Supplement to “Risk ratios for contagious outcomes”

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1 Risk ratio in clusters of size two

Consider a cluster of two subjects, both uninfected at baseline, with $x_1 = 1, x_2 = 0$. The hazard functions for these subjects are

$$\lambda_1(t) = e^{\beta}[\alpha + \omega Y_2(t)]$$
$$\lambda_2(t) = \alpha + \omega e^{\gamma} Y_1(t)$$

and we are interested in understanding the properties of the risk ratio evaluated at time t,

$$RR = \frac{\mathbb{E}[Y_1(t)]}{\mathbb{E}[Y_2(t)]}.$$

First, let T_1 and T_2 be the infection times of subjects 1 and 2, and let $S = \min\{T_1, T_2\}$ be the time of first infection. Let I be the identity of the first infected subject. The random variables S has density

$$f(s) = \alpha(e^{\beta} + 1)\exp[-\alpha(e^{\beta} + 1)s]$$

and

$$\Pr(I = 1) = e^{\beta}/(1 + e^{\beta})$$

Furthermore S and I are independent. By the law of iterated expectations, we expand

$$\begin{aligned}
\mathbb{E}[Y_1(t)] &= \mathbb{E}_S[\mathbb{E}_I[Y_1(t)|S]] \\
&= \mathbb{E}_S\left[\sum_{j\in\{1,2\}} \mathbb{E}[Y_1(t)|I = j, S = s]\Pr(I = j|S = s)\right] = \mathbb{E}_S\left[\sum_{j\in\{1,2\}} \mathbb{E}[Y_1(t)|I = j, S = s]\Pr(I = j)\right] \\
&= \mathbb{E}_S\left[\Pr(I = 1) + \mathbb{E}[Y_1(t)|I = 2, S = s]\Pr(I = 2)\right] \\
&= \mathbb{E}_S\left[\frac{e^{\beta}}{1 + e^{\beta}} + \mathbb{E}[Y_1(t)|I = 2, S = s]\frac{1}{1 + e^{\beta}}\right]
\end{aligned}$$

In the above expectation with respect to S, it is implicit that $s < t$. The remaining inner expectation is

$$\begin{aligned}
\mathbb{E}[Y_1(t)|I = 2, S = s] &= \Pr(T_1 < t|I = 2, S = s) \\
&= \Pr(T_1 < t|T_1 > s) \\
&= 1 - \exp[-e^{\beta}(\alpha + \omega)(t - s)]
\end{aligned}$$

by the memoryless property of the exponential distribution. Putting these pieces together,

$$\begin{aligned}
\mathbb{E}[Y_1(t)] &= \int_0^\infty \mathbb{1}\{s<t\}\left[\frac{e^\beta}{1+e^\beta}+\frac{1}{1+e^\beta}(1-\exp[-e^\beta(\alpha+\omega)(t-s)])\right]\alpha(e^\beta+1)\exp[-\alpha(e^\beta+1)s]\ \mathrm{d}s \\
&= \alpha\int_0^t \left[e^\beta+1-\exp[-e^\beta(\alpha+\omega)(t-s)]\right]\exp[-\alpha(e^\beta+1)s]\ \mathrm{d}s \\
&= \alpha(e^\beta+1)\int_0^t \exp[-\alpha(e^\beta+1)s]\ \mathrm{d}s-\alpha\exp[-e^\beta(\alpha+\omega)t]\int_0^t \exp[(e^\beta\omega-\alpha)s]\ \mathrm{d}s
\end{aligned}$$

When $e^\beta\omega\neq\alpha$,

$$\begin{aligned}
\mathbb{E}[Y_1(t)] &= \frac{\alpha(e^\beta+1)}{-\alpha(e^\beta+1)}\Big[\exp[-\alpha(e^\beta+1)t]-1\Big]-\frac{\alpha}{e^\beta\omega-\alpha}\exp[-e^\beta(\alpha+\omega)t]\Big[\exp[(e^\beta\omega-\alpha)t]-1\Big] \\
&= 1-\exp[-\alpha(e^\beta+1)t]-\frac{\alpha}{e^\beta\omega-\alpha}\exp[-\alpha(e^\beta+1)t]+\frac{\alpha}{e^\beta\omega-\alpha}\exp[-e^\beta(\alpha+\omega)t] \\
&= \frac{e^\beta\omega}{\alpha-e^\beta\omega}\exp[-\alpha(e^\beta+1)t]-\frac{\alpha}{\alpha-e^\beta\omega}\exp[-e^\beta(\alpha+\omega)t]+1
\end{aligned}$$

and when $e^\beta\omega=\alpha$,

$$\begin{aligned}
\mathbb{E}[Y_1(t)] &= 1-\exp[-\alpha(e^\beta+1)t]-\alpha t\exp[-e^\beta(\alpha+\omega)t] \\
&= 1-\exp[-\alpha(e^\beta+1)t](1+\alpha t)
\end{aligned}$$

Similarly for $\mathbb{E}[Y_2(t)]$, if $\alpha e^\beta\neq\omega e^\gamma$,

$$\mathbb{E}[Y_2(t)] = \frac{\omega e^\gamma}{\alpha e^\beta-\omega e^\gamma}\exp[-\alpha(e^\beta+1)t]-\frac{\alpha e^\beta}{\alpha e^\beta-\omega e^\gamma}\exp[-(\alpha+\omega e^\gamma)t]+1$$

and if $\alpha e^\beta=\omega e^\gamma$,

$$\mathbb{E}[Y_2(t)] = 1-\exp[-\alpha(e^\beta+1)t](1+\alpha e^\beta t)$$

Therefore the ratio of expectations is:

$$RR = \begin{cases}
\frac{\frac{e^\beta\omega}{\alpha-e^\beta\omega}\exp[-\alpha(e^\beta+1)t]-\frac{\alpha}{\alpha-e^\beta\omega}\exp[-e^\beta(\alpha+\omega)t]+1}{\frac{\omega e^\gamma}{\alpha e^\beta-\omega e^\gamma}\exp[-\alpha(e^\beta+1)t]-\frac{\alpha e^\beta}{\alpha e^\beta-\omega e^\gamma}\exp[-(\alpha+\omega e^\gamma)t]+1}, & e^\beta\omega\neq\alpha, \alpha e^\beta\neq\omega e^\gamma \\
\frac{1-\exp[-\alpha(e^\beta+1)t](1+\alpha t)}{\frac{\omega e^\gamma}{\alpha e^\beta-\omega e^\gamma}\exp[-\alpha(e^\beta+1)t]-\frac{\alpha e^\beta}{\alpha e^\beta-\omega e^\gamma}\exp[-(\alpha+\omega e^\gamma)t]+1}, & e^\beta\omega=\alpha, \alpha e^\beta\neq\omega e^\gamma \\
\frac{\frac{e^\beta\omega}{\alpha-e^\beta\omega}\exp[-\alpha(e^\beta+1)t]-\frac{\alpha}{\alpha-e^\beta\omega}\exp[-e^\beta(\alpha+\omega)t]+1}{1-\exp[-\alpha(e^\beta+1)t](1+\alpha e^\beta t)}, & e^\beta\omega\neq\alpha, \alpha e^\beta=\omega e^\gamma \\
\frac{1-\exp[-\alpha(e^\beta+1)t](1+\alpha t)}{1-\exp[-\alpha(e^\beta+1)t](1+\alpha e^\beta t)}, & e^\beta\omega=\alpha, \alpha e^\beta=\omega e^\gamma.
\end{cases} \tag{1}$$

In some of the proofs that follow, it will be useful to consider the risk difference $\mathbb{E}[Y_1]-\mathbb{E}[Y_2]$, whose sign is the same as that of the RD^*, where

$$RD^* = \begin{cases}
\frac{\omega(e^{2\beta}-e^\gamma)\exp[-\alpha(e^\beta+1)t]+(\omega e^\gamma-\alpha e^\beta)\exp[-e^\beta(\alpha+\omega)t]+e^\beta(\alpha-\omega e^\beta)\exp[-(\alpha+\omega e^\gamma)t]}{(\alpha-\omega e^\beta)(\alpha e^\beta-\omega e^\gamma)}, & e^\beta\omega\neq\alpha, \alpha e^\beta\neq\omega e^\gamma \\
\frac{e^\beta\exp[-(\alpha+\omega e^\gamma)t]-(e^\beta+t(\alpha e^\beta-\omega e^\gamma))\exp[-\alpha(e^\beta+1)t]}{\alpha e^\beta-\omega e^\gamma}, & e^\beta\omega=\alpha, \alpha e^\beta\neq\omega e^\gamma \\
\frac{(1+te^\beta(\alpha-\omega e^\beta))\exp[-\alpha(e^\beta+1)t]-\exp[-e^\beta(\alpha+\omega)t]}{\alpha-\omega e^\beta}, & e^\beta\omega\neq\alpha, \alpha e^\beta=\omega e^\gamma \\
t(e^\beta-1), & e^\beta\omega=\alpha, \alpha e^\beta=\omega e^\gamma.
\end{cases} \tag{2}$$

2 Proofs

2.1 Households of size two

We first state and prove a simple Lemma that will ease exposition in what follows.

Lemma 1. *Suppose* $0 < a < b < c$. *Then*

$$(c-b)(e^{-a}-e^{-b})-(b-a)(e^{-b}-e^{-c})>0.$$

Proof. Let $f(x)=e^{-x}$, so $f'(x)=\mathrm{d}f(x)/\mathrm{d}x=-e^{-x}$. By the mean value theorem, there exist $x_1 \in (a,b)$ and $x_2 \in (b,c)$ such that

$$f'(x_1)=-e^{-x_1}=\frac{e^{-b}-e^{-a}}{b-a} \quad \text{and} \quad f'(x_2)=-e^{-x_2}=\frac{e^{-c}-e^{-b}}{c-b}.$$

But since $x_1 < x_2$, it follows that $-e^{-x_1} < -e^{-x_2}$ and so $f'(x_1) < f'(x_2)$. Therefore

$$\frac{e^{-b}-e^{-a}}{b-a} < \frac{e^{-c}-e^{-b}}{c-b},$$

and rearranging this inequality gives $(c-b)(e^{-a}-e^{-b})-(b-a)(e^{-b}-e^{-c})>0$, as claimed. □

Result 1: No within-cluster contagion

Proof. Suppose $\alpha > 0$ and $\omega = 0$. We only need to consider the first case in (2), and the sign of this expression at time T is the same as that of

$$\exp[-\alpha T]-\exp[-\alpha e^{\beta} T].$$

Since α and T are non-negative, the risk ratio is less than one for every $t \in (0,T]$ when $\beta < 0$, one when $\beta = 0$, and greater than one when $\beta > 0$. Therefore the risk ratio is direction-unbiased. □

Result 2: Under the null

Proof. Suppose $\beta = 0$. The sign of (2) is the same as the sign of $RD^*_{\beta=0}$, where

$$RD^*_{\beta=0}=\begin{cases} \frac{\omega(1-e^{\gamma})\exp[-\alpha t]+(\omega e^{\gamma}-\alpha)\exp[-\omega t]+(\alpha-\omega)\exp[-\omega e^{\gamma} t]}{(\alpha-\omega)(\alpha-\omega e^{\gamma})}, & \alpha \neq \omega, \alpha \neq \omega e^{\gamma} \\ \frac{\exp[-\alpha e^{\gamma} t]-(1+t\alpha(1-e^{\gamma}))\exp[-\alpha t]}{\alpha(1-e^{\gamma})}, & \alpha = \omega, \alpha \neq \omega e^{\gamma} \\ \frac{(1+t(\omega e^{\gamma}-\omega))\exp[-\omega e^{\gamma} t]-\exp[-\omega t]}{\omega(e^{\gamma}-1)}, & \alpha \neq \omega, \alpha = \omega e^{\gamma} \\ 0, & \alpha = \omega, \alpha = \omega e^{\gamma}. \end{cases} \tag{3}$$

First, note that when $\gamma = 0$, $RD^*_{\beta=0} = 0$, so $RR = 1$.

Now suppose $\gamma \neq 0$. The proof is divided into cases for $\gamma < 0$ and $\gamma > 0$. These cases are further divided into several sub-cases defined by the relationship between the parameters of the model.

Case 1: Let $\gamma < 0$. We will show that for any $t > 0$, expression in (3) is positive, and hence $RR > 1$.
Sub-case 1.1: Suppose $0 < \alpha < \omega e^{\gamma} < \omega$. The denominator of (3) is positive, and the expressions in the numerator have the following signs:

$$\omega(1 - e^{\gamma}) > 0, \quad \omega e^{\gamma} - \alpha > 0, \quad \text{and} \quad \alpha - \omega < 0.$$

Multiplying the numerator of (3) by $t > 0$ gives the following expression:

$$(\omega t - \omega e^{\gamma} t) \exp[-\alpha t] + (\omega e^{\gamma} t - \alpha t) \exp[-\omega t] - (\omega t - \alpha t) \exp[-\omega e^{\gamma} t].$$

Splitting $\omega t - \alpha t$ into $(\omega t - \omega e^{\gamma} t) + (\omega e^{\gamma} t - \alpha t)$ and rearranging, the numerator of (3) equals:

$$(\omega t - \omega e^{\gamma} t) (\exp[-\alpha t] - \exp[-\omega e^{\gamma} t]) - (\omega e^{\gamma} t - \alpha t) (\exp[-\omega e^{\gamma} t] - \exp[-\omega t])$$

Let $a = \alpha t$, $b = \omega e^{\gamma} t$, and $c = \omega t$. By Lemma 1, the numerator of (3) is positive for any $t > 0$, so $RR > 1$.

Sub-case 1.2: Suppose $0 < \omega e^{\gamma} < \alpha < \omega$. The denominator of (3) is negative, and the expressions in the numerator have the following signs:

$$\omega(1 - e^{\gamma}) > 0, \quad \omega e^{\gamma} - \alpha < 0, \quad \text{and} \quad \alpha - \omega < 0.$$

Multiplying the numerator of (3) by $t > 0$ and rearranging gives the following expression:

$$(\alpha t - \omega e^{\gamma} t) (\exp[-\alpha t] - \exp[-\omega t]) - (\omega t - \alpha t) (\exp[-\omega e^{\gamma} t] - \exp[-\alpha t])$$

By Lemma 1, the numerator of (3) is negative for any $t > 0$, so $RR > 1$.

Sub-case 1.3: Suppose $0 < \omega e^{\gamma} < \omega < \alpha$. The denominator of (3) is positive, and the expressions in the numerator have the following signs:

$$\omega(1 - e^{\gamma}) > 0, \quad \omega e^{\gamma} - \alpha < 0, \quad \text{and} \quad \alpha - \omega > 0.$$

Multiplying the numerator of (3) by $t > 0$ and rearranging gives the following expression:

$$(\alpha t - \omega t)(\exp[-\omega e^{\gamma} t] - \exp[-\omega t]) - (\omega t - \omega e^{\gamma} t)(\exp[-\omega t] - \exp[-\alpha t])$$

By Lemma 1, numerator of (3) is positive for any $t > 0$, so $RR > 1$.

Sub-case 1.4: Suppose $\alpha - \omega = 0$. Since $e^{\gamma} < 1$, the denominator of (3) is positive. Dividing the numerator by $\exp[-\alpha t]$ and rearranging gives:

$$\exp[\alpha t(1 - e^{\gamma})] - (1 + \alpha t(1 - e^{\gamma})),$$

which is positive for any $t > 0$, since $\exp[a] > 1 + a$ for $a \neq 0$, so $RR > 1$.

Sub-case 1.5: Suppose $\alpha - \omega e^{\gamma} = 0$. Since $e^{\gamma} < 1$, the denominator of (3) is negative. Dividing the numerator by $\exp[-\omega e^{\gamma} t]$ and rearranging gives:

$$(1 + \omega t(e^{\gamma} - 1)) - \exp[\omega t(e^{\gamma} - 1)],$$

which is negative for any $t > 0$, since $\exp[a] > 1 + a$ for $a \neq 0$, so $RR > 1$.

