Supplementary Material for "Quantifying Direct and Indirect Effects Through Joint Modeling of Terminal Events and Gap Times Between Recurrent Events" by Fang Niu, Cheng Zheng, and Lei Liu.

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I. Details on the parameter estimation

Here we would like to give detailed methods for parameter estimation based on the following joint model of gap time and survival time:

$$
\begin{aligned}
r_{ik}(z, g_k) &= r_{0k}(g_k)\exp\{\beta_{zk} z + \boldsymbol{\beta}_{xk}^\top \boldsymbol{X}_i + \nu_i\}, k \geq 1 \\
\lambda_i(z, \underline{m}, t) &= \lambda_0(t)\exp\{\eta_z z + \eta_m m(t) + \boldsymbol{\eta}_x^\top \boldsymbol{X}_i + \delta_1 \nu_i + \delta_2 \nu_i m(t)\}
\end{aligned}
$$

where $\nu_i \sim N(0, \sigma_\nu^2)$ is a shared random effect and independent of $\boldsymbol{X}_i$, z. $r_{ik}(z, g_k)$ is the intensity function for the kth gaps of recurrent event process $M_i(z, t)$, we assume they are independent of each other conditioning on the shared random effect. Define $\Theta = (r_{0k}(g_k), \lambda_0(t), \beta_{xk}, \beta_{zk}, \eta_x, \eta_z, \eta_m, \delta_1, \delta_2, \sigma_\nu)$, under the independent censoring assumption, we have $T \perp\!\!\!\perp C \mid \boldsymbol{X}$. The (partial) log-likelihood for the joint models when treating ν as fixed can be written as:

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$$
\begin{aligned}
l(\Theta) &= \sum_{i=1}^{n}\{\sum_{k=1}^{J_i(Z_i)}[\log(r_{0k}(G_{ik}))+\beta_{zk}Z_i+\boldsymbol{\beta}_{xk}^{\top}\boldsymbol{X}_i+\nu_i] \\
&- \sum_{k=1}^{J_i(Z_i)}\exp(\beta_{zk}Z_i+\boldsymbol{\beta}_{xk}^{\top}\boldsymbol{X}_i+\nu_i)\int_0^{G_{ik}}r_{0k}(u)du \\
&- \exp(\beta_{z(J_i(Z_i)+1)}Z_i+\boldsymbol{\beta}_{x(J_i(Z_i)+1)}^{\top}\boldsymbol{X}_i+\nu_i)\int_0^{T_i^{\star}-\sum_{k=1}^{J_i(Z_i)}colorblackG_{ik}}r_{0(J_i(Z_i)+1)}(u)du]\} \\
&+ \sum_{i=1}^{n}\{\Delta_i[\log(\lambda_0(T_i^{\star}))+\eta_z Z_i+\eta_m M_i(T_i^{\star})+\boldsymbol{\eta}_x^{\top}\boldsymbol{X}_i+\delta_1\nu_i+\delta_2\nu_i M_i(T_i^{\star})] \\
&- \exp(\eta_z Z_i+\boldsymbol{\eta}_x^{\top}\boldsymbol{X}_i+\delta_1\nu_i)\int_0^{T_i^{\star}}\lambda_0(u)\exp(\eta_m M_i(u)+\delta_2\nu_i M_i(u))du\} \\
&+ \sum_{i=1}^{n}\log f_{\nu}(\nu_i),
\end{aligned}
$$

where $J_i(Z_i)$ is the number of jumping points within $[0,\tau]$ and $G_{i1},\cdots,G_{iJ_i(Z_i)}$ are corresponding gap time points. Here $f_\nu(\cdot)$ is the probability density function for the normal distribution with mean 0 and variance σ_ν^2. Since the parameter is of infinite dimension, it is computationally intensive to compute the nonparametric maximum likelihood. Therefore we approximate both $\lambda_0(t)$ and $r_{0k}(g_k)$ by piecewise constant functions with knots $0=g_{rk0}<g_{rk1}<\cdots<g_{rkJ_{rk}}<\tau$, $0=t_{\lambda 0}<t_{\lambda 1}<\cdots<t_{\lambda J_\lambda}=\tau$:

$$
\begin{aligned}
\lambda_0(t) &= \sum_{j=1}^{J_\lambda}\lambda_{0j}I(t_{\lambda j-1}\le t<t_{\lambda j}), \\
r_{0k}(g_k) &= \sum_{j=1}^{J_{rk}}r_{0kj}I(g_{rkj-1}\le g_k<g_{rkj}),
\end{aligned}
$$

where τ is the largest follow-up time.

