Supporting Information for ‘Estimation of Incubation Period and Generation Time Based on Observed Length-biased Epidemic Cohort with Censoring for COVID-19 Outbreak in China’ by Deng et al.

Web Appendix A.

Here three parametric forms are used to fit the distribution of incubation period (inter-arrival time) $I$, they are Gamma distribution, Weibull distribution and Log-normal distribution. Let $f_I$ and $h$ be the pdf of $I$ and $V$ respectively, and let $F_I$ and $H$ be the cdf of $I$ and $V$ respectively.

Example 1. Suppose that $I \sim \Gamma(\alpha, \beta)$ with density

$$f_I(t; \theta) = \frac{\beta^\alpha}{\Gamma(\alpha)} t^{\alpha-1} e^{-\beta t} \quad (t > 0),$$

where $\theta = (\alpha, \beta)^T$ is unknown ($\alpha > 0$, $\beta > 0$), then

$$h(t; \theta) = \frac{\beta}{\alpha} [1 - \Gamma(t, \alpha, \beta)] \quad (t > 0),$$

$$H(t; \theta) = \Gamma(t, \alpha + 1, \beta) + \frac{\beta t}{\alpha} [1 - \Gamma(t, \alpha, \beta)] \quad (t > 0),$$

where $\Gamma(u, \alpha, \beta)$ is the cdf of $\Gamma(\alpha, \beta)$ at $u$.

Example 2. Suppose that $I \sim W(k, \lambda)$ with density

$$f_I(t; \theta) = \frac{k}{\lambda} \left( \frac{t}{\lambda} \right)^{k-1} \exp \left\{ - \left( \frac{t}{\lambda} \right)^k \right\} \quad (t > 0),$$

where $\theta = (k, \lambda)^T$ is unknown ($k > 0$, $\lambda > 0$), then

$$h(t; \theta) = \frac{k}{\lambda} \Gamma \left( \frac{1}{k} \right)^{-1} \exp \left\{ - \left( \frac{t}{\lambda} \right)^k \right\} \quad (t > 0),$$

$$H(t; \theta) = \Gamma \left( \left( \frac{t}{\lambda} \right)^k, \frac{1}{k}, 1 \right) \quad (t > 0).$$
Example 3. Suppose that $I \sim LN(\mu, \sigma^2)$ with density
\[
f_I(t; \theta) = \frac{1}{\sqrt{2\pi\sigma^2 t}} \exp\left\{ \frac{-(\log t - \mu)^2}{2\sigma^2} \right\} \quad (t > 0),
\]
where $\theta = (\mu, \sigma^2)^\top$ is unknown ($\sigma > 0$), then
\[
h(t; \theta) = \exp\left\{ -\mu - \frac{1}{2} \sigma^2 \right\} \left[ 1 - \Phi(\log t; \mu, \sigma^2) \right] \quad (t > 0),
\]
\[
H(t; \theta) = \Phi(\log t; \mu + \sigma^2, \sigma^2) + t \exp\left\{ -\mu - \frac{1}{2} \sigma^2 \right\} \left[ 1 - \Phi(\log t; \mu, \sigma^2) \right] \quad (t > 0),
\]
where $\Phi(u, \mu, \sigma^2)$ is the cdf of normal distribution $N(\mu, \sigma^2)$ at $u$.

Web Appendix B. Likelihood approach for the mixture distribution

The log-likelihood of the mixture distribution can be derived by introducing a latent variable. Specifically, denote $\delta_j = 1$ if the $j$th individual in our cohort got infected at the departure, $\delta_j = 0$ if the individual got infected before departure, and $t_j$ to be the observed time difference from the event of leaving Wuhan to symptoms onset for $j = 1, \ldots, m.$ Note that only \{\(t_1, \ldots, t_m\)\} are observed, and \{\(\delta_1, \ldots, \delta_m\)\} are unobserved. We can rewrite this problem as a mixture distribution below,
\[
\delta_j \sim Bin(1, \pi), \quad j = 1, \ldots, m.
\]
\[
t_j \mid (\delta_j = 1) \sim f^p_I(\cdot; \theta), \quad t_j \mid (\delta_j = 0) \sim h^p(\cdot; \theta),
\]
and the conditional likelihood is
\[
L(\theta; t_1, \ldots, t_m \mid \delta_1, \ldots, \delta_m) = \prod_{j=1}^{m} \{f^p_I(t_j; \theta)\}^{\delta_j} \{h^p(t_j; \theta)\}^{1-\delta_j}
= \prod_{j=1}^{m} \{\delta_j f^p_I(t_j; \theta) + (1 - \delta_j) h^p(t_j; \theta)\}.
\]