Case 2: Let $\gamma > 0$. We will show that for any $t > 0$, the expression in (3) is negative, and hence $RR < 1$.
Sub-case 2.1: Suppose $0 < \alpha < \omega < \omega e^{\gamma}$. The denominator of (3) is positive, and the expressions in the numerator have the following signs:

$$\omega(1 - e^{\gamma}) < 0, \quad \omega e^{\gamma} - \alpha > 0, \quad \text{and} \quad \alpha - \omega < 0.$$

Multiplying the numerator of (3) by $t > 0$ and rearranging gives the following expression:

$$(\omega t - \alpha t)(\exp[-\omega t] - \exp[-\omega e^{\gamma} t]) - (\omega e^{\gamma} t - \omega t)(\exp[-\alpha t] - \exp[-\omega t])$$

By Lemma 1, the numerator of (3) is negative for any $t > 0$, so $RR < 1$.

Sub-case 2.2: Suppose $0 < \omega < \alpha < \omega e^{\gamma}$. The denominator of (3) is negative, and the expressions in the numerator have the following signs:

$$\omega(1 - e^{\gamma}) < 0, \quad \omega e^{\gamma} - \alpha > 0, \quad \text{and} \quad \alpha - \omega > 0.$$

Multiplying the numerator of (3) by $t > 0$ and rearranging gives the following expression:

$$(\omega e^{\gamma} t - \alpha t)(\exp[-\omega t] - \exp[-\alpha t]) - (\alpha t - \omega t)(\exp[-\alpha t] - \exp[-\omega e^{\gamma} t])$$

By Lemma 1, the numerator of (3) is positive for any $t > 0$, so $RR < 1$.

Sub-case 2.3: Suppose $0 < \omega < \omega e^{\gamma} < \alpha$. The denominator of (3) is positive, and the expressions in the numerator have the following signs:

$$\omega(1 - e^{\gamma}) < 0, \quad \omega e^{\gamma} - \alpha < 0, \quad \text{and} \quad \alpha - \omega > 0.$$

Multiplying the numerator of (3) by $t > 0$ and rearranging gives the following expression:

$$(\omega e^{\gamma} t - \omega t)(\exp[-\omega e^{\gamma} t] - \exp[-\alpha t]) - (\alpha t - \omega e^{\gamma} t)(\exp[-\omega t] - \exp[-\omega e^{\gamma} t])$$

By Lemma 1, the numerator of (3) is negative for any $t > 0$, so $RR < 1$.

Sub-case 2.4: Suppose $\alpha - \omega = 0$. Since $e^{\gamma} > 1$, the denominator of (3) is negative. Dividing the numerator by $\exp[-\alpha t]$ and rearranging gives:

$$\exp[\alpha t(1 - e^{\gamma})] - (1 + \alpha t(1 - e^{\gamma})),$$

which is positive for any $t > 0$, since $\exp[a] > 1 + a$ for $a \neq 0$, so $RR < 1$.

Sub-case 2.5: Suppose $\alpha - \omega e^{\gamma} = 0$. Since $e^{\gamma} > 1$, the denominator of (3) is positive. Dividing the numerator by $\exp[-\omega e^{\gamma} t]$ and rearranging gives:

$$(1 + \omega t(e^{\gamma} - 1)) - \exp[\omega t(e^{\gamma} - 1)],$$

which is negative for any $t > 0$, since $\exp[a] > 1 + a$ for $a \neq 0$, so $RR < 1$. $\square$

Result 3: Homogeneous infectiousness

Proof. Suppose $\gamma = 0$. The sign of (2) is the same as the sign of $RD^*_{\gamma=0}$, where

$$RD^*_{\gamma=0} = \begin{cases} \frac{\omega(e^{2\beta}-1)\exp[-\alpha(e^{\beta}+1)t]+(\omega-\alpha e^{\beta})\exp[-e^{\beta}(\alpha+\omega)t]+e^{\beta}(\alpha-\omega e^{\beta})\exp[-(\alpha+\omega)t]}{(\alpha-\omega e^{\beta})(\alpha e^{\beta}-\omega)}, & e^{\beta}\omega \neq \alpha, \alpha e^{\beta} \neq \omega \\ \frac{e^{\beta}\exp[-\omega t]-(e^{\beta}+t\omega(e^{2\beta}-1))\exp[-\omega e^{2\beta}t]}{\omega(e^{2\beta}-1)}, & e^{\beta}\omega = \alpha, \alpha e^{\beta} \neq \omega \\ \frac{(1+t\alpha e^{\beta}(1-e^{2\beta}))\exp[-\alpha t]-\exp[-\alpha e^{2\beta}t]}{\alpha(1-e^{2\beta})}, & e^{\beta}\omega \neq \alpha, \alpha e^{\beta} = \omega \\ t(e^{\beta}-1), & e^{\beta}\omega = \alpha, \alpha e^{\beta} = \omega. \end{cases} \tag{4}$$

First note that when $\gamma = 0$, $RD^*_{\beta=0} = 0$, so $RR = 1$.

Now suppose $\beta \neq 0$. The proof is divided into cases for $\beta < 0$ and $\beta > 0$. These cases are further divided into several sub-cases defined by the relationship between the parameters of the model.

Case 1: Suppose $\beta < 0$. We will show that for any $t > 0$, expression in (4) is negative.
Sub-case 1.1: Suppose $0 < \alpha < \omega e^{\beta}$. It follows from this condition that $\alpha e^{\beta} < \omega e^{2\beta} < \omega$, $\alpha e^{\beta} < \omega$ and $\exp[-e^{\beta}(\alpha+\omega)t] < \exp[-(\alpha+\omega e^{2\beta})t]$. The denominator of (4) is positive, and the expressions in the numerator have the following signs:

$$\omega(e^{2\beta}-1) < 0, \quad \omega - \alpha e^{\beta} > 0, \quad \text{and} \quad e^{\beta}(\alpha - \omega e^{\beta}) < 0.$$

The numerator of (4) is less than

$$\omega(e^{2\beta}-1)\exp[-\alpha(e^{\beta}+1)t] + (\omega-\alpha e^{\beta})\exp[-(\alpha+\omega e^{2\beta})t] + e^{\beta}(\alpha-\omega e^{\beta})\exp[-(\alpha+\omega)t] \tag{5}$$

which has the same sign as

$$\omega(e^{2\beta}-1)\exp[-\alpha e^{\beta}t] + (\omega-\alpha e^{\beta})\exp[-\omega e^{2\beta}t] + e^{\beta}(\alpha-\omega e^{\beta})\exp[-\omega t]. \tag{6}$$

Multiplying (6) by $t > 0$ and rearranging gives the following expression:

$$(\omega e^{2\beta}t - \alpha e^{\beta}t)(\exp[-\omega e^{2\beta}t] - \exp[-\omega t]) - (\omega t - \omega e^{2\beta}t)(\exp[-\alpha e^{\beta}t] - \exp[-\omega e^{2\beta}t]).$$

By Lemma 1, (6) is negative for any $t > 0$, so $RR < 1$.

Sub-case 1.2: Suppose $0 < \omega e^{2\beta} < \alpha e^{\beta} < \omega$. It follows from this condition that $\alpha e^{\beta} < \omega$, $\omega e^{\beta} < \alpha$, and $\exp[-e^{\beta}(\alpha+\omega)t] > \exp[-(\alpha+\omega e^{2\beta})t]$. The denominator of (4) is negative, and the expressions in the numerator have the following signs:

$$\omega(e^{2\beta}-1) < 0, \quad \omega - \alpha e^{\beta} > 0, \quad \text{and} \quad e^{\beta}(\alpha - \omega e^{\beta}) > 0.$$

The numerator of (4) is greater than (5), which has the same sign as (6). Multiplying (6) by $t > 0$ and rearranging gives the following expression:

$$(\omega t - \alpha e^{\beta}t)(\exp[-\omega e^{2\beta}t] - \exp[-\alpha e^{\beta}t]) - (\alpha e^{\beta}t - \omega e^{2\beta}t)(\exp[-\alpha e^{\beta}t] - \exp[-\omega t]).$$

By Lemma 1, (6) is positive for any $t > 0$, so $RR < 1$.

Sub-case 1.3: Suppose $0 < \omega < \alpha e^\beta$. It follows from this condition that $\omega e^{2\beta} < \omega < \alpha e^\beta$, $\omega e^\beta < \alpha$ and $\exp[-e^\beta(\alpha+\omega)t] > \exp[-(\alpha+\omega e^{2\beta})t]$. The denominator of (4) is positive, and the expressions in the numerator have the following signs:

$$\omega(e^{2\beta}-1) < 0, \quad \omega - \alpha e^\beta < 0, \quad \text{and} \quad e^\beta(\alpha - \omega e^\beta) > 0.$$

The numerator of (4) is less than (5), which has the same sign as (6). Multiplying (6) by $t > 0$ and rearranging gives the following expression:

$$(\omega t - \omega e^{2\beta} t)(\exp[-\omega t] - \exp[-\alpha e^\beta t]) - (\alpha e^\beta t - \omega t)(\exp[-\omega e^{2\beta} t] - \exp[-\omega t]).$$

By Lemma 1, (6) is negative for any $t > 0$, so $RR < 1$.

Sub-case 1.4: Suppose $\alpha - \omega e^\beta = 0$ and $\alpha e^\beta - \omega \neq 0$. Since $e^\beta < 1$, the denominator of (4) is negative. Dividing the numerator by $e^\beta \exp[-\omega e^{2\beta} t]$ and rearranging gives:

$$\exp[\omega t(e^{2\beta}-1)] - (1 + \omega \frac{t}{e^\beta}(e^{2\beta}-1)) > \exp[\omega t(e^{2\beta}-1)] - (1 + \omega t(e^{2\beta}-1)).$$

The right hand side of this expression is positive for any $t > 0$, since $\exp[a] > 1 + a$ for $a \neq 0$, so $RR < 1$.

Sub-case 1.5: Suppose $\alpha - \omega e^\beta \neq 0$ and $\alpha e^\beta - \omega = 0$. Since $e^\beta < 1$, the denominator of (4) is positive. Dividing the numerator by $\exp[-\alpha t]$ and rearranging gives:

$$1 + \alpha e^\beta t(1 - e^{2\beta}) - \exp[\alpha t(1-e^{2\beta})] < 1 + \alpha t(1 - e^{2\beta}) - \exp[\alpha t(1 - e^{2\beta})].$$

The right hand side of this expression is negative for any $t > 0$, since $\exp[a] > 1 + a$ for $a \neq 0$, so $RR < 1$.

Sub-case 1.6: Suppose $\alpha - \omega e^\beta = 0$ and $\alpha e^\beta - \omega = 0$. Since $e^\beta < 1$, (4) is negative for any $t > 0$, so $RR < 1$.

Case 2: Suppose $\beta > 0$. We will show that for any $t > 0$, expression in (4) is positive, and hence $RR > 1$.
Sub-case 2.1: Suppose $0 < \alpha e^\beta < \omega$. It follows from this condition that $\alpha e^\beta < \omega < \omega e^{2\beta}$, $\alpha < \omega e^\beta$ and $\exp[-e^\beta(\alpha+\omega)t] > \exp[-(\alpha+\omega e^{2\beta})t]$. The denominator of (4) is positive, and the expressions in the numerator have the following signs:

$$\omega(e^{2\beta}-1) > 0, \quad \omega - \alpha e^\beta > 0, \quad \text{and} \quad e^\beta(\alpha - \omega e^\beta) < 0.$$

The numerator of (4) is greater than (5), which has the same sign as (6). Multiplying (6) by $t > 0$ and rearranging gives the following expression:

$$(\omega e^{2\beta} t - \omega t)(\exp[-\alpha e^\beta t] - \exp[-\omega t]) - (\omega t - \alpha e^\beta t)(\exp[-\omega t] - \exp[-\omega e^{2\beta} t]).$$

By Lemma 1, (6) is positive for any $t > 0$, so $RR > 1$.

Sub-case 2.2: Suppose $0 < \omega < \alpha e^\beta < \omega e^{2\beta}$. It follows from this condition that $\alpha < \omega e^\beta$, $\alpha e^\beta > \omega$ and $\exp[-e^\beta(\alpha+\omega)t] > \exp[-(\alpha+\omega e^{2\beta})t]$. The denominator of (4) is negative, and the expressions in the numerator have the following signs:

$$\omega(e^{2\beta}-1) > 0, \quad \omega - \alpha e^\beta < 0, \quad \text{and} \quad e^\beta(\alpha - \omega e^\beta) < 0.$$

The numerator of (4) is less than (5), which has the same sign as (6). Multiplying (6) by $t > 0$ and rearranging gives the following expression:

$$(\alpha e^{\beta}t - \omega t)(\exp[-\alpha e^{\beta}t] - \exp[-\omega e^{2\beta}t]) - (\omega e^{2\beta}t - \alpha e^{\beta}t)(\exp[-\omega t] - \exp[-\alpha e^{\beta}t]).$$

By Lemma 1, (6) is negative for any $t > 0$, so $RR > 1$.

Sub-case 2.3: Suppose $0 < \omega e^{\beta} < \alpha$. It follows from this condition that $\omega < \omega e^{2\beta} < \alpha e^{\beta}$, $\alpha e^{\beta} > \omega$ and $\exp[-e^{\beta}(\alpha + \omega)t] < \exp[-(\alpha + \omega e^{2\beta})t]$. The denominator of (4) is positive, and the expressions in the numerator have the following signs:

$$\omega(e^{2\beta} - 1) > 0, \quad \omega - \alpha e^{\beta} < 0, \quad \text{and} \quad e^{\beta}(\alpha - \omega e^{\beta}) > 0.$$

The numerator of (4) is greater than (5), which has the same sign as (6). Multiplying (6) by $t > 0$ and rearranging gives the following expression:

$$(\alpha e^{\beta}t - \omega e^{2\beta}t)(\exp[-\omega t] - \exp[-\omega e^{2\beta}t]) - (\omega e^{2\beta}t - \omega t)(\exp[-\omega e^{2\beta}t] - \exp[-\alpha e^{\beta}t]).$$

By Lemma 1, (6) is positive for any $t > 0$, so $RR < 1$.

Sub-case 2.4: Suppose $\alpha - \omega e^{\beta} = 0$ and $\alpha e^{\beta} - \omega \neq 0$. Since $e^{\beta} > 1$, the denominator of (4) is positive. Dividing the numerator by $e^{\beta}\exp[-\omega e^{2\beta}t]$ and rearranging gives:

$$\exp[\omega t(e^{2\beta} - 1)] - (1 + \omega\frac{t}{e^{\beta}}(e^{2\beta} - 1)) > \exp[\omega t(e^{2\beta} - 1)] - (1 + \omega t(e^{2\beta} - 1)).$$

The right hand side of this expression is positive for any $t > 0$, since $\exp[a] > 1 + a$ for $a \neq 0$, so $RR < 1$.

Sub-case 2.5: Suppose $\alpha - \omega e^{\beta} \neq 0$ and $\alpha e^{\beta} - \omega = 0$. Since $e^{\beta} > 1$, the denominator of (4) is negative. Dividing the numerator by $\exp[-\alpha t]$ and rearranging gives:

$$1 + \alpha e^{\beta}t(1 - e^{2\beta}) - \exp[\alpha t(1 - e^{2\beta})] < 1 + \alpha t(1 - e^{2\beta}) - \exp[\alpha t(1 - e^{2\beta})].$$

The right hand side of this expression is negative for any $t > 0$, since $\exp[a] > 1 + a$ for $a \neq 0$, so $RR < 1$.

Sub-case 2.6: Suppose $\alpha - \omega e^{\beta} = 0$ and $\alpha e^{\beta} - \omega = 0$. Since $e^{\beta} > 1$, (4) is positive for any $t > 0$, so $RR < 1$. □

Result 4: Direction bias

Proof. The proof is divided into cases for $\beta < 0$ and $\beta > 0$. These cases are further divided into several sub-cases defined by the relationship between the parameters of the model.

