BETS: The dangers of selection bias in early analyses of the coronavirus disease (COVID-19) pandemic

Qingyuan Zhao∗1, Nianqiao Ju2, Sergio Bacallado1, and Rajen D. Shah1

1Statistical Laboratory, Department of Pure Mathematics and Mathematical Statistics, University of Cambridge
2Department of Statistics, Harvard University

May 7, 2020

Abstract

The coronavirus disease 2019 (COVID-19) has quickly grown from a regional outbreak in Wuhan, China to a global pandemic. Early estimates of the epidemic growth and incubation period of COVID-19 may have been biased due to sample selection. Using detailed case reports from 14 locations in and outside mainland China, we obtained 378 Wuhan-exported cases who left Wuhan before an abrupt travel quarantine. We developed a generative model we call BETS for four key epidemiological events—Beginning of exposure, End of exposure, time of Transmission, and time of Symptom onset (BETS)—and derived explicit formulas to correct for the sample selection. We gave a detailed illustration of why some early and highly influential analyses of the COVID-19 pandemic were severely biased. All our analyses, regardless of which subsample and model were being used, point to an epidemic doubling time of $2^{\frac{5}{2}}$ days during the early outbreak in Wuhan. A Bayesian nonparametric analysis further suggests that about 5% of the symptomatic cases may not develop symptoms within 14 days of infection and that men may be much more likely than women to develop symptoms within 2 days of infection.

∗Correspondence to: Dr. Qingyuan Zhao, Centre for Mathematical Sciences, Wilberforce Road, Cambridge, CB3 0WB, United Kingdom. Email:qyzhao@statslab.cam.ac.uk
1 Introduction

On December 31, 2019, the Health Commission in Wuhan, China, announced 27 cases of unknown viral pneumonia and alerted the World Health Organization. The causative pathogen was quickly identified as a novel coronavirus and the disease was later designated as the coronavirus disease 2019 (COVID-19) [4]. The regional outbreak in Wuhan quickly turned into a global pandemic. As of April 15, 2020, COVID-19 has reached almost every country in the world, infected at least 2 million people, and killed at least 130,000 [2].

Researchers around the world quickly responded to the COVID-19 outbreak. In particular, many have examined early outbreak data to estimate the initial epidemic growth, using COVID-19 cases confirmed in Wuhan or elsewhere. Two early studies published in premier medical journals by the end of January estimated that the epidemic doubling time in Wuhan was about 6 to 7 days [17, 28], but other studies appearing around the same time found that the doubling time was drastically shorter, about 2 to 3 days [23, 25, 29]. How the pandemic subsequently developed around the world seems to suggest that the latter estimates were much closer to truth. By simply plotting the cumulative cases and deaths over time, it is evident now that the number of cases (and deaths) grew more than 100 times 20 days after the first 100 cases (and 10 deaths) in countries most heavily hit by the pandemic such as Italy, Spain, and the United States (Figure 1). That growth rate almost exactly corresponds to a doubling time of 3 days. Nevertheless, to our knowledge there is no formal explanation for this drastic difference, and it might have caused confusion during the early phase of containment of COVID-19. For example, during the UK government’s daily briefing on March 16, it was acknowledged that “without drastic action, cases could double every five or six days” [3]. Less than two weeks later, that number was revised to “three to four days” [1].

For infectious diseases, another key epidemiological parameter is the incubation period. Several studies have attempted to estimate the incubation period distribution of COVID-19 using cases exported from Wuhan [5, 15, 18] and the results have been influential in shaping guidelines to manage confirmed COVID-19 patients. For example, the interim clinical guidance for managing COVID-19 patients published by the Centers for Disease Control and Prevention (CDC) [6] quoted the results of Lauer et al. [15] that “97.5% of persons with COVID-19 who develop symptoms will do so within 11.5 days of SARS-CoV-2 infection.” However, as we will demonstrate below in Section 4, the design and statistical inference of these studies are highly susceptible to selection bias.

In general, there are several potential sources of bias in early analyses of the COVID-19 pandemic (see also Table 1):

(i) **Under-ascertainment:** Because COVID-19 is a new disease, the testing capacity was very limited during the early stage of the outbreak. The eligibility criterion for testing was initially very strict. This may explain why Li et al. [17] under-estimated the epidemic growth as they only used cases in Wuhan who showed symptoms before January 5, 2020.

(ii) **Non-random sample selection:** Not all public health agencies reported detailed information of COVID-19 cases. Many stopped doing so after the first few cases. Studies which only collect complete or conveniently available data may be biased by non-random sample selection. For example, it is often impossible to know the exact time when the cases were infected. If one simply uses cases with known infection time, the incubation period may be under-estimated because it is more difficult to discern the infection time for cases with longer incubation period.

(iii) **Travel quarantine:** Wuhan is a major transportation hub in central China. To control the spread of the virus, all outbound travels from Wuhan were abruptly halted on January 23, 2020. For studies using cases exported from Wuhan (COVID-19 cases who were infected in
(a) Cumulative cases.

(b) Cumulative deaths.

Figure 1: Growth of the COVID-19 pandemic around the world (data retrieved from [https://www.worldometers.info/](https://www.worldometers.info/) on April 15, 2020).

Wuhan and confirmed elsewhere), ignoring the sample selection due to the travel quarantine leads to biased estimates of the epidemic growth.

(iv) **Ignoring epidemic growth:** Because the epidemic was rapidly growing, patients were more likely to be infected towards the end of their exposure period. Ignoring the growth and using a simple uniform distribution for the infection time over a prolonged exposure period may lead to over-estimation of the incubation period.

(v) **Right-truncation:** Early analyses of the epidemic were limited to using cases confirmed before a certain date, when the number of infections was still growing rapidly. This may lead to under-estimation of the incubation period, as people with milder symptoms or longer incubation period are less likely to be included in the study.

In this article, we address these challenges by carefully constructing a study sample and a statistical model. We collected key epidemiological information for 1,460 confirmed COVID-19 cases across 14 locations in and outside mainland China. By focusing on locations where the local health agencies made great efforts to contain the initial outbreaks and published detailed case reports, the biases due to (i) under-ascertainment and (ii) non-random selection are minimized. Section 2 describes how our data were collected and the Wuhan-exported cases were discerned.

We addressed potential biases due to (iii) the travel quarantine, (iv) ignoring epidemic growth, and (v) right-truncation by constructing a generative statistical model. We call it the BETS model, as it models four key epidemiological events: Beginning of exposure, End of exposure, time of Transmission, and time of Symptom onset. The travel quarantine puts a constraint on the support of the observed data for Wuhan-exported cases, for which we carefully worked out the selection probability and used it to adjust the likelihood function. Epidemic growth is naturally considered in the estimation of the incubation period because they are estimated jointly using the likelihood
| Bias                                      | Susceptible studies                                                                 | Direction                                    | Solutions                                                                 |
|------------------------------------------|-----------------------------------------------------------------------------------|----------------------------------------------|---------------------------------------------------------------------------|
| **(i) Under-ascertainment:** Symptomatic patients did not seek health-care or could not be diagnosed. | All studies using cases confirmed when testing is insufficient.                   | **Varied**, depending on the pattern of under-ascertainment and parameter of interest. | Use carefully considered and planned study designs.                      |
| **(ii) Non-random sample selection:** Cases included in the study are not representative of the population. | All studies, as detailed information of COVID-19 cases is sparse, but especially those without clear inclusion criteria. | **Varied.**                                  | Follow a protocol for data collection and exclude data that do not meet the sample inclusion criterion. |
| **(iii) Travel quarantine:** Outbound travel from Wuhan was banned from January 23, 2020 to April 8, 2020. | Studies that analyze cases exported from Wuhan.                                   | **Under-estimation** of epidemic growth [28] and infection-to-recovery time [8]. | Derive tailored likelihood functions to account for travel restrictions. (See Section 4.1) |
| **(iv) Epidemic growth:** Patients were more likely to be infected towards the end of their exposure period. | Studies that treat infections as uniformly distributed over the exposure period.    | **Over-estimation** of incubation period [5, 15, 18] and serial interval [9, 22]. | Derive tailored likelihood functions to account for epidemic growth. (See Section 4.2) |
| **(v) Right-truncation:** Cases confirmed after a certain time are excluded from the dataset. | Studies that only use cases detected early in an epidemic.                         | **Under-estimation** of incubation period [5, 15, 18], serial interval [9, 22], and disease severity. | 1. Collect all cases that meet a selection criterion, do not end data collection prematurely; 2. Derive tailored likelihood functions to correct for right-truncation. (See Section 4.2) |

Table 1: Summary of potential biases in analyses of the COVID-19 pandemic.
functions we derived. Sample selection due to right-truncation can also be characterized and adjusted for. Details of the generative model and likelihood inference can be found in Section 3.

We then give a detailed explanation in Section 4 of why some early analyses of the COVID-19 outbreak were severely biased, including the estimation of epidemic growth by Wu et al. [28] and the estimation of incubation period by Backer et al. [5], Lauer et al. [15], Linton et al. [18]. Because these analyses did not start from a generative model, they could not correctly adjust for sample selection in their statistical inference.

In order to obtain closed-form likelihood functions in Section 3, we introduced some parametric assumptions which necessarily restrict the shape of the tail of the incubation period distribution. To avoid biased tail estimates, we model the distribution nonparametrically and also relax the other assumptions in Section 5. Because the likelihood function is no longer available in closed form, a Markov Chain Monte Carlo (MCMC) sampler is needed for Bayesian nonparametric inference. Finally, we summarize our findings and discuss potential limitations of our study in Section 6. All technical derivations can be found in the appendix; our dataset and statistical programs are publicly available as an R package from https://github.com/qingyuanzhao/bets.covid19.

2 Data

2.1 Data Collection

We identified 14 locations where the local health agencies have published continuous reports for every confirmed COVID-19 case since the first local case. Out of the 14 locations, 8 are cities/provinces in mainland China: Hefei, Guilin, Jinan, Shaanxi, Shenzhen, Yangzhou, Xinyang, Zhanjiang and 6 are countries/regions in East Asia: Hong Kong, Japan, South Korea, Macau, Singapore, and Taiwan (Figure 2). These locations have varied levels of economic development and patterns of traveling to/from Wuhan. Key information (close contact, travel history, symptom onset) of the confirmed COVID-19 cases was collected based on press releases of the official health agencies (Table 2). In total, there are 1,460 COVID-19 cases in the collected dataset.

For the mainland Chinese locations, the dataset included all the cases confirmed as of February 29, 2020. In Chinese cities outside the Hubei province, local epidemics were considered to be successfully contained by the end of February. For the international locations, the dataset included all the cases confirmed before February 15, more than three weeks after the outbound travel quarantine of Wuhan on January 23. It is thus safe to say that our dataset contains almost all Wuhan-exported cases confirmed in these locations.

