Web Material

On the causal interpretation of rate-change methods:

the prior event rate ratio and rate difference

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Web Appendix Contents

Web Appendix 1   Identification of the causal incidence rate ratio by PERR

1.1   Identifiability conditions

We restate the identifiability conditions from the main text:

1. Consistency among the actually treated: $r_{\text{post}}^{a=1}(A=1) = r_{\text{post}}(A=1)$.

2. Hypothetical intervention to implement the control strategy does not affect the pretreatment event rate among the treated: $r_{\text{pre}}^{a=0}(A=1) = r_{\text{pre}}(A=1)$.

3. Common rate-change assumption on the multiplicative scale: $\dfrac{r_{\text{post}}^{a=0}(A=1)}{r_{\text{pre}}^{a=0}(A=1)} = \dfrac{r_{\text{post}}(A=0)}{r_{\text{pre}}(A=0)}$.

4. Positivity of the treatment probability: $1 > \Pr[A=1] > 0$.

5. Positivity of event rates: for $a \in \{0,1\}$, $r_{\text{pre}}(A=a) > 0$ and $r_{\text{post}}(A=a) > 0$.

1.2   Identification

We will show that under the identifiability conditions described above, the causal incidence rate ratio $\text{IRR}_{\text{causal}}(A=1)$ equals the prior event rate ratio (PERR), defined as

$$\text{PERR} \equiv \frac{r_{\text{post}}(A=1)/r_{\text{post}}(A=0)}{r_{\text{pre}}(A=1)/r_{\text{pre}}(A=0)}.$$

Starting with the right-hand-side of the above expression,

$$
\begin{aligned}
\frac{r_{\text{post}}(A=1)/r_{\text{post}}(A=0)}{r_{\text{pre}}(A=1)/r_{\text{pre}}(A=0)} &= \frac{r_{\text{post}}(A=1)}{r_{\text{pre}}(A=1)} \times \frac{r_{\text{pre}}(A=0)}{r_{\text{post}}(A=0)} \\
&= \frac{r_{\text{post}}^{a=1}(A=1)}{r_{\text{pre}}^{a=0}(A=1)} \times \frac{r_{\text{pre}}^{a=0}(A=1)}{r_{\text{post}}^{a=0}(A=1)} \\
&= \frac{r_{\text{post}}^{a=1}(A=1)}{r_{\text{post}}^{a=0}(A=1)} \\
&\equiv \text{IRR}_{\text{causal}}(A=1),
\end{aligned}
$$

where the first equality follows from algebraic re-writing of the definition of PERR, the second from assumptions *1* through *3*, the third from cancellation of terms, and the last from the definition of the causal incidence rate ratio.

1.3 Examples of violations of the identifiability conditions

As noted in the main text, identifiability conditions *1* through *3*, which directly involve counterfactual quantities, make up the core of the PERR method and cannot be verified using observed data (i.e., they are untestable). Their plausibility is context- dependent, and can only be assessed using background knowledge. To develop intuition for these three conditions, we now discuss how they might be violated in applications.

Assumption *1* is violated if the treated group ($A = 1$), would have a different outcome rate in the posttreatment period under intervention to implement the treatment strategy $a = 1$, for example, if the implementation of the intervention has an effect on the outcome not through treatment itself. Furthermore, implicit in our notation is that $a = 1$ is a *well-defined* intervention. For example, assumption *1* is not meaningful when treatment variation irrelevance [1] does not hold for different proton pump inhibitors (i.e., when different proton pump inhibitors in use have different effects on the outcome).

Assumption *2* is violated if the intervention to implement the control strategy (i.e., to set $a = 0$) would lead to behavior changes among members of the treated group ($A = 1$) that would change the rate in the pretreatment period. For example, if the group that normally would have received treatment, upon learning that treatment might be denied, changes their behavior in a way that affects the pretreatment event rate (e.g., by adopting ancillary interventions during the pretreatment period).