Case 1: Suppose $\beta < 0$ and $e^{\gamma} < \min\{e^{2\beta}, e^{\beta} + \frac{\alpha}{\omega}(e^{\beta} - 1)\}$. It follows that $e^{\beta} > \alpha/(\alpha + \omega)$, and that the equalities $e^{\beta}\omega = \alpha$ and $\alpha e^{\beta} = \omega e^{\gamma}$ cannot hold simultaneously. We will show that for every combination of other parameters there exists $t^* > 0$, such that for all $t > t^*$, the corresponding expression in (2) is positive, and hence $RR > 1$.
Sub-case 1.1: Suppose $\alpha/\omega < e^{\beta} < 1$, $\alpha e^{\beta} \neq \omega e^{\gamma}$ and consider the first line of (2). When $\alpha e^{\beta} - \omega e^{\gamma} < 0$, the denominator is positive, and the expressions in the numerator have the following signs:

$$\omega(e^{2\beta} - e^{\gamma}) > 0, \quad \omega e^{\gamma} - \alpha e^{\beta} > 0, \quad \text{and} \quad e^{\beta}(\alpha - \omega e^{\beta}) < 0.$$

Therefore for any $t > 0$ the numerator of (2) is greater than

$$\omega(e^{2\beta} - e^{\gamma}) \exp[-\alpha(e^{\beta} + 1)t] + e^{\beta}(\alpha - \omega e^{\beta}) \exp[-(\alpha + \omega e^{\gamma})t] \tag{7}$$

which has positive sign whenever

$$\omega(e^{2\beta} - e^{\gamma}) \exp[-\alpha(e^{\beta} + 1)t] > -e^{\beta}(\alpha - \omega e^{\beta}) \exp[-(\alpha + \omega e^{\gamma})t]. \tag{8}$$

This inequality holds for any $t > \frac{\log[e^{\beta}(\omega e^{\beta}-\alpha)]-\log[\omega(e^{2\beta}-e^{\gamma})]}{\omega e^{\gamma}-\alpha e^{\beta}}$. Note that this threshold for t is positive and finite.

When $\alpha e^{\beta} - \omega e^{\gamma} > 0$, the denominator of (2) is negative, and the coefficients in the numerator have the following signs:

$$\omega(e^{2\beta} - e^{\gamma}) > 0, \quad \omega e^{\gamma} - \alpha e^{\beta} < 0, \quad \text{and} \quad e^{\beta}(\alpha - \omega e^{\beta}) < 0.$$

Therefore for any $t > 0$ the numerator of (2) is less than

$$\omega(e^{2\beta} - e^{\gamma}) \exp[-\alpha(e^{\beta} + 1)t] + e^{\beta}(\alpha - \omega e^{\beta}) \exp[-(\alpha + \omega e^{\gamma})t] \tag{9}$$

which is negative whenever

$$\omega(e^{2\beta} - e^{\gamma}) \exp[-\alpha(e^{\beta} + 1)t] < -e^{\beta}(\alpha - \omega e^{\beta}) \exp[-(\alpha + \omega e^{\gamma})t]. \tag{10}$$

This inequality holds for any $t > \frac{\log[\omega(e^{2\beta}-e^{\gamma})]-\log[e^{\beta}(\omega e^{\beta}-\alpha)]}{\alpha e^{\beta}-\omega e^{\gamma}}$. Note that this threshold for t is positive and finite.

Sub-case 1.2: Suppose $e^{\beta} < \alpha/\omega$ and $\alpha e^{\beta} \neq \omega e^{\gamma}$. It follows that $\alpha e^{\beta} - \omega e^{\gamma} > 0$, the denominator of (2) is positive, and the expressions in the numerator have the following signs:

$$\omega(e^{2\beta} - e^{\gamma}) > 0, \quad \omega e^{\gamma} - \alpha e^{\beta} < 0, \quad \text{and} \quad e^{\beta}(\alpha - \omega e^{\beta}) > 0.$$

Therefore for any $t > 0$, the numerator of (2) is greater than

$$(\omega e^{\gamma} - \alpha e^{\beta}) \exp[-e^{\beta}(\alpha + \omega)t] + e^{\beta}(\alpha - \omega e^{\beta}) \exp[-(\alpha + \omega e^{\gamma})t], \tag{11}$$

which is positive whenever

$$(\omega e^{\gamma} - \alpha e^{\beta}) \exp[-e^{\beta}(\alpha + \omega)t] > -e^{\beta}(\alpha - \omega e^{\beta}) \exp[-(\alpha + \omega e^{\gamma})t]. \tag{12}$$

This inequality holds for any $t > \frac{\log[\alpha e^{\beta}-\omega e^{\gamma}]-\log[e^{\beta}(\alpha-\omega e^{\beta})]}{e^{\beta}(\alpha+\omega)-(\alpha+\omega e^{\gamma})}$. Note that this threshold for t is positive and finite.

Sub-case 1.3: Suppose that $\alpha = \omega e^{\beta}$ and $\alpha e^{\beta} \neq \omega e^{\gamma}$. It follows that $\alpha/\omega < 1$ and $\alpha e^{\beta} - \omega e^{\gamma} > 0$. The denominator of (2) is positive, and the expressions in the numerator have the following signs:

$$e^{\beta} > 0 \quad \text{and} \quad e^{\beta} + t(\alpha e^{\beta} - \omega e^{\gamma}) > 0.$$

Therefore (2) has positive sign whenever

$$e^{\beta} \exp[-(\alpha + \omega e^{\gamma})t] > (e^{\beta} + t(\alpha e^{\beta} - \omega e^{\gamma})) \exp[-\alpha(e^{\beta} + 1)t]. \tag{13}$$

Since $t > 0$ and $a > 0$, $\log(1 + at)$ is a monotonic function of t that grows more slowly than t. Therefore there exists $t^* > 0$ such that for any $t > t^*$, $t > \frac{\log(1+\frac{t}{e^{\beta}}(\alpha e^{\beta}-\omega e^{\gamma}))}{\alpha e^{\beta}-\omega e^{\gamma}}$. Therefore (13) holds for $t > t^*$.

Sub-case 1.4: Suppose $\alpha \neq \omega e^\beta$ and $\alpha e^\beta = \omega e^\gamma$. It follows that $\alpha/\omega < 1$, and $\alpha - \omega e^\beta < 0$. The denominator of (2) is negative, and (2) is positive when $1 + te^\beta(\alpha - \omega e^\beta) < 0$. This inequality holds for any $t > [e^\beta(\omega e^\beta - \alpha)]^{-1}$. Note that this threshold value for t is positive and finite.

Case 2: Suppose $\beta > 0$ and $e^\gamma > \max\{e^{2\beta}, e^\beta + \frac{\alpha}{\omega}(e^\beta - 1)\}$. It follows that the equalities $e^\beta \omega = \alpha$ and $\alpha e^\beta = \omega e^\gamma$ cannot hold simultaneously. We will show that for every combination of other parameters there exists $t^* > 0$, such that for all $t > t^*$, the corresponding expression in (2) is negative.

Sub-case 2.1: Suppose $1 < e^\beta < \alpha/\omega$ and $\alpha e^\beta \neq \omega e^\gamma$. When $\alpha e^\beta - \omega e^\gamma < 0$, the denominator of (2) is negative, and the coefficients in the numerator have the following signs:

$$\omega(e^{2\beta} - e^\gamma) < 0, \quad \omega e^\gamma - \alpha e^\beta > 0, \quad \text{and} \quad e^\beta(\alpha - \omega e^\beta) > 0.$$

Therefore for any $t > 0$ the numerator of (2) is greater than

$$\omega(e^{2\beta} - e^\gamma)\exp[-\alpha(e^\beta + 1)t] + (\omega e^\gamma - \alpha e^\beta)\exp[-e^\beta(\alpha + \omega)t], \tag{14}$$

which has positive sign whenever

$$(\omega e^\gamma - \alpha e^\beta)\exp[-e^\beta(\alpha + \omega)t] > -\omega(e^{2\beta} - e^\gamma)\exp[-\alpha(e^\beta + 1)t]. \tag{15}$$

This inequality holds for any $t > \frac{\log[\omega(e^\gamma - e^{2\beta})] - \log[\omega e^\gamma - \alpha e^\beta]}{\alpha - \omega e^\beta}$. Note that this threshold for t is positive and finite.

When $\alpha e^\beta - \omega e^\gamma > 0$, the denominator of (2) is positive, and the coefficients in the numerator have the following signs:

$$\omega(e^{2\beta} - e^\gamma) < 0, \quad \omega e^\gamma - \alpha e^\beta < 0, \quad \text{and} \quad e^\beta(\alpha - \omega e^\beta) > 0.$$

Therefore for any $t > 0$ the numerator of (2) is less than

$$(\omega e^\gamma - \alpha e^\beta)\exp[-e^\beta(\alpha + \omega)t] + e^\beta(\alpha - \omega e^\beta)\exp[-(\alpha + \omega e^\gamma)t] \tag{16}$$

which is negative whenever

$$e^\beta(\alpha - \omega e^\beta)\exp[-(\alpha + \omega e^\gamma)t] < -(\omega e^\gamma - \alpha e^\beta)\exp[-e^\beta(\alpha + \omega)t]. \tag{17}$$

This inequality holds for any $t > \frac{\log[e^\beta(\alpha - \omega e^\beta)] - \log[\alpha e^\beta - \omega e^\gamma]}{(\alpha - \omega e^\beta) - (\alpha e^\beta - \omega e^\gamma)}$. Note that this threshold for t is positive and finite.

Sub-case 2.2: Suppose $e^\beta > \alpha/\omega$ and $\alpha e^\beta \neq \omega e^\gamma$. It follows that $\alpha e^\beta - \omega e^\gamma < 0$. The denominator of (2) is positive, and the expressions in the numerator have the following signs:

$$\omega(e^{2\beta} - e^\gamma) < 0, \quad \omega e^\gamma - \alpha e^\beta > 0, \quad \text{and} \quad e^\beta(\alpha - \omega e^\beta) < 0.$$

Therefore for any $t > 0$ the numerator of (2) is less than

$$\omega(e^{2\beta} - e^\gamma)\exp[-\alpha(e^\beta + 1)t] + (\omega e^\gamma - \alpha e^\beta)\exp[-e^\beta(\alpha + \omega)t] \tag{18}$$

which is negative whenever

$$(\omega e^\gamma - \alpha e^\beta)\exp[-e^\beta(\alpha + \omega)t] < -\omega(e^{2\beta} - e^\gamma)\exp[-\alpha(e^\beta + 1)t]. \tag{19}$$

This inequality holds for any $t > \frac{\log[\omega e^{\gamma}-\alpha e^{\beta}]-\log[\omega(e^{\gamma}-e^{2\beta})]}{\omega e^{\beta}-\alpha}$. Note that this threshold for t is positive and finite.

Sub-case 2.3: Suppose $\alpha = \omega e^{\beta}$ and $\alpha e^{\beta} \neq \omega e^{\gamma}$. It follows that $\alpha/\omega > 1$ and $(\alpha e^{\beta} - \omega e^{\gamma}) < 0$. The denominator of (2) is negative, and (2) is negative when $e^{\beta} + t(\alpha e^{\beta} - \omega e^{\gamma}) < 0$. This inequality holds for any $t > \frac{e^{\beta}}{\omega e^{\gamma}-\alpha e^{\beta}}$. Note that this threshold for t is positive and finite.

Sub-case 2.4: Suppose that $\alpha \neq \omega e^{\beta}$ and $\alpha e^{\beta} = \omega e^{\gamma}$. It follows from this condition that $\alpha/\omega > 1$, and $\alpha - \omega e^{\beta} > 0$. The denominator of (2) is positive, and the expression in the numerator has the following sign:

$$1 + te^{\beta}(\alpha - \omega e^{\beta}) > 0$$

Therefore (2) has negative sign whenever

$$(1 + te^{\beta}(\alpha - \omega e^{\beta})) \exp[-\alpha(e^{\beta} + 1)t] < \exp[-e^{\beta}(\alpha + \omega)t]. \tag{20}$$

Since $t > 0$ and $a > 0$, $\log(1 + at)$ is a monotonic function of t that grows more slowly than t. Therefore there exists $t^* > 0$ such that for any $t > t^*$, $t > \frac{\log(1+te^{\beta}(\alpha-\omega e^{\beta}))}{\alpha-\omega e^{\beta}}$. Therefore (20) holds for $t > t^*$. □

2.2 General clusters

We begin with notation that will simplify exposition. Let $H_i = (\alpha_i(t), \omega_{ikj}(t), n_i, T_i)$ represent cluster-level variables. Let $\mathbb{E}_{t_{ij}}[\cdot]$ denote expectation with respect to the infection time of j, and let $\mathbb{E}_{\mathbf{t}_{i,-j}}[\cdot]$ denote expectation with respect to infection times t_{ik} for $k \neq j$ (and implicitly, outcomes $Y_{ik}(T_i)$). Since $Y_{ij}(t) = \mathbb{1}\{t_{ij} < t\}$, we will employ expectation with respect to $Y_{ij}(t)$ and t_{ij} interchangeably, so $\mathbb{E}_{t_{ij}}[Y_{ij}(t)] = \mathbb{E}_{Y_{ij}(t)}[Y_{ij}(t)]$. Let $\mathbf{x}_i = (x_{i1}, \ldots, x_{in_i})$ be the vector of covariate x in cluster i, and $\mathbb{E}_{\mathbf{x}_{i,-j}}[\cdot]$ denote expectation with respect to x_{ik} for $k \neq j$. By iterating expectations, we can decompose the conditional expectations that comprise the risk ratio as follows,

$$\mathbb{E}[Y_{ij}(T_i)|x_{ij} = x] = \mathbb{E}_{H_i}\left[\mathbb{E}_{\mathbf{x}_{i,-j}}\left[\mathbb{E}_{\mathbf{t}_{i,-j}}\left[\mathbb{E}_{t_{ij}}[Y_{ij}(T_i) \mid x_{ij} = x, \mathbf{t}_{i,-j}, \mathbf{x}_{i,-j}, H_i] \mid x_{ij} = x, \mathbf{x}_{i,-j}, H_i\right] \mid x_{ij} = x, H_i\right] \mid x_{ij} = x\right].$$

At time T_i, the innermost expectation is

$$\mathbb{E}_{t_{ij}}[Y_{ij}(T_i) \mid x_{ij} = x, \mathbf{x}_{i,-j}, \mathbf{t}_{i,-j}, H_i] = 1 - \exp\left(-e^{x\beta}\int_0^{T_i}\left(\alpha_i(t) + \sum_{k=1}^{n_i}\mathbb{1}\{t_{ik} < t\}\omega_{ikj}(t - t_{ik})e^{x_{ik}\gamma}\right) \mathrm{d}t\right).$$

Lemma 2. *Let X be a non-negative random variable that takes at least some positive values, and let a be a non-negative constant. Then*

$$\frac{\mathbb{E}_X[1 - \exp(-aX)]}{\mathbb{E}_X[1 - \exp(-X)]} < 1 \text{ iff } a < 1$$

$$\frac{\mathbb{E}_X[1 - \exp(-aX)]}{\mathbb{E}_X[1 - \exp(-X)]} > 1 \text{ iff } a > 1$$

$$\frac{\mathbb{E}_X[1 - \exp(-aX)]}{\mathbb{E}_X[1 - \exp(-X)]} = 1 \text{ iff } a = 1$$

Proof. Let $a < 1$.

$$\frac{\mathbb{E}_X[1 - \exp(-aX)]}{\mathbb{E}_X[1 - \exp(-X)]} < 1 \Leftrightarrow \mathbb{E}_X[\exp(-aX)] - \mathbb{E}_X[\exp(-X)] > 0$$

$$\mathbb{E}_X[\exp(-aX)] - \mathbb{E}_X[\exp(-X)] = \int_0^\infty [\exp(-ax) - \exp(-x)]f(x)\ \mathrm{d}x > 0 \Leftrightarrow a < 1.$$