2.2 Discerning Wuhan-exported cases

We define Wuhan-exported cases as those who were infected in Wuhan and confirmed elsewhere. In total, 614 cases in our dataset are potentially exported from Wuhan because they had stayed in Wuhan before got diagnosed elsewhere. Because Wuhan was the first center of epidemic outbreak and traveling from/to Wuhan was not restricted before January 23, it is reasonable to assume that most of these 614 cases were infected there. However, some uncertainty arises if a case had contact with other confirmed cases outside their stay in Wuhan, in one of the following scenarios:

- The case already had contact with other confirmed cases before their stay in Wuhan (4 cases);
- The case had contact with other confirmed cases only after they left Wuhan but before they arrived at their destination, for example in trains or flights (4 cases);
| Column name | Description | Example | Summary statistics |
|------------|-------------|---------|--------------------|
| **Case**   | Unique identifier for each case | HongKong-05 | 1460 in total |
| **Residence** | Nationality or residence of the case | Wuhan | 21.5% reside in Wuhan |
| **Gender** | Gender | Male/Female | 52.1%/47.7% (0.2% unknown) |
| **Age** | Age | 63 | Mean=45.6, IQR=[34, 57] |
| **Known Contact** | Have known epidemiological contact? | Yes/No | 84.7%/15.3% |
| **Cluster** | Relationship with other cases | Husband of HongKong-04 | 32.1% known |
| **Outside** | Transmitted outside Wuhan? | Yes/Likely/No | 58.5%/7.7%/33.8% |
| **Begin Wuhan** | Begin of stay in Wuhan (B) | 30-Nov | 58.9% known period/date |
| **End Wuhan** | End of stay in Wuhan (E) | 22-Jan | 8.2% known date |
| **Exposure** | Period of exposure | 1-Dec to 22-Jan | 58.9% known period/date |
| **Arrived** | Final arrival date at the location where confirmed a COVID-19 case | 22-Jan | 40.6% did not travel outside |
| **Symptom** | Date of symptom onset (S) | 23-Jan | 9.0% unknown |
| **Initial** | Date of first medical visit/quarantine | 23-Jan | 6.5% unknown |
| **Confirmed** | Date confirmed as a COVID-19 case | 24-Jan | |

Table 2: A summary of the key columns in the collected dataset. Boxed entries correspond to the recorded values of the example (HongKong-05).

1Description of this case in Hong Kong government’s press release on January 24, 2020: “The other two cases are a married couple of residents of in Wuhan, a 62-year-old female [HongKong-04] and a 63-year-old male [HongKong-05], with good prior health conditions. Based on information provided by the patients, They took a high-speed train departing from Wuhan at 2:20pm, January 22, and arrived at the West Kowloon station around 8pm. The female patient had a fever since yesterday with no respiratory symptoms. The male patient started to cough yesterday and had a fever today. They went to the emergency department at the Prince of Wales Hospital yesterday and were admitted to the hospital for treatment in isolation. Currently their health conditions are stable. Respiratory samples of the two patients were tested positive for the novel coronavirus.” (translated from Chinese).

2A case is considered to have known epidemiological contact if he/she had contact with people from the Hubei province or had contact with another case confirmed earlier.

3See the main text for the criterion we used to classify the cases.

4The beginning of stay is treated as November 30 if the case resides in Wuhan and has no known beginning of stay.
- The case had close contact with other confirmed cases (usually family members who traveled together from Wuhan) after they reached their travel destination (131 cases).

To discern a dataset of Wuhan-exported cases, the principle we followed is to exclude cases if there is a “reasonable doubt” that they could be infected outside Wuhan. We assumed in the first two scenarios above, the cases were transmitted outside Wuhan. For the third scenario, it is likely that the cases were transmitted outside Wuhan, but at least one of the cases in each cluster were transmitted in Wuhan. (Two cases are considered to belong two the same cluster if they are in the family or had other recorded contact.) We used a column called **Outside** in our dataset to record our best judgment on whether the cases were transmitted outside Wuhan using the following rules:

(i) **Outside** = “Yes”: Cases with no recorded stay in Wuhan between December 1, 2019 and January 23, 2020, and the 8 cases in the first two scenarios above (854 cases).

(ii) **Outside** = “Likely”: Wuhan-exposed cases who did not show symptoms during the recorded stay in Wuhan and had recorded contact with another confirmed COVID-19 case with an earlier symptom onset (112 cases).

(iii) **Outside** = “No”: Wuhan-exposed cases who had no recorded contact with other confirmed
Figure 3: Epidemic curves in different locations stratified by whether the cases were transmitted outside Wuhan. “China - Other” includes four Chinese cities: Guilin, Jinan, Yangzhou, Zhanjiang; “International” includes six Asian countries/regions: Hong Kong, Japan, Korea, Macau, Singapore, Taiwan. The dashed vertical lines correspond to the abrupt travel quarantine of Wuhan from January 23, 2020.

Figure 3 shows the local epidemic curves stratified by the Transmitted outside Wuhan? column in different locations.

The dataset we collected has relatively few missing values in the key entries needed for epidemic modeling. Among the Transmitted outside = “No” cases, only 6.5% do not have the exact date they left Wuhan and only 8.1% have missing symptom onset date (including those showing no symptoms at the time of confirmation). We imputed the missing end of exposure to Wuhan by the day of the travel quarantine (January 23) and excluded the cases with missing symptom onset. This left us with 458 cases. We further excluded cases who arrived at the location where they are diagnosed with COVID-19 after January 23 as they have a different traveling pattern than the other cases. In the end we obtained 378 cases who were exported from Wuhan.

3 Statistical model and parametric inference

3.1 BETS: A generative model
On a high level, our goal is to make inference about the epidemic in Wuhan using its “shadows” observed in other locations. To properly consider the consequences of sample selection, we will first outline a generative model for (which is also named after) four key epidemiological events: the beginning of stay in Wuhan \(B\), the end of stay in Wuhan \(E\), the usually unobserved time of transmission \(T\), and the time of symptom onset \(S\) (BETS). These four variables are well defined regardless of whether the person has been to Wuhan, contracted the pathogenic coronavirus, or showed symptoms of COVID-19.

**Study population: Exposed to Wuhan**

Consider the population of all people who stayed in Wuhan any time between 12AM December 1, 2019 (time \(0\)) and 12AM January 24, 2020 (time \(L\) when outbound travel from Wuhan was banned, \(L = 54\)) in local time. We introduce the following conventions to define the population with exposure to Wuhan:

- \(B = 0\): The person started their stay in Wuhan before December 2019.
- \(E = \infty\): The person did not arrive in the 14 locations we are considering before the travel quarantine (time \(L\)). For the purpose of this study, we need not differentiate between people who stayed in Wuhan or went to a location different from the ones we are considering.
- \(T = \infty\): The person did not contract the pathogenic virus during their stay in Wuhan. For the purpose of this study, we need not differentiate between people who contracted the virus outside their Wuhan stay and people who never contracted the virus.
- \(S = \infty\): The person did not show symptoms of COVID-19, either because they never contracted the virus or they were asymptomatic.

Because we are only considering people exposed to Wuhan, we have \(B \leq L\). Two other natural constraints are \(B \leq E\) and \(T \leq S\) (where we allow \(\infty \leq \infty\)). Therefore, the support of \((B, E, T, S)\) for the Wuhan-exposed population is

\[
P = \{(b, e, t, s) \mid b \in [0, L], e \in [b, L] \cup \{\infty\}, t \in [b, e] \cup \{\infty\}, s \in [t, \infty]\}.
\]

(1)

Notice that although \(B\) is supported on \([0, L]\), \(B = 0\) is a point mass representing Wuhan residents and is categorically different from \(B = \epsilon\) for some small positive \(\epsilon\). All density functions of \(B\) below are defined with respect to the sum of Lebesgue measure on the real line and degenerate counting measure for \(\{0\}\). Similarly, for \(E, T,\) and \(S\) the dominating measure is the sum of Lebesgue measure and the counting measure for \(\{\infty\}\). Joint densities of \((B, E, T, S)\) below are defined with respect to their product measure.

**Full data BETS model: Independence of traveling and disease transmission/progression**

In Section 3.2 below we will define the constraints corresponding to our sample selection. But first, we will introduce a generative statistical model for \((B, E, T, S)\) in the whole study population \(P\). The joint density of \((B, E, T, S)\) can always be factorized as:

\[
f(b, e, t, s) = f_B(b) \cdot f_E(e \mid b) \cdot f_T(t \mid b, e) \cdot f_S(s \mid b, e, t).
\]

(2)

Throughout this article we will maintain two general assumptions about two conditional densities in this factorization:
Figure 4: Directed acyclic graph (DAG) for the BETS model. B is the beginning of exposure, E is the end of exposure, T is the time of transmission, and S is the time of symptom onset.

**Assumption 1.** The conditional density $f_T(t \mid b, e)$ does not depend on $b$ and $e$ in the range $b \leq t \leq e$, so it can be written as

$$f_T(t \mid b, e) = \begin{cases} g(t), & \text{if } b < t < e, \\ 1 - \int_b^e g(x) \, dx, & \text{if } t = \infty. \end{cases}$$

(3)

Here $g(t) \geq 0$ models the epidemic growth in Wuhan before the citywide quarantine on January 23; it can be interpreted as the instantaneous probability of being infected in Wuhan at time $t$ and satisfies the constraint $\int_0^L g(x) \, dx \leq 1$.

**Assumption 2.** The conditional density $f_S(s \mid b, e, t)$ does not depend on $b$ and $e$, so it can be written as

$$f_S(s \mid b, e, t) = \begin{cases} \nu \cdot h(s-t), & \text{if } s < \infty, \\ 1 - \nu, & \text{if } s = \infty. \end{cases}$$

(4)

Here $h(s-t)$ is the conditional density of the incubation period $S - T$ given that $S - T < \infty$ (the case is not asymptomatic), so $h(\cdot)$ satisfies $\int_0^\infty h(x) \, dx = 1$.

Assumptions 1 and 2 essentially mean that the disease transmission and progression are independent of traveling, which allows us to extend conclusions learned from the Wuhan-exported sample to the whole population. Assumption 2 is equivalent to the conditional independence $S \perp \perp (B, E) \mid T$, which can be represented as a directed acyclic graphical (DAG) model (Figure 4) on the distribution of $(B, E, T, S)$ [16]. Assumption 1 further restricts the dependence of $T$ on $(B, E)$. Under these two assumptions, the BETS model is then parameterized by two kinds of parameters: the nuisance parameters for the traveling pattern $f_B(\cdot)$ and $f_E(\cdot \mid \cdot)$, and the parameters of interest for disease transmission $g(\cdot)$ and progression $h(\cdot)$.

Like any other assumptions in epidemic models, Assumptions 1 and 2 represent approximations to the underlying dynamics. Assumptions 1 and 2 can be violated if, for example, short-term visitors were exposed to more infectious cases or if people were less likely to travel if they felt sick. Nevertheless, we think they are reasonable approximations to the reality during the initial outbreak, when little was known about the new infectious disease.

**Parametric assumptions for closed-form likelihood functions**

Assumptions 1 and 2 are general assumptions on the dependence of $T$ and $S$ on $B$ and $E$. We consider two parametric assumptions that simplify the interpretation of our results:

**Assumption 3.** The probability of contracting the virus in Wuhan was increasing exponentially before the quarantine:

$$g(t) = g_{\kappa, r}(t) \triangleq \kappa \cdot \exp(rt), \quad t \leq L,$$

(5)

where $(\kappa, r)$ satisfies $\int_0^L g_{\kappa, r}(t) \, dt \leq 1$. 

10
Assumption 4. The incubation period $T - S$, given that it is finite (the case is not asymptomatic), follows a Gamma distribution with shape $\alpha > 0$ and rate $\beta > 0$:

$$h(s - t) = h_{\alpha, \beta}(s - t) = \frac{\beta^\alpha}{\Gamma(\alpha)}(s - t)^{\alpha-1}\exp\{-\beta(s - t)\}.$$  

(6)

Assumption 3 says that the epidemic size in Wuhan was growing exponentially before the quarantine, which is a common assumption for early epidemic outbreaks. We think it is quite reasonable given that little was known about the novel coronavirus before January 23. Assumption 4 restricts the density function $h(\cdot)$ to the Gamma family, which is commonly used to model the distribution of the incubation period. These two assumptions will be used later in this and the next sections to calculate closed-form likelihood functions. Later in Section 5, we will relax the parametric assumptions to allow more flexible patterns for the epidemic growth and more general distributions of the incubation period.