The parameters $\tilde{\Theta}=(r_{011},\cdots,r_{01J_{r1}},\cdots,r_{0K1},\cdots,r_{0KJ_{rK}},$
$\lambda_{01},\cdots,\lambda_{0J_\lambda},\boldsymbol{\beta}_x,\boldsymbol{\beta}_z,\boldsymbol{\eta}_x,\eta_z,\eta_m,\delta_1,\delta_2,\sigma_\nu)$ were estimated using parametric maximum likelihood where the likelihood integrated over random effect is approximated by using the numerical integration technique - Gaussian quadrature and the optimization is performed using the quasi-Newton method, which is built in standard statistical packages Proc NLMIXED in SAS.

When the parametric model is correctly specified (i.e., the true baseline hazard functions are piecewise constant with known knots), we know that the parameters estimated by the maximum likelihood estimation (MLE) are efficient. Since the model is fully parametric without infinite-dimension nuisance parameters, the invariant of MLE property guarantees that the NDE and NIE estimator using the plug-in parameter from these MLE parameters are also MLE and thus is consistent and efficient. When the parametric model is incorrectly specified and the semiparametric model is assumed, there can be bias in the estimation of the model parameters as well as NIE and NDE when the numbers of pieces for the baseline hazard functions are fixed. However, such bias can be reduced and asymptotically converge to 0 when the numbers of pieces, J_{rk} and J_λ, are allowed to be grown with sample size n. The theoretical results about the specific growth rate that is most efficient and the semi-parametric efficiency bound for the estimation of NDE and NIE are challenging to obtain because the most efficient estimate for nuisance parameters cannot guarantee the most efficient estimate for the plug-in estimators (Van der Laan, 2014). The theoretical development of the most efficient NDE and NIE estimators is beyond the scope of this paper and is worth future research.

We denote the specific set of parameter estimators obtained from fitting the joint model as $\hat{r}_{011},\cdots,\hat{r}_{01J_{r1}}$, $,\cdots,$ $\hat{r}_{0K1},\cdots,\hat{r}_{0KJ_{rK}}$, $\hat{\lambda}_{01},\cdots,\hat{\lambda}_{0J_\lambda}$, $\hat{\beta}_{z1},\cdots,\hat{\beta}_{zK}$, $\hat{\boldsymbol{\beta}}_{x1},\cdots,\hat{\boldsymbol{\beta}}_{xK}$, $\hat{\eta}_z$, $\hat{\eta}_m$, $\hat{\boldsymbol{\eta}}_x$, $\hat{\delta}_1$, $\hat{\delta}_2$, $\hat{\sigma}_\nu^2$. For the model without an interaction term, we just fix $\hat{\delta}_2$ at 0 and for the model assuming SI, we just fix $\hat{\delta}_1=\hat{\delta}_2=0$. For the model assuming no frailty, we can further set $\hat{\sigma}_\nu=0$.

II. Details on the estimation of NDE and NIE

After estimation of parameters, we could calculate NDE(t) and NIE(t) for $t \in [0, \tau]$. For NDE and NIE estimation based on each simulated data set, we repeated B times, and the detailed algorithms are described below:

- Step 1: Sample $\nu_1, \cdots, \nu_B$ independently from $N(0, \hat{\sigma}_\nu^2)$.
- Step 2: For each ν_b, then for each individual i, we independently sample two corresponding potential mediator process $M_{ib}^0(s)$ and $M_{ib}^1(s)$ for $s \in [0, \tau]$ with $i = 1, \cdots, n$ and $b = 1, \cdots, B$ by first sampling each gap time separately using hazard function of gap time models $\hat{r}_{0k}(g_k) \exp\{\hat{\boldsymbol{\beta}}_{xk}^\top \boldsymbol{X}_i + \nu_b\}$ and $\hat{r}_{0k}(g_k) \exp\{\hat{\beta}_{zk} + \hat{\boldsymbol{\beta}}_{xk}^\top \boldsymbol{X}_i + \nu_b\}$ correspondingly by inversion approach (Çinlar, 1975).
- Step 3: Compute the survival functions $S_{ib}^{00}(t)$, $S_{ib}^{01}(t)$, $S_{ib}^{10}(t)$, $S_{ib}^{11}(t)$ by plugging in the estimated parameters from Section I and the formula below:

$$\begin{aligned}
S_{ib}^{00}(t) &= \exp\{-\exp(\hat{\boldsymbol{\eta}}_x^\top \boldsymbol{X}_i + \hat{\delta}_1 \nu_b) \int_0^t \hat{\lambda}_0(u) \exp\{(\hat{\eta}_m + \hat{\delta}_2 \nu_b) M_{ib}^0(u)\}\, du\}, \\
S_{ib}^{01}(t) &= \exp\{-\exp(\hat{\eta}_z + \hat{\boldsymbol{\eta}}_x^\top \boldsymbol{X}_i + \hat{\delta}_1 \nu_b) \int_0^t \hat{\lambda}_0(u) \exp\{(\hat{\eta}_m + \hat{\delta}_2 \nu_b) M_{ib}^0(u)\}\, du\}, \\
S_{ib}^{10}(t) &= \exp\{-\exp(\hat{\boldsymbol{\eta}}_x^\top \boldsymbol{X}_i + \hat{\delta}_1 \nu_b) \int_0^t \hat{\lambda}_0(u) \exp\{(\hat{\eta}_m + \hat{\delta}_2 \nu_b) M_{ib}^1(u)\}\, du\}, \\
S_{ib}^{11}(t) &= \exp\{-\exp(\hat{\eta}_z + \hat{\boldsymbol{\eta}}_x^\top \boldsymbol{X}_i + \hat{\delta}_1 \nu_b) \int_0^t \hat{\lambda}_0(u) \exp\{(\hat{\eta}_m + \hat{\delta}_2 \nu_b) M_{ib}^1(u)\}\, du\}.
\end{aligned}$$

- Step 4: Estimate $\widehat{\text{NDE}}(t, z, z', \boldsymbol{X}_i)$ and $\widehat{\text{NIE}}(t, z, z', \boldsymbol{X}_i)$ as

$$\widehat{\text{NDE}}(t, z, z', \boldsymbol{X}_i) = B^{-1} \sum_{b=1}^{B} \left(S_{ib}^{zz'}(t) - S_{ib}^{zz}(t) \right),$$

$$\widehat{\text{NIE}}(t, z, z', \boldsymbol{X}_i) = B^{-1} \sum_{b=1}^{B} \left(S_{ib}^{z'z'}(t) - S_{ib}^{zz'}(t) \right).$$

- Step 5: Estimate $\widehat{\text{NDE}}(t, z, z')$ and $\widehat{\text{NIE}}(t, z, z')$ as

$$\widehat{\text{NDE}}(t, z, z') = n^{-1} \sum_{i=1}^{n} \widehat{\text{NDE}}(t, z, z', \boldsymbol{X}_i),$$

$$\widehat{\text{NIE}}(t, z, z') = n^{-1} \sum_{i=1}^{n} \widehat{\text{NIE}}(t, z, z', \boldsymbol{X}_i).$$

- Step 6: Report $\widehat{\text{NDE}}(t) = [\widehat{\text{NDE}}(t, 0, 1) - \widehat{\text{NDE}}(t, 1, 0)]/2$, $\widehat{\text{NIE}}(t) = [\widehat{\text{NIE}}(t, 0, 1) - \widehat{\text{NIE}}(t, 1, 0)]/2$ and proportion mediated $\widehat{\text{NIE}}(t)/[\widehat{\text{NIE}}(t) + \widehat{\text{NDE}}(t)]$.

As a remark, for step one, we do not need to sample $\nu_{1i}, \cdots, \nu_{Bi}$ differently for each individual i because the goal is just to integrate out the effect of ν for each individual using the Monte-Carlo integration and the final estimation of NDE and NIE is just the average of the estimation of individual NDE and NIE.