The proof for $a > 1$ and $a = 1$ is similar. □

Result 5: No within-cluster contagion

Proof. Suppose $\omega_{ikj}(t) = 0$ for all t and $\mathbf{x}_i \perp\!\!\!\perp \{\alpha_i(t), n_i, T_i\}$. Then

$$\begin{aligned}
RR &= \frac{\mathbb{E}[Y_{ij}(T_i) \mid x_{ij} = 1]}{\mathbb{E}[Y_{ij}(T_i) \mid x_{ij} = 0]} \\
&= \frac{\mathbb{E}_{H_i}[\mathbb{E}_{\mathbf{x}_{i,-j}}[\mathbb{E}_{\mathbf{t}_{i,-j}}[1 - \exp(-e^\beta \int_0^{T_i} \alpha_i(t)\ \mathrm{d}t) \mid x_{ij} = 1, \mathbf{x}_{i,-j}, H_i] \mid x_{ij} = 1, H_i] \mid x_{ij} = 1]}{\mathbb{E}_{H_i}[\mathbb{E}_{\mathbf{x}_{i,-j}}[\mathbb{E}_{\mathbf{t}_{i,-j}}[1 - \exp(- \int_0^{T_i} \alpha_i(t)\ \mathrm{d}t) \mid x_{ij} = 0, \mathbf{x}_{i,-j}, H_i] \mid x_{ij} = 0, H_i] \mid x_{ij} = 0]} \\
&= \frac{\mathbb{E}_{H_i}[\mathbb{E}_{\mathbf{x}_{i,-j}}[\mathbb{E}_{\mathbf{t}_{i,-j}}[1 - \exp(-e^\beta \int_0^{T_i} \alpha_i(t)\ \mathrm{d}t) \mid H_i] \mid x_{ij} = 1, H_i] \mid x_{ij} = 1]}{\mathbb{E}_{H_i}[\mathbb{E}_{\mathbf{x}_{i,-j}}[\mathbb{E}_{\mathbf{t}_{i,-j}}[1 - \exp(- \int_0^{T_i} \alpha_i(t)\ \mathrm{d}t) \mid H_i] \mid x_{ij} = 0, H_i] \mid x_{ij} = 0]} \\
&= \frac{\mathbb{E}_{H_i}[\mathbb{E}_{\mathbf{x}_{i,-j}}[1 - \exp(-e^\beta \int_0^{T_i} \alpha_i(t)\ \mathrm{d}t) \mid x_{ij} = 1, H_i] \mid x_{ij} = 1]}{\mathbb{E}_{H_i}[\mathbb{E}_{\mathbf{x}_{i,-j}}[1 - \exp(- \int_0^{T_i} \alpha_i(t)\ \mathrm{d}t) \mid x_{ij} = 0, H_i] \mid x_{ij} = 0]} \\
&= \frac{\mathbb{E}_{H_i}[1 - \exp(-e^\beta \int_0^{T_i} \alpha_i(t)\ \mathrm{d}t) \mid x_{ij} = 1]}{\mathbb{E}_{H_i}[1 - \exp(- \int_0^{T_i} \alpha_i(t)\ \mathrm{d}t) \mid x_{ij} = 0]} \\
&= \frac{\mathbb{E}_{H_i}[1 - \exp(-e^\beta \int_0^{T_i} \alpha_i(t)\ \mathrm{d}t)]}{\mathbb{E}_{H_i}[1 - \exp(- \int_0^{T_i} \alpha_i(t)\ \mathrm{d}t)]},
\end{aligned}$$

where the third line follows because the distribution of $Y_{ij}(T_i)$ does not depend on $\mathbf{x}_{i,-j}$, and only depends on x_{ij} via multiplicative constant e^β; the fourth line follows because $Y_{ij}(T_i)$ does not depend on $\mathbf{t}_{i,-j}$, and the fifth line follows because $Y_{ij}(T_i)$ is independent of $\mathbf{x}_{i,-j}$ and $\mathbf{x}_i$ is independent of H_i. Since the only difference between the numerator and denominator is the multiplicative constant e^β, by Lemma 2 the risk ratio is direction-unbiased. □

Result 6: Independent x

Proof of Result 6. Suppose the covariates $\mathbf{x}_i$ are jointly independent and $\mathbf{x}_i \perp\!\!\!\perp \{\alpha_i(t), \omega_{ikj}(t), n_i, T_i\}$. For any time $t > 0$, we can write the cumulative hazard to subject j in cluster i as

$$\Lambda_{ij}(t) = e^{x_{ij}\beta} \int_0^{T_i} (1 - Y_{ij}(s)) \left(\alpha_i(s) + \sum_{k=1}^{n_i} Y_{ik}(s)\omega_{ikj}(s - t_{ik})e^{x_{ik}\gamma} \right)\ \mathrm{d}s$$

For ease of exposition, let

$$\xi_i(t) = \alpha_i(t) + \sum_{k=1}^{n_i} Y_{ik}(t)\omega_{ikj}(t - t_{ik})e^{x_{ik}\gamma}.$$

Then

$$
\begin{aligned}
RR &= \frac{\mathbb{E}[Y_{ij}(T_i) \mid x_{ij}=1]}{\mathbb{E}[Y_{ij}(T_i) \mid x_{ij}=0]} \\
&= \frac{\mathbb{E}_{H_i}[\mathbb{E}_{\mathbf{x}_{i,-j}}[\mathbb{E}_{\mathbf{t}_{i,-j}}[1-\exp(-e^{\beta}\int_0^{T_i}(1-Y_{ij}(t))\xi_i(t)\ \mathrm{d}t) \mid \mathbf{x}_{i,-j}, x_{ij}=1, H_i] \mid x_{ij}=1, H_i] \mid x_{ij}=1]}{\mathbb{E}_{H_i}[\mathbb{E}_{\mathbf{x}_{i,-j}}[\mathbb{E}_{\mathbf{t}_{i,-j}}[1-\exp(-\int_0^{T_i}(1-Y_{ij}(t))\xi_i(t)\ \mathrm{d}t) \mid \mathbf{x}_{i,-j}, x_{ij}=0, H_i] \mid x_{ij}=0, H_i] \mid x_{ij}=0]} \\
&= \frac{\mathbb{E}_{H_i}[\mathbb{E}_{\mathbf{x}_{i,-j}}[\mathbb{E}_{\mathbf{t}_{i,-j}}[1-\exp(-e^{\beta}\int_0^{T_i}(1-Y_{ij}(t))\xi_i(t)\ \mathrm{d}t) \mid \mathbf{x}_{i,-j}, H_i] \mid H_i]]}{\mathbb{E}_{H_i}[\mathbb{E}_{\mathbf{x}_{i,-j}}[\mathbb{E}_{\mathbf{t}_{i,-j}}[1-\exp(-\int_0^{T_i}(1-Y_{ij}(t))\xi_i(t)\ \mathrm{d}t) \mid \mathbf{x}_{i,-j}, H_i] \mid H_i]]},
\end{aligned}
$$

because the distribution of $\mathbf{t}_{i,-j}$ is invariant to conditioning on $x_{ij}=1$ or $x_{ij}=0$, when subject j is susceptible, and because by joint independence of $\mathbf{x}_i$, the expectation $\mathbb{E}_{\mathbf{x}_{i,-j}}[\cdot]$ is also invariant to conditioning on $x_{ij}=1$ or $x_{ij}=0$, and x_{ij} is independent of H_i. By Lemma 2 the risk ratio is direction-unbiased. □

3 Risk ratio maps

3.1 Exact risk ratio maps for clusters of size two

Figures 1 and 2 provide the plots that illustrate analytic result (1) for different combinations of force of infection parameters α and ω as a function of susceptibility (β) and infectiousness (γ) parameters. Figure 1 shows the exact expected value of the $log[RR]$, and Figure 2 shows the regions of the direction bias of the risk ratio as an approximation of the hazard ratio for the same combinations of parameters α, ω and observation time T_i. We have demonstrated in Result 4 that for a given combination of (β, γ), direction bias depends on the observation time and the ratio of ω/α. In Figures 1 and 2 observation time is chosen such that cumulative incidence when $\beta = 0$ and $\gamma = 0$ is kept constant around 0.15 for a given ratio of ω/α. With observation time chosen this way, the behavior of the bias is exactly the same for the same ratio of ω/α regardless of the absolute values of these two parameters.

3.2 Simulation results

Exact expression for the expectation of the risk ratio is intractable in general case. This section provides a summary of the simulation results for different study designs and combinations of epidemiologic parameters. In simulations we vary:

- Distribution of covariate x: block randomization, independent Bernoulli, cluster randomization;
- Cluster size distribution: fixed size, Poisson distributed;
- Observation period: constant at different values, variable;
- Subjects infected at baseline: $Pr[Y(0) = 1] = 0$; $Pr[Y(0) = 1] > 0$.
- Ratio ω/α.

3.2.1 Distribution of covariate x when cluster size is constant

First, we look at the behavior of the bias of the risk ratio as an approximation of the hazard ratio for different types of the distribution of covariate x when cluster size is constant. Figure 3 shows simulation results for block randomized distribution of x, Figure 4 - for independent Bernoulli distribution of x, and Figure 5 - for cluster randomized distribution of x. In all simulations presented in this subsection (Figures 3 - 5) the following parameters are held constant:

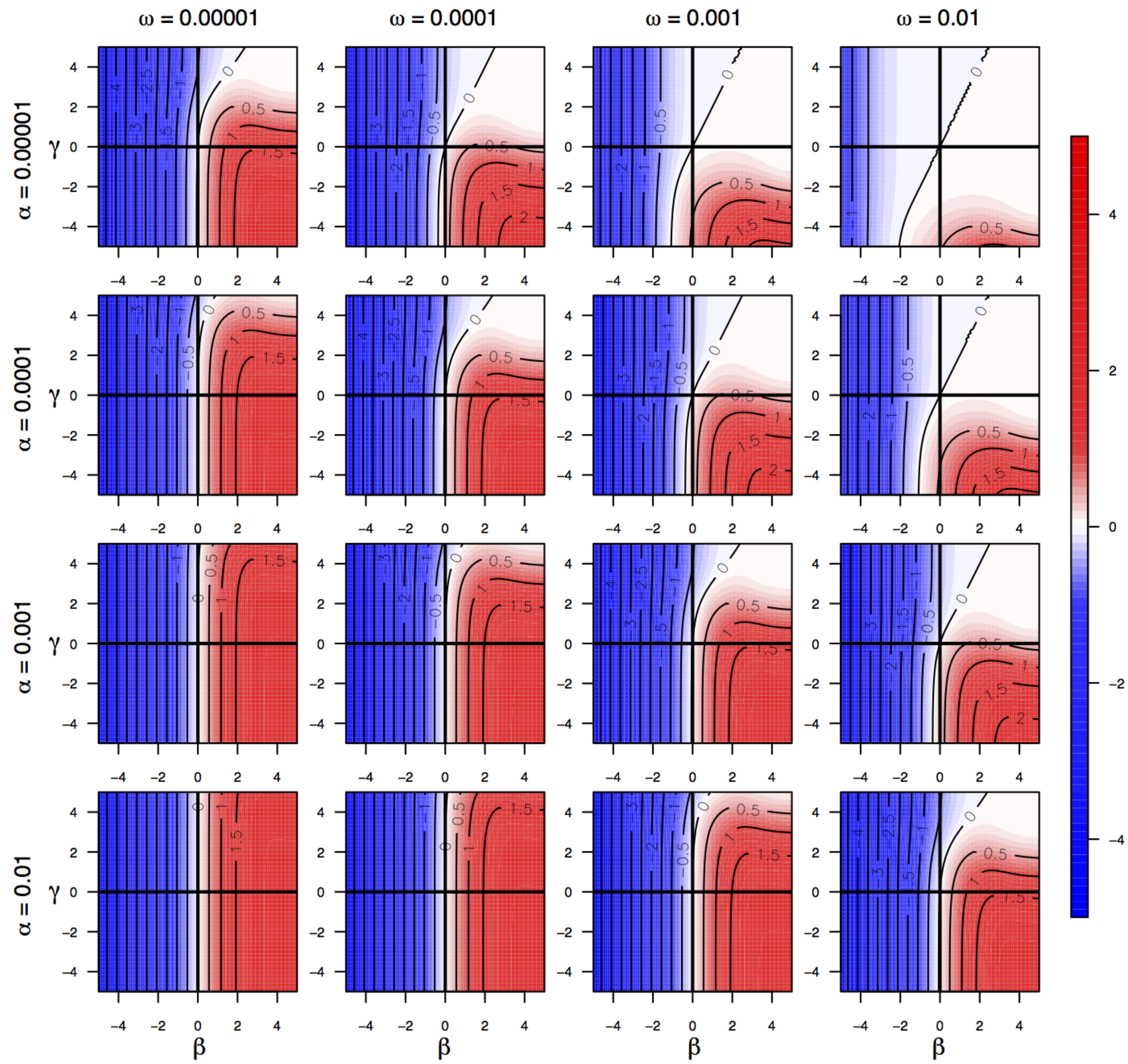

Figure 1: Computed $\log[RR]$ as a function of β and γ in clusters of size two, when exactly one subject per cluster has a value of $x = 1$. Observation time is constant and chosen such that the cumulative incidence when $\beta = 0$ and $\gamma = 0$ is approximately 0.15 for a given combination of α and ω.

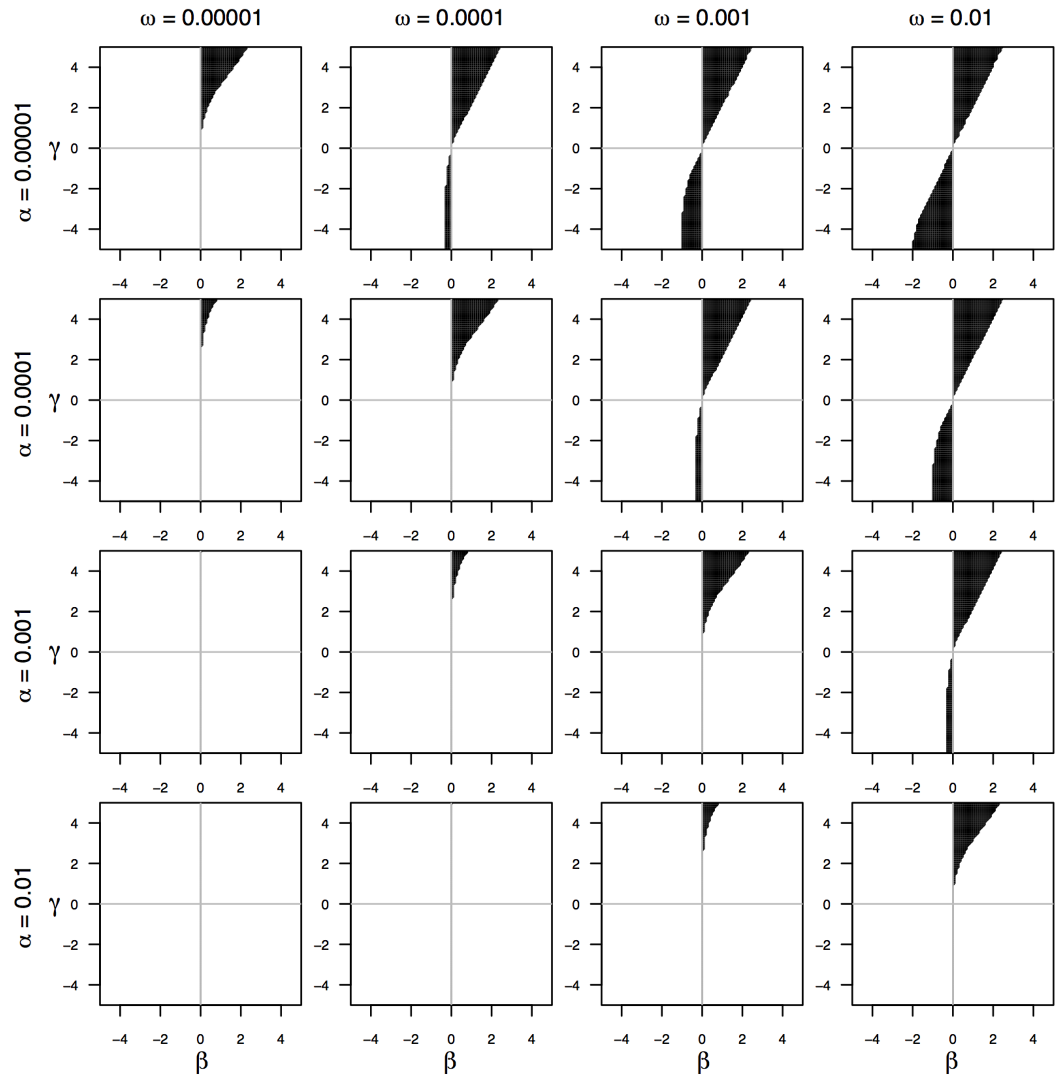

Figure 2: Regions of direction bias of computed $\log[RR]$ as a function of β and γ in clusters of size two, when exactly one subject per cluster has a value of $x = 1$. Observation time is constant and chosen such that the cumulative incidence when $\beta = 0$ and $\gamma = 0$ is approximately 0.15 for a given combination of α and ω.

