{11}\notin y_c,Y_{10}\notin y_c,Y_{01}\in y_c,Y_{00}\notin y_c\right)\\
&\quad+P\left(Y_{11}\in y_c,Y_{10}\in y_c,Y_{01}\notin y_c,Y_{00}\in y_c\right)+P\left(Y_{11}\in y_c,Y_{10}\notin y_c,Y_{01}\in y_c,Y_{00}\in y_c\right)\\
&\quad+P\left(Y_{11}\notin y_c,Y_{10}\notin y_c,Y_{01}\notin y_c,Y_{00}\in y_c\right).
\end{aligned}
$$

When X_1 and X_2 both have positive monotonic effects on $Y\in y_c$, the contrast

$$
\begin{aligned}
&P\left(Y\in y_c\mid X_1=1,X_2=1\right)-P\left(Y\in y_c\mid X_1=1,X_2=0\right)\\
&-P\left(Y\in y_c\mid X_1=0,X_2=1\right)+P\left(Y\in y_c\mid X_1=0,X_2=0\right)
\end{aligned}
$$

is equal to

$$P\left(Y_{11} \in y_c, Y_{10} \notin y_c, Y_{01} \notin y_c, Y_{00} \notin y_c\right).$$

As a sensitivity analysis of the monotonic condition the expression

$$\begin{aligned}
&P\left(Y \in y_c \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_c \mid X_1 = 1, X_2 = 0\right) \\
&- P\left(Y \in y_c \mid X_1 = 0, X_2 = 1\right) + P\left(Y \in y_c \mid X_1 = 0, X_2 = 0\right) \\
&- c,
\end{aligned}$$

where

$$\begin{aligned}
c = {} & 2P\left(Y_{11} \in y_c, Y_{10} \notin y_c, Y_{01} \notin y_c, Y_{00} \in y_c\right) + P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \notin y_c, Y_{00} \in y_c\right) \\
& + P\left(Y_{11} \in y_c, Y_{10} \notin y_c, Y_{01} \in y_c, Y_{00} \in y_c\right) + P\left(Y_{11} \notin y_c, Y_{10} \notin y_c, Y_{01} \notin y_c, Y_{00} \in y_c\right) \\
& - P\left(Y_{11} \notin y_c, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \notin y_a\right) + P\left(Y_{11} \notin y_c, Y_{10} \in y_c, Y_{01} \notin y_c, Y_{00} \notin y_c\right) \\
& - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \notin y_c\right) - P\left(Y_{11} \notin y_c, Y_{10} \in y_c, Y_{01} \in v, Y_{00} \in y_c\right) \\
& - P\left(Y_{11} \notin y_c, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \notin y_c\right) - P\left(Y_{11} \notin y_c, Y_{10} \notin y_c, Y_{01} \in y_c, Y_{00} \notin y_c\right)
\end{aligned}$$

is equal to

$$P\left(Y_{11} \in y_c, Y_{10} \notin y_c, Y_{01} \notin y_c, Y_{00} \notin y_c\right).$$

$\square$

Proof of Theorem S6.3. The contrast

$$\begin{aligned}
&P\left(Y \in y_b \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_b \mid X_1 = 1, X_2 = 0\right) \\
&- P\left(Y \in y_b \mid X_1 = 0, X_2 = 1\right) + P\left(Y \in y_b \mid X_1 = 0, X_2 = 0\right) \\
&+ P\left(Y \in y_c \mid X_1 = 0, X_2 = 0\right) - P\left(Y \in y_c \mid X_1 = 1, X_2 = 0\right)
\end{aligned}$$

is equal to

$$P\left(Y_{11} \in y_b\right) - P\left(Y_{10} \in y_b\right) - P\left(Y_{01} \in y_b\right) + P\left(Y_{00} \in y_b\right) + P\left(Y_{00} \in y_c\right) - P\left(Y_{10} \in y_c\right)$$

under $Y_{x_1 x_2} \amalg X_1 X_2$. Applying the law of total probability, we have the following results:

$$P\left(Y_{10} \in y_b\right) = \sum_{(y_{11}, y_{01}, y_{00}) \in \{(y_a, y_b, y_c)^3\}} P\left(Y_{11} \in y_{11}, Y_{10} \in y_b, Y_{01} \in y_{01}, Y_{00} \in y_{00}\right)$$
$$P\left(Y_{01} \in y_b\right) = \sum_{(y_{11}, y_{10}, y_{00}) \in \{(y_a, y_b, y_c)^3\}} P\left(Y_{11} \in y_{11}, Y_{10} \in y_{10}, Y_{01} \in y_b, Y_{00} \in y_{00}\right)$$
$$P\left(Y_{00} \in y_b\right) = \sum_{(y_{11}, y_{10}, y_{01}) \in \{(y_a, y_b, y_c)^3\}} P\left(Y_{11} \in y_{11}, Y_{10} \in y_{10}, Y_{01} \in y_b, Y_{00} \in y_b\right)$$
$$P\left(Y_{00} \in y_c\right) = \sum_{(y_{11}, y_{10}, y_{01}) \in \{(y_a, y_b, y_c)^3\}} P\left(Y_{11} \in y_{11}, Y_{10} \in y_{10}, Y_{01} \in y_b, Y_{00} \in y_c\right)$$
$$P\left(Y_{10} \in y_c\right) = \sum_{(y_{11}, y_{01}, y_{00}) \in \{(y_a, y_b, y_c)^3\}} P\left(Y_{11} \in y_{11}, Y_{10} \in y_c, Y_{01} \in y_{01}, Y_{00} \in y_{00}\right)$$

As an example, of this cartesian product notation, we have

$$P\left(Y_{11} \in y_b\right) = \sum_{(y_{10}, y_{01}, y_{00}) \in \{(y_a, y_b, y_c)^3\}} P\left(Y_{11} \in y_b, Y_{10} \in y_{10}, Y_{01} \in y_{01}, Y_{00} \in y_{00}\right)$$

is equivalent to writing

$$
\begin{aligned}
&P\left(Y_{11} \in y_b\right) \\
&= P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \in y_a\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_b, Y_{01} \in y_a, Y_{00} \in y_a\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_c, Y_{01} \in y_a, Y_{00} \in y_a\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_b, Y_{00} \in y_a\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_a\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_a\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_c, Y_{00} \in y_a\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_b, Y_{01} \in y_c, Y_{00} \in y_a\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_a\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \in y_b\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_b, Y_{01} \in y_a, Y_{00} \in y_b\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_c, Y_{01} \in y_a, Y_{00} \in y_b\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_b, Y_{00} \in y_b\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_b\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_b\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_c, Y_{00} \in y_b\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_b, Y_{01} \in y_c, Y_{00} \in y_b\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_b\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \in y_c\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_b, Y_{01} \in y_a, Y_{00} \in y_c\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_c, Y_{01} \in y_a, Y_{00} \in y_c\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_b, Y_{00} \in y_c\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_c\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_c\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_c, Y_{00} \in y_c\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_b, Y_{01} \in y_c, Y_{00} \in y_c\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_c\right).
\end{aligned}
$$

Simplifying this equality, we have

$$
\begin{aligned}
&P\left(Y \in y_b \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_b \mid X_1 = 1, X_2 = 0\right) \\
&\; - P\left(Y \in y_b \mid X_1 = 0, X_2 = 1\right) + P\left(Y \in y_b \mid X_1 = 0, X_2 = 0\right) \\
&\; + P\left(Y \in y_c \mid X_1 = 0, X_2 = 0\right) - P\left(Y \in y_c \mid X_1 = 1, X_2 = 0\right)
\end{aligned}
$$

is equal to

$$
\begin{aligned}
&P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \in y_a\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_c, Y_{00} \in y_a\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \in y_b\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_c, Y_{00} \in y_b\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \in y_c\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_c, Y_{00} \in y_c\right) \\
&\quad - P\left(Y_{11} \in y_a, Y_{10} \in y_b, Y_{01} \in y_a, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_a, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_a, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_a, Y_{10} \in y_b, Y_{01} \in y_c, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_c, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_b, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_a, Y_{01} \in y_b, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_a, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_b, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_a, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_a, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_b\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_b\right) - P\left(Y_{11} \in y_a, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_c\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_c\right) + P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \in y_b\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \in y_b\right) + P\left(Y_{11} \in y_c, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \in y_b\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_b, Y_{01} \in y_a, Y_{00} \in y_b\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_c, Y_{01} \in y_a, Y_{00} \in y_b\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_b, Y_{00} \in y_b\right) + P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_c, Y_{00} \in y_b\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_c, Y_{00} \in y_b\right) + P\left(Y_{11} \in y_c, Y_{10} \in y_a, Y_{01} \in y_c, Y_{00} \in y_b\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_b, Y_{01} \in y_c, Y_{00} \in y_b\right) + P\left(Y_{11} \in y_a, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_b\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_b\right) + P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \in y_c\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \in y_c\right) + P\left(Y_{11} \in y_c, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \in y_c\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_b, Y_{01} \in y_a, Y_{00} \in y_c\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_c, Y_{01} \in y_a, Y_{00} \in y_c\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_b, Y_{00} \in y_c\right) + P\left(Y_{11} \in y_a, Y_{10} \in y_a, Y_{01} \in y_c, Y_{00} \in y_c\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_c, Y_{00} \in y_c\right) + P\left(Y_{11} \in y_c, Y_{10} \in y_a, Y_{01} \in y_c, Y_{00} \in y_c\right) \\
&\quad + P\left(Y_{11} \in y_b, Y_{10} \in y_b, Y_{01} \in y_c, Y_{00} \in y_c\right) + P\left(Y_{11} \in y_b, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_c\right) \\
&\quad - P\left(Y_{11} \in y_a, Y_{10} \in y_c, Y_{01} \in y_a, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_a, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_a, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_b, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_a, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_a\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_a, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_b\right) \\
&\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_b\right) - P\left(Y_{11} \in y_a, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_b\right) \\
&\quad - P\left(Y_{11} \in y_a, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_c\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_c\right).
\end{aligned}
$$