3.2 Accounting for sample selection in the likelihood

Study sample: Wuhan-exported cases

To use Wuhan-exported cases to study the epidemic growth and incubation period, it is crucial to consider the effect of sample selection on Wuhan-exported cases. Using the notation above, the Wuhan-exported cases confirmed in the 14 locations we consider can be written as an event $(B, E, T, S) \in D$ where

$$D = \{(b, e, t, s) \in \mathcal{P} \mid b \leq t \leq e \leq L, t \leq s < \infty\}.$$  

(7)

Compared to the full population $\mathcal{P}$ of people with exposure to Wuhan in [1], the set $D$ makes three further restrictions:

(i) $B \leq T \leq E$, because we only use cases who contracted the virus during their stay in Wuhan;

(ii) $E \leq L$, because the case can only be observed in the dataset if they left Wuhan before the travel quarantine;

(iii) $S < \infty$, because not all locations report asymptomatic cases, which motivates us to only consider COVID-19 cases who showed symptoms.

Selection-adjusted likelihood functions

In an ideal world where we could take independent observations $(B_i, E_i, T_i, S_i)$, $i = 1, \ldots, n$ from the exposed population $\mathcal{P}$, the likelihood function would be given by a product of the density $f(B_i, E_i, T_i, S_i)$ in (2) over $i$. However, that is almost impossible for the initial COVID-19 outbreak in Wuhan. Because of limited testing capacity in the beginning of the outbreak, many COVID-19 patients in Wuhan were not identified.

Instead, in Section 2 we have obtained a high-quality dataset of Wuhan-exported cases which can be considered as “shadows” of the epidemic in Wuhan. To use this dataset, it is crucial that the statistical inference takes into account the sample selection because we do not have independent observations from $\mathcal{P}$. Instead, we may view our sample as independent observations generated from the following density:

$$f(b, e, t, s \mid D) \overset{\Delta}{=} f(b, e, t, s \mid (B, E, T, S) \in D) = \frac{f(b, e, t, s) \cdot 1\{(b, e, t, s) \in D\}}{\mathbb{P}((B, E, T, S) \in D)},$$  

(8)
where $1_{\{\cdot\}}$ is the indicator function. To reduce cluttering, we will omit the indicator $1_{\{(b,e,t,s)\in D\}}$ if it is clear from the context that we are considering sample from the Wuhan-exported cases $\mathcal{D}$. We can then use the product
\[
\prod_{i=1}^{n} f(B_i, E_i, T_i, S_i \mid \mathcal{D}),
\]
as the likelihood function, under the assumption that we have observed an independent and identically distributed sample $(B_i, E_i, T_i, S_i)$, $i = 1, \ldots, n$ from the density $f_{B}$. A further difficulty is that the time of transmission $T$ is usually unobserved in our dataset. To solve this problem, we can either treat $T$ as a latent variable and maximize the likelihood over both the modeling parameters and the unobserved $T_i$, or simply marginalize over $T$ in the full data likelihood and use the following observed data likelihood,
\[
L_{\text{uncond}}(\theta) = \prod_{i=1}^{n} \int f_{T,S}(t, S_i \mid B_i, E_i, \mathcal{D}) dt,
\]
where $\theta = (f_B(\cdot), f_E(\cdot \mid \cdot), g(\cdot), h(\cdot))$ contains all the parameters of interest.

We can also condition on $(B, E)$ to formulate a conditional likelihood function that does not depend on the marginal distribution of $(B, E)$:
\[
L_{\text{cond}}(\theta) = \prod_{i=1}^{n} \int f_{T,S}(t, S_i \mid B_i, E_i, \mathcal{D}) dt,
\]
where $\theta = (g(\cdot), h(\cdot))$ and
\[
f_{T,S}(t, s \mid b, e, \mathcal{D}) = f_{T,S}(t, s \mid B = b, E = e, (B, E, T, S) \in \mathcal{D}) = \frac{f_{T,S}(t, s \mid b, e)}{\mathbb{P}((B, E, T, S) \in \mathcal{D} \mid B = b, E = e)}.
\]
The information about the epidemic growth $g(\cdot)$ and the incubation period $h(\cdot)$ contained in the density $f_{B,E}(b, e \mid \mathcal{D})$ is not used in the conditional likelihood, but the benefit is that it does not require us to specify the nuisance parameters $f_B(\cdot)$ and $f_E(\cdot \mid \cdot)$ to model the traveling. In other words, the conditional likelihood is less efficient than the unconditional likelihood but more robust.

Next we derive the likelihood functions (10) and (11). For the unconditional likelihood function we will make additional parametric modeling assumptions on the traveling pattern $f_B(\cdot)$ and $f_E(\cdot \mid \cdot)$.

**Computing the selection probability**

The first technical problem is to compute the denominators in (8) and (12). This is straightforward for the conditional likelihood:

**Lemma 1.** Under Assumptions 1 and 2, for $(b, e, t, s) \in \mathcal{D}$,
\[
\mathbb{P}((B, E, T, S) \in \mathcal{D} \mid B = b, E = e) = \nu[G(e) - G(b)], \quad \text{and} \quad f_{T,S}(t, s \mid b, e, \mathcal{D}) = \frac{g(t)h(s - t)}{G(e) - G(b)}. \tag{13}
\]
where $G(t) = \int_{-\infty}^{t} g(x) dx$. If we additionally assume $g(t)$ is growing exponentially (Assumption 3), we have
\[
f_{T,S}(t, s \mid b, e, \mathcal{D}) = \begin{cases} 
    r \exp(rt) & \text{for } r \neq 0, \\
    \frac{\exp(re) - \exp(rb)}{r} h(s - t) & \text{for } r = 0,
\end{cases}
\]
\[
\frac{1}{e - b} h(s - t), \quad \text{for } r = 0. \tag{14}
\]
An important observation here is that \((14)\) does not depend on \(\nu\) (proportion of symptomatic cases) and \(\kappa\) (absolute scale of the epidemic). Conditional likelihood \(L_{\text{cond}}(\theta)\) can then be derived by integrating \((14)\) over \(t\) and the precise formula can be found in Proposition 1 below.

For the denominator in the unconditional likelihood, we need to integrate \(P((B, E, T, S) \in \mathcal{D} | B = b, E = e)\) in Lemma 1 over the marginal distribution of \(B\) and \(E\). We make the following simplifying assumptions on \(f_B(b)\) and \(f_E(e | b)\) which heuristically say that the travel pattern is stable during the study period:

**Assumption 5.** The beginning of stay in Wuhan \(B\), conditioning on \(0 < B \leq L\), follows a uniform distribution from \(0\) to \(L\). More specifically,

\[
f_B(b) = \begin{cases} 
1 - \pi, & \text{for } b = 0, \\
\pi/L, & \text{for } 0 < b \leq L,
\end{cases}
\]

where \(0 \leq \pi \leq 1\) is the proportion of visitors (non-residents of Wuhan) in the Wuhan-exposed population.

**Assumption 6.** The end of stay \(E\) follows an uniform distribution from \(B\) to \(L\) given \(E \leq L\), with rate depending on whether the person resides in Wuhan:

\[
f_E(e | b = 0) = \begin{cases} 
\lambda_W, & \text{if } 0 \leq e \leq L, \\
1 - L\lambda_W, & \text{if } e = \infty,
\end{cases}
\]

\[
f_E(e | b, b > 0) = \begin{cases} 
\lambda_V, & \text{if } b \leq e \leq L, \\
1 - (L - b)\lambda_V, & \text{if } e = \infty,
\end{cases}
\]

where the parameters \(\lambda_W, \lambda_V \leq 1/L\).

For \(b > 0\), Assumption 4 implies that \(P(E = \infty | b, b > 0) = b\lambda_V + (1 - L\lambda_V)\) increases as \(b\) increases. This is consistent with our intuition that the later someone arrives in Wuhan, the more likely that person stays there after the travel quarantine on January 23.

By using the parametric forms \((5), (15), (16)\) when integrating \(P((B, E, T, S) \in \mathcal{D} | B = b, E = e)\) and using the approximation \((1 + rL)/\exp(rL) \approx 0\) for \(rL > 5\), we obtain the following result.

**Lemma 2.** Under Assumptions 1 to 3, 5 and 6, for \(r > 5/L\), the selection probability is given by

\[
P((B, E, T, S) \in \mathcal{D}) \approx \frac{\kappa \exp(rL) \nu}{r^2} \left[ (1 - \pi)\lambda_W + \pi\lambda_V \left(1 - \frac{2}{rL}\right) \right],
\]

and for \((b, e, t, s) \in \mathcal{D}\), the density in \((8)\) is given by

\[
f(b, e, t | \mathcal{D}) \approx r^2 \cdot \frac{1_{\{b=0\}} + (\rho/L)1_{\{b>0\}} \cdot \exp(rt)}{[1 + \rho(1 - 2/(rL))] \cdot \exp(rL)} \cdot h(s - t),
\]

where \(1_{\{\cdot\}}\) is the indicator function and \(\rho = (\lambda_V/\lambda_W) \cdot \pi/(1 - \pi)\).

Similar to \((14)\), the conditional density \((17)\) does not depend on \(\nu\) and \(\kappa\). Moreover, it only depends on the traveling parameters \(\pi, \lambda_V\) and \(\lambda_W\) through a single transformed parameter \(\rho\). The approximation \((1 + rL)/\exp(rL) \approx 0\) we used in the Appendix to obtain the analytical formulae in Lemma 2 is quite reasonable for \(rL > 5\) (if the doubling time is 4 days, \(rL = \log(2)/4 \times 54 = 9.34\)).
Observed data likelihood

As explained after equation (9), we cannot immediately use the densities in (14) and (17) for statistical inference because we do not observe the time of transmission $T$. The final step in the derivation of our likelihood function is to marginalize over $t$ in the density functions. The parametric form of $h(\cdot)$ in Assumption 4 allows us to derive closed-form formulae.

Proposition 1. Under Assumptions 1 to 4, the observed data conditional likelihood (11) is given by

$$L_{\text{cond}}(r, \alpha, \beta) = \begin{cases} r^n \left( \beta \over \beta + r \right)^{na} \cdot \prod_{i=1}^{n} \frac{\exp(rS_i)[H_{\alpha,\beta+r}(S_i - B_i) - H_{\alpha,\beta+r}((S_i - E_i)_+)]}{\exp(rE_i) - \exp(rB_i)}, & \text{for } r > 0, \\ \prod_{i=1}^{n} \frac{H_{\alpha,\beta}(S_i - B_i) - H_{\alpha,\beta}((S_i - E_i)_+)}{E_i - B_i}, & \text{for } r = 0, \end{cases}$$

(18)

where $H_{\alpha,\beta}(\cdot)$ is the cumulative distribution function of the Gamma distribution with shape $\alpha$ and rate $\beta$ and $(x)_+ = \max(x, 0)$ is the positive part of $x$. Under Assumptions 1 to 6, the observed data unconditional likelihood (10) for $r > 5/L$ is approximately given by

$$L_{\text{uncond}}(\rho, r, \alpha, \beta) \approx r^{2n} \left( \beta \over \beta + r \right)^{na} \cdot \prod_{i=1}^{n} \left\{ \frac{1_{\{B_i=0\}} + (\rho/L)1_{\{B_i>0\}}}{1 + \rho(1 - 2/(rL))} \exp \left\{ r(S_i - L) \right\} \right. \left. \times [H_{\alpha,\beta+r}(S_i - B_i) - H_{\alpha,\beta+r}((S_i - E_i)_+)] \right\}.$$  

(19)

It is worthwhile to point out that if $r = 0$ (the epidemic was stationary), our conditional likelihood function $L_{\text{cond}}(r, \alpha, \beta)$ reduces to the likelihood function for interval-censored exposure in Reich et al. [23]. However, COVID-19 was growing quickly during its early outbreak in Wuhan, so the growth exponent $r$ is very different from 0. It is thus inappropriate to use the likelihood $L_{\text{cond}}(0, \alpha, \beta)$ to estimate the incubation period of COVID-19, as done in some previous analyses also using Wuhan-exported cases [5, 15, 18]. See Section 4.2 for further discussion and an illustration of the bias due to ignoring the epidemic growth.