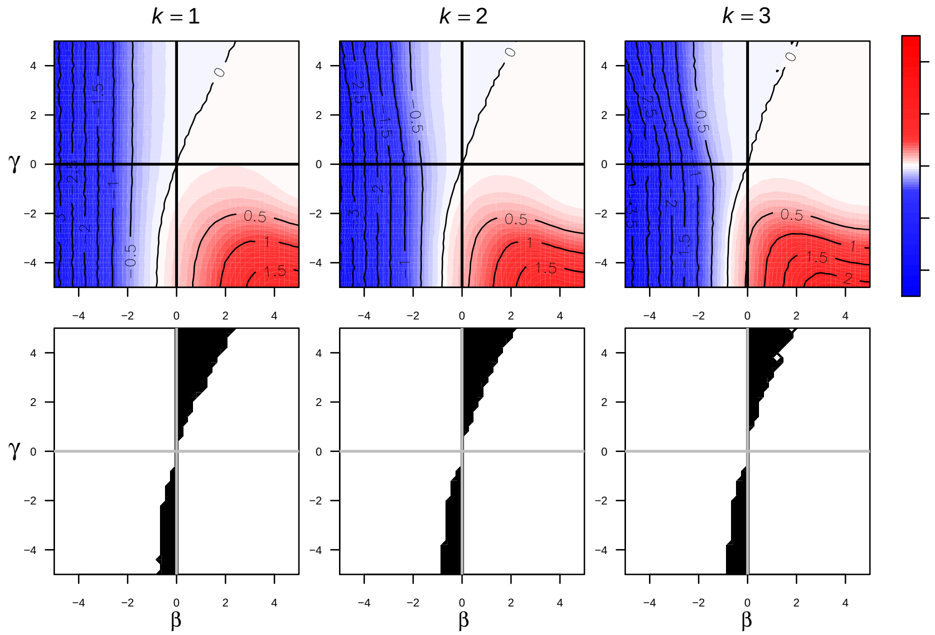

Figure 3: $\log[RR]$ (top row) and region of direction bias (bottom row) as a function of β and γ when cluster size is constant and x is block randomized: $\sum_{j=1}^{n_i} x_{ij} = k$.

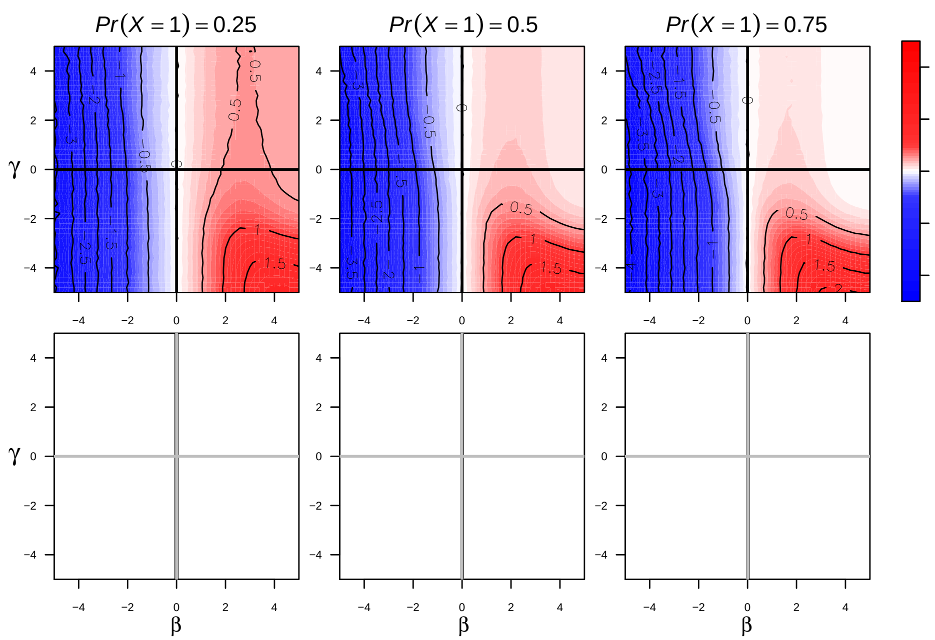

Figure 4: $\log[RR]$ (top row) and region of direction bias (bottom row) as a function of β and γ when cluster size is constant and x has independent Bernoulli distribution with varying $Pr[x = 1]$.

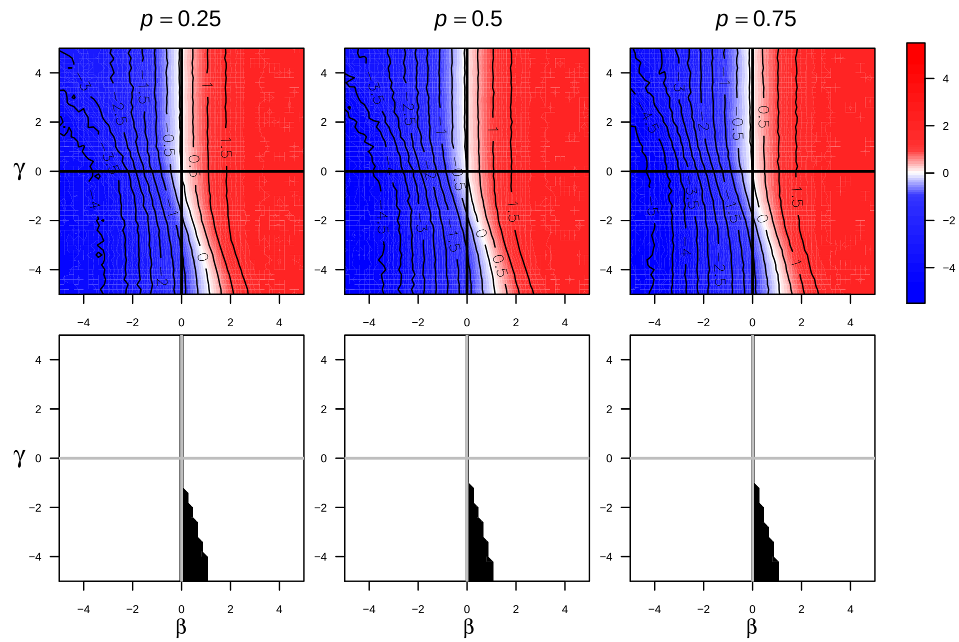

Figure 5: $\log[RR]$ (top row) and region of direction bias (bottom row) as a function of β and γ when cluster size is constant and x is cluster randomized: proportion p of clusters have $\sum_{j=1}^{n_i} x_{ij} = 4$, and remaining $1-p$ have $\sum_{j=1}^{n_i} x_{ij} = 0$.

- Force of infection parameters: $\alpha = 0.0001$, $\omega = 0.01$;
- Cluster size: $n_i = 4$ for $i = 1, \ldots, N$;
- Observation time: $T_i = 450$ for $i = 1, \ldots, N$ (giving cumulative incidence of approximately 0.15 when $\beta = 0$ and $\gamma = 0$);
- All subjects uninfected at baseline: $Y_{ij}(0) = 0$ for $i = 1, \ldots, N$ and $j = 1, 2, 3, 4$;
- Simulation parameters: number of clusters $N = 500$, number of simulations per combination of parameters = 200.

As demonstrated analytically in the Result 6, independent Bernoulli distribution of x results in the direction-unbiased risk ratio (Figure 4). Lack of joint independence in the distribution of x, however, generally results in the risk ratio exhibiting direction bias in some regions of the (β, γ) parameter space. Figure 3 shows that bias patterns under block randomization and constant cluster size mimic that of the simple two-person cluster case. Figure 5 shows that cluster randomized distribution of x leads to the direction bias in the regions where β and γ have opposite signs, and when the risk ratio is direction unbiased, it is not necessarily biased towards the null, but may be biased away from the null.

3.2.2 Variable cluster size under different distributions of covariate x

In this subsection we explore the behavior of the risk ratio bias under variable cluster size, which follows Poisson distribution with different means. Figures 6 - 9 show simulation results for the average cluster size between two and five, under different distributions of covariate x. In Figure 6 covariate x is block randomized such that for any cluster size only one subject per cluster has $x = 1$; Figure 7 shows block randomization of x, when in any cluster half of the subjects have $x = 1$; in Figure 8 covariate x has Bernoulli distribution with $Pr[x = 1] = 0.5$, and Figure 9 shows the results for cluster randomized

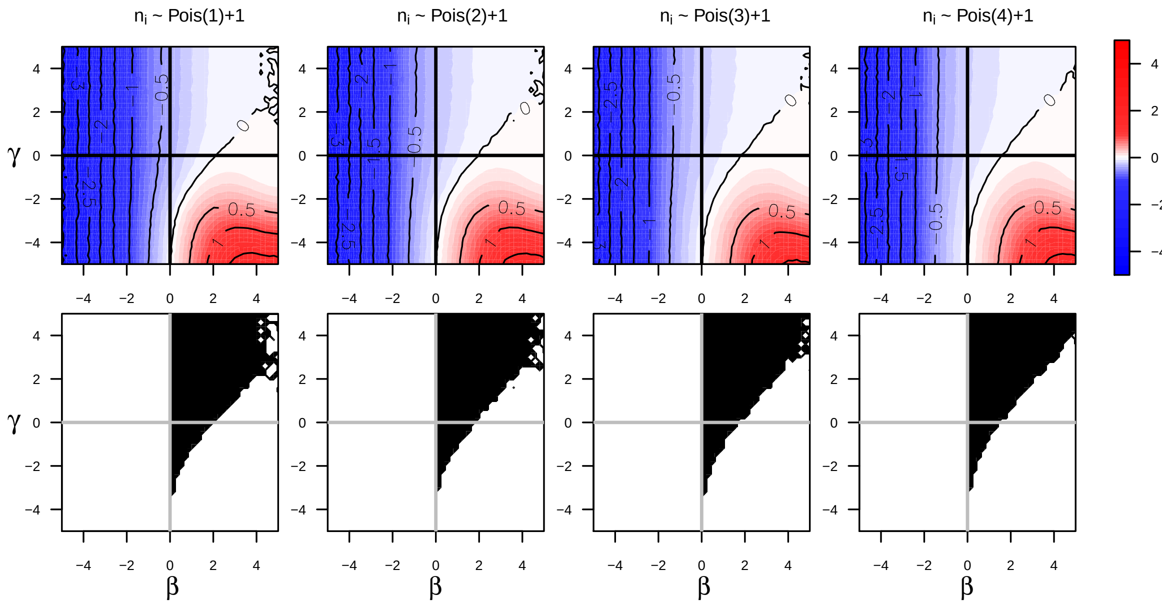

Figure 6: $\log[RR]$ (top row) and region of direction bias (bottom row) as a function of β and γ when cluster size $n_i \sim \text{Pois}(\mu) + 1$ and x is block randomized such that $\sum_{j=1}^{n_i} x_{ij} = 1$ for all i.

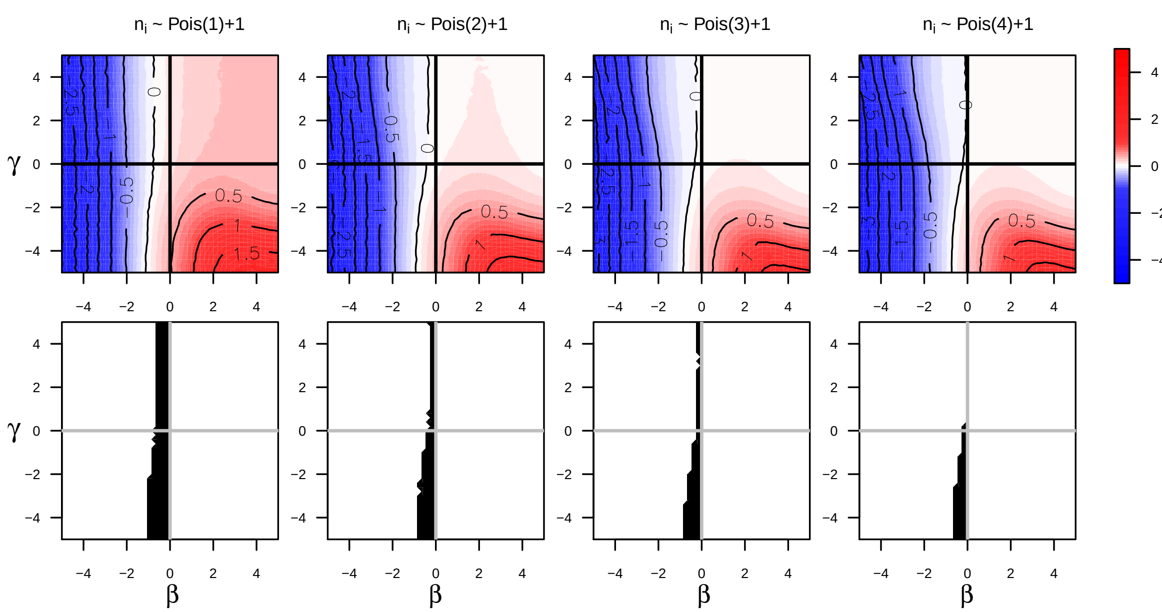

Figure 7: $\log[RR]$ (top row) and region of direction bias (bottom row) as a function of β and γ when cluster size $n_i \sim \text{Pois}(\mu) + 1$ and x is block randomized such that $\sum_{j=1}^{n_i} x_{ij} = \lfloor n_i/2 \rfloor$ for all i.

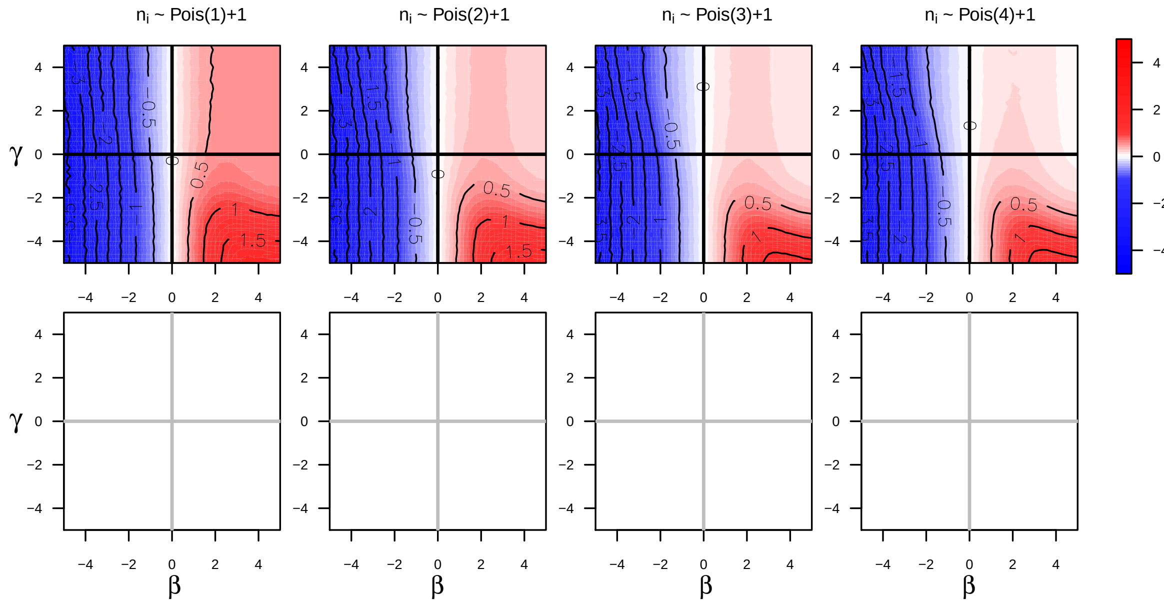

Figure 8: $\log[RR]$ (top row) and region of direction bias (bottom row) as a function of β and γ when cluster size $n_i \sim \text{Pois}(\mu) + 1$ and x has independent Bernoulli distribution with $Pr[x = 1] = 0.5$.