By integrating the unobservable \{\(\delta_1, \ldots, \delta_m\)\} out, the likelihood is reduced to
\[
L(\theta, \pi; t_1, \ldots, t_m) = \prod_{j=1}^{m} \{\pi f^p_I(t_j; \theta) + (1 - \pi) h^p(t_j; \theta)\}.
\]
Hence, the estimates of parameters can be obtained by Newton-Raphson or EM algorithm (Dempster et al., 1977; Booth and Hobert, 1999). Note that extra cautions need to be taken when an EM algorithm is implemented due to the local maximum issue.

**Web Appendix C. Proof of Theorem 1 and 2**

To study the large-sample properties of the MLE and the likelihood ratio statistics $R_1(\theta_0, \pi_0)$ and $R_2(\pi_0)$, we consider the behavior of $\ell(\theta, \pi)$ for $(\theta^\top, \pi)^\top = (\theta_0^\top, \pi_0)^\top + n^{-1/2}\xi$ with $\xi = (\xi_1^\top, \xi_2^\top) = O_p(1)$.

By second-order Taylor expansion and weak law of large numbers, we have

$$\ell((\theta^\top, \pi_0)^\top + m^{-1/2}\xi) = \ell(\theta_0, \pi_0) + u_m^\top \xi - \frac{1}{2} \xi^\top U \xi + r_m \xi^\top \xi,$$

(S1)

where $r_m = o_p(1)$ uniformly for all $(\theta, \pi)$ in a neighborhood of $(\theta_0, \pi_0)$,

$$u_m = m^{-1/2} \sum_{i=1}^m \frac{\pi_0 \nabla_\theta f_i^p(t; \theta_0) + (1 - \pi_0) \nabla_\theta h^p(t; \theta_0)}{\pi_0 f_i^p(t; \theta_0) + (1 - \pi_0) h^p(t; \theta_0)},$$

and $U = (U_{ij})_{1 \leq i,j \leq 2}$ with

$$U_{11} = E \left\{ \frac{\pi_0 \nabla_\theta f_i^p(t; \theta_0) + (1 - \pi_0) \nabla_\theta h^p(t; \theta_0)}{\pi_0 f_i^p(t; \theta_0) + (1 - \pi_0) h^p(t; \theta_0)} \right\}^2,$$

$$U_{12} = E \left\{ \frac{\{\pi_0 \nabla_\theta f_i^p(t; \theta_0) + (1 - \pi_0) \nabla_\theta h^p(t; \theta_0)\} \{\nabla_\theta f_i^p(t; \theta_0) - \nabla_\theta h^p(t; \theta_0)\}^\top}{\pi_0 f_i^p(t; \theta_0) + (1 - \pi_0) h^p(t; \theta_0)} \right\}^2,$$

$$U_{22} = E \left\{ \frac{f_i^p(t; \theta_0) - h^p(t; \theta_0)}{\pi_0 f_i^p(t; \theta_0) + (1 - \pi_0) h^p(t; \theta_0)} \right\}^2.$$

Here $A^{\otimes 2} = AA^\top$ for a vector or matrix $A$. It is straightforward to see that $\text{var}(u_m) = U$ and $u_m \xrightarrow{d} N(0, U)$.

Let $\tilde{\xi} = (\tilde{\xi}_1^\top, \tilde{\xi}_2^\top) = \sqrt{m}(\tilde{\theta} - \theta_0)^\top, \tilde{\pi} - \pi_0)^\top$. If $(\theta_0, \pi_0)$ is an interior point of the parameter space, it follows from (S1) that the MLE $(\hat{\theta}^\top, \hat{\pi})^\top = (\theta_0^\top, \pi_0)^\top + m^{-1/2}\tilde{\xi}$ satisfies

$$\hat{\xi} = U^{-1} u_m + o_p(1) \xrightarrow{d} N(0, U^{-1}).$$
and that
\[ R(\theta_0, \pi_0) = 2u_m^\top \hat{\xi} - \hat{\xi}^\top U \hat{\xi} + o_p(1) = u_m^\top U^{-1} u_m + o_p(1) \xrightarrow{d} \chi_{q_\theta + 1}^2, \]
where \( q_\theta \) is the dimension of \( \theta \). Similarly it is straightforward to see that \( R_2(\pi_0) \xrightarrow{d} \chi_1^2 \). This proves Theorem 1.