Assumption *3* is violated when time-varying factors that affect the outcome differ between the treated and control groups. For example, if the control group receives ancillary interventions during the posttreatment period that affect the outcome and are not provided to the treated group, then the observed ratio of the pretreatment and posttreatment period rates in the control group may not be representative of the ratio of the counterfactual pretreatment and posttreatment period rates in the treated group under intervention to implement the control strategy. Furthermore, environmental (e.g., epidemic waves in infectious disease applications) or policy changes (e.g., implementation of clinical practice guidelines or reimbursement deci-

sions) that occur over time and differentially impact the treated and control group can lead to violations of the assumption.

1.4 Identification conditional on covariates

For completeness, we show how to extend the results in the previous section to use baseline time-fixed covariates. Let X denote these covariates (unaffected by treatment); $r_{\text{post}}^{a=0}(X = x, A = 1)$ the conditional counterfactual (potential) posttreatment event rate had we intervened to implement the control strategy $a = 0$ in the treated group with covariate pattern $X = x$; $r_{\text{post}}^{a=1}(X = x, A = 1)$ the conditional counterfactual posttreatment event rate had we intervened to implement the treatment strategy $a = 1$ to the treated group with covariate pattern $X = x$; $r_{\text{pre}}^{a=0}(X = x, A = 1)$ the conditional counterfactual pretreatment event rate had we intervened to implement the control strategy $a = 0$ in the treated group; and $r_{\text{pre}}(X = x, A = a)$ and $r_{\text{post}}(X = x, A = a)$ denote the factual pretreatment and posttreatment event rate, respectively, among individuals with covariate pattern $X = x$ who received treatment $A = a$. Last, for covariate pattern $X = x$ define the conditional prior event rate ratio as

$$\text{PERR}(x) \equiv \frac{r_{\text{post}}(X = x, A = 1)/r_{\text{post}}(X = x, A = 0)}{r_{\text{pre}}(X = x, A = 1)/r_{\text{pre}}(X = x, A = 0)},$$

and the conditional causal incidence rate ratio as

$$\text{IRR}_{\text{causal}}(X = x, A = 1) \equiv \frac{r_{\text{post}}^{a=1}(X = x, A = 1)}{r_{\text{post}}^{a=0}(X = x, A = 1)}.$$

The modified identifiability conditions for the conditional causal incidence rate ratio are:

1. *Consistency among the actually treated:* $r_{\text{post}}^{a=1}(X = x, A = 1) = r_{\text{post}}(X = x, A = 1)$.

2. *Hypothetical intervention to implement the control strategy does not affect the pretreatment event rate among the treated:* $r_{\text{pre}}^{a=0}(X = x, A = 1) = r_{\text{pre}}(X = x, A = 1)$.

3. *Common rate-change assumption on the multiplicative scale:* $\dfrac{r_{\text{post}}^{a=0}(X = x, A = 1)}{r_{\text{pre}}^{a=0}(X = x, A = 1)} = \dfrac{r_{\text{post}}(X = x, A = 0)}{r_{\text{pre}}(X = x, A = 0)}.$

4. *Positivity of the treatment probability:* $1 > \Pr[A = 0|X = x] > 0$ for for all x with positive density $f_{X,A}(x, A = 1) > 0$.

5. *Positivity of the conditional event rates:* for $a \in \{0, 1\}$ and for all x with positive density $f_{X,A}(x, A = a) > 0$, $r_{\text{pre}}(X = x, A = a) > 0$ and $r_{\text{post}}(X = x, A = a) > 0$.

Under these identifiability conditions, the conditional causal incidence rate ratio is identified by the conditional prior event rate ratio; that is,

$$\text{IRR}_{\text{causal}}(X = x, A = 1) = \text{PERR}(x).$$

Web Appendix 2 Identification of the causal incidence rate difference by PERD

2.1 Identifiability conditions

1. Consistency among the actually treated: $r_{\text{post}}^{a=1}(A=1) = r_{\text{post}}(A=1)$.

2. Hypothetical intervention to implement the control treatment does not affect the pretreatment event rate among the treated: $r_{\text{pre}}^{a=0}(A=1) = r_{\text{pre}}(A=1)$.