When both X_1 and X_2 have positive monotonic effects on $Y \in y_c$, the contrast

$$\begin{aligned}&P\left(Y \in y_b \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_b \mid X_1 = 1, X_2 = 0\right)\\ &- P\left(Y \in y_b \mid X_1 = 0, X_2 = 1\right) + P\left(Y \in y_b \mid X_1 = 0, X_2 = 0\right)\\ &+ P\left(Y \in y_c \mid X_1 = 0, X_2 = 0\right) - P\left(Y \in y_c \mid X_1 = 1, X_2 = 0\right)\end{aligned}$$

is equal to

$$\begin{aligned}&P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_a, Y_{00} \in y_a\right)\\ &\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_c, Y_{00} \in y_a\right)\\ &\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_a, Y_{01} \in y_b, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_b, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_a\right)\\ &\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_a\right)\\ &\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_b, Y_{01} \in y_b, Y_{00} \in y_b\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_a, Y_{00} \in y_a\right)\\ &\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_a\right) - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_a\right)\\ &\quad - P\left(Y_{11} \in y_c, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_b\right) - P\left(Y_{11} \in y_a, Y_{10} \in y_c, Y_{01} \in y_c, Y_{00} \in y_b\right).\\ &\quad - P\left(Y_{11} \in y_a, Y_{10} \in y_c, Y_{01} \in y_b, Y_{00} \in y_c\right).\end{aligned}$$

Therefore,

$$\begin{aligned}&P\left(Y \in y_b \mid X_1 = 1, X_2 = 1\right) - P\left(Y \in y_b \mid X_1 = 1, X_2 = 0\right)\\ &- P\left(Y \in y_b \mid X_1 = 0, X_2 = 1\right) + P\left(Y \in y_b \mid X_1 = 0, X_2 = 0\right)\\ &+ P\left(Y \in y_c \mid X_1 = 0, X_2 = 0\right) - P\left(Y \in y_c \mid X_1 = 1, X_2 = 0\right)\end{aligned}$$

is a lower bound on

$$P\left(Y_{11} \in y_b, Y_{10} \in y_a, Y_{01} \in y_a, Y_{00} \in y_a\right).$$

For the second result, interchange the roles of Y_{01} and Y_{10}. □

S6.1 Appendix 3: Inference

The log-likelihood for an ordinal outcome with two binary exposures is

$$\begin{aligned} l(\mathbf{p}) \quad = \quad & \sum_{(x_1,x_2)\in\{0,1\}^2} n^A_{x_1x_2}\log(p^A_{x_1x_2}) + \sum_{(x_1,x_2)\in\{0,1\}^2} n^C_{x_1x_2}\log(p^C_{x_1x_2})\\ & + \sum_{(x_1,x_2)\in\{0,1\}^2} n^D_{x_1x_2}\log(p^D_{x_1x_2})\end{aligned}$$

where $\mathbf{p} = (p^A_{11}, p^A_{10}, p^A_{01}, p^A_{00}, p^C_{11}, p^C_{10}, p^C_{01}, p^C_{00}, p^D_{11}, p^D_{10}, p^D_{01}, p^D_{00})$, and $n^L_{x_1x_2} = \sum_{i=1}^n I(X_{1i} = x_1, X_{2i} = x_2, Y_i \in L)$. Here, Y_i denotes the outcome for the i^{th} individual. Similarly, X_{1i} denotes individual i's X_1 exposure status, and X_{2i} denotes individual i's X_2 exposure status. The likelihood ratio statistic is $T = \max\{2(\sup_{\mathbf{p}\in(0,1)^{12}\setminus\mathbf{p}_0} l(\mathbf{p}) - \sup_{\mathbf{p}\in\mathbf{p}_0} l(\mathbf{p})), 0\}$. Finally, $\mathbf{p}_0$ denotes the null space that is defined by the relevant inequality constraints.

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