3.3 Results of the parametric inference

Implementation

To fit the statistical model, we used the 378 Wuhan-exported cases that satisfy our sample selection criterion and do not have missing symptom onset date. We fitted separate models for different locations to compare the results across the locations.

As the model in Section 3 is a regular parametric model, we performed the usual frequentist inference using the likelihood function (19). In particular, point estimators of the parameters $(\rho, r, \alpha, \beta)$ were obtained by maximizing the likelihood function (19), and confidence intervals for the parameters were obtained by inverting the likelihood ratio $\chi^2$-test. As we are more interested in quantiles of the incubation period instead of the shape and rate parameters, we parametrized the Gamma distribution in Assumption 4 by its median and 95% quantile and mapped them to $\alpha$ and $\beta$ when calculating the likelihood function. The growth exponent $r$ was also transformed to the more interpretable doubling time (in days) using doubling time $= \log(2)/r$.

Because we only observed the date instead of the exact time for $B$, $E$, and $S$, we applied a simple transformation before computing the likelihood function. Instead of using the integer date which corresponds to the end of a day, we used $B - 3/4$, $E - 1/4$, and $S - 1/2$ in places of $B$, $E$, and $S$.
| Location     | Sample size | $\rho$               | Doubling time (in days) | Incubation period | Conditional likelihood |
|--------------|-------------|----------------------|-------------------------|-------------------|------------------------|
|               |             |                      |                         |                   | All locations          |
| China - Hefei| 34          | Not estimated        | 2.1 (1.2–3.7)           | 4.3 (2.9–6.0)     | 12.0 (9.1–17.3)        |
| China - Shaanxi| 53        | Not estimated        | 1.7 (1.0–2.8)           | 4.5 (3.1–6.2)     | 14.6 (11.5–19.8)       |
| China - Shenzhen| 129      | Not estimated        | 2.2 (1.7–3.0)           | 3.5 (2.8–4.3)     | 11.2 (9.5–13.6)        |
| China - Xinyang| 74        | Not estimated        | 2.3 (1.5–3.5)           | 6.8 (5.4–8.2)     | 16.4 (13.8–20.1)       |
| China - Other| 42          | Not estimated        | 2.0 (1.1–3.4)           | 5.1 (3.6–6.7)     | 12.3 (9.8–16.4)        |
| International| 46          | Not estimated        | 2.1 (1.4–3.4)           | 3.8 (2.5–5.3)     | 10.9 (8.4–15.1)        |
| All locations| 378         | Not estimated        | 2.1 (1.8–2.5)           | 4.5 (4.0–5.0)     | 13.4 (12.2–14.8)       |
| All except Xinyang| 304 | Not estimated | 2.1 (1.7–2.5)           | 4.0 (3.5–4.6)     | 12.2 (11.0–13.7)       |

| Location     | Sample size | $\rho$               | Doubling time (in days) | Incubation period | Unconditional likelihood |
|--------------|-------------|----------------------|-------------------------|-------------------|------------------------|
|               |             |                      |                         |                   | All locations          |
| China - Hefei| 34          | 0.40 (0.18–0.82)     | 1.8 (1.4–2.4)           | 4.1 (2.8–5.5)     | 11.9 (9.0–17.2)        |
| China - Shaanxi| 53        | 0.24 (0.11–0.46)     | 2.5 (2.0–3.1)           | 5.3 (3.9–6.8)     | 15.0 (12.0–20.0)       |
| China - Shenzhen| 129      | 0.75 (0.52–1.06)     | 2.4 (2.1–2.8)           | 3.6 (2.9–4.3)     | 11.3 (9.6–13.7)        |
| China - Xinyang| 74        | 0.45 (0.27–0.74)     | 2.4 (2.0–2.9)           | 6.8 (5.6–8.1)     | 16.4 (13.9–20.2)       |
| China - Other| 42          | 0.45 (0.22–0.86)     | 2.1 (1.7–2.8)           | 5.3 (4.0–6.6)     | 12.4 (10.0–16.4)       |
| International| 46          | 0.14 (0.05–0.32)     | 2.0 (1.6–2.6)           | 3.7 (2.5–5.0)     | 10.8 (8.4–15.1)        |
| All locations| 378         | 0.45 (0.36–0.56)     | 2.3 (2.1–2.5)           | 4.6 (4.1–5.1)     | 13.5 (12.3–14.9)       |
| All except Xinyang| 304 | 0.45 (0.35–0.57) | 2.2 (2.1–2.5)           | 4.1 (3.7–4.6)     | 12.3 (11.1–13.8)       |

Table 3: Results of the parametric inference. For each location and parameter, the maximum likelihood estimator and the 95% confidence interval (in brackets) based on inverting the likelihood ratio test are reported.

to compute (18) and (19). This transformation also avoids a singularity in the likelihood function when $B$ and $E$ are exactly equal.

**Results**

Results of the parametric model in Section 3 are reported in Table 3. We give some remarks about the results:

(i) There is considerable heterogeneity of the estimated $\rho$ (a parameter capturing the traveling pattern) using the unconditional likelihood. This is not surprising given that the locations we are considering are different in many ways.

(ii) Regardless of the location, our model shows that the epidemic doubling time in Wuhan was less than 3 days. There is no substantial heterogeneity among estimates in different locations.

(iii) The estimated incubation periods are similar for most locations except Xinyang, a less developed city neighboring the Hubei province.

(iv) The conditional likelihood (18) and unconditional likelihood (19) give very similar results. Confidence intervals for the doubling time computed using the unconditional likelihood are slightly shorter than those computed using the conditional likelihood.
In conclusion, inferences based on our parametric model suggest that the initial doubling time of the COVID-19 epidemic in Wuhan was between 2 to 2.5 days, the median incubation period of COVID-19 is around 4 days, and the 95% quantile of the incubation period is between 11 to 15 days.

4 Why some previous COVID-19 analyses were severely biased

4.1 Estimating the epidemic growth: Bias due to ignoring the travel quarantine

In this section we discuss the selection bias in some early COVID-19 analyses. Like the present study, a highly influential article published in the *Lancet* in late January also used Wuhan-exported cases to estimate the epidemic growth during the early outbreak [28]. However, their estimated doubling time was 6.4 days (95% credible interval: 5.8–7.1), drastically higher than the estimates in Table 3.

A closer look at the model in Wu et al. [28] shows that the most likely reason is that their model did not consider how sample selection (in particular, the travel quarantine of Wuhan) changes the likelihood function. This issue is best illustrated by examining the marginal distribution of symptom onset in Wuhan-exported cases, which can be obtained by integrating the conditional density (17) obtained earlier. In the Proposition below we focus on the exported cases who are Wuhan residents \((B = 0)\), whose marginal distributions of \(T\) and \(S\) are slightly cleaner than those who visited Wuhan \((B > 0)\).

**Proposition 2.** Under Assumptions 1 to 3, 5 and 6, the marginal density of \(T\) given \((D, B = 0) \in \mathcal{D}\) for \(r > 5/L\) is approximately given by

\[
 f_T(t | D, B = 0) \propto \exp(rt)(L - t) \cdot 1_{\{t \leq L\}}, \tag{20}
\]

where \(\propto\) means approximately proportional to. If in addition the incubation period \(S - T\) follows a Gamma\((\alpha, \beta)\) distribution (Assumption 4) and \(L > 4(\alpha + 5)/(\beta + r)\), the marginal density of \(S\) of the exported cases is approximately given by, for \(s \geq L/2\),

\[
 f_S(s | D, B = 0) \propto \exp(rs) \cdot \left\{ (L - s)[1 - H_{\alpha,\beta+r}((s-L)+)] + \frac{\alpha}{\beta + r}[1 - H_{\alpha+1,\beta+r}((s-L)+)] \right\}, \tag{21}
\]

As a consequence,

\[
 f_S(s | D, B = 0) \propto \exp(rs) \cdot \left( L + \frac{\alpha}{\beta + r} - s \right) \text{ for } L/2 \leq s \leq L. \tag{22}
\]

The technical assumption \(L > 4(\alpha + 5)/(\beta + r)\) is used to control the tail probability of a Gamma distribution so we may replace \(H_{\alpha,\beta+r}(s)\) and \(H_{\alpha+1,\beta+r}(s)\) by 1 in (21). It is usually satisfied if \(L\) is larger than several times the mean incubation period \(\alpha/\beta\) and is satisfied here with the maximum likelihood estimator of \((r, \alpha, \beta)\) in Section 3.3.

Figure 3 shows the histogram of the symptom onset of the exported cases in our dataset who are Wuhan residents \((B = 0)\) and the theoretical fit based on (21) and the maximum unconditional likelihood estimator in Table 3 using all the locations \((r = 0.30, \alpha = 1.86, \beta = 0.33)\). The theoretical density provided good fit to the observed distribution of \(S\) (Pearson’s \(\chi^2\) goodness-of-fit test: \(p\)-value = 0.94).

Wu et al. [28] fitted a Susceptible-Exposed-Infectious-Recovered (SEIR) model using Wuhan-exported cases but did not consider sample selection due to the travel quarantine. In the early phase of epidemic outbreaks, the SEIR model can be well approximated by an exponential growth for cases in Wuhan:

\[
 f_S(s) \propto \exp(rs). \tag{23}
\]
However, Proposition 2, in particular equation (22), shows that the marginal distribution of $S$ for exported Wuhan residents $f_S(s \mid D, B = 0)$ does not follow the same exponential growth as $f_S(s)$. 

Equation (22) not only shows that fitting a simple exponential growth to the initial symptom onsets among Wuhan-exported cases will under-estimate the epidemic growth $r$, it can also be used to derive a simple bias-correction formula. We can approximate the log-linear regression for symptom incidence counts from $L - c$ to $L$ by a first-order Taylor expansion at the midpoint:

$$
\log f_S(s \mid D, B = 0) \approx rs + \log \left(L + \frac{\alpha}{\beta + r} - s\right) + \text{constant}
$$

$$= rs + \log \left(\frac{\alpha}{\beta + r} + c/2 + (L - c/2 - s)\right) + \text{constant}$$

$$\approx rs + \log \left(\frac{\alpha}{\beta + r} + \frac{c}{2}\right) + \frac{L - c/2 - s}{\alpha/(\beta + r) + c/2} + \text{constant}$$

$$= \left[r - \frac{1}{\alpha/(\beta + r) + c/2}\right]s + \text{constant}.
$$

Therefore the under-estimation bias is about $(\alpha/(\beta + r) + c/2)^{-1}$. As most of the symptom onsets of Wuhan-exported cases before the travel quarantine happened within two weeks, it might be reasonable to choose $c = 14$. Using our estimate of $(r, \alpha, \beta)$ in Table 3, the under-estimation bias is about $((1.86)/(0.3 + 0.33) + 14/2)^{-1} \approx 0.1$.

Using Wuhan-exported cases confirmed outside Mainland China by January 28, 2020, Wu et al. [28] estimated that the doubling time of COVID-19 was about 6.4 days, which corresponds to
\[ r = \log(2)/6.2 \approx 0.11. \] With the above correction, the estimated \( r \) would be 0.11 + 0.1 \( \approx 0.21 \), or doubling time of 3.3 days. In other words, this simple correction already shows that the epidemic could be doubling twice as fast as estimated by Wu et al. [28].

The actual bias of the analysis in Wu et al. [28] is more complicated than the inexact calculations above. This is because Wu et al. [28] fitted their SEIR model also using symptom onset after January 23 (time \( L \)). Our theory in Proposition 2 suggests that the \( f_S(s \mid D) \) not only has slower and slower growth as \( s \) approaches \( L \) but also decreases eventually. This means that the inclusion of symptom onsets after January 23 may lead to further under-estimation of \( r \). This also explains why, after the simple correction above, the epidemic growth estimate of Wu et al. [28] is still not as fast as ours in Table 3.