3*. Common rate-change assumption on the difference scale: $r_{\text{post}}^{a=0}(A=1) - r_{\text{pre}}^{a=0}(A=1) = r_{\text{post}}(A=0) - r_{\text{pre}}(A=0)$

4. Positivity of the treatment probability: $1 > \Pr[A=1] > 0$.

In addition to these conditions, we assume that all subjects can be observed from the start of the pretreatment period until the end of the posttreatment period (i.e., no censoring and no competing risks).

2.2 Identification

We will show that under the identifiability conditions described above, the causal incidence risk difference $\text{IRD}_{\text{causal}}(A=1)$ equals the prior event rate difference, PERD, defined as

$$\text{PERD} \equiv \big\{r_{\text{post}}(A=1) - r_{\text{post}}(A=0)\big\} - \big\{r_{\text{pre}}(A=1) - r_{\text{pre}}(A=0)\big\}$$

Starting with the right-hand-side of the above expression,

$$r_{\text{post}}(A = 1) - r_{\text{post}}(A = 0) - r_{\text{pre}}(A = 1) + r_{\text{pre}}(A = 0)$$

$$= r_{\text{post}}^{a=1}(A = 1) - r_{\text{pre}}^{a=0}(A = 1) - r_{\text{post}}(A = 0) + r_{\text{pre}}(A = 0)$$

$$= \left\{ r_{\text{post}}^{a=1}(A = 1) - r_{\text{pre}}^{a=0}(A = 1) \right\} - \left\{ r_{\text{post}}^{a=0}(A = 1) - r_{\text{pre}}^{a=0}(A = 1) \right\}$$

$$= r_{\text{post}}^{a=1}(A = 1) - r_{\text{post}}^{a=0}(A = 1)$$

$$\equiv \text{IRD}_{\text{causal}}(A = 1),$$

where the first equality follows from conditions *1* and *2*; the second from condition *3**, the third from cancellation of terms; and the last from the definition of the causal incide rate difference.

2.3   Identification conditional on covariates

For completeness, we again show how to extend the results in the previous section to use baseline time-fixed covariates. As for the PERR results presented above, X denotes these baseline covariates. For covariate pattern $X = x$ define the conditional prior event rate difference as

$$\text{PERD}(x) \equiv \left\{ r_{\text{post}}(X = x, A = 1) - r_{\text{post}}(X = x, A = 0) \right\} - \left\{ r_{\text{pre}}(X = x, A = 1) - r_{\text{pre}}(X = x, A = 0) \right\},$$

and the conditional causal incidence rate difference as

$$\text{IRD}_{\text{causal}}(X = x, A = 1) \equiv r_{\text{post}}^{a=1}(X = x, A = 1) - r_{\text{post}}^{a=0}(X = x, A = 1).$$

The modified identifiability condition for the conditional causal incidence rate difference is:

3*. *Common rate-change assumption on the additive scale:*

$$r_{\text{post}}^{a=0}(X = x, A = 1) - r_{\text{pre}}^{a=0}(X = x, A = 1) = r_{\text{post}}(X = x, A = 0) - r_{\text{pre}}(X = x, A = 0);$$

Furthermore, we retain conditions *1*, *2*, and *4*, but no longer need condition *5* (i.e., we no longer need to assume that the event rates are strictly positive).

