

eAppendix to On the Nondifferential Misclassification of a Binary Confounder

Result 2 For A , and C binary, the partial control result holds for the effect of treatment on the treated on the RD, RR, and OR scales.

Proof: We will show that $E_{C'|A=1}[Y|A = 1]=E[Y|A = 1]=E[Y_1|A = 1]$ and that $E_{C'|A=1}[Y|A = 0]$ is between $E[Y|A = 0]$ and $E[Y_0|A = 1]$. It then follows immediately that the observed adjusted effect is between the crude and true effects on the RD, RR, and OR scales. First, note that $E[Y_1|A = 1] = E[Y|A = 1]$ by the consistency assumption, and

$$\begin{aligned} E_{C'|A=1}[Y|A = 1] &= E[Y|A = 1, C' = 1]P[C' = 1|A = 1] + E[Y|A = 1, C' = 0]P[C' = 0|A = 1] \\ &= E[Y|A = 1] \end{aligned}$$

We now prove that $E_{C'|A=1}[Y|A = 0]$ is between $E[Y|A = 0]$ and $E[Y_0|A = 1]$. It is enough to show that $E[Y_0|A = 1] - E_{C'|A=1}[Y|A = 0]$ and $E_{C'|A=1}[Y|A = 0] - E[Y|A = 0]$ have the same sign, where

$$\begin{aligned} &E[Y_0|A = 1] - E_{C'|A=1}[Y|A = 0] \\ &= (E[Y|A = 0, C = 1] - E[Y|A = 0, C = 0]) \\ &\quad \times (\{E[C|A = 1, C' = 1] - E[C|A = 0, C' = 1]\} E[C'|A = 1] \\ &\quad + \{E[C|A = 1, C' = 0] - E[C|A = 0, C' = 0]\} (1 - E[C'|A = 1])) \end{aligned}$$

and

$$\begin{aligned}
& E_{C'|A=1}[Y|A=0] - E[Y|A=0] \\
= & (E[Y_0|A=1] - E[Y|A=0]) - (E[Y_0|A=1] - E_{C'|A=1}[Y|A=0]) \\
= & (E[Y|A=0, C=1] - E[Y|A=0, C=0]) (E[C|A=1] - E[C|A=0]) \\
& - (E[Y|A=0, C=1] - E[Y|A=0, C=0]) \\
& \times (\{E[C|A=1, C'=1] - E[C|A=0, C'=1]\} E[C'|A=1] \\
& + \{E[C|A=1, C'=0] - E[C|A=0, C'=0]\} (1 - E[C'|A=1])) \\
= & (E[Y|A=0, C=1] - E[Y|A=0, C=0]) \\
& \times (E[C|A=0, C'=1] \{E[C'|A=1] - E[C'|A=0]\} \\
& - E[C|A=0, C'=0] \{E[C'|A=1] - E[C'|A=0]\})
\end{aligned}$$

Then, it is enough to show that

$$\begin{aligned}
& \{E[C|A=1, C'=1] - E[C|A=0, C'=1]\} E[C'|A=1] \\
& + \{E[C|A=1, C'=0] - E[C|A=0, C'=0]\} (1 - E[C'|A=1])
\end{aligned} \tag{1}$$

and

$$\begin{aligned}
& E[C|A=0, C'=1] \{E[C'|A=1] - E[C'|A=0]\} \\
& - E[C|A=0, C'=0] \{E[C'|A=1] - E[C'|A=0]\}
\end{aligned} \tag{2}$$

have the same sign. We will prove this by showing that (1) and (2) are simultaneously either maximized or minimized at 0.

We consider two cases: $e \geq 1 - f$ and $e \leq 1 - f$, where e is sensitivity and f is specificity. In the first case $E[C|A=a, C']$ is increasing in C' for all a , while in the

second case it is decreasing in C' for all a , with equality in both cases when $e = f = 0.5$.

We now prove that $E[C|A = 1] \leq E[C|A = 0] \iff E[C'|A = 1] \leq E[C'|A = 0]$ when $e \geq 1 - f$. That $E[C|A = 1] \leq E[C|A = 0] \iff E[C'|A = 1] \geq E[C'|A = 0]$ when $e \leq 1 - f$ follows by a similar argument. Note that

$$E[C'|A = 1] = E[C|A = 1]e + (1 - E[C|A = 1])(1 - f)$$

and

$$E[C'|A = 0] = E[C|A = 0]e + (1 - E[C|A = 0])(1 - f)$$

are both convex combinations of e and $(1 - f)$. If $E[C|A = 1] > E[C|A = 0]$, then $E[C|A = 1] : (1 - E[C|A = 1]) > E[C|A = 0] : (1 - E[C|A = 0])$ and $E[C'|A = 1]$ will be closer to e and therefore greater than $E[C'|A = 0]$. If $E[C|A = 1] < E[C|A = 0]$, the reverse relationship holds and $E[C'|A = 1] < E[C'|A = 0]$.