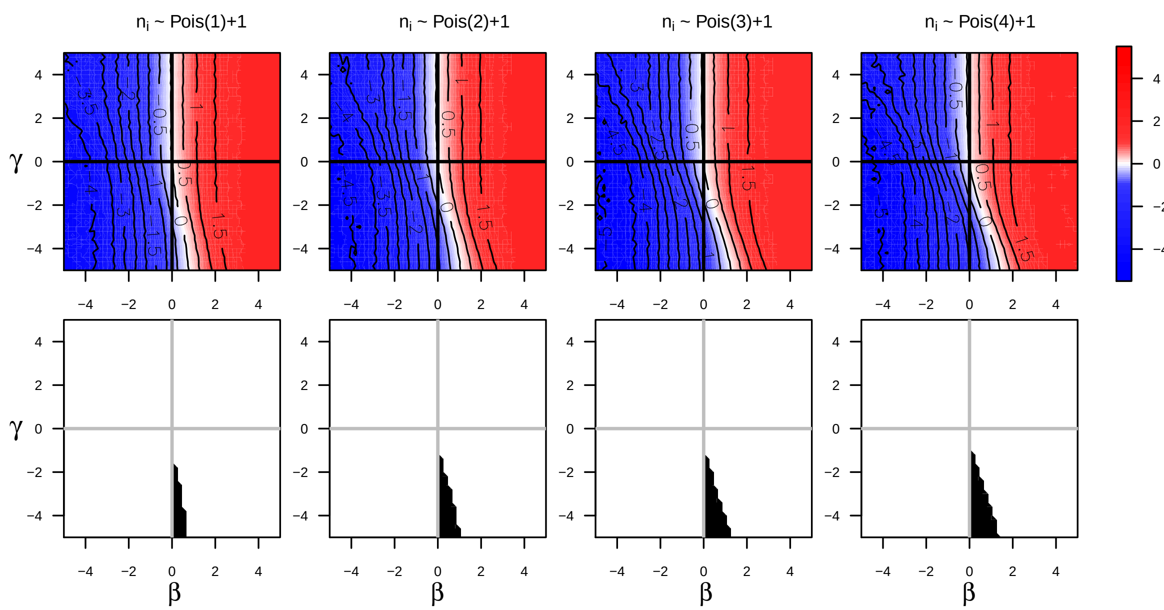

Figure 9: $\log[RR]$ (top row) and region of direction bias (bottom row) as a function of β and γ when cluster size $n_i \sim \text{Pois}(\mu) + 1$ and x is cluster randomized: half of clusters have $\sum_{j=1}^{n_i} x_{ij} = n_i$, and remaining half have $\sum_{j=1}^{n_i} x_{ij} = 0$.

distribution of x such that in half of clusters all subjects have $x = 1$, and in the remaining half everyone has $x = 0$. In all simulations presented in this subsection (Figures 6 - 9) the following parameters are held constant:

- Force of infection parameters: $\alpha = 0.0001$, $\omega = 0.01$;
- Observation time: $T_i = 750$, when $n_i \sim \text{Pois}(1) + 1$; $T_i = 525$, when $n_i \sim \text{Pois}(2) + 1$; $T_i = 450$, when $n_i \sim \text{Pois}(3) + 1$; and $T_i = 330$, when $n_i \sim \text{Pois}(4) + 1$ (giving cumulative incidence of approximately 0.15 when $\beta = 0$ and $\gamma = 0$);
- All subjects uninfected at baseline: $Y_{ij}(0) = 0$ for $i = 1, \ldots, N$ and $j = 1, \ldots, n_i$;
- Simulation parameters: number of clusters $N = 500$, number of simulations per combination of parameters = 200.

When covariate x is block randomized, the behavior of risk ratio bias changes substantially when we allow cluster size to vary compared to holding it constant. Figures 6, 7 and 3 demonstrate very different patterns of bias behavior, while all having block randomized distribution of x. When cluster size is fixed (Figure 3), risk ratio is direction-unbiased when $\gamma = 0$, and bias in direction requires γ being more extreme than and having the same sign as β. However, when cluster size varies under block randomized x, the risk ratio is not necessarily direction-unbiased when $\gamma = 0$, or when γ and β have opposite signs. Figures 6 and 7 show that under variable cluster size and block randomized x, bias behaves very differently depending on proportion of subjects with $x = 1$ per cluster. Increasing imbalance in the distribution of x generally makes things worse under such study design (compare Figure 6 to Figure 7).

When x has independent Bernoulli or cluster randomized distribution, bias of the risk ratio as an approximation of hazard ratio generally behaves similarly for constant or variable cluster size (compare Figure 8 to Figure 4 for Bernoulli distributed x, and Figure 9 to Figure 5 for cluster randomized distribution of x).

3.2.3 Duration and variability of observation time T_i

This subsection looks at the impact of duration and variability of observation time on the risk ratio bias under different distributions of covariate x. Figures 10 - 12 show simulation results for three constant durations of observation ($T_i = 50$, 450 and 1500) and one, where observation time is exponentially distributed with rate = 1/450. Figure 10 shows the results for constant cluster size and block randomized distribution of x, Figure 11 - for variable cluster size and independent Bernoulli distribution of x, and Figure 12 - for constant cluster size and cluster randomized distribution of x. In all simulations presented in this subsection (Figures 10 - 12) the following parameters are held constant:

- Force of infection parameters: $\alpha = 0.0001$, $\omega = 0.01$;
- All subjects uninfected at baseline: $Y_{ij}(0) = 0$ for $i = 1, \ldots, N$ and $j = 1, \ldots, n_i$;
- Simulation parameters: number of clusters $N = 500$, number of simulations per combination of parameters = 200.

With all other parameters held the same, increasing duration of observation leads to the increase in cumulative incidence. Under block randomized (Figure 10) and independent Bernoulli (Figure 11) distribution of x higher cumulative incidence increases the bias of the risk ratio as an approximation of the hazard ratio. However, under cluster randomized distribution of x (Figure 12) increasing duration of observation reduces the region, where the risk ratio exhibits direction bias, but does not necessarily reduce the bias in absolute value. Under any of the three distributions of x variable duration of observation does not appreciably change the behavior of risk ratio bias compared to constant T_i.

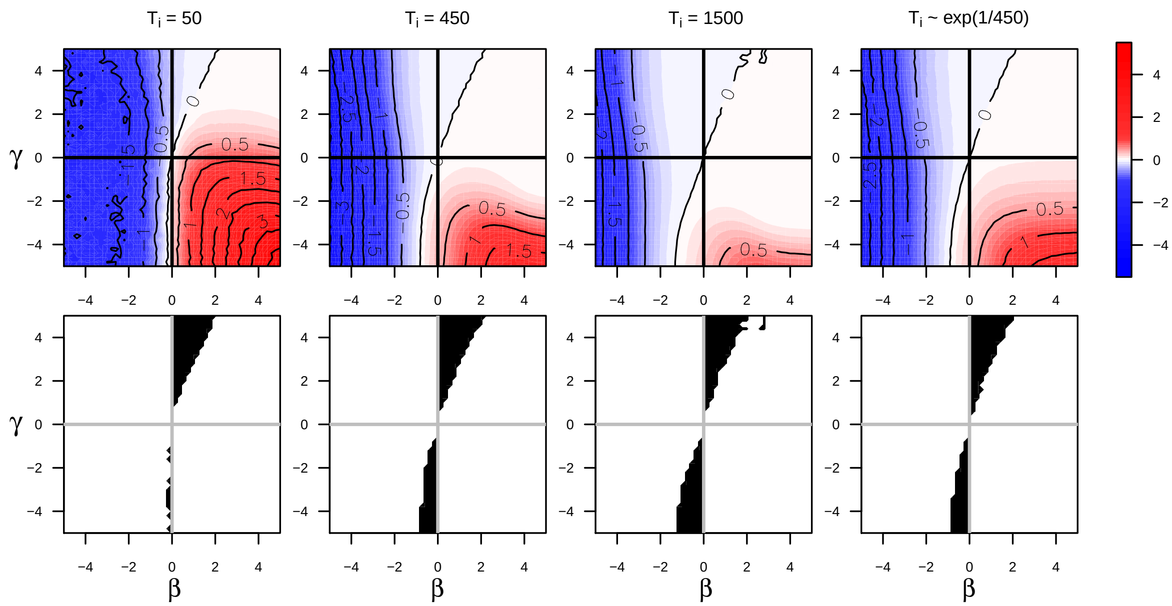

Figure 10: log[RR] (top row) and region of direction bias (bottom row) as a function of β and γ for different observation time T_i, when cluster size is constant ($n_i = 4$ for all i), and x is block randomized such that $\sum_{j=1}^{n_i} x_{ij} = 2$.

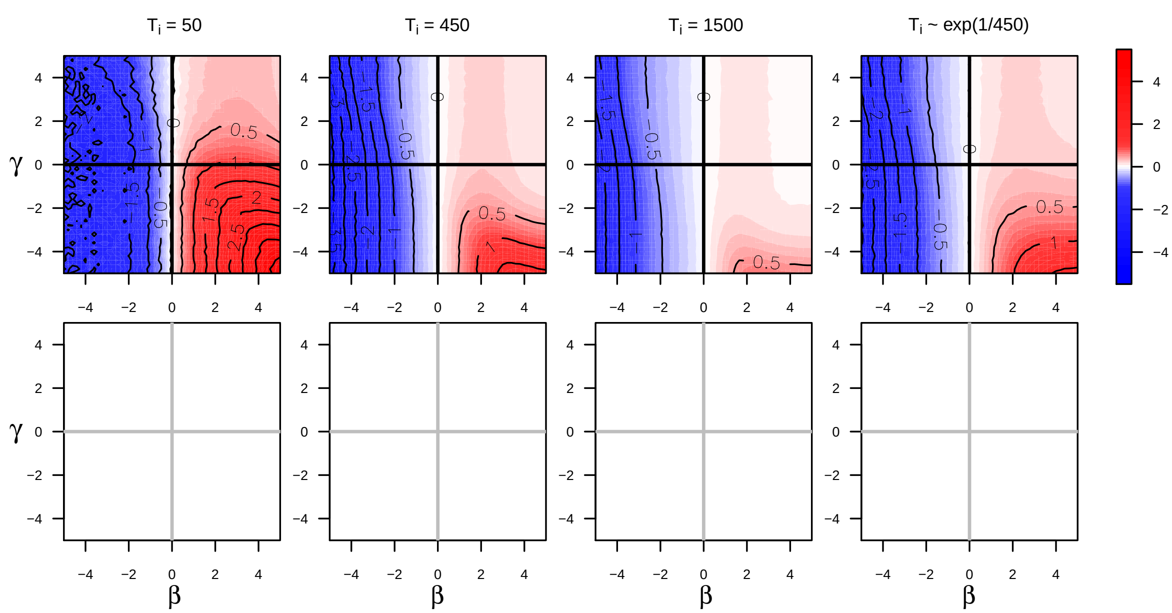

Figure 11: log[RR] (top row) and region of direction bias (bottom row) as a function of β and γ for different observation time T_i, when cluster size $n_i \sim$ Pois(3) + 1 and x has independent Bernoulli distribution with $Pr[x = 1] = 0.5$.

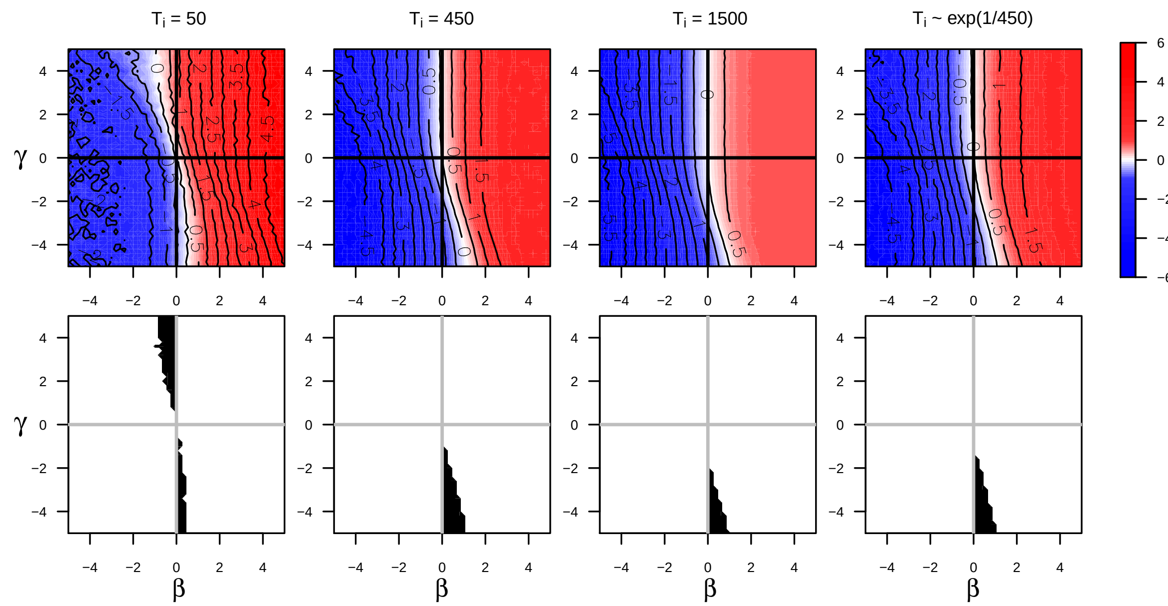

Figure 12: $\log[RR]$ (top row) and region of direction bias (bottom row) as a function of β and γ for different observation time T_i, when cluster size is constant ($n_i = 4$ for all i), and x is cluster randomized: half of clusters have $\sum_{j=1}^{n_i} x_{ij} = 4$, and remaining half have $\sum_{j=1}^{n_i} x_{ij} = 0$.

3.2.4 Infections at time zero

In the simple case of clusters of size two and in all previous simulations we assumed that all subjects are uninfected at time zero (baseline). In practice, however, such study design is rarely a case. When researchers study infection transmission, they often select these clusters based on having at least one infected subject per cluster at baseline assessment (often called "index" case). Sometimes studies would include a mix of clusters with and without infected subjects at baseline. In observational studies the distribution of covariate x is given, and if β and/or γ is not zero, then the distribution of infections at baseline assessment is not independent of x. In experimental studies baseline distribution of infections may be independent of treatment x, and researchers can choose, whether subjects infected at baseline may or may not be assigned to treatment ($x = 1$). In this subsection we explore the behavior of the risk ratio bias under the presence of infections at time zero.

Figures 13 and 14 show the estimate of $\log[RR]$ and regions of direction bias for a range of values of $Pr[Y(0) = 1|X = 1]$ and $Pr[Y(0) = 1|X = 0]$ under block randomized distribution of x and constant cluster size, and Figures 15 and 16 - under independent Bernoulli distribution of x and variable cluster size. In all plots the observation time T_i was chosen such that cumulative incidence when $\beta = 0$ and $\gamma = 0$ is approximately 0.15. The risk ratio was computed among subjects uninfected at time zero. In most of the simulations presented in Figures 13 - 16 number of clusters $N = 500$. In some of the plots we increased N to 1,000 and 5,000 to ensure convergence of the averages to expectations. For the same reason the number of simulations per combination of parameters varies between 100 and 2,000.