Under these identifiability conditions, the conditional causal incidence rate difference is identified by the conditional prior event rate difference; that is,

$$\mathrm{IRD}_{\mathrm{causal}}(X = x, A = 1) = \mathrm{PERD}(x).$$

Web Appendix 3   Identification of the causal hazard ratio by PEHR

3.1   Observed data

We assume a common time origin at the beginning of the pretreatment period ($t = 0$); the interval T_{pre} represents time from the origin to the end of the pretreatment period and the interval T_{post} represents time from the start of treatment to the end of the posttreatment period (i.e., the end of the study). Let $h_{\text{pre}}(t, A = a)$ be the pretreatment hazard rate at time $t \in T_{\text{pre}}$, among individuals who received treatment $A = a$; and $h_{\text{post}}(t, A = a)$ be the posttreatment hazard rate at time $t \in T_{\text{post}}$, among individuals who received treatment $A = a$. As in the main text, we take treatment A to be binary, so that $a \in \{0, 1\}$, and we assume that the outcome of interest can recur (i.e., it is not a terminal outcome). This simple scheme for failure-time outcomes allows us to illustrate an identification strategy for the causal hazard ratio among the treated that relates closely to the strategies we used to identify the causal rate ratio and rate difference. The strategy can be extended to more complex schemes for failure-time outcomes (e.g., see [2]) but a detailed treatment of each of these schemes is outside the scope of this paper.

3.2   Causal quantities of interest

For time $t \in T_{\text{post}}$, let $h_{\text{post}}^{a=0}(t, A = 1)$ be the counterfactual posttreatment hazard rate under intervention to implement the control strategy $a = 0$ in the treated group and $h_{\text{post}}^{a=1}(t, A = 1)$ be the counterfactual posttreatment hazard rate under intervention to implement the treatment strategy $a = 1$ in the treated group. For time $t \in T_{\text{pre}}$, let $h_{\text{pre}}^{a=0}(t, A = 1)$ be the counterfactual pretreatment hazard rate had we intervened to implement the control strategy $a = 0$ in the treated group. We define the causal hazard ratio (HR) among the treated at time $t \in T_{\text{post}}$, as

$$\text{HR}_{\text{causal}}(t, A = 1) \equiv \frac{h_{\text{post}}^{a=1}(t, A = 1)}{h_{\text{post}}^{a=0}(t, A = 1)}.$$

Under this definition, the hazard ratio in the posttreatment period may vary over time.

3.3 Identification of the causal hazard rate ratio by PEHR

3.3.1 Identifiability conditions

We assume that the following identifiability conditions hold:

HR1. Consistency among the actually treated: $h_{\text{post}}^{a=1}(t, A = 1) = h_{\text{post}}(t, A = 1)$, $t \in T_{\text{post}}$; among the treated group, the posttreatment counterfactual hazard rate under intervention to assign treatment strategy $a = 1$ is equal to the factual hazard rate.

HR2. Hypothetical intervention to withhold treatment does not affect the pretreatment period hazard rate among the treated: $h_{\text{pre}}^{a=0}(t, A = 1) = h_{\text{pre}}(t, A = 1)$, $t \in T_{\text{pre}}$; the factual pretreatment hazard rate among the treated equals the counterfactual hazard rate of the same group under intervention to implement the control strategy.

HR3. Proportional hazards in the pretreatment period: $h_{\text{pre}}(t, A = 1) = h_{\text{pre}}(t, A = 0) \exp(\beta_{\text{pre}})$, $t \in T_{\text{pre}}$; this assumption states that the hazard ratio comparing the treated and untreated group during the pretreatment period does not vary over time.

HR4. Proportional hazards in the posttreatment period: $h_{\text{post}}(t, A = 1) = h_{\text{post}}(t, A = 0) \exp(\beta_{\text{post}})$, $t \in T_{\text{post}}$; this assumption states that the hazard ratio comparing the treated and untreated group during the posttreatment period does not vary over time.

HR5. Common hazard ratio assumption:

$$\frac{h_{\text{post}}^{a=0}(t, A = 1)}{h_{\text{post}}(t, A = 0)} = \frac{h_{\text{pre}}^{a=0}(t', A = 1)}{h_{\text{pre}}(t', A = 0)}, \text{ for every } t \in T_{\text{post}} \text{ and every } t' \in T_{\text{pre}}.$$

HR6. Positivity of the treatment probability: $1 > \Pr[A = 1] > 0$.