### 4.2 Estimating the incubation period: When two biases do not “balance out”

Like the present study, several influential articles also estimated the incubation period of COVID-19 using Wuhan-exported cases [5, 15, 18]. Their results are roughly in line with our estimates in Table 3 with lighter tails, but a closer look shows that the existing methods actually suffer from two biases:

(i) **Bias due to right-truncation**: The three previous studies only used Wuhan-exported cases confirmed before the end of January. In our dataset, about 70% of the Wuhan-exported cases were confirmed by that time. However, the other 30% would have an incubation period of at least 8 days as they must have left Wuhan before January 23. The right truncation, if not accounted for, leads to under-estimation of the incubation period.

(ii) **Bias due to ignoring epidemic growth**: The three previous studies all used the interval-censored likelihood function for the incubation period in Reich et al. [24]. As discussed after Proposition 1, this likelihood corresponds to our conditional likelihood \( L_{\text{cond}}(\alpha, \beta) \) with \( r \) fixed at 0 and thus does not account for the rapid growth of COVID-19. Intuitively, a person in Wuhan has a much higher prior probability of contracting the virus on January 20 than on January 1, but the likelihood function in Reich et al. [24] does not take that into account. Ignoring the epidemic growth leads to over-estimation of the incubation period.

It is possible to correct for the right-truncation by further conditioning on \( S \leq M \) (\( M \) is some truncation time) in our likelihood function.

**Proposition 3.** Under Assumptions 1 and 2, for \((b, e, t, s) \in D\) and \( s \leq M \),

\[
f_{T,S}(t, s \mid b, e, D, S \leq M) = \frac{g(t)h(s-t)}{\int_b^{\max(e, s)} g(t)H(M-t)dt},
\]

where \( H(s) = \int_0^s h(x) dx \) is the distribution function of the incubation period. Furthermore, under the exponential growth model (Assumption 3) and Gamma-distributed incubation period (Assumption 4), the conditional observed data likelihood under the right truncation \( S \leq M \) is given by

\[
L_{\text{cond, trunc}}(r, \alpha, \beta; M) = \begin{cases} 
\left(\frac{\beta}{\beta + r}\right)^n \prod_{i=1}^{n} \frac{\exp\{r(S_i - M)\} [H_{\alpha, \beta + r}(S_i - B_i) - H_{\alpha, \beta + r}((S_i - E_i)_{+})]}{Z_r(M - B_i) - Z_r((M - E_i)_{+})}, & \text{if } r \neq 0, \\
\prod_{i=1}^{n} \frac{H_{\alpha, \beta}(S_i - B_i) - H_{\alpha, \beta}((S_i - E_i)_{+})}{Z_0(M - B_i) - Z_0((M - E_i)_{+})}, & \text{if } r = 0,
\end{cases}
\]
where
\[
Z_r(x) = \begin{cases} 
\left(\frac{\beta}{\beta + r}\right)^\alpha H_{\alpha,\beta+r}(x) - \exp(-rx)H_{\alpha,\beta}(x), & \text{if } r \neq 0, \\
xH_{\alpha,\beta}(x) - \left(\frac{\alpha}{\beta}\right)H_{\alpha+1,\beta}(x), & \text{if } r = 0.
\end{cases}
\]

It is straightforward to show that \(L_{\text{cond, trunc}}(r, \alpha, \beta; M)\) reduces to the conditional likelihood \(L_{\text{cond}}(r, \alpha, \beta)\) without the right truncation in (18) when \(M \to \infty\).

We demonstrate the two kinds of biases in the estimation of the incubation period using a retrospective experiment. In this experiment, we assumed the incubation period follows a Gamma distribution and estimated its median and the 95% quantile by maximizing one of the following three likelihood functions:

(i) **Adjusted for nothing:** This is the likelihood function in Reich et al. [24] that is equal to our \(L_{\text{cond}}(0, \alpha, \beta)\) by setting \(r = 0\).

(ii) **Adjusted for growth:** This is our conditional likelihood function \(L_{\text{cond}}(r, \alpha, \beta)\).

(iii) **Adjusted for both growth and right-truncation:** This is our conditional likelihood \(L_{\text{cond, trunc}}(r, \alpha, \beta; M)\) with adjustment for sample selection due to the right-truncation \(S \leq M\).

For each day from January 23 to February 18, we estimated the incubation distribution using Wuhan-exported cases in our dataset confirmed by that day. For the third method, we choose \(M\) to be a week prior to the truncation date for confirmation, as most Wuhan-exported cases were confirmed within a week of symptom onset. Figure 6 shows the estimated medians and 95% quantiles of the incubation period of COVID-19, with pointwise confidence intervals in the plot computed using the basic nonparametric bootstrap with 1000 resamples [10].

The bias due to not accounting for right-truncation can be clearly visualized from the dotted blue curves in Figure 6. Had we fitted our conditional likelihood function \(L_{\text{cond}}(r, \alpha, \beta)\) using cases confirmed by January 31 (265 cases), the estimated median incubation period would be 3.5 days and the 95% quantile would be 9.5 days. In comparison, when the entire dataset is used, the estimated median and 95% quantile are 4.6 days and 13.5 days (Table 3).

The bias due to ignoring the epidemic growth is even more dramatic. Had we fitted the incubation period using the likelihood function in Reich et al. [24] (the same as setting \(r = 0\) in our conditional likelihood) to all the cases in our dataset (387 cases), the estimated median incubation period would be 9.2 days and the 95% quantile would be a whopping 24.9 days!

The truncation-corrected conditional likelihood \(L_{\text{cond, trunc}}(r, \alpha, \beta; M)\) derived in Proposition 3 successfully corrected for the right-truncation bias. The estimated median and 95% quantile of the incubation using \(L_{\text{cond, trunc}}(r, \alpha, \beta; M)\) were roughly unbiased starting from the end of January. Had we fitted this likelihood using all cases confirmed by January 31 and having shown symptoms a week prior (220 cases), the estimated median incubation period would be 4.8 days (95% CI: 3.0 to 6.0) and the estimated 95% quantile would be 14.4 days (95% CI: 6.7 to 18.5). These estimates are less precise than the estimates obtained using the entire dataset (Table 3), but they correctly reflect the uncertainty due to the right-truncation. In contrast, using the wrong likelihood functions not only results in biased point estimates but also narrow and misleading confidence intervals.

Because the right-truncation bias and epidemic growth bias are towards opposite directions, coincidentally they were almost “balanced out” in the previous studies. As a consequence, their estimates were not drastically different from ours. To be fair in our criticism, the previous studies did acknowledge that under-ascertainment of mild cases could bias their analyses. Backer et al. [7] mentioned the over-estimation due to ignoring epidemic growth in their discussion. Linton et al. [18]...
Figure 6: An illustration of two kinds of biases in the estimation of the incubation period of COVID-19. The curves (region) in the plot are maximum likelihood estimators (and bootstrap confidence intervals) using three likelihood functions and cases confirmed by each day. Likelihood functions used in this experiment are: $L_{cond}(0, \alpha, \beta)$ (dashed orange), $L_{cond}(r, \alpha, \beta)$ (dotted blue), and $L_{cond,trunc}(r, \alpha, \beta; M)$ (solid green). Results of some previous studies [5, 15, 18] (essentially using our conditional likelihood with $r$ set to 0 on different datasets) are also shown in this plot.

(Lauer et al. [15] did not report an estimated 95% quantile of the incubation period. Here we imputed it based on the reported median and 97.5% quantile, assuming a Gamma distribution for the incubation period. Although Lauer et al. [15] used COVID-19 cases confirmed as late as late February, only 4 out of their 181 cases were confirmed in February. In this Figure it is thus treated as using cases confirmed up till February 1.)
attempted to use a formula to correct for right-truncation which bears some similarity to (23), which resulted in slightly longer estimates of the incubation period. However, Linton et al. [18] did not give any justification to the formula and we could not derive it from our generative model. In any case, our experiments in Figure 6 clearly show that these early estimates of the incubation period (especially their tail estimates) are unreliable to guide health policies.

5 Nonparametric inference

5.1 Time discretization

So far we have used parametric assumptions (e.g. Gamma-distributed incubation period) to explicitly derive likelihood functions for the observed data. To assess the robustness of our results, we next relax some of these parametric assumptions. In particular, we will model the distribution of the incubation period nonparametrically so the tail probabilities are not determined by any parametric form. Because analytic forms of the sample selection probabilities \( \mathbb{P}(\{b,e,t,s\} \in \mathcal{D} | b,e) \) and \( \mathbb{P}(\{b,e,t,s\} \in \mathcal{D}) \) are generally unavailable, we will put prior distributions on the model parameters and use Markov Chain Monte Carlo (MCMC) to compute their posterior distributions.

We start by discretizing all the time variables in the model, which are measured in days. This will simplify the Bayesian computation. Instead of working with continuous time \((B, E, T, S) \in \mathcal{P}\), we use the discretization:

\[
\begin{aligned}
B^* &= \lfloor B \rfloor, \quad E^* = \lfloor E \rfloor, \quad T^* = \lfloor T \rfloor, \quad S^* = \lfloor S \rfloor, \\
\end{aligned}
\]

where \( \lfloor \cdot \rfloor \) is the ceiling function (\( \lfloor x \rfloor \) is the smallest integer larger than \( x \)). The support of \((B^*, E^*, T^*, S^*)\) is then \( \mathcal{P} \), the set of all 4-tuples of integers and \( \infty \). The general continuous distributions in Assumptions 1 and 2 can be modified accordingly:

\[
\begin{aligned}
\mathbb{P}(T^* = t^* | B^* = b^*, E^* = e^*) &= \begin{cases} 
 g^*(t^*), & \text{if } b^* \leq t^* \leq e^*, \\
 1 - \sum_{t^* = b^*}^{e^*} g^*(t^*), & \text{if } t^* = \infty; 
\end{cases} \\
\mathbb{P}(S^* = s^* | B^* = b^*, E^* = e^*, T^* = t^*) &= \begin{cases} 
 \nu \cdot h^*(s^* - t^*), & \text{if } t^* \leq s^* < \infty, \\
 1 - \nu, & \text{if } s^* = \infty, 
\end{cases} 
\end{aligned}
\]

where \( g^*(\cdot) \) satisfies \( \sum_{x^*=0}^{L} g^*(x^*) \leq 1 \) and \( h^*(\cdot) \) is a probability mass function on nonnegative integers: \( \sum_{x^*=0}^{\infty} h^*(x^*) = 1 \).

5.2 Relaxing the parametric assumptions

Our parametric assumptions (Assumptions 3 to 6) on the distribution of \((B, E, T, S)\) can be translated to the following assumptions on \((B^*, E^*, T^*, S^*)\) after discretization:

\[
\begin{aligned}
 g^*(t^*) &\approx g_{\kappa, \tau}(t^*) = \kappa \exp(\tau t^*), \\
 h^*(t^* - s^*) &\approx h_{\alpha, \beta}(t^* - s^*), \\
 \mathbb{P}(B^* = b^*) &= \begin{cases} 
 (1 - \pi), & \text{for } b^* = 0, \\
 \pi / L, & \text{for } b^* = 1, \ldots, L, 
\end{cases} \\
\mathbb{P}(E^* = e^* | B^* = b^*) &= \begin{cases} 
 \lambda_{b^*}, & \text{for } b^* \leq e^* \leq L, \\
 1 - (L - b^* + 1) \lambda_{b^*}, & \text{for } e^* = \infty, 
\end{cases} 
\end{aligned}
\]

where \( \lambda_0 = \lambda_{\infty} \) and \( \lambda_1 = \cdots = \lambda_{L} = \lambda_{V} \).

In the nonparametric model we consider the following relaxations:
(i) **Nonparametric distribution for the incubation period:** Besides putting a prior to encourage smoothness and log-concavity, we do not put any parametric restrictions on the distribution of the incubation period.