To proving Theorem 2, we re-express (S1) as
\[
\ell((\theta_0^\top, \pi_0)^\top + m^{-1/2} \xi) = \ell(\theta_0, \pi_0) + u_m^\top \xi_1 + u_m^\top \xi_2 \\
- \frac{1}{2} \xi_1^\top U_{11} \xi_1 - \frac{1}{2} \xi_1^\top U_{12} \xi_2 - \frac{1}{2} \xi_2^\top U_{22} \xi_2 + r_m \xi^\top \xi \\
= \ell(\theta_0^\top, \pi_0)^\top + \frac{1}{2} u_m^\top U_{11}^{-1} u_m \\
- \frac{1}{2} \{ \xi_1 - U_{11}^{-1}(u_m - U_{12} \xi_2) \}^\top U_{11} \{ \xi_1 - U_{11}^{-1}(u_m - U_{12} \xi_2) \} \\
+ u_m^\top U_{11}^{-1} U_{12} \xi_2 - \frac{1}{2} \xi_2^\top (U_{22} - U_{12} U_{11}^{-1} U_{12}) \xi_2 + r_m \xi^\top \xi. \quad (S2)
\]
Because \( \theta_0 \) is an interior point, when \( m \) is large, \( \xi_1 \) is free from any constraint. For any fixed \( \xi_2 \), taking maximum in (S2) with respect to \( \xi_1 \) leads to
\[
\xi_1 = U_{11}^{-1}(u_m - U_{12} \xi_2) + r_m, \quad (S3)
\]
where \( r_m = o_p(1) \) uniformly. Putting this back in (S2), we have the profile log-likelihood
\[
\ell_p(\pi_0 + m^{-1/2} \xi_2) = (u_m - U_{21} U_{11}^{-1} u_m) \xi_2 - \frac{1}{2} (U_{22} - U_{12} U_{11}^{-1} U_{12}) \xi_2^2 + C + r_m \xi_2^2,
\]
where \( C \) does not depend on \( \xi_2 \) and \( r_m = o_p(1) \) uniformly.

Because \( \pi \leq \pi_0 = 1 \), \( \xi_2 \) takes only non-positive values, and \( \ell_p(\pi_0 + m^{-1/2} \xi_2) \) takes its maximum at
\[
\hat{\xi}_2 = (U_{22} - U_{12} U_{11}^{-1} U_{12})^{-1}(u_m - U_{21} U_{11}^{-1} u_m)_- + o_p(1),
\]
where \( x_- = \min\{x, 0\} \). Putting \( \hat{\xi}_2 \) back into (S3) leads to an approximate of \( \hat{\xi}_1 \), i.e.,
\[
\hat{\xi}_1 = U_{11}^{-1} \{ u_m - U_{12}(U_{22} - U_{12} U_{11}^{-1} U_{12})^{-1}(u_m - U_{21} U_{11}^{-1} u_m)_- \} + o_p(1).
\]
The fact \( u_m \xrightarrow{d} N(0, U) \) implies that \( u_m \xrightarrow{d} N(0, U_{11}) \) and
\[
u m \xrightarrow{d} N(0, U) \xrightarrow{d} N(0, U_{11}),
\]
and
\[
u m \xrightarrow{d} N(0, U_{11}).
\]
and that they are asymptotically independent. This immediately implies result (a) of Theorem 3.

It follows from the approximates of the MLEs and (S2) that

\[ R_2(\pi_0) = \mathcal{S}_2^\top (U_{22} - U_{12}^{-1}U_{11}^{-1}U_{12}) \mathcal{S}_2 + o_p(1) \]

\[ = (u_{m2} - U_{21}U_{11}^{-1}u_{m1})_2^2 + o_p(1) \]

\[ \xrightarrow{d} \frac{1}{2} \chi_0^2 + \frac{1}{2} \chi_1^2, \]

and

\[ R_1(\theta_0, \pi_0) = u_{m1}U_{11}^{-1}u_{m1} + (u_{m2} - U_{21}U_{11}^{-1}u_{m1})_2^2 \]

\[ \xrightarrow{d} \frac{1}{2} \chi_0^2 + \frac{1}{2} \chi_1^2 + \frac{1}{2} \chi_2^2. \]