HR7. Positivity of the hazard rates: $h_{\text{pre}}(t, A = 0) > 0$, for $t \in T_{\text{pre}}$; and $h_{\text{post}}(t, A = 0) > 0$, for $t \in T_{\text{post}}$; and β_{pre} and β_{post} are real numbers (i.e., not infinite).

In addition to these conditions, we assume that all subjects can be observed from the start of the pretreatment until the end of the posttreatment period. Extensions to address identification in the presence

of drop-out or competing events are possible but beyond the scope of this paper.

3.3.2 Identification

We will show that under identifiability conditions *HR1* through *HR7* described above, the causal hazard ratio among the treated $\mathrm{HR}_{\mathrm{causal}}(t, A = 1)$ does not vary over time and is identifiable by the population prior event ratio of hazard ratios (PEHR),

$$\mathrm{PEHR} \equiv \frac{\exp(\beta_{\mathrm{post}})}{\exp(\beta_{\mathrm{pre}})}, \text{ which also does not vary over time.}$$

To derive the identification result, first, note that PEHR is well-defined by assumption *HR7* and throuhgout this derivation all quantities conditional on $A = a$, for $a \in \{0, 1\}$ are well-defined by condition *HR6*.

Next, by assumptions *HR3* and *HR7*, $\exp(\beta_{\mathrm{pre}}) = \dfrac{h_{\mathrm{pre}}(t, A = 1)}{h_{\mathrm{pre}}(t, A = 0)}$, which does not vary over $t \in T_{\mathrm{pre}}$ and is positive. Using assumption *HR2*, this result implies that

$$\exp(\beta_{\mathrm{pre}}) = \frac{h_{\mathrm{pre}}^{a=0}(t, A = 1)}{h_{\mathrm{pre}}(t, A = 0)}, \tag{3.1}$$

where the right-hand-side also does not vary over $t \in T_{\mathrm{pre}}$ and is positive.

By assumptions *HR4* and *HR7*, $\exp(\beta_{\mathrm{post}}) = \dfrac{h_{\mathrm{post}}(t, A = 1)}{h_{\mathrm{post}}(t, A = 0)}$, which does not vary over $t \in T_{\mathrm{post}}$ and is positive. Using assumption *HR1*, this result implies that

$$\exp(\beta_{\mathrm{post}}) = \frac{h_{\mathrm{post}}^{a=1}(t, A = 1)}{h_{\mathrm{post}}(t, A = 0)}, \tag{3.2}$$

where the right-hand-side also does not vary over $t \in T_{\mathrm{post}}$ and is positive.

Using the definition of PEHR, and the results in equations (3.1) and (3.2), we obtain

$$\mathrm{PEHR} \equiv \frac{\exp(\beta_{\mathrm{post}})}{\exp(\beta_{\mathrm{pre}})} = \frac{h_{\mathrm{post}}^{a=1}(t, A = 1)/h_{\mathrm{post}}(t, A = 0)}{h_{\mathrm{pre}}^{a=0}(t', A = 1)/h_{\mathrm{pre}}(t', A = 0)}, \text{ for every } t' \in T_{\mathrm{pre}} \text{ and every } t \in T_{\mathrm{post}},$$

and where the far right-hand-side does not vary over $t' \in T_{\mathrm{pre}}$ or $t \in T_{\mathrm{post}}$.

By assumption *HR5*, we can re-write the above result as

$$
\begin{aligned}
\text{PEHR} \equiv \frac{\exp(\beta_{\text{post}})}{\exp(\beta_{\text{pre}})} &= \frac{h_{\text{post}}^{a=1}(t, A=1)/h_{\text{post}}(t, A=0)}{h_{\text{pre}}^{a=0}(t', A=1)/h_{\text{pre}}(t', A=0)} \\
&= \frac{h_{\text{post}}^{a=1}(t, A=1)/h_{\text{post}}(t, A=0)}{h_{\text{post}}^{a=0}(t, A=1)/h_{\text{post}}(t, A=0)} \\
&= \frac{h_{\text{post}}^{a=1}(t, A=1)}{h_{\text{post}}^{a=0}(t, A=1)} \\
&\equiv \text{HR}_{\text{causal}}(t, A=1),
\end{aligned}
$$

where all ratios or ratios-of-ratios do not vary over $t' \in T_{\text{pre}}$ or $t \in T_{\text{post}}$.