(ii) **Two-stage exponential growth:** Human-to-human transmissibility of COVID-19 is first confirmed to the public in the evening of January 20. We modify the exponential growth model to allow for a different growth exponent after January 20:

\[
g^*(t^*) = g^*_{r_1, r_2}(t^*) = \begin{cases} 
\kappa \exp(r_1 t^*) & \text{if } t \leq L_1, \\
\kappa \exp(r_2(t^* - L_1) + r_1^* L_1) & \text{if } L_1 < t \leq L_2,
\end{cases}
\]

where \(L_1 = 51\) (January 20) and \(L_2 = L = 54\) (January 23). The simple exponential growth model is a special case of this model with both \(L_1\) and \(L_2\) set to \(L\).

(iii) **Geometric distribution for \(E^* \mid B^*\):** As a sensitivity analysis to our assumption that \(E^* \mid B^*\) is uniformly distributed between \(B^*\) and \(L\), this relaxation assumes a geometric distribution for \(E^* \mid B^*\):

\[
P(E^* = e^* \mid E^* \geq e^*, B^*) = \begin{cases} 
\eta_{B^*, 1} & \text{if } e^* < L_{\text{chunyun}}, \\
\eta_{B^*, 2} & \text{if } e^* \geq L_{\text{chunyun}},
\end{cases}
\]

where \(L_{\text{chunyun}} = 41\) corresponds to January 10, the start of the Chinese New Year travel season known as “chunyun”. We assume \(\eta_{0,i} = \eta_{W,i}\) and \(\eta_{1,i} = \cdots = \eta_{L,i} = \eta_{V,i}\), for \(i = 1, 2\).

(iv) **Gender-specific and age-specific incubation periods:** To assess whether the distribution of incubation period varies with gender, we use different densities, \(h^*_M(\cdot)\) for men and \(h^*_F(\cdot)\) for women. Like in (i), we put no parametric restrictions on these distributions apart from the same prior that encourages smoothness and log-concavity. Similarly, we can use different densities for different age groups. To avoid fitting incubation period with too few observations, we only consider two age groups: above 50 years old and below 50 years old. Notice that the same exponential growth model for \(g\) is used for different gender or age groups, as we expect the growth of the chance of infection is the same for all strata.

Under these different modeling assumptions, likelihood functions for the parameters can be computed in the same way as in Section 3.2, with integrals replaced by finite sums. We omit the details here.

### 5.3 Prior distributions and details of the implementation

To simplify the computation, we assume the incubation period of COVID-19 is less than 30 days. It is common to use a unimodal distribution with a smooth density function to model the incubation period. We use the following prior distribution on \(h^*(\cdot)\) to encourage smoothness and log-concavity:

\[
\pi(h^*(0), \ldots, h^*(29)) \propto \left( \prod_{x^* = 0}^{29} h^*(x^*)^{\mu \cdot h_0(x^*) - 1} \right) \times \exp \left\{ \sum_{x^* = 1}^{28} \left( 2 \log h^*(x^*) - \log h^*(x^* - 1) - \log h^*(x^* + 1) \right)_- \right\},
\]

where \((\cdot)_-\) is the negative part function. The first part of the right hand side of (25) is proportional to the density of a Dirichlet distribution with concentration parameters \(\{\mu \cdot h_0(0), \ldots, \mu \cdot h_0(29)\}\).
We choose \( h_0(\cdot) \) to be a discretization of Gamma\((9, 1.5)\), whose tail probability of \( \geq 14 \) days is less than 0.01. The second part of the right hand side of (25) is an exponential tilt which penalizes lack of log-concavity.

We put uninformative priors on other parameters in the model:

\[
r_1 \sim \text{Exp}(1), \ r_2 \sim \text{N}(0, 4), \kappa \sim \text{Unif}(0, 1), \lambda_W, \lambda_V \sim \text{Unif}(0, 1/L).
\]

Note that \( r_2 \) is allowed to be negative (exponential decrease after January 20). For the model with a geometric distribution for \( E^* | B^* \), we put Unif\((0, 1)\) priors on \( \eta_{W,1}, \eta_{W,2}, \eta_{V,1}, \eta_{V,2} \).

A random walk Metropolis–Hastings algorithm targeting the posterior distribution of \( h^*(\cdot) \) and \( r_1, r_2 \) was implemented using the TensorFlow Probability library in Python [7]. We simulated chains of 80,000 steps, discarding a burn-in period of 50%. The convergence of the sampler was assessed by simulating 8 parallel Markov chains with initial values overdispersed with respect to the target distribution, and computing the potential of scale reduction factor [12] for \( r_1 \), the mean of the incubation period distribution, and the probability of an incubation period of 14 days or more. In every case, the statistic was confidently below 1.1.

5.4 Results of Bayesian nonparametric inference

Aggregated results

Table 4 reports the results of the Bayesian nonparametric inference in 7 different scenarios. Overall, they are not too dissimilar to the results of the parametric model in Table 3. Without restricting the tail to follow that of a Gamma distribution, the estimated tail probabilities are slightly higher than those in Table 3. The posterior mean for \( \mathbb{P}(S^* - T^* \geq 14 \) days) exceeds 0.03 in all scenarios, even when we exclude the cases confirmed in Xinyang who seemed to have longer incubation periods in Table 3. Moreover, prior and posterior distributions of \( \mathbb{P}(S^* - T^* \geq 14 \) days) show a large discrepancy (Figure 7b), indicating that the posterior estimates of the tail probabilities are driven by the data instead of the prior. Employing the two-stage epidemic growth model suggests that the epidemic growth may have slowed down after January 20, but this more flexible model did not alter the estimated doubling time and incubation period distribution substantially. Taken together, our nonparametric models suggest that the probability of an incubation period of at least 14 days (among symptomatic cases) may be about 5%.

Gender-specific and age-specific incubation periods

The gender-specific and age-specific estimates of the incubation period can be found in Table 5 and Figure 8a. The estimated distributions of incubation periods for men and women are notably different, with the distribution of men peaking earlier and having a heavier tail than women. In particular, men seem to be much more likely than women to develop symptoms within two days of infection. A related phenomenon can be directly seen from the raw distribution of \( S - E \) (days from leaving Wuhan to symptom onset; can be negative if a person showed symptoms during the stay in Wuhan) for the cases exported from Wuhan (Figure 8b). The difference \( S - E \) appears to be more spread out in men. A nonparametric Ansari-Bradley test for the dispersion gives a \( p \)-value \( \approx 0.0025 \), while the Wilcoxon signed-rank test for the location gives a \( p \)-value \( \approx 0.48 \) [14].

The difference of incubation period distributions for older and younger cases seem less pronounced in Figure 8a. Their distributions of \( S - E \) also appear to be quite similar in Figure 8b (Ansari-Bradley test for dispersion: \( p \)-value \( \approx 0.56 \); Wilcoxon test for location: \( p \)-value \( \approx 0.1 \)).
(a) A comparison of the estimated parametric and nonparametric incubation period distributions. Orange curve: Gamma distribution with median = 4.5 and 95% quantile = 13.4. Blue error bars: Posterior mean and 95% credible interval, computed in the model with a two-stage exponential growth, and geometric $E^* | B^*$, with $\mu = 10$.

(b) A comparison of the prior and posterior $P(\text{Incubation} \geq 14 \text{ days})$ in the first two simulation scenarios of Table 4. Two panels correspond to two choices for the prior distribution \((25)\) of $h^*(\cdot)$.

Figure 7: An illustration of the nonparametric Bayesian fit to the incubation period distribution.
(a) Gender-specific (left) and age-specific (right) distributions of the incubation period.

(b) Gender-specific (left) and age-specific (right) distributions of $S - E$ (days from leaving Wuhan to symptom onset). Dots represent the exact proportions in the dataset and the curves are kernel density estimates with bandwidth set to 1 day.

Figure 8: Results of the Bayesian nonparametric inference after stratification by gender and age. Blue solid curves are for men and cases younger than 50 and orange dashed curves are for women and cases older than 50.
Table 4: Results of the nonparametric Bayesian inference where we do not impose a parametric form for the distribution of the incubation period. As sensitivity analyses, we also vary the study sample, model for the epidemic growth, distribution of $E^*$ given $B^*$, and the hyperprior parameter $\mu$. Numbers reported in the table are posterior means and 95% credible intervals (in brackets).

| Sample growth | All $r_1$ | All $r_1$ | Shenzhen $r_1$ | Wuhan residents $r_1$ | All except Xinyang $r_1$ | All $r_1$ | All $r_1$, $r_2$ | All $r_1$, $r_2$ |
|---------------|-----------|-----------|----------------|--------------------------|--------------------------|-----------|----------------|----------------|
| $E^* | B^*$ | Uniform | Uniform | Uniform | Uniform | Uniform | Uniform | Uniform | Geometric |
| $\mu$ | $\mu = 1$ | $\mu = 10$ | $\mu = 1$ | $\mu = 1$ | $\mu = 10$ | $\mu = 1$ | $\mu = 1$ | $\mu = 1$ |
| Doubling days for $r_1$ | 2.4 (2.2–2.6) | 2.4 (2.2–2.6) | 2.5 (2.2–2.9) | 2.3 (2.1–2.6) | 2.4 (2.2–2.6) | 2.2 (2.0–2.4) | 2.2 (1.9–2.4) | 2.2 (1.9–2.4) |
| $r_2$ (Growth in Jan. 21–23) | – | – | – | – | – | – | – | – |
| Incubation period | Mean | 5.5 (5.0–5.9) | 5.4 (5.0–5.9) | 4.4 (3.7–5.1) | 5.6 (5.0–6.1) | 5.0 (4.6–5.5) | 5.6 (5.1–6.1) | 5.6 (5.2–6.1) |
| $\mathbb{P}(\geq 7)$ | .31 (.25–.38) | .31 (.25–.37) | .22 (.13–.31) | .30 (.22–.38) | .26 (.19–.32) | .05 (.02–.08) | .06 (.03–.08) | .06 (.03–.08) |
| $\mathbb{P}(\geq 10)$ | .19 (.14–.24) | .18 (.14–.22) | .10 (.05–.17) | .21 (.14–.28) | .14 (.10–.19) | .19 (.14–.23) | .19 (.15–.24) | .19 (.15–.24) |
| $\mathbb{P}(\geq 14)$ | .05 (.02–.08) | .04 (.02–.07) | .03 (.01–.06) | .04 (.01–.07) | .03 (.01–.06) | .05 (.02–.08) | .06 (.03–.08) | .06 (.03–.08) |
| $\mathbb{P}(\geq 21)$ | .00 (.00–.01) | .00 (.00–.00) | .01 (.00–.03) | .01 (.00–.02) | .00 (.00–.01) | .00 (.00–.01) | .00 (.00–.01) | .00 (.00–.01) |
### Table 5: Estimated distributions of incubation period in different subgroups.

| Subgroup | Men | Women | Difference | Age < 50 | Age ≥ 50 | Difference |
|----------|-----|-------|------------|---------|---------|------------|
| Mean     | 5.8 (5.1–6.6) | 5.3 (4.7–5.9) | 0.5 (-0.4–1.5) | 5.4 (4.7–6.1) | 5.8 (5.2–6.5) | -0.5 (-1.4–0.4) |
| P(≥ 2)  | .82 (.73–.92) | .97 (.91–1.00) | -.15 (-.25–.04) | .90 (.78–.97) | .89 (.81–.96) | .01 (-.11–.13) |
| P(≥ 4)  | .59 (.50–.69) | .55 (.42–.69) | .04 (-.13–.20) | .53 (.41–.65) | .62 (.50–.72) | -.09 (-.25–.07) |
| P(≥ 7)  | .37 (.29–.46) | .24 (.17–.32) | .13 (.01–.24) | .31 (.22–.40) | .34 (.26–.42) | -.03 (-.14–.09) |
| P(≥ 10) | .20 (.13–.28) | .17 (.11–.23) | .03 (-.06–.14) | .20 (.13–.28) | .18 (.13–.24) | .01 (-.08–.11) |
| P(≥ 14) | .07 (.04–.12) | .03 (.01–.07) | .04 (.01–.09) | .03 (.01–.07) | .07 (.04–.11) | -.03 (-.08–.01) |
| P(≥ 21) | .01 (.00–.03) | .00 (.00–.02) | .00 (.01–.02) | .01 (.00–.03) | .01 (.00–.01) | .00 (.01–.02) |

### 6 Discussion

In this article, we have proposed the generative BETS model for four key epidemiological events: beginning of exposure, end of exposure, time of transmission, and time of symptom onset. Under parametric models, we have derived the sample inclusion probability for exported cases and used it to correct for selection bias in the likelihood functions. Across different sub-samples and modeling assumptions, the initial epidemic doubling time for COVID-19 in Wuhan is consistently estimated to be between 2 to 2.5 days. Our nonparametric Bayesian analysis suggests that the parametric fit likely under-estimated the tail of the incubation period, and among all the COVID-19 patients who develop symptoms, about 5% of them could develop the symptoms at least 14 days after contracting the pathogenic virus. Gender-specific analysis shows that men may have a more variable incubation period than women. In particular, more men appear to show symptoms within two days of infection, which could be related to the men’s higher death rate across the world [13]. We hope the generality of our model makes it extensible in further studies of the current pandemic and other outbreaks in the future.