For step 2, since we use piece-wise estimator for kth gap time $\hat{r}_{0k}(g_k) = \sum_{j=0}^{J_r} \hat{r}_{0kj} I(g_{rkj} \leq g_k < g_{rk(j+1)})$ for $0 = g_{rk0} < g_{rk1} < \cdots < g_{rkJ_r} < g_{rk(J_r+1)} = \tau$, we have the following piece-wise linear cumulative density function:

$$\Lambda_{rki}^z(g_k) = \int_0^{g_k} \hat{r}_{ik}^z(u) du = \exp(\beta_{zk} z + \boldsymbol{\beta}_{xk}^\top \boldsymbol{X}_i + \nu_i) \left\{ \sum_{j=0}^{J_{rk}} (\hat{r}_{0kj} - \hat{r}_{0k(j-1)}) \left(g_k - g_{rkj}\right)_+ \right\},$$

for $g_k \in [0,\tau]$ where $\hat{rk}_{0(-1)} = 0$ and its inverse is also piece-wise linear function:

$$(\Lambda^z_{rki})^{-1}(\lambda) = \exp(-\beta_{zk}z - \boldsymbol{\beta}_{xk}^\top \boldsymbol{X}_i - \nu_i)\left\{\sum_{j=0}^{J_{rk}} (\hat{r}^{-1}_{0kj} - \hat{r}^{-1}_{0k(j-1)})(\lambda - \Lambda^z_{rki}(g_{rkj}))_+\right\}.$$

So we can generate the jumping time process using Çinlar's Method ((Çinlar, 1975)) as below:

- Initialize $s = 0$, $j = 0$, $t = 0$
- While $t < \tau$, do the following:
  - Generate $u_j \sim U(0,1)$
  - Set $s = -\log(u_j)$
  - Set $j = j+1$, $G_j = \Lambda_j^{-1}(s)$
  - Set $t = t + G_j$
- Output $J = j - 1$, gap times $G_1, \cdots, G_J$ and then compute $R_1, \cdots, R_{J-1}$.

For step 3, since we use piece-wise estimator $\hat{\lambda}_0(t) = \sum_{j=0}^{J_\lambda} \hat{\lambda}_{0j} I(t_{\lambda_j} \le t < t_{\lambda(j+1)})$ for $0 = t_{\lambda 0} < t_{\lambda 1} < \cdots < t_{\lambda J_\lambda} < t_{\lambda(J_\lambda+1)} = \tau$, let $\hat{\lambda}_{0(-1)} = 0$, we have:

$$\begin{aligned}
S^{00}_{ib}(t) &= \exp\left[-\exp\left(\hat{\boldsymbol{\eta}}_x^\top \boldsymbol{X}_i + \hat{\delta}_1\nu_b\right)\sum_{j=0}^{J_\lambda}\sum_{j'=0}^{J^0_{ib}} c_{ibjj'}\left\{t - (t_{\lambda j} \vee R^0_{ibj'})\right\}_+\right],\\
S^{01}_{ib}(t) &= \exp\left[-\exp\left(\hat{\eta}_z + \hat{\boldsymbol{\eta}}_x^\top \boldsymbol{X}_i + \hat{\delta}_1\nu_b\right)\sum_{j=0}^{J_\lambda}\sum_{j'=0}^{J^0_{ib}} c_{ibjj'}\left\{t - (t_{\lambda j} \vee R^0_{ibj'})\right\}_+\right],\\
S^{10}_{ib}(t) &= \exp\left[-\exp\left(\hat{\boldsymbol{\eta}}_x^\top \boldsymbol{X}_i + \hat{\delta}_1\nu_b\right)\sum_{j=0}^{J_\lambda}\sum_{j'=0}^{J^1_{ib}} c_{ibjj'}\left\{t - (t_{\lambda j} \vee R^1_{ibj'})\right\}_+\right],\\
S^{11}_{ib}(t) &= \exp\left[-\exp\left(\hat{\eta}_z + \hat{\boldsymbol{\eta}}_x^\top \boldsymbol{X}_i + \hat{\delta}_1\nu_b\right)\sum_{j=0}^{J_\lambda}\sum_{j'=0}^{J^1_{ib}} c_{ibjj'}\left\{t - (t_{\lambda j} \vee R^1_{ibj'})\right\}_+\right],
\end{aligned}$$

where $a \vee b$ means taking the maximum of a and b, $0 < R^1_{ib1} < \cdots < R^1_{ibJ^1_{ib}} < \tau$ are all jumping points of $M^1_{ib}(s)$, $s \in [0,\tau]$ and $0 < R^0_{ib1} < \cdots < R^0_{ibJ^0_{ib}} < \tau$ are all jumping points of $M^0_{ib}(s)$, $s \in [0,\tau]$ and

$$\begin{aligned}
c_{ibj0} &= \hat{\lambda}_{0j} - \hat{\lambda}_{0(j-1)},\\
c_{ibjj'} &= \left(\hat{\lambda}_{0j} - \hat{\lambda}_{0(j-1)}\right)\exp\left\{(\hat{\eta}_m + \hat{\delta}_2\nu_b)(j'-1)\right\}\left\{\exp(\hat{\eta}_m + \hat{\delta}_2\nu_b) - 1\right\}, \forall j' \ge 1.
\end{aligned}$$