Remark: As shown above, $\exp(\beta_{\text{pre}}) = \dfrac{h_{\text{pre}}^{a=0}(t', A=1)}{h_{\text{pre}}(t', A=0)}$, and thus, using assumption *HR5*,

$$
\exp(\beta_{\text{pre}}) = \frac{h_{\text{pre}}^{a=0}(t', A=1)}{h_{\text{pre}}(t', A=0)} = \frac{h_{\text{post}}^{a=0}(t, A=1)}{h_{\text{post}}(t, A=0)} \text{ for every } t' \in T_{\text{pre}} \text{ and every } t \in T_{\text{post}}.
$$

Because the far left-hand-side does not vary over time, it has to be that

$$
\frac{h_{\text{post}}^{a=0}(t, A=1)}{h_{\text{pre}}^{a=0}(t', A=1)} = \frac{h_{\text{post}}(t, A=0)}{h_{\text{pre}}(t', A=0)} \text{ for every } t' \in T_{\text{pre}} \text{ and every } t \in T_{\text{post}}.
$$

This expression is analogous to the rate-change assumptions in the main text.

Web Appendix 4   Should we use PERR or PERD?

4.1   Observed data implications of the identifiability conditions for PERR and PERD

Suppose that the conditions needed for both PERR and PERD to have a causal interpretation held simultaneously. Then, the two rate-change conditions, would be

$$\frac{r_{\text{post}}^{a=0}(A=1)}{r_{\text{pre}}^{a=0}(A=1)} = \frac{r_{\text{post}}(A=0)}{r_{\text{pre}}(A=0)}$$

and

$$r_{\text{post}}^{a=0}(A=1) - r_{\text{pre}}^{a=0}(A=1) = r_{\text{post}}(A=0) - r_{\text{pre}}(A=0).$$

By rewriting the first condition as $r_{\text{post}}^{a=0}(A=1) = r_{\text{pre}}^{a=0}(A=1)\dfrac{r_{\text{post}}(A=0)}{r_{\text{pre}}(A=0)}$, inserting the result into the expression for the second condition, and using straightforward algebraic manipulations, we obtain

$$\left\{ r_{\text{post}}(A=0) - r_{\text{pre}}(A=0) \right\} \left\{ \frac{r_{\text{pre}}^{a=0}(A=1)}{r_{\text{pre}}(A=0)} - 1 \right\} = 0,$$

which implies that

$$\left\{ r_{\text{post}}(A=0) = r_{\text{pre}}(A=0) \text{ or } r_{\text{pre}}^{a=0}(A=1) = r_{\text{pre}}(A=0) \right\},$$

and, by condition 2, that

$$\left\{ r_{\text{post}}(A=0) = r_{\text{pre}}(A=0) \text{ or } r_{\text{pre}}(A=1) = r_{\text{pre}}(A=0) \right\}.$$

In summary, if the conditions that are needed to endow both PERR and PERD with a causal interpretation hold simultaneously, then it has to be that the pretreatment and posttreatment event rates among the control group are equal (i.e., there was no change over time in the control group) *or* the pretreatment event rates of the treated and control group are equal (i.e., there is an indication that the treatment and control groups are "similar" during the pretreatment period).