A key epidemiological parameter we decided not to study in this article is the basic reproduction number, commonly denoted by $R_0$. Intuitively, $R_0$ is the expected number of secondary infections produced by a typical case in a population where everyone is susceptible. In early outbreak analysis, $R_0$ can be estimated from the epidemic growth exponent $r$ by $R_0 = 1/M(-r)$ [23], where $M(\cdot)$ is the moment generating function for the distribution of the serial interval (time between successive cases in a chain of transmission). Several studies have attempted to estimate the serial interval of COVID-19 in Wuhan by using observed pairs of infector-infectedees [17, 22, 9]. The reported point estimate of the mean serial interval ranging from 4.0 [9] to 7.5 days [17]. However, for most COVID-19 cases it seems impossible to ascertain the infector, so these early estimates of the serial interval could be severely biased by sample selection just like the early estimates of epidemic growth and incubation period as seen in Section 4.

Our findings in this article should be viewed together with the limitations of our methodology. First of all, symptom onset time were usually reported by patients, who could be under social pressure to report a later symptom onset (for example, so they did not travel when showing symptoms). This can make estimated incubation longer than the truth. Second, although the contact tracing for travelers from Wuhan was intensive in the locations included in our dataset, some degree of under-ascertainment of Wuhan-exported cases is perhaps inevitable. If patients who showed symptoms earlier were less likely to be ascertained, our analysis may have over-estimated the speed of the epidemic growth. Third, the discernment of Wuhan-exported cases in Section 2.2 is not perfect; for example, there is ambiguity about where some COVID-19 cases were infected if they both had
stayed in Wuhan and were exposed to other confirmed cases after their stay. Another potential limitation is the core assumptions that the disease transmission and progression are independent of traveling. This assumption is necessary to extend the conclusions from a “shadow” of the epidemic (Wuhan-exported cases) to the center of the outbreak, but it can be violated if, for example, some people canceled travel plans due to feeling sick. Finally, it is possible that the population of travelers is not representative of the general population in a meaningful way.

Nevertheless, these limitations are perhaps minor compared to the selection bias identified in this article. Several authors have warned about selection bias and other statistical issues in COVID-19 studies [19, 20, 21, 11, 27]. By constructing a generative model and deriving the likelihood functions from first principles, we gave a quantitative assessment of the selection bias in several high-impact studies. We found that the biases were indeed startling. This highlights the lesson that data quality and methodical consideration of selection bias are often much more important than data quantity and specific models. This is especially important in high-stakes decisions like the ones for the COVID-19 pandemic. In a world where data science is playing an ever-larger role in policy making, ignoring selection bias could become the most costly of bets.

Acknowledgement

We thank Cindy Chen, Yang Chen, Yunjin Choi, Hera He, Michael Levy, Marc Lipsitch, James Robins, Andrew Rosenfeld, Dylan Small, Yachong Yang, and Zilu Zhou for their helpful suggestions. We thank citizens living in the first author’s hometown, Wuhan, whose enduring adherence to the travel quarantine not only saved many lives but also made our analysis possible.

References

[1] Michael Gove: rate of coronavirus infection in UK doubling every three to four days – video. https://www.theguardian.com/world/video/2020/mar/27/michael-gove-rate-of-coronavirus-infection-in-uk-doubling-every-three-to-four-days-video Retrieved: April 15, 2020.

[2] COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). https://coronavirus.jhu.edu/map.html Retrieved: April 15, 2020.

[3] Boris Johnson coronavirus speech transcript: UK PM tells UK to avoid non-essential travel & contact. https://www.rev.com/blog/transcripts/ boris-johnson-coronavirus-speech-transcript-uk-pm-tells-uk-to-avoid-non-essential-travel-contact Retrieved: April 15, 2020.

[4] WHO statement regarding cluster of pneumonia cases in Wuhan, China. https://www.who.int/china/news/detail/09-01-2020-who-statement-regarding-cluster-of-pneumonia-cases-in-wuhan-china 2020. Retrieved: April 15, 2020.

[5] J. A. Backer, D. Klinkenberg, and J. Wallinga. Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travellers from Wuhan, China, 20–28 January 2020. Eurosurveillance, 25(5):2000062, 2020. doi: 10.2807/1560-7917.ES.2020.25.5.2000062.
[6] Centers for Disease Control and Prevention. Interim clinical guidance for management of patients with confirmed coronavirus disease (COVID-19). [https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html](https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html). Retrieved: April 15, 2020.

[7] J. V. Dillon, I. Langmore, D. Tran, E. Brevdo, S. Vasudevan, D. Moore, B. Patton, A. Alemi, M. Hoffman, and R. A. Saurous. Tensorflow distributions. arXiv preprint arXiv:1711.10604, 2017.

[8] I. Dorigatti, L. Okell, A. Cori, N. Imai, M. Baguelin, S. Bhatia, A. Boonyasiri, Z. Cucunubá, G. Cuomo-Dannenburg, R. FitzJohn, et al. Report 4 - Severity of 2019 novel coronavirus (nCoV). Technical report, Imperial College London, MRC Centre for Global Infectious Disease Analysis, 2020.

[9] Z. Du, X. Xu, Y. Wu, L. Wang, B. J. Cowling, and L. A. Meyers. The serial interval of covid-19 from publicly reported confirmed cases. Emerging Infectious Diseases, 26(6), 2020.

[10] B. Efron and R. J. Tibshirani. An Introduction to the Bootstrap. CRC press, 1994.

[11] A. Gelman. Concerns with that stanford study of coronavirus prevalence. [https://statmodeling.stat.columbia.edu/2020/04/19/fatal-flaws-in-stanford-study-of-coronavirus-prevalence/](https://statmodeling.stat.columbia.edu/2020/04/19/fatal-flaws-in-stanford-study-of-coronavirus-prevalence/), 2020.

[12] A. Gelman, D. B. Rubin, et al. Inference from iterative simulation using multiple sequences. Statistical science, 7(4):457–472, 1992.

[13] Global Health 5050. Covid-19 sex-disaggregated data tracker. [https://globalhealth5050.org/covid19/](https://globalhealth5050.org/covid19/). Retrieved: April 28, 2020.

[14] J. Hájek, Z. Šidák, and P. K. Sen. Theory of Rank Tests. Academic Press, 1999.

[15] S. A. Lauer, K. H. Grantz, Q. Bi, F. K. Jones, Q. Zheng, H. R. Meredith, A. S. Azman, N. G. Reich, and J. Lessler. The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. Annals of Internal Medicine, 2020.

[16] S. L. Lauritzen. Graphical Models. Clarendon Press, 1996.

[17] Q. Li, X. Guan, P. Wu, X. Wang, L. Zhou, Y. Tong, R. Ren, K. S. Leung, E. H. Lau, J. Y. Wong, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. New England Journal of Medicine, 2020.

[18] N. M. Linton, T. Kobayashi, Y. Yang, K. Hayashi, A. R. Akhmetzhanov, S.-m. Jung, B. Yuan, R. Kinoshita, and H. Nishiura. Incubation period and other epidemiological characteristics of 2019 novel coronavirus infections with right truncation: a statistical analysis of publicly available case data. Journal of Clinical Medicine, 9(2):E538, 2020.

[19] M. Lipsitch. Estimating case fatality rates of COVID-19. Lancet Infectious Diseases, 2020.

[20] M. Lipsitch, K. Joshi, and S. E. Cobey. Comment on "Association of Public Health Interventions With the Epidemiology of the COVID-19 Outbreak in Wuhan, China " by Pan et al. [https://github.com/keyajoshi/Pan_response](https://github.com/keyajoshi/Pan_response), 2020.
[21] R. Niehus, P. Martinez de Salazar Munoz, A. Taylor, and M. Lipsitch. Quantifying bias of COVID-19 prevalence and severity estimates in Wuhan, China that depend on reported cases in international travelers. Technical report, Harvard T.H. Chan School of Public Health, 2020.

[22] H. Nishiura, N. M. Linton, and A. R. Akhmetzhanov. Serial interval of novel coronavirus (COVID-19) infections. International Journal of Infectious Diseases, 2020.

[23] J. M. Read, J. R. Bridgen, D. A. Cummings, A. Ho, and C. P. Jewell. Novel coronavirus 2019-ncov: early estimation of epidemiological parameters and epidemic predictions. medRxiv, 2020. doi: 10.1101/2020.01.23.20018549. URL https://www.medrxiv.org/content/early/2020/01/28/2020.01.23.20018549.

[24] N. G. Reich, J. Lessler, D. A. T. Cummings, and R. Brookmeyer. Estimating incubation period distributions with coarse data. Statistics in Medicine, 28(22):2769–2784, 2009. doi: 10.1002/sim.3659.

[25] S. Sanche, Y. Lin, C. Xu, E. Romero-Severson, N. Hengartner, and R. Ke. High contagiousness and rapid spread of Severe Acute Respiratory Syndrome Coronavirus 2. Emerging Infectious Diseases, 26(7), 2020.

[26] J. Wallinga and M. Lipsitch. How generation intervals shape the relationship between growth rates and reproductive numbers. Proceedings of the Royal Society B: Biological Sciences, 274(1609):599–604, 2007.

[27] J. C. Wong and C. Bergstrom. ‘there is no absolute truth’: an infectious disease expert on Covid-19, misinformation and ‘bullshit’. https://www.theguardian.com/world/2020/apr/28/there-is-no-absolute-truth-an-infectious-disease-expert-on-covid-19-misinformation-and-bullshit, 2020. Retrieved: May 3, 2020.

[28] J. T. Wu, K. Leung, and G. M. Leung. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. Lancet, 395(10225):689–697, 2020.