III. Details on the Data Simulation

First, we would like to describe the details of the data simulation. We generate data with one covariate $X \sim N(0,1)$, binary treatment $Z \sim Bernoulli(0.5)$. Gap times were independent of each other and generated separately. For $k = 1$, the first order of gap time, $\beta_{x1} = 0.5$ and $\beta_{z1} = -0.5$. We assume that the baseline hazard function is $r_{01}(g_1) = 3I(0 \le g_1 < 0.1) + 3.2I(g_1 \ge 0.1)$. For $k = 2$, the second order of gap time, $\beta_{x2} = 0.5$ and $\beta_{z2} = -0.4$. We assume that the baseline hazard function is $r_{02}(g_2) = 3.6I(0 \le g_2 < 0.1) + 4.5I(g_2 \ge 0.1)$. For $k \ge 3$, the third or later order of the gap time, $\beta_{x3} = 0.5$ and $\beta_{z3} = -0.3$. We assume that the baseline hazard function is $r_{03}(g_3) = 4.2I(0 \le g_3 < 0.1) + 5I(g_3 \ge 0.1)$. Then we independently sample two non-homogeneous Poisson processes of recurrent event mediators $\boldsymbol{M}^z(s)$ for z =0 or 1 and $s \in [0,\tau]$ using Cinlar's Inversion Method (Çinlar, 1975) as provided in section Appendix II. We assume the baseline hazard for the terminal event is $\lambda_0(t) = 0.9I(0 \leq t < 1) + I(1 \leq t < 2) + 1.1I(t \geq 2)$ and the regression coefficients are $\eta_z = -1$, $\eta_m = 0.25$, $\eta_x = 1$, $\delta_1 = 1$. Using the previous setting, the potential survival time $T(z, \boldsymbol{M})$ can be sampled by the inversion approach.

We performed simulations under five different settings. For the first two settings, we assume that our random effect is correctly specified as $\nu \sim N(0, 1)$. For setting I, we assume no interaction and set $\delta_2 = 0$; for setting II, we have interaction by setting $\delta_2 = 0.15$. For setting III, we want to evaluate the robustness of our method to the misspecification of random effect distribution, so we generate ν using log gamma distribution with shape parameter 1 and scale parameter 1. For setting IV, we misfit our model without the interaction term while the data are generated with the interaction term. For setting V, we introduced variable baseline rates for each order of gap time, while keeping (β_{x1}, β_{x2}, β_{x3}, β_{z1}, β_{z2}, β_{z3}) same as previous settings. For $k = 1$, the first order of gap time, baseline hazard function is $r_{01}(g_1) = 1I(0 \leq g_1 < 2) + 3I(g_1 \geq 2)$. For $k = 2$, the second order of gap time, the baseline hazard function is $r_{02}(g_2) = 5I(0 \leq g_2 < 2) + 2I(g_2 \geq 2)$. For $k \geq 3$, the third or later order of gap time, the baseline hazard function is $r_{03}(g_3) = 6I(0 \leq g_3 < 2) + 1I(g_3 \geq 2)$.

We set administrative censoring times at $\tau = 4$ and additional early drop-out times are sampled from the uniform distribution on $[2, 4]$. The sample size is set to 400 for five simulation scenarios. In settings I and II, the simulated data exhibit a censoring rate of approximately 11-14% of the terminal event, with around 72% of the sample experiencing at least one recurrent event, and a mean of about two recurrent events per subject. In Setting V, the censoring rate of the terminal event is approximately 16%, with 51% of the sample experiencing at least one recurrent event, and the mean number of recurrent events remains around two.

IV. Additional Simulation Results

We perform 200 simulations for each simulation setting in order to estimate the bias, standard deviation (SD), median estimated standard error (MeSE) and coverage rate for 95% nominal confidence interval (CR) for the parameters. Taking simulated datasets and estimated parameters, we calculated the NDE and NIE with $B = 10,000$ at time points $(1, 2, 3)$. All bias, SD, MeSE, and 95% CR are computed using 100 parametric Bootstrap samples.

