eAppendix of “Conditional and Unconditional Infectiousness Effects in Vaccine Trials”

Proofs of Results 1 and 2

To prove Results 1 and 2, it is enough to show that

$$\mathrm{E}[Y_{i2}(a_{i1}, Y_{i1}(1))] = \mathrm{E}[Y_{i2}(a_{i1}) \mid Y_{i1}(1) = 1, Y_{i1}(0) = 1] \times \Pr(Y_{i1} = 1 \mid A_{i1} = 1)$$

holds under Assumptions 1 and 2. Under these assumptions, $\mathrm{E}[Y_{i2}(a_{i1},Y_{i1}(1))]$ can be expressed as follows:

$$\begin{aligned}
\mathrm{E}\left[Y_{i2}(a_{i1}, Y_{i1}(1))\right] &= \sum_{s=0}^{1}\sum_{t=0}^{1} \mathrm{E}\left[Y_{i2}(a_{i1}, Y_{i1}(1)) \mid Y_{i1}(1) = s, Y_{i1}(0) = t\right]\Pr\left(Y_{i1}(1) = s, Y_{i1}(0) = t\right) \\
&= \mathrm{E}\left[Y_{i2}(a_{i1}, Y_{i1}(1)) \mid Y_{i1}(1) = 1, Y_{i1}(0) = 1\right]\Pr\left(Y_{i1}(1) = 1, Y_{i1}(0) = 1\right) \\
&\quad + \mathrm{E}\left[Y_{i2}(a_{i1}, Y_{i1}(1)) \mid Y_{i1}(1) = 0, Y_{i1}(0) = 1\right]\Pr\left(Y_{i1}(1) = 0, Y_{i1}(0) = 1\right) \\
&\quad + \mathrm{E}\left[Y_{i2}(a_{i1}, Y_{i1}(1)) \mid Y_{i1}(1) = 0, Y_{i1}(0) = 0\right]\Pr\left(Y_{i1}(1) = 0, Y_{i1}(0) = 0\right) \\
&= \mathrm{E}\left[Y_{i2}(a_{i1}, 1) \mid Y_{i1}(1) = 1, Y_{i1}(0) = 1\right]\Pr\left(Y_{i1}(1) = 1, Y_{i1}(0) = 1\right) \\
&\quad + \mathrm{E}\left[Y_{i2}(a_{i1}, 0) \mid Y_{i1}(1) = 0, Y_{i1}(0) = 1\right]\Pr\left(Y_{i1}(1) = 0, Y_{i1}(0) = 1\right) \\
&\quad + \mathrm{E}\left[Y_{i2}(a_{i1}, 0) \mid Y_{i1}(1) = 0, Y_{i1}(0) = 0\right]\Pr\left(Y_{i1}(1) = 0, Y_{i1}(0) = 0\right) \\
&= \mathrm{E}\left[Y_{i2}(a_{i1}, 1) \mid Y_{i1}(1) = 1, Y_{i1}(0) = 1\right]\Pr\left(Y_{i1}(1) = 1\right), \qquad \text{(A1)}
\end{aligned}$$

where the second equation is by Assumption 2 and the fourth is by Assumptions 1 and 2. In the last equation, $\mathrm{E}[Y_{i2}(a_{i1},1) \mid Y_{i1}(1) = 1, Y_{i1}(0) = 1]$ can be expressed as:

$$\begin{aligned}
\mathrm{E}\left[Y_{i2}(a_{i1}, 1) \mid Y_{i1}(1) = 1, Y_{i1}(0) = 1\right] &= \mathrm{E}\left[Y_{i2}(a_{i1}, Y_{i1}(a_{i1})) \mid Y_{i1}(1) = 1, Y_{i1}(0) = 1\right] \\
&= \mathrm{E}\left[Y_{i2}(a_{i1}) \mid Y_{i1}(1) = 1, Y_{i1}(0) = 1\right], \qquad \text{(A2)}
\end{aligned}$$

and $\Pr(Y_{i1}(1) = 1)$ can be expressed as:

$$\Pr(Y_{i1}(1) = 1) = \Pr(Y_{i1}(1) = 1 \mid A_{i1} = 1) = \Pr(Y_{i1} = 1 \mid A_{i1} = 1) \qquad \text{(A3)}$$

by random assignment to person 1 and the consistency assumption. Substituting (A2) and (A3) into (A1) completes the proof.

Outlines of Methods for the Inference of the Conditional Infectiousness Effect

Marginal Structural Model

To yield a CIE estimate by the marginal structural model under Assumption 2 and the assumption that $Y_{i2}(a_{i1})$ is independent of A_{i1} conditional on Y_{i1} and C_i, we need only data for households with $Y_{i1} = 1$. The analysis can be conducted using a weighted regression model of A_{i1} on Y_{i2} with the weights $w_i = 1$ for households with $A_{i1} = 1$ and $w_i = \Pr(A_{i1} = 1 \mid Y_{i1} = 1, C_i) / \Pr(A_{i1} = 0 \mid Y_{i1} = 1, C_i)$ for households with $A_{i1} = 0$.[7] The following is an SAS code, which was applied to the data in Table. Note that the data file “IPW” contains only data for households with $Y_{i1} = 1$ in the original data file.

```
/* Estimation of Predicted Values */
proc logistic data=IPW descending;
  model A1=X;
  output out=PRED p=P;
run;
/* Calculation of the Weights */
data CIE;
  set PRED;
  if A1=1 then WEIGHT=1; else WEIGHT=P/(1-P);
run;
/* Weighted Analysis */
proc genmod data=CIE;
  class i;
  model Y2=A1/dist=poisson link=log;
  weight WEIGHT;
  repeated sub=i/type=ind;
  estimate 'beta' A1 1/exp;
run;
```