This proves Theorem 3. It is similar to prove the circumstance if \( \pi_0 = 0 \). □

Web Appendix D. Conditions and properties for deconvolution

Suppose the incubation period \( I \) follows a Gamma distribution \( \Gamma(\alpha, \beta) \) with pdf \( f_I \), then the characteristic function (chf) of \( I \) satisfies

\[ \phi_I(t) = \left(1 - \frac{it}{\beta}\right)^{-\alpha} \text{ and } |\phi_I(t)|^2 = \left(\frac{\beta^2}{\beta^2 + t^2}\right)^{\alpha}. \]

According to Liu and Taylor (1989) and Devroye (1989), under the following conditions, the estimator for \( f_G \) in (13) at its interior point is consistent:

(C1). \( \phi_S(t)/|\phi_I(t)|^2 \) is absolutely integrable.

(C2). The second order derivative of \( f_G(y) \) exists and is continuous on \([0, +\infty)\).

(C3). The chf of \( I \phi_I(t) \neq 0 \) for almost all \( t \).

(C4). The kernel chf \( \phi_K(t) \) vanishes at \( |t| > M \) for some \( M \).

(C5). \( M_n \to \infty \) and \( h_n \to 0 \) as \( n \to \infty \).

The aim of the kernel \( K(\cdot) \) is to smooth the empirical chf of \( S \) into an integrable function. It is known that the best kernels are those whose chfs are the flattest near the
origin (Davis, 1975, 1977). The bias of \( \hat{f}_G(y) \) is

\[
\text{bias}\{\hat{f}_G(y)\} = \frac{1}{2} h^2 f_G(y) \int_{-\infty}^{y/h_n} t^2 K_c(t) dt + o(h_n^2),
\]

where \( K_c(t) = a_0 K(t) + a_1 K'(t) \) and

\[
\begin{pmatrix} a_0 \\ a_1 \end{pmatrix} = \begin{pmatrix} \int_{-\infty}^{y/h_n} K(t) dt & \int_{-\infty}^{y/h_n} K'(t) dt \\ \int_{-\infty}^{y/h_n} tK(t) dt & \int_{-\infty}^{y/h_n} tK'(t) dt \end{pmatrix}^{-1} \begin{pmatrix} 1 \\ 0 \end{pmatrix}.
\]

The variance of \( \hat{f}_G(y) \) is given in Karunamuni (2009).

An alternative to nonparametric density estimation is the parametric approach. To accord with the generation mechanism of serial interval, it is more reasonable to post a parametric model on generation time rather than serial interval theoretically. A potential weakness for directly modeling the serial interval is model misspecification. An additional condition should be satisfied to make \( \hat{\phi}_G \) a proper chf:

\((C6). \ |\hat{\phi}_S(t)|/|\phi_I(t)|^2 \leq 1.\)

This condition requires that the norm of estimated chf for \( S \) be declining fast near the origin and is too strong for modeling observed data. For example, normal \( S \) and Gamma \( I \) may not satisfy \((C6).\)

**Web Appendix E. The goodness-of-fit test for incubation period modeling**

The goodness-of-fit test is performed as follows. Divide the non-negative real line into 17 parts: \([k - 1.5, k - 0.5)\) for \( k = 1, \ldots, 16, \) and \([15.5, +\infty)\). The goodness-of-fit \( \chi^2 \) statistic is

\[
X^2 = \sum_{k=1}^{17} \frac{(O_k - E_k)^2}{E_k},
\]

where \( E_k \) and \( O_k \) are the expected and observed number of cases in the \( k \)th interval:

\[
E_k = m[\hat{\pi} F_I(k - 0.5; \hat{\theta}) + (1 - \hat{\pi}) H(k - 0.5; \hat{\theta})] - m[\hat{\pi} F_I(k - 1.5; \hat{\theta}) + (1 - \hat{\pi}) H(k - 1.5; \hat{\theta})].
\]

The degree of freedom of \( X^2 \) is \( 17 - 3 - 1 = 13 \), since there are three parameters in total. The 0.95 quantile of chi-squared distribution with 13 degrees of freedom is 22.36.
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