Now we turn our attention to the minima and maxima of expressions (1) and (2); we will find the extreme values with respect to $E[C|A, C']$. The derivative of (2) with respect to $E[C|A = 0, C' = 1]$ is $E[C'|A = 1] - E[C'|A = 0]$ and the derivative with respect to $E[C|A = 0, C' = 0]$ is $-\{E[C'|A = 1] - E[C'|A = 0]\}$. Therefore (2) is monotonic in both $E[C|A = 0, C' = 1]$ and $E[C|A = 0, C' = 0]$, and furthermore it is non-decreasing in one and non-increasing in the other. Therefore, the unconstrained extrema occur at $E[C|A = 0, C' = 1] = 1$ and $E[C|A = 0, C' = 0] = 0$, and at $E[C|A = 0, C' = 1] = 0$ and $E[C|A = 0, C' = 0] = 1$. But we know that when $e \geq 1 - f$ these conditional expectations are constrained to be nondecreasing in C' ; therefore the constrained extrema occur at $E[C|A = 0, C' = 1] = 1$ and $E[C|A = 0, C' = 0] = 0$ and at $E[C|A = 0, C' = 1] = E[C|A = 0, C' = 0] = 1$. On the other hand, when $e \leq 1 - f$

these conditional expectations are constrained to be nonincreasing in C' and therefore the constrained extrema occur at $E[C|A = 0, C' = 1] = 0$ and $E[C|A = 0, C' = 0] = 1$ and at $E[C|A = 0, C' = 1] = E[C|A = 0, C' = 0] = 1$.

When $E[C|A = 0, C' = 1] = E[C|A = 0, C' = 0]$, (2) equals 0. If $E[C'|A = 1] < E[C'|A = 0]$, then this is the maximum of (2) if $e \geq 1 - f$ and the minimum if $e \leq 1 - f$. If $E[C'|A = 1] > E[C'|A = 0]$ then (2) is maximized at 0 if $e \leq 1 - f$ and minimized at 0 if $e \geq 1 - f$.

To find the extrema of (1), we restrict our attention to the case where $E[C'|A = 0] < E[C'|A = 1]$ and $e \geq 1 - f$. We will show that (1) is also minimized at 0. Because (1) is equal to

$$E[C|A = 1] - E[C|A = 0, C' = 1]P[C' = 1|A = 1] - E[C = 1|A = 0, C' = 0]P[C' = 0|A = 1]$$

proving that it is minimized at 0 is equivalent to proving that

$$E[C|A = 0, C' = 1]P[C' = 1|A = 1] + E[C = 1|A = 0, C' = 0]P[C' = 0|A = 1] \quad (3)$$

is maximized at $E[C|A = 1]$. We will maximize (3) with respect to e and f .

Let $D = E[C|A = 0]$ and $B = E[C|A = 1]$.

$$\begin{aligned} & E[C|A = 0, C' = 1]P[C' = 1|A = 1] - E[C = 1|A = 0, C' = 0]P[C' = 0|A = 1] \\ &= D \left(e \frac{Be + (1 - B)(1 - f)}{De + (1 - D)(1 - f)} + (1 - e) \frac{1 - \{Be + (1 - B)(1 - f)\}}{1 - \{De + (1 - D)(1 - f)\}} \right) \end{aligned} \quad (4)$$

If $e \geq 1 - f$, then $D \leq B$ and (4) is increasing in e (the derivative with respect to e is

positive), so in order to maximize it we set $e = 1$. Now (4) reduces to $D \frac{B+(1-B)(1-f)}{D+(1-D)(1-f)}$, which is increasing in f (the derivative with respect to f is positive) and is therefore maximized at $f = 1$. At $e = f = 1$, $\sum_{C'} E[C|A = 0, C']P[C'|A = 1] = E[C|A = 1]$. Therefore, (1) is minimized at 0.

That (1) is minimized at 0 when $E[C'|A = 0] < E[C'|A = 1]$ and $e \leq 1 - f$, and that it is maximized at 0 when $E[C'|A = 0] < E[C'|A = 1]$ and $e \geq 1 - f$ or when $E[C'|A = 0] > E[C'|A = 1]$ and $e \leq 1 - f$, follow by analogous arguments.

Result 3 For A and C binary, if sensitivity+specificity ≥ 1 then the bias of the observed adjusted effect of treatment on the treated decreases with increasing sensitivity and specificity. If in addition $E[Y|A, C]$ is monotonic in C , then the bias of the observed adjusted average treatment effect decreases with increasing sensitivity and specificity.

Proof: Under monotonicity, $E_{C'}[Y|A = a]$ lies between $E[Y_a]$ and $E[Y|A = a]$ for $a = 0, 1$. We will show that $E_{C'}[Y|A = 1]$ and $E_{C'}[Y|A = 0]$ move further from $E[Y|A = a]$ and closer to $E[Y_a]$ as e and f increase. The result follows immediately.

When $e + f \geq 1$, the signs of $\frac{\partial}{\partial e} E_{C'}[Y|A = 1]$ and $\frac{\partial}{\partial f} E_{C'}[Y|A = 1]$ depend only on the sign of $\{E[Y|A = 1, C = 1] - E[Y|A = 1, C = 0]\}\{E[A|C = 0] - E[A|C = 1]\}$. When $E[Y|A, C]$ and $E[A|C]$ are both either non-increasing or non-decreasing in C this product is negative (or 0) and $E_{C'}[Y|A = 1]$ is non-increasing in e and f , i.e. as e and f increase $E_{C'}[Y|A = 1]$ moves closer to $E[Y_1]$ and farther from $E[Y|A = 1]$. (Recall that $E[Y_1] \leq E[Y|A = 1]$ when both conditional expectations are either non-increasing or non-decreasing in C .) When one of $E[Y|A, C]$ and $E[A|C]$ is non-increasing and the other non-decreasing then the product is non-negative and $E_{C'}[Y|A = 1]$ is non-

increasing in e and f , which again entails that as e and f increase $E_{C'}[Y|A = 1]$ moves closer to $E[Y_1]$ and further from $E[Y|A = 1]$.

The proof that $E_{C'}[Y|A = 0]$ approaches $E[Y_0]$ as e and f increase is similar.