The conditions $r_{\mathrm{post}}(A = 0) = r_{\mathrm{pre}}(A = 0)$ and $r_{\mathrm{pre}}(A = 1) = r_{\mathrm{pre}}(A = 0)$ are testable using the observed data and thus if one of them is rejected by the data with high confidence, then we could infer that at least one of the conditions needed for both PERR and PERD to have a causal interpretation does not hold. Such rejection does not imply that either PERR or PERD have a causal interpretation; it only implies that at most one of PERR or PERD can have a causal interpretation in the particular application. In such cases, it is not sensible to conduct both PERR and PERD analyses on the same data. In fact, because neither of the observed data conditions we derived above is likely to hold in practice, it will usually be necessary to rely on background knowledge to choose on which scale a rate-change condition is most likely to hold and, thus, to decide whether PERR or PERD analysis is most appropriate.

4.2 Implications for the counterfactual event rate among the treated under intervention to implement the control strategy

When the assumptions needed to endow both PERR and PERD with a causal interpretation hold, the two methods lead to the same inferences about the counterfactual posttreatment rate in the treated group, under intervention to implement the control strategy, $r_{\mathrm{post}}^{a=0}(A = 1)$. Using the identification result for PERR, consistency among the actually treated (condition 1), and positivity of $r_{\mathrm{post}}(A = 1)$ (condition 5), we obtain

$$r_{\mathrm{post}}^{a=0}(A = 1) = r_{\mathrm{pre}}(A = 1)\frac{r_{\mathrm{post}}(A = 0)}{r_{\mathrm{pre}}(A = 0)}. \tag{4.1}$$

Similarly, using the identification result for PERD and consistency among the actually treated, we obtain

$$r_{\mathrm{post}}^{a=0}(A = 1) = r_{\mathrm{pre}}(A = 1) + r_{\mathrm{post}}(A = 0) - r_{\mathrm{pre}}(A = 0). \tag{4.2}$$

It is now easy to see that the quantities on the right-hand-side of the above two expressions are equal when $r_{\mathrm{pre}}(A = 0) > 0$, which is assumed by condition 5 needed for PERR to be well defined, and

$$r_{\mathrm{pre}}(A = 1)\frac{r_{\mathrm{post}}(A = 0)}{r_{\mathrm{pre}}(A = 0)} = r_{\mathrm{pre}}(A = 1) + r_{\mathrm{post}}(A = 0) - r_{\mathrm{pre}}(A = 0),$$

or equivalently, when

$$\left\{ r_{\text{post}}(A=0) - r_{\text{pre}}(A=0) \right\} \left\{ r_{\text{pre}}(A=1) - r_{\text{pre}}(A=0) \right\} = 0.$$

As shown in the previous section of this Appendix, when the assumptions needed to endow both PERR and PERD with a causal interpretation hold, it has to be that either $r_{\text{pre}}(A=1) = r_{\text{pre}}(A=0)$ or $r_{\text{post}}(A=0) = r_{\text{pre}}(A=0)$. Thus, we conclude that PERR and PERD produce the same inferences about $r_{\text{post}}^{a=0}(A=1)$, whenever PERR and PERD have a causal interpretation.

When one or both of the methods do not have a causal interpretation (i.e., whenever the assumptions needed for a causal interpretation fail to hold for at least one of PERR or PERD) then, in general, we do not expect PERR and PERD to lead to the same inferences about $r_{\text{post}}^{a=0}(A=1)$. The expressions on the right-hand-side of equations (4.1) and (4.2), however, will always be equal to each other whenever (1) $r_{\text{pre}}(A=0) > 0$; and (2) $r_{\text{pre}}(A=1) = r_{\text{pre}}(A=0)$ or $r_{\text{post}}(A=0) = r_{\text{pre}}(A=0)$.

Web Appendix References

[1] Tyler J VanderWeele. Concerning the consistency assumption in causal inference. *Epidemiology*, 20(6):880–883, 2009.

[2] Nan Xuan Lin and William Edward Henley. Prior event rate ratio adjustment for hidden confounding in observational studies of treatment effectiveness: a pairwise cox likelihood approach. *Statistics in Medicine*, 35(28):5149–5169, 2016.