Figures 17-18 summarize simulations that represent observational study design, which includes clusters based on having at least one "index" case at baseline. These simulations were conducted as follows. We started with all subjects being uninfected and ran simulation for $T_i = 75$ (Figure 17) or $T_i = 150$ (Figure 18). This time point then became the time of "baseline" assessment, at which we selected clusters with at least one infected subject. For different values of β the initial number of clusters N was chosen

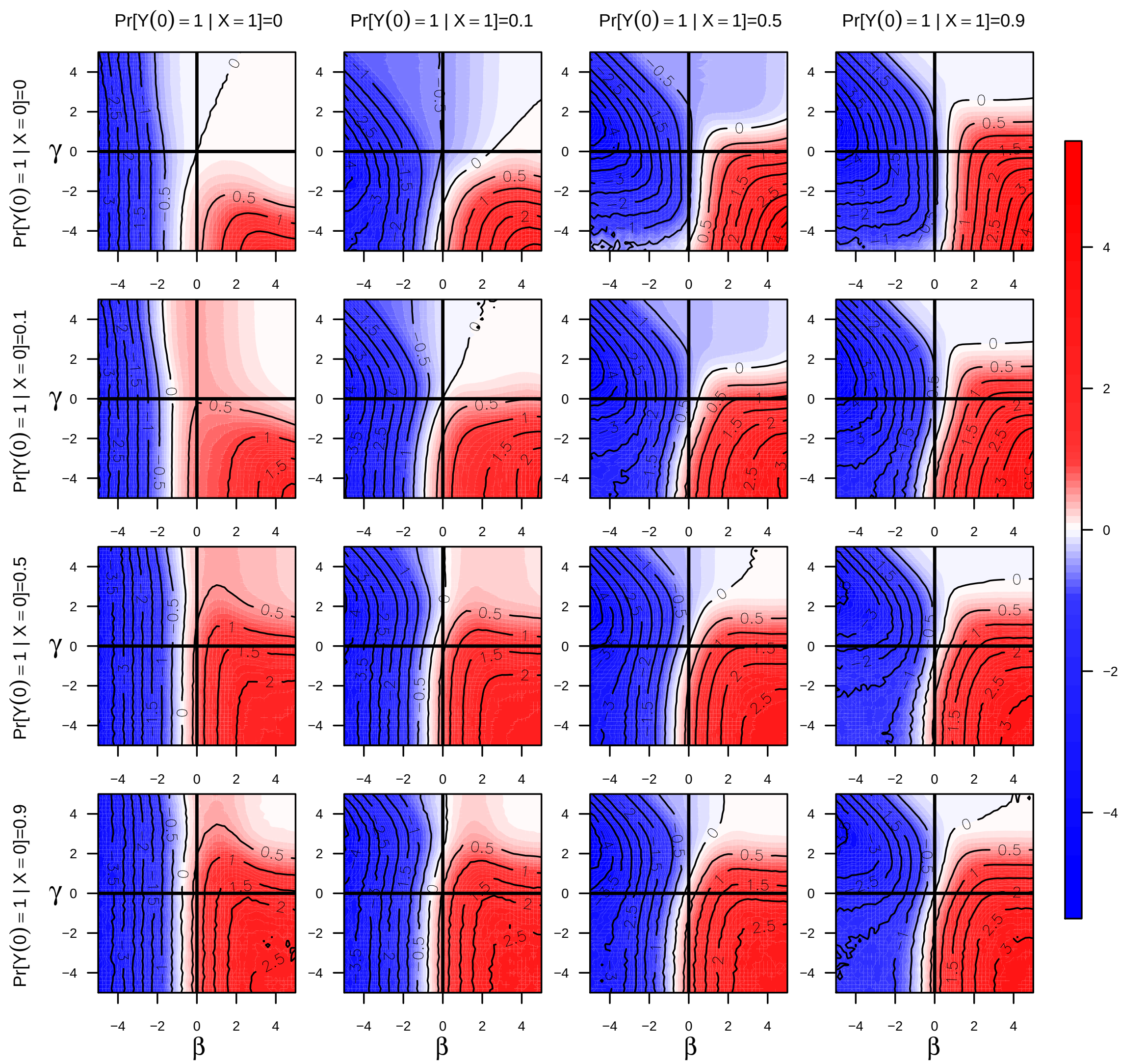

Figure 13: $\log[RR]$ as a function of β and γ for a range of $Pr[Y(0) = 1|X = 1]$ and $Pr[Y(0) = 1|X = 0]$, when cluster size is constant ($n_i = 4$ for all i), and x is block randomized such that $\sum_{j=1}^{n_i} x_{ij} = 2$.

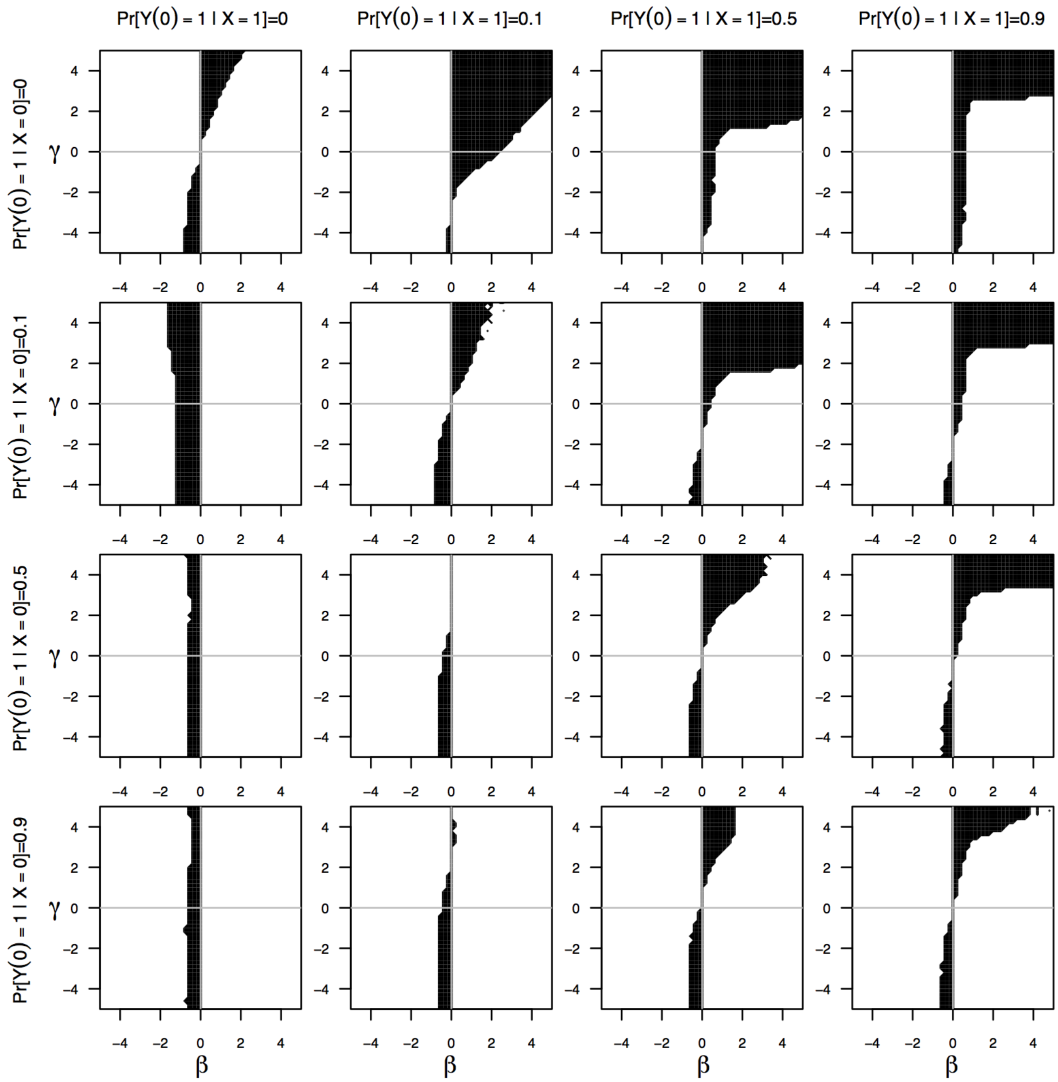

Figure 14: Regions of direction bias of $\log[RR]$ as a function of β and γ for a range of $Pr[Y(0) = 1|X = 1]$ and $Pr[Y(0) = 1|X = 0]$, when cluster size is constant ($n_i = 4$ for all i), and x is block randomized such that $\sum_{j=1}^{n_i} x_{ij} = 2$.

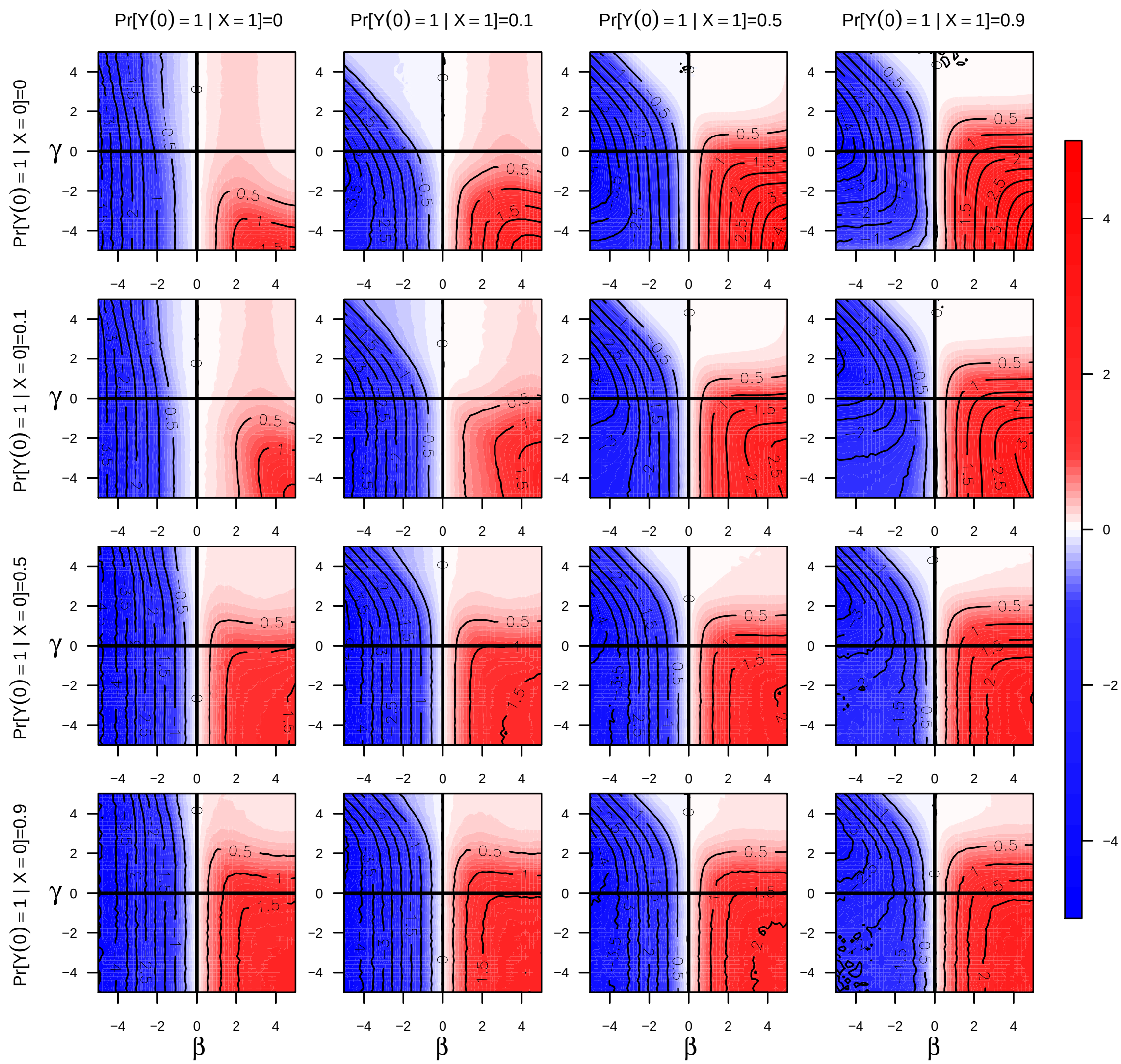

Figure 15: $\log[RR]$ as a function of β and γ for a range of $Pr[Y(0) = 1|X = 1]$ and $Pr[Y(0) = 1|X = 0]$, when cluster size $n_i \sim \text{Pois}(3) + 1$ and x has independent Bernoulli distribution with $Pr[x = 1] = 0.5$.

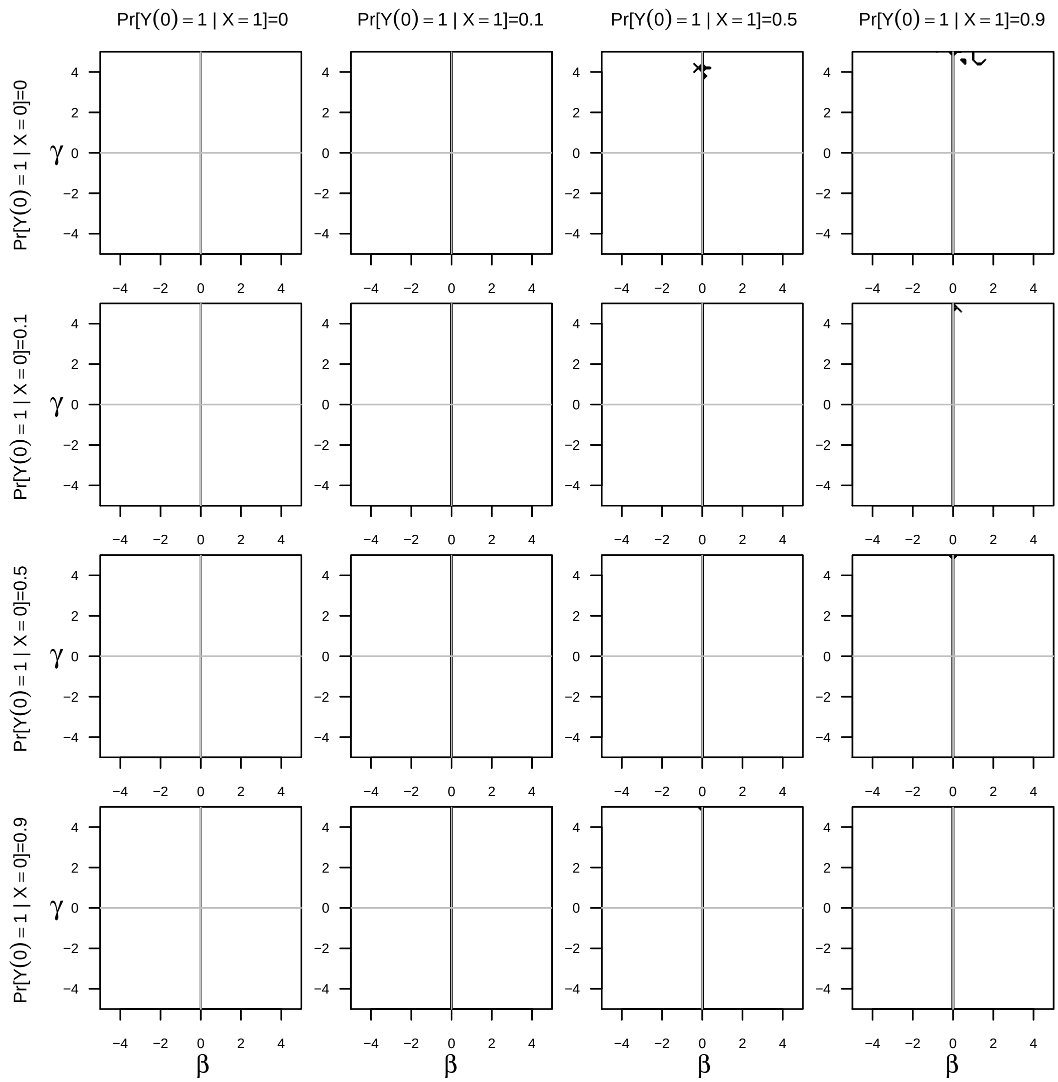

Figure 16: Regions of direction bias of $\log[RR]$ as a function of β and γ for a range of $Pr[Y(0) = 1|X = 1]$ and $Pr[Y(0) = 1|X = 0]$, when cluster size $n_i \sim \text{Pois}(3)+1$ and x has independent Bernoulli distribution with $Pr[x = 1] = 0.5$.

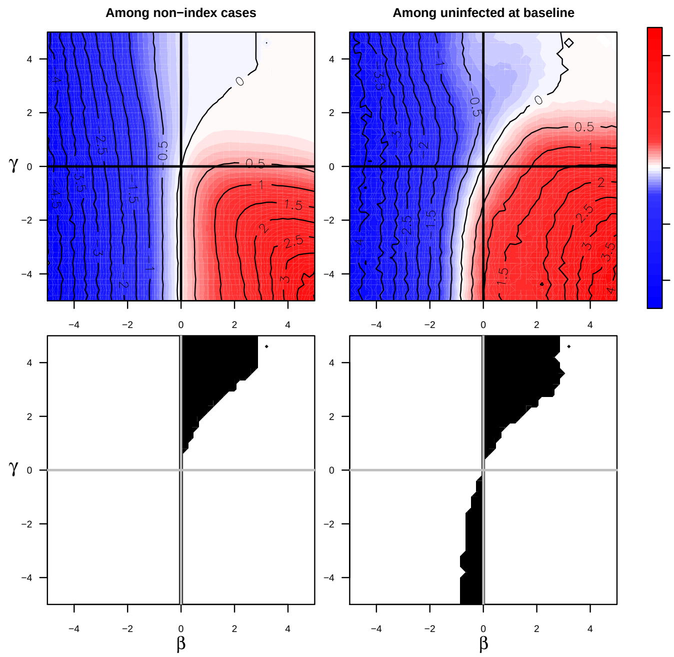

Figure 17: $\log[RR]$ (top row) and region of direction bias (bottom row) as a function of β and γ for clusters selected based on having at least one infection at "baseline", when cluster size is constant ($n_i = 4$ for all i), and x is block randomized such that $\sum_{j=1}^{n_i} x_{ij} = 2$. Risk ratio is calculated in two ways: among all "non-index" cases, and among cases uninfected at "baseline".

