eAppendix 1: Detailed derivations

Where VanderWeele had rewritten condition (VanderWeele-9) as:

$$(½)e^{\beta_1+\beta_2+\beta_3} - e^{\beta_1} + (½)e^{\beta_1+\beta_2+\beta_3} - e^{\beta_2} > 0$$

We rewrite condition (VanderWeele-9) as:

$$xe^{\beta_1+\beta_2+\beta_3} - e^{\beta_1} + (1-x)e^{\beta_1+\beta_2+\beta_3} - e^{\beta_2} > 0 \quad \text{where } 0 < x < 1. \qquad (1)$$

This can be rewritten as:

$$e^{\beta_1}\{xe^{\beta_2+\beta_3} - 1\} + e^{\beta_2}\{(1-x)e^{\beta_1+\beta_3} - 1\} > 0$$

It is easy to see the previous condition is true if both

$$\{xe^{\beta_2+\beta_3} - 1\} > 0 \text{ and } \{(1-x)e^{\beta_1+\beta_3} - 1\} > 0.$$

These two conditions can be rewritten as

$$e^{\beta_2+\beta_3} > 1/x \text{ and } e^{\beta_1+\beta_3} > 1/(1-x) \text{ or as}$$

$$e^{\beta_3} > (1/x)e^{-\beta_2} \text{ and } e^{\beta_3} > (1/(1-x))e^{-\beta_1}.$$

Whereby the conditions for $\beta_3 > 0$ to imply sufficient cause interaction become:

$$\beta_3 > \log(1/x) - \beta_2 \text{ and } \beta_3 > \log(1/(1-x)) - \beta_1$$

As $\beta_1 = \log(RR_{10})$ and $\beta_2 = \log(RR_{01})$ this leads to

$$\mathbf{RR_{01} \geq 1/x} \quad \text{and} \qquad (2a)$$

$$\mathbf{RR_{10} \geq 1/(1\text{-}x)} \qquad (2b)$$

When x is chosen to be equal to $1/RR_{01}$, condition (2b) becomes:

$$RR_{10} \geq 1/(1-(1/RR_{01}))$$

which can be rewritten as:

$$(1 - (1/RR_{01})) \times RR_{10} \geq 1$$

$$RR_{10} - (RR_{10}/RR_{01}) \geq 1$$

$$(RR_{01} \times RR_{10}) - RR_{10} \geq RR_{01}$$

$$RR_{01} \times RR_{10} \geq RR_{01} + RR_{10} \qquad (3)$$

Leading to the easy to remember rule that: *"If the product of separate relative risks is greater than or equal to their sum, testing for β_3>0 implies sufficient cause interaction".*

eAppendix 2

Three-Way Sufficient Cause Interaction in Log-Linear and Logistic Models

Define a saturated log-linear model like VanderWeele's model 21:

$P(D=1|X_1 = x_1, X_2 = x_2, X_3 = x_3)$

$$= \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_4 x_1 x_2 + \beta_5 x_1 x_3 + \beta_6 x_2 x_3 + \beta_7 x_1 x_2 x_3$$

Without the assumption that the effects of X_1, X_2, and X_3 on D are monotonic, VanderWeele comes to condition (22) to imply a 3-way sufficient cause interaction:

$$e^{\beta_1+\beta_2+\beta_4}(\tfrac{1}{3}\, e^{\beta_3+\beta_5+\beta_6+\beta_7}-1) + e^{\beta_1+\beta_3+\beta_5}(\tfrac{1}{3}\, e^{\beta_2+\beta_4+\beta_6+\beta_7}-1) + e^{\beta_2+\beta_3+\beta_6}(\tfrac{1}{3}\, e^{\beta_1+\beta_4+\beta_5+\beta_7}-1) > 0$$

To allow an unequal division of $e^{\beta_0+\beta_1+\beta_2+\beta_3+\beta_4+\beta_5+\beta_6+\beta_7}$ this condition can be rewritten as:

$$e^{\beta_1+\beta_2+\beta_4}(\alpha_1\, e^{\beta_3+\beta_5+\beta_6+\beta_7}-1) + e^{\beta_1+\beta_3+\beta_5}(\alpha_2\, e^{\beta_2+\beta_4+\beta_6+\beta_7}-1) + e^{\beta_2+\beta_3+\beta_6}(\alpha_3\, e^{\beta_1+\beta_4+\beta_5+\beta_7}-1) > 0$$

where $\alpha_1 + \alpha_2 + \alpha_3 = 1$ and $0 < \alpha_{1,2,3} < 1$ (Ap1)

It is easily verified that if: $\alpha_1 > e^{-(\beta_3+\beta_5+\beta_6+\beta_7)}$ and $\alpha_2 > e^{-(\beta_2+\beta_4+\beta_6+\beta_7)}$ and $\alpha_3 > e^{-(\beta_1+\beta_4+\beta_5+\beta_7)}$ this condition is satisfied. Condition (Ap1) also holds true if only one $\alpha > e^{-(\beta\ldots)}$, and the two other α's equal $e^{-(\beta\ldots)}$, for instance if $\alpha_1 > e^{-(\beta3+\beta5+\beta6+\beta7)}$ and $\alpha_2 = e^{-(\beta2+\beta4+\beta6+\beta7)}$ and $\alpha_3 =.\ e^{-(\beta1+\beta4+\beta5+\beta7)}$. Since $\alpha_1 + \alpha_2 + \alpha_3 = 1$, this first condition $\alpha_1 > e^{-(\beta3+\beta5+\beta6+\beta7)}$ can be rewritten into:

$$1 - \alpha_2 - \alpha_3 > e^{-(\beta3+\beta5+\beta6+\beta7)}$$

which can be derived into:

$$1 - e^{-(\beta_2+\beta_4+\beta_6+\beta_7)} - e^{-(\beta_1+\beta_4+\beta_5+\beta_7)} > e^{-(\beta_3+\beta_5+\beta_6+\beta_7)}$$

and $$1 > e^{-(\beta_3+\beta_5+\beta_6+\beta_7)} + e^{-(\beta_2+\beta_4+\beta_6+\beta_7)} + e^{-(\beta_1+\beta_4+\beta_5+\beta_7)}$$

illustrating in this phase of the derivation that it doesn't make a difference which of the α's was initially selected $> e^{-(\beta\ldots)}$.

Further derivation leads to:

$$e^{\beta_7} > e^{-(\beta_3+\beta_5+\beta_6)} + e^{-(\beta_2+\beta_4+\beta_6)} + e^{-(\beta_1+\beta_4+\beta_5)}$$

$$\frac{1}{e^{\beta_1+\beta_4+\beta_5}} + \frac{1}{e^{\beta_2+\beta_4+\beta_6}} + \frac{1}{e^{\beta_3+\beta_5+\beta_6}} \le 1 \mid \beta_7 > 0 \qquad \text{(Ap2)}$$

So when $e^{-(\beta_3+\beta_5+\beta_6)} + e^{-(\beta_2+\beta_4+\beta_6)} + e^{-(\beta_1+\beta_4+\beta_5)} < 1$, a test for a 3-way statistical interaction, $\beta_7 > 0$, implies a 3-way sufficient cause interaction. Here also, VanderWeele's conditions [$\beta_3 + \beta_5 + \beta_6$

$> \log(3)$ and $\beta_2 + \beta_4 + \beta_6 > \log(3)$ and $\beta_1 + \beta_4 + \beta_5 > \log(3)$] describe only a selection of the possible ways to fulfill condition (Ap2).