Bounds

Under Assumption 2, $E_{11}(a_{i1}) \equiv \mathrm{E}[Y_{i2}(a_{i1}) \mid Y_{i1}(1) = 1, Y_{i1}(0) = 1]$ can be expressed as:

$$\begin{aligned}\mathrm{E}\left[Y_{i2}(a_{i1}) \mid Y_{i1}(1) = 1, Y_{i1}(0) = 1\right] &= \mathrm{E}\left[Y_{i2}(a_{i1}) \mid Y_{i1}(1) = 1\right] \\ &= \mathrm{E}\left[Y_{i2}(a_{i1}) \mid A_{i1} = 1, Y_{i1} = 1\right].\end{aligned}$$

For $a_{i1} = 1$,

$$\mathrm{E}[Y_{i2}(1) \mid Y_{i1}(1) = 1, Y_{i1}(0) = 1] = \mathrm{E}[Y_{i2} \mid A_{i1} = 1, Y_{i1} = 1]$$

by the consistency assumption, and for $a_{i1} = 0$,

$$\mathrm{E}[Y_{i2}(0) \mid A_{i1} = 1, Y_{i1} = 1] \le \frac{\Pr(Y_{i1} = 1 \mid A_{i1} = 0)}{\Pr(Y_{i1} = 1 \mid A_{i1} = 1)} \mathrm{E}[Y_{i2} \mid A_{i1} = 0, Y_{i1} = 1],$$

because under Assumption 2,

$$\begin{aligned}
\mathrm{E}\left[Y_{i2} \mid A_{i1} = 0, Y_{i1} = 1\right] &= \mathrm{E}\left[Y_{i2}(0) \mid A_{i1} = 0, Y_{i1} = 1\right] \\
&= \mathrm{E}\left[Y_{i2}(0) \mid Y_{i1}(0) = 1\right] \\
&= \mathrm{E}\left[Y_{i2}(0) \mid Y_{i1}(1) = 0, Y_{i1}(0) = 1\right]\Pr\left(Y_{i1}(1) = 0 \mid Y_{i1}(0) = 1\right) \\
&\quad + \mathrm{E}\left[Y_{i2}(0) \mid Y_{i1}(1) = 1, Y_{i1}(0) = 1\right]\Pr\left(Y_{i1}(1) = 1 \mid Y_{i1}(0) = 1\right) \\
&\ge \mathrm{E}\left[Y_{i2}(0) \mid Y_{i1}(1) = 1, Y_{i1}(0) = 1\right]\Pr\left(Y_{i1}(1) = 1 \mid Y_{i1}(0) = 1\right) \\
&= \frac{\Pr\left(Y_{i1}(1) = 1\right)}{\Pr\left(Y_{i1}(0) = 1\right)} \mathrm{E}\left[Y_{i2}(0) \mid Y_{i1}(1) = 1\right] \\
&= \frac{\Pr\left(Y_{i1} = 1 \mid A_{i1} = 1\right)}{\Pr\left(Y_{i1} = 1 \mid A_{i1} = 0\right)} \mathrm{E}\left[Y_{i2}(0) \mid A_{i1} = 1, Y_{i1} = 1\right].
\end{aligned}$$

Therefore, under Assumption 1, the lower bound for $\mathrm{CIE}_{\mathrm{r}} \equiv E_{11}(1) / E_{11}(0)$ becomes

$$\begin{aligned}
\mathrm{CIE}_{\mathrm{r}} &\ge \frac{\mathrm{E}[Y_{i2} \mid A_{i1} = 1, Y_{i1} = 1]}{\frac{\Pr(Y_{i1} = 1 \mid A_{i1} = 0)}{\Pr(Y_{i1} = 1 \mid A_{i1} = 1)} \mathrm{E}[Y_{i2} \mid A_{i1} = 0, Y_{i1} = 1]} \\
&= \frac{\mathrm{E}[Y_{i2} \mid A_{i1} = 1, Y_{i1} = 1]\Pr(Y_{i1} = 1 \mid A_{i1} = 1) + \mathrm{E}[Y_{i2} \mid A_{i1} = 1, Y_{i1} = 0]\Pr(Y_{i1} = 0 \mid A_{i1} = 1)}{\mathrm{E}[Y_{i2} \mid A_{i1} = 0, Y_{i1} = 1]\Pr(Y_{i1} = 1 \mid A_{i1} = 0) + \mathrm{E}[Y_{i2} \mid A_{i1} = 0, Y_{i1} = 0]\Pr(Y_{i1} = 0 \mid A_{i1} = 0)} \\
&= \frac{\mathrm{E}[Y_{i2} \mid A_{i1} = 1]}{\mathrm{E}[Y_{i2} \mid A_{i1} = 0]}.
\end{aligned}$$

Under the assumption that $\mathrm{E}[Y_{i2}(0) \mid A_{i1} = 1, Y_{i1} = 1] \ge \mathrm{E}[Y_{i2}(0) \mid A_{i1} = 0, Y_{i1} = 1]$,

$$\mathrm{CIE}_{\mathrm{r}} \le \frac{\mathrm{E}[Y_{i2} \mid A_{i1} = 1, Y_{i1} = 1]}{\mathrm{E}[Y_{i2}(0) \mid A_{i1} = 0, Y_{i1} = 1]} = \frac{\mathrm{E}[Y_{i2} \mid A_{i1} = 1, Y_{i1} = 1]}{\mathrm{E}[Y_{i2} \mid A_{i1} = 0, Y_{i1} = 1]}.$$