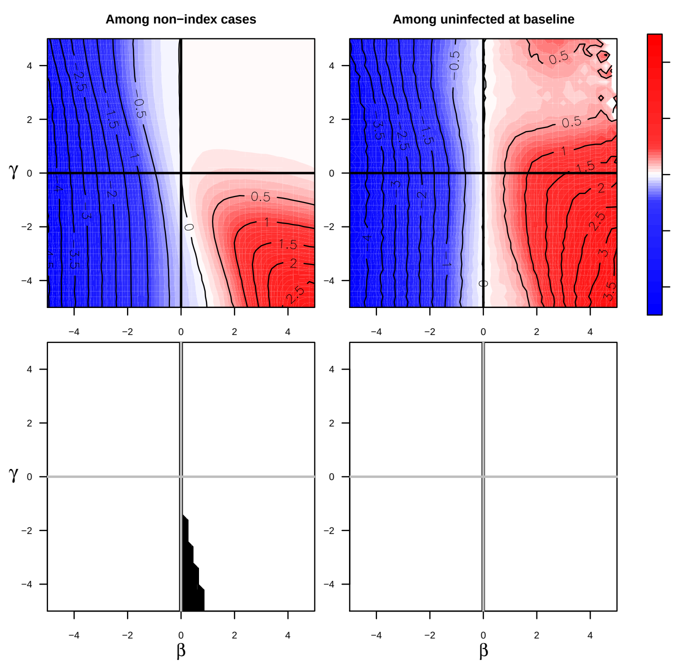

Figure 18: $\log[RR]$ (top row) and region of direction bias (bottom row) as a function of β and γ for clusters selected based on having at least one infection at "baseline", when cluster size $n_i \sim \text{Pois}(2) + 2$ and x has independent Bernoulli distribution with $Pr[x = 1] = 0.5$. Risk ratio is calculated in two ways: among all "non-index" cases, and among cases uninfected at "baseline".

such that the number of clusters with at least one infected at "baseline" assessment was approximately 500. If there were more than one subject per cluster infected at baseline, an "index" case was selected randomly from among them. We then ran simulation for $T_i = 10$ (resulting in cumulative incidence of approximately 0.15 among subjects uninfected at "baseline" when $\beta = 0$ and $\gamma = 0$) and calculated the risk ratio in two ways: among all subjects uninfected at "baseline", and among "non-index" cases. In Figure 17 number of simulations per combination of parameters = 50, and in Figure 18 - 200.

In all simulations presented in this subsection (Figures 13 - 18) force of infection parameters are held constant at the following values: $\alpha = 0.0001$, $\omega = 0.01$.

Introducing subjects infected at baseline with different probabilities conditional on the value of covariate x may result in substantial direction bias that generally increases with the increase of the difference in these conditional probabilities. Under constant cluster size and block randomized distribution of x, when $Pr[Y(0) = 1|X = 1] = Pr[Y(0) = 1|X = 0]$, bias generally behaves in the way similar to the same study design with no subjects infected at baseline (Figures 13 and 14). Under variable cluster size and independent Bernoulli distribution of x (Figures 15 and 16), the risk ratio is direction-unbiased.

When study clusters are selected based on having at least one subject per cluster infected at baseline ("index" case), bias behavior under constant cluster size and block randomized distribution of x is similar to having no subjects infected at baseline. Whether risk ratio is calculated among subjects uninfected at baseline, or excluding only "index" cases the risk ratio exhibits direction bias in the same regions of the (β, γ) parameter space. Under independent Bernoulli distribution of x, when we start with no subjects infected at time zero, the risk ratio is always direction-unbiased (Result 6). When we include clusters based on infections at "baseline", and calculate the risk ratio excluding all subjects infected at the start of observation, we still have this nice property of the risk ratio. However, when the risk ratio is calculated excluding only the "index" cases under the same conditions, direction-unbiasedness does not necessarily hold (Figure 18).

3.2.5 Ratio ω/α

This subsection looks at the influence of the ratio ω/α of per-subject within-cluster to exogenous force of infection. Figure 19 shows simulation results for different values of ω and α under constant cluster size and block randomized distribution of x; Figure 20 - under variable cluster size and independent Bernoulli distribution of x, Figure 21 - under variable cluster size and block randomized distribution of x, when exactly one subject per cluster has a value of $x = 1$, and Figure 22 - under variable cluster size and cluster randomized distribution of x. Similarly to the previous subsection, in all plots the observation time T_i was chosen such that the cumulative incidence when $\beta = 0$ and $\gamma = 0$ is approximately 0.15. In all simulations presented in this subsection (Figures 19 - 22) the following parameters are held constant:

- All subjects uninfected at baseline: $Y_{ij}(0) = 0$ for $i = 1, \ldots, N$ and $j = 1, \ldots, n_i$;
- Simulation parameters: number of clusters $N = 500$, number of simulations per combination of parameters = 200.

In the simple case of clusters of size two, for which we have derived analytic expression for the risk ratio bias, we have demonstrated that bias behavior is exactly the same for the same ratio of ω/α when observation time T_i is chosen such that it keeps cumulative incidence the same (Figures 1 and 2). Figures 19 and 20 show that this property holds for more complex study designs. Figure 21 shows that under the same conditions on T_i and block randomized distribution of x, the region of the (β, γ) space, where risk ratio exhibits direction bias increases with the increase of the ratio ω/α as proportionally more infections get attributed to within-cluster transmission. However, under cluster randomized distribution of x (Figure 22) region, where the risk ratio is not direction-unbiased, is largest when ratio ω/α gets closer to one.

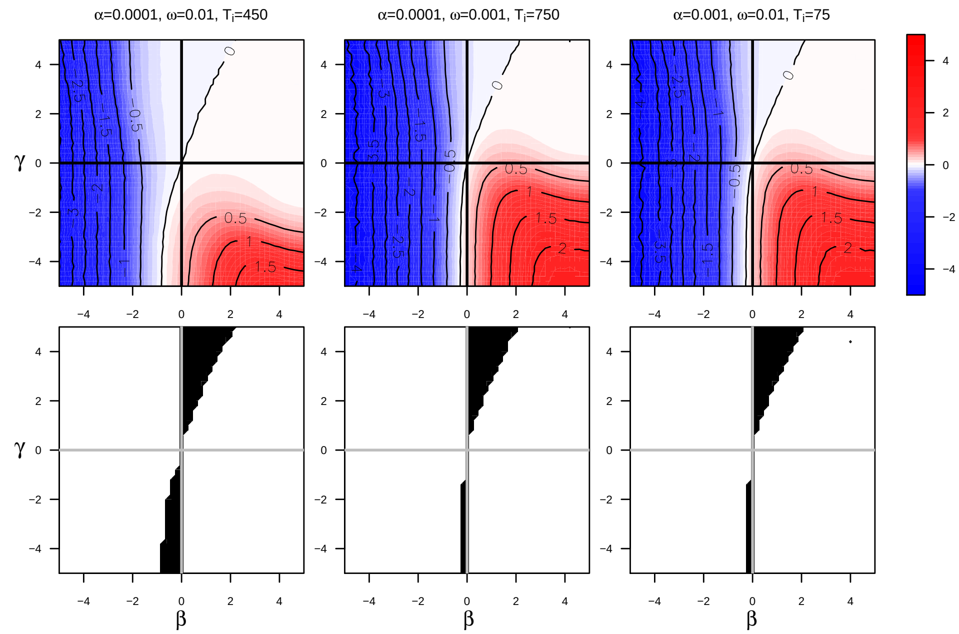

Figure 19: $\log[RR]$ (top row) and region of direction bias (bottom row) as a function of β and γ for different combinations of ratio ω/α and observation time T_i, when cluster size is constant ($n_i = 4$ for all i), and x is block randomized such that $\sum_{j=1}^{n_i} x_{ij} = 2$. In all plots observation time is constant and chosen such that the cumulative incidence when $\beta = 0$ and $\gamma = 0$ is approximately 0.15 for a given combination of α and ω.

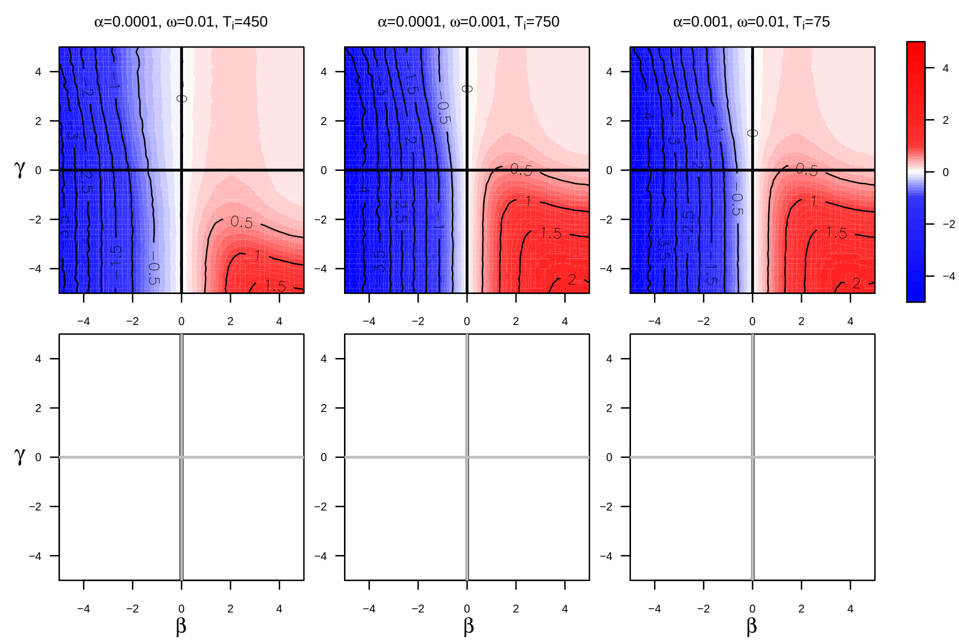

Figure 20: $\log[RR]$ (top row) and region of direction bias (bottom row) as a function of β and γ for different combinations of ratio ω/α and observation time T_i, when cluster size $n_i \sim \text{Pois}(3) + 1$ and x has independent Bernoulli distribution with $Pr[x = 1] = 0.5$. In all plots observation time is constant and chosen such that the cumulative incidence when $\beta = 0$ and $\gamma = 0$ is approximately 0.15 for a given combination of α and ω.

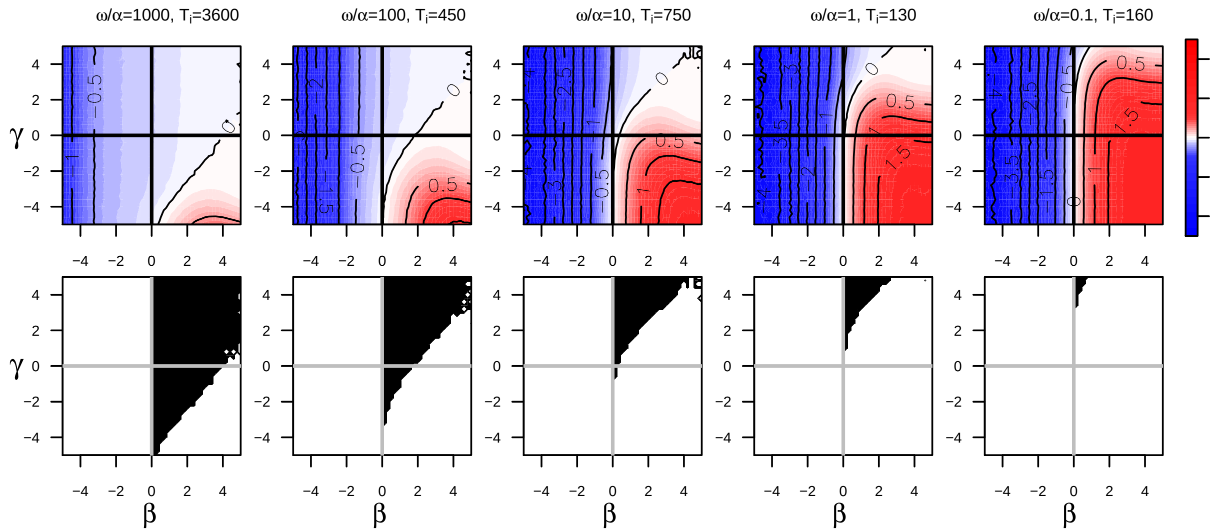

Figure 21: $\log[RR]$ (top row) and region of direction bias (bottom row) as a function of β and γ for different combinations of ratio ω/α and observation time T_i, when cluster size $n_i \sim \text{Pois}(3) + 1$ and x is block randomized such that $\sum_{j=1}^{n_i} x_{ij} = 1$ for all i. In all plots observation time is constant and chosen such that the cumulative incidence when $\beta = 0$ and $\gamma = 0$ is approximately 0.15 for a given combination of α and ω.

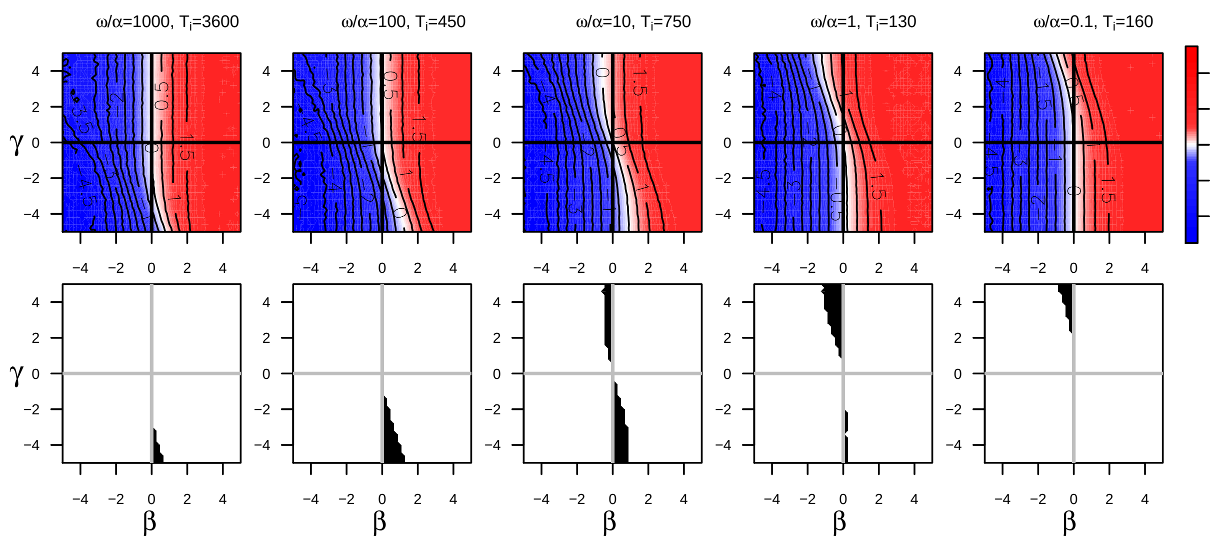

Figure 22: $\log[RR]$ (top row) and region of direction bias (bottom row) as a function of β and γ for different combinations of ratio ω/α and observation time T_i, when cluster size $n_i \sim \text{Pois}(3) + 1$ and x is cluster randomized: half of clusters have $\sum_{j=1}^{n_i} x_{ij} = n_i$, and remaining half have $\sum_{j=1}^{n_i} x_{ij} = 0$. In all plots observation time is constant and chosen such that the cumulative incidence when $\beta = 0$ and $\gamma = 0$ is approximately 0.15 for a given combination of α and ω.