The simulation results for the estimation of model parameters under settings I to IV can be found in Tables S1-S4.

Data Availability Statement

The data that support the findings of this study are from a trial (ClinicalTrials.gov Identifier: NCT00001022) conducted by the CPCRA, which is funded by the National Institute of Allergy and Infectious Diseases (NIAID). Any data request needs to be submitted to the trial PIs (Drs. Saravolatz LD and Winslow DL dwinslow@stanford.edu) and the CPCRA.

Table S1: Bias, empirical standard deviation (SD), median estimated standard error (MeSE), and coverage rate for 95% nominal confidence interval (CR) from simulation settings I.

Effect	Bias	SD	MeSE	CR
β_{z1}	0.009	0.153	0.161	94.0%
β_{z2}	0.016	0.187	0.180	94.0%
β_{z3}	0.027	0.154	0.157	95.5%
β_{x1}	-0.029	0.275	0.277	95.5%
β_{x2}	-0.032	0.322	0.310	93.0%
β_{x3}	0.008	0.274	0.268	95.0%
$log(\sigma_\nu^2)$	-0.021	0.13	0.129	96.0%
$\log(r_{01}(g_1))$: $g_1 \in [0, 0.1)$	0.008	0.184	0.193	96.5%
$\log(r_{01}(g_1))$: $g_1 \in [0.1, \infty]$	0.017	0.181	0.187	95.0%
$\log(r_{02}(g_2))$: $g_2 \in [0, 0.1)$	0.007	0.228	0.215	93.0%
$\log(r_{02}(g_2))$: $g_2 \in [0.1, \infty]$	0.004	0.218	0.211	94.5%
$\log(r_{03}(g_3))$: $g_3 \in [0, 0.1)$	-0.027	0.182	0.186	94.5%
$\log(r_{03}(g_3))$: $g_3 \in [0.1, \infty]$	-0.018	0.187	0.185	94.5%
η_z	0.017	0.160	0.159	95.0%
η_x	0.002	0.281	0.268	94.0%
η_m	0.008	0.028	0.027	94.0%
δ_1	-0.005	0.127	0.117	93.0%
$\log(\lambda_0(t))$: $t \in [0, 1)$	-0.018	0.195	0.179	94.5%
$\log(\lambda_0(t))$: $t \in [1, 2)$	-0.022	0.247	0.248	96.0%
$\log(\lambda_0(t))$: $t \in [2, \infty]$	-0.039	0.348	0.330	94.5%

References

Çinlar E (1975). *Introduction to stochastic processes.* Prentice-Hall, New Jersey.

Van der Laan M (2014). Targeted estimation of nuisance parameters to obtain valid statistical inference. *The International Journal of Biostatistics*, 10(1): 29–57.

Table S2: Bias, empirical standard deviation (SD), median estimated standard error (MeSE), and coverage rate for 95% nominal confidence interval (CR) from simulation settings II.

Effect	Bias	SD	MeSE	CR
β_{z1}	0.007	0.153	0.160	93.8%
β_{z2}	0.017	0.184	0.177	93.8%
β_{z3}	0.026	0.147	0.149	94.8%
β_{x1}	-0.025	0.267	0.274	96.4%
β_{x2}	-0.030	0.313	0.304	94.3%
β_{x3}	0.009	0.261	0.254	95.4%
$log(\sigma_\nu^2)$	-0.023	0.136	0.134	94.3%
$\log(r_{01}(g_1))$: $g_1 \in [0, 0.1)$	0.009	0.182	0.192	96.4%
$\log(r_{01}(g_1))$: $g_1 \in [0.1, \infty]$	0.016	0.176	0.186	96.4%
$\log(r_{02}(g_2))$: $g_2 \in [0, 0.1)$	0.009	0.224	0.213	93.3%
$\log(r_{02}(g_2))$: $g_2 \in [0.1, \infty]$	0.004	0.213	0.207	94.8%
$\log(r_{03}(g_3))$: $g_3 \in [0, 0.1)$	-0.022	0.181	0.180	95.9%
$\log(r_{03}(g_3))$: $g_3 \in [0.1, \infty]$	-0.016	0.184	0.176	93.8%
η_z	0.029	0.179	0.179	94.3%
η_x	0.005	0.313	0.305	95.4%
η_m	0.011	0.038	0.036	93.3%
δ_1	0.000	0.144	0.148	97.4%
δ_2	-0.001	0.049	0.048	93.8%
$\log(\lambda_0(t))$: $t \in [0, 1)$	-0.026	0.209	0.201	95.4%
$\log(\lambda_0(t))$: $t \in [1, 2)$	-0.044	0.279	0.271	94.3%
$\log(\lambda_0(t))$: $t \in [2, \infty]$	-0.083	0.410	0.372	93.8%

Table S3: Bias, empirical standard deviation (SD), median estimated standard error (MeSE), and coverage rate for 95% nominal confidence interval (CR) from simulation settings III.

Effect	Bias	SD	MeSE	CR
β_{z1}	-0.003	0.178	0.174	93.5%
β_{z2}	0.014	0.197	0.195	93.0%
β_{z3}	0.006	0.162	0.168	96.0%
β_{x1}	-0.046	0.318	0.298	92.0%
β_{x2}	-0.065	0.346	0.335	94.5%
β_{x3}	-0.044	0.283	0.289	95.0%
$log(\sigma_\nu^2)$	0.276	0.124	0.134	44.5%
$\log(r_1(g_1))$: $g_1 \in [0, 0.1)$	-0.521	0.222	0.217	31.5%
$\log(r_1(g_1))$: $g_1 \in [0.1, \infty]$	-0.532	0.217	0.200	25.5%
$\log(r_2(g_2))$: $g_2 \in [0, 0.1)$	-0.533	0.263	0.242	42.5%
$\log(r_2(g_2))$: $g_2 \in [0.1, \infty]$	-0.463	0.230	0.225	46.5%
$\log(r_3(g_3))$: $g_3 \in [0, 0.1)$	-0.506	0.216	0.207	30.5%
$\log(r_3(g_3))$: $g_3 \in [0.1, \infty]$	-0.461	0.194	0.199	36.5%
η_z	0.048	0.197	0.193	93.5%
η_x	-0.110	0.305	0.329	94.0%
η_m	-0.030	0.038	0.039	88.0%
δ_1	-0.002	0.141	0.144	95.0%
δ_2	-0.050	0.046	0.047	80.0%
$\log(\lambda_0(t))$: $t \in [0, 1)$	-0.492	0.207	0.219	38.0%
$\log(\lambda_0(t))$: $t \in [1, 2)$	-0.610	0.264	0.275	40.0%
$\log(\lambda_0(t))$: $t \in [2, \infty]$	-0.763	0.345	0.353	42.5%

Table S4: Bias, empirical standard deviation (SD), median estimated standard error (MeSE), and coverage rate for 95% nominal confidence interval (CR) from simulation settings IV.

Effect	Bias	SD	MeSE	CR
β_{z1}	0.007	0.152	0.159	94.3%
β_{z2}	0.011	0.187	0.178	94.3%
β_{z3}	0.009	0.151	0.155	94.8%
β_{x1}	-0.023	0.274	0.274	95.9%
β_{x2}	-0.022	0.321	0.306	94.8%
β_{x3}	0.035	0.276	0.266	93.8%
$log(\sigma_\nu^2)$	-0.061	0.135	0.133	93.3%
$\log(r_1(g_1))$: $g_1 \in [0, 0.1)$	0.029	0.182	0.191	96.4%
$\log(r_1(g_1))$: $g_1 \in [0.1, \infty]$	0.014	0.181	0.185	94.3%
$\log(r_2(g_2))$: $g_2 \in [0, 0.1)$	0.045	0.225	0.212	90.7%
$\log(r_2(g_2))$: $g_2 \in [0.1, \infty]$	0.022	0.216	0.208	93.8%
$\log(r_3(g_3))$: $g_3 \in [0, 0.1)$	-0.011	0.183	0.184	95.4%
$\log(r_3(g_3))$: $g_3 \in [0.1, \infty]$	-0.002	0.187	0.181	94.3%
η_z	0.082	0.173	0.175	92.3%
η_x	-0.053	0.314	0.297	93.8%
η_m	0.017	0.037	0.031	88.7%
δ_1	0.239	0.122	0.126	57.2%
$\log(\lambda_0(t))$: $t \in [0, 1)$	0.026	0.209	0.198	95.4%
$\log(\lambda_0(t))$: $t \in [1, 2)$	-0.145	0.269	0.266	92.8%
$\log(\lambda_0(t))$: $t \in [2, \infty]$	-0.455	0.382	0.349	74.2%