[29] Q. Zhao, Y. Chen, and D. S. Small. Analysis of the epidemic growth of the early 2019-nCoV outbreak using internationally confirmed cases. medRxiv, 2020. doi: 10.1101/2020.02.06.20020941. URL https://www.medrxiv.org/content/early/2020/02/09/2020.02.06.20020941
A Technical proofs

A.1 Derivation of Lemma 1

Using eqs. (3) and (4), it is straightforward to show that

\[ P((B,E,T,S) \in \mathcal{D} | B = b, E = e) = \int_{t \in (b,e)} f_T(t | b, e) \int_{s \in (t, \infty)} f_S(s | b, e, t) \, ds \, dt \]

\[ = \int_{t \in (b,e)} f_T(t | b, e) \left\{ \int_{s \in (t, \infty)} \nu \cdot h(s-t) \, ds \right\} \, dt \]

\[ = \int_{t \in (b,e)} f_T(t | b, e) \cdot \nu \, dt \]

\[ = \nu [G(e) - G(b)]. \]

A.2 Derivation of Lemma 2

By Assumption 3, \( G_{\kappa,r}(t) = \int_{-\infty}^{t} g_{\kappa,r}(s) \, ds = (\kappa/r) \exp(rt) \). Thus for \( b > 0 \), we have

\[ P((B,E,T,S) \in \mathcal{D} | B = b) = \nu \int_{e \in (b,L)} f_E(e | b) \left[ G_{\kappa,r}(e) - G_{\kappa,r}(b) \right] \, de \]

\[ = \nu \int_{b}^{L} \lambda_V (\kappa/r) \{\exp(re) - \exp(rb)\} \, de \]

\[ = \frac{\lambda_V \kappa \nu}{r} \left[ \frac{1}{r} \left( \exp(reL) - \exp(rb) \right) - (L - b) \exp(rb) \right] \]

\[ = \frac{\lambda_V \kappa \nu}{r^2} \exp(rL) - \frac{\lambda_V \kappa \nu}{r} \left( r^{-1} + L - b \right) \exp(rb) \]

\[ = \frac{\lambda_V \kappa \nu}{r^2} \exp(rL) \left[ 1 - (1 + r(L - b)) \exp(-r(L - b)) \right]. \] (26)

For \( b = 0 \), we can replace \( \lambda_V \) in the above equation by \( \lambda_W \).

The idea is that, if \( rL \) is much larger than 1 (in our preliminary analysis \( rL \approx 0.25 \times 54 = 13.5 \)), then

Right hand side of (26) \( \approx \frac{\nu \lambda_W \kappa}{r^2} \exp(rL) \) when \( b = 0 \).

Using this approximation, we obtain

\[ P((B,E,T,S) \in \mathcal{D}) \]

\[ = \int_{0 \leq b < L} P((b, E, T, S) \in \mathcal{D} | B = b) \, f_B(b) \, db \]

\[ = \int_{0 \leq b < L} P((b, E, T, S) \in \mathcal{D} | B = b) \, f_B(b) \, db \]

\[ \approx \frac{(1 - \pi) \lambda_W \kappa \nu}{r^2} \exp(rL) + \int_{0 < b < L} P((b, E, T, S) \in \mathcal{D} | B = b) \, f_B(b) \, db \]

\[ = \frac{(1 - \pi) \lambda_W \kappa \nu}{r^2} \exp(rL) + \pi \int_{0}^{L} \frac{1}{L} \frac{\lambda_W \kappa \nu}{r^2} \exp(rL) \left[ 1 - (1 + r(L - b)) \exp(-r(L - b)) \right] \, db \]
The following Lemma is useful to marginalize over $\rho$ where

$$\text{Lemma 3.}$$

In the last step we used the approximation $e^{rL} \approx 1 + rL$:

$$A_1 = \int_0^L (1 + rx) \exp(-rx) \, dx = -\frac{\exp(-rx)(rx + 2)}{r} \bigg|_{x=0}^{x=L} = 2 - \frac{\exp(-rL)(rL + 2)}{r} \approx \frac{2}{r}.$$

Therefore, the density is given by

$$f(b, e, t | D) \approx \frac{r^2}{r^2 \exp(rL) \nu} \left[ (1 - \pi)\lambda_W 1_{\{b=0\}} + (\pi/L)\lambda_V 1_{\{b>0\}} \right] \cdot \frac{\exp(rt) \cdot \nu h(s-t)}{r \exp(1 - \pi)\lambda_W + \pi \lambda_V (1 - 2/(rL))} \cdot \exp(rL) \cdot h(s-t),$$

where $\rho = (\lambda_V/\lambda_W)\pi/(1 - \pi)$.

**A.3 Derivation of Proposition**

The following Lemma is useful to marginalize over $T$ when the incubation period follows a Gamma($\alpha, \beta$) distribution:

**Lemma 3.** For any $r > 0$ and $b \leq e \leq s$,

$$\int_b^{\min(s,e)} \exp(rt) h_{\alpha,\beta}(s-t) \, dt = \left(\frac{\beta}{\beta + r}\right)^\alpha \exp(rs) \left[H_{\alpha,\beta+r}(s-b) - H_{\alpha,\beta+r}((s-e)+)\right].$$

**Proof.** By a change of variables,

$$\int_b^{\min(s,e)} \exp(rt) h_{\alpha,\beta}(s-t) \, dt$$

$$= \int_b^{\min(s,e)} \exp(rt) \frac{\beta^\alpha}{\Gamma(\alpha)} (s-t)^{\alpha-1} \exp\{-\beta(s-t)\} \, dt$$

$$= \left(\frac{\beta}{\beta + r}\right)^\alpha \exp(rs) \int_b^{\min(s,e)} \frac{(\beta + r)^\alpha}{\Gamma(\alpha)} (s-t)^{\alpha-1} \exp\{-(\beta + r)(s-t)\} \, dt$$

$$= \left(\frac{\beta}{\beta + r}\right)^\alpha \exp(rs) \left[H_{\alpha,\beta+r}(s-b) - H_{\alpha,\beta+r}((s-e)+)\right].$$

The time of contraction $T$ is not observed. Should it be observed, the full data unconditional likelihood is given by

$$L_{\text{uncond}}(\rho, r, h(\cdot); T)$$

32
\[= \prod_{i=1}^{n} f(B_i, E_i, T_i, S_i \mid (B_i, E_i, T_i, S_i) \in \mathcal{D})
\approx r^{2n} \prod_{i=1}^{n} \frac{1_{\{B_i = 0\}} + (\rho/L)1_{\{B_i > 0\}}}{1 + \rho(1 - 2/(rL))} \cdot \prod_{i=1}^{n} 1_{\{B_i \leq T_i \leq \min(E_i, S_i)\}} \cdot \exp(r(T_i - L)) \cdot h(S_i - T_i).\]

If we assume \(h(\cdot)\) is the density of a Gamma distribution:

\[h(x) = h_{\alpha, \beta}(x) = \frac{\beta^\alpha}{\Gamma(\alpha)} x^{\alpha-1} \exp(-\beta x) \quad (x > 0),\]

then we can marginalize over \(T_i\) using Lemma \ref{lemma:marginalize}:

\[\int A_{2,i} dT_i = \exp \left\{ r(S_i - L) \right\} \left( \frac{\beta}{\beta + r} \right)^\alpha \cdot \left[ H_{\alpha, \beta + r}(S_i - B_i) - H_{\alpha, \beta + r}(S_i - E_i) \right].\]

In conclusion, the unconditional observed data likelihood is given by

\[L_{\text{uncond}}(\rho, r, \alpha, \beta) \approx r^{2n} \left( \frac{\beta}{\beta + r} \right)^\alpha \prod_{i=1}^{n} \left\{ \frac{1_{\{B_i = 0\}} + (\rho/L)1_{\{B_i > 0\}}}{1 + \rho(1 - 2/(rL))} \cdot \exp(r(L - T_i)) \cdot h(S_i - T_i) \right\} \cdot \exp(rL) \cdot h(s - t) \cdot ds \cdot de \]

The conditional observed data likelihood can be derived in the same way. Details are omitted.

### A.4 Derivation of Proposition \ref{proposition:conditional}

By integrating the conditional density \eqref{conditional_density} over \((b, e, s)\), the marginal distribution of \(T\) conditional on \((B, E, T, S) \in \mathcal{D}\) is given by

\[f_T(t \mid \mathcal{D}, B = 0) \propto \int \int \int f(b, e, t, s \mid \mathcal{D}) \cdot 1_{\{(b, e, t, s) \in \mathcal{D}\}} \cdot 1_{\{b = 0\}} \cdot db \cdot de \cdot ds \]
\[\approx \int_t^L \int_t^L \int_t^\infty r^2 \cdot \frac{1_{\{b = 0\}} \cdot \exp(rt)}{1 + \rho(1 - 2/(rL))} \cdot \exp(rL) \cdot h(s - t) \cdot ds \cdot de \]
\[= \int_t^L \exp(rt) \cdot h(s - t) \cdot ds \]
\[= (L - t) \exp(rt).\]

Assumption \ref{assumption:symptom_onset} says that the distribution of the symptom onset \(S\) only depends on the time of transmission \(T\) \((S \perp B, E \mid T)\). Therefore the marginal distribution of \(S\) in exported Wuhan resident cases is given by convolving the distribution of \(T\) with the distribution of the incubation period \(S - T\):

\[f_S(s \mid \mathcal{D}, B = 0) = \int_0^{\min(L, s)} f_T(t \mid \mathcal{D}, B = 0) h(s - t) dt\]
Under the parametric assumption that \( S - T \) follows a Gamma distribution (Assumption 4), we have, for \( s \geq L/2 \),

\[
f_s(s \mid D, B = 0) \propto \int_0^{\min(L,s)} (L - t) \exp(rt) \cdot (s - t)^{\alpha-1} \exp\{-\beta(s - t)\} \, dt
\]

\[
= \exp(rs) \cdot \int_0^{\min(L,s)} [(L - s) + (s - t)](s - t)^{\alpha-1} \exp\{-(\beta + r)(s - t)\} \, dt
\]

\[
= \exp(rs) \cdot \int_{(s-L)+}^{s} [(L - s)x^{\alpha-1} + x^{\alpha}] \exp\{-(\beta + r)x\} \, dx
\]

\[
= \exp(rs) \cdot \left\{ (L - s) \frac{\Gamma(\alpha)}{H_{\alpha+1}(\beta + r)} \left[ H_{\alpha+1}(\beta + r)(s - L) + H_{\alpha+1}(\beta + r)(s - L)\right] \right\}
\]

\[
\propto \exp(rs) \cdot \left\{ (L - s) \left[ H_{\alpha+1}(\beta + r)(s - L) + H_{\alpha+1}(\beta + r)(s - L)\right] \right\}
\]

\[
\approx \exp(rs) \cdot \left\{ (L - s)[1 - H_{\alpha+1}(\beta + r)(s - L)] + \frac{\alpha}{\beta + r}[1 - H_{\alpha+1}(\beta + r)(s - L)] \right\}
\]

The last step uses the approximation that

\[
1 \approx H_{\alpha+1,\beta+r}(L/2) \leq H_{\alpha+1,\beta+r}(s) \leq H_{\alpha,\beta+r}(s).
\]

We next show that this is reasonable under the technical assumption \( L > 4(\alpha + 5)/(\beta + r) \) in Proposition 2. Suppose \( X \sim \text{Gamma}(\alpha + 1, \beta + r) \). The Chernoff tail bound says that

\[
1 - H_{\alpha+1,\beta+r}(L/2) = \mathbb{P}(X > L/2) \leq \mathbb{E}[\exp(cX)] / \exp(cL/2) = \frac{(1 - c/(\beta + r))^{-(\alpha+1)}}{\exp(cL/2)} \text{ for } a < \beta + r.
\]

By choosing \( c = (1 - \exp(-1))(\beta + r) \approx 0.63(\beta + r) \), we have

\[
1 - H_{\alpha+1,\beta+r}(L/2) \leq \frac{\exp(\alpha + 1)}{\exp\{0.31(\beta + r)L\}} < \frac{\exp(\alpha + 1)}{\exp\{0.31 \times 4(\alpha + 5)\}} < \exp(1 - 0.31 \times 20) < 0.01.
\]

### A.5 Derivation of Proposition 3

Let \( e_- = \min(e, M) \). Then under Assumptions 1 and 2 for \((b, e, t, s) \in \mathcal{D} \) and \( s \leq M \),

\[
f_{T,S}(t, s \mid b, e, \mathcal{D}, S \leq M) = \frac{f_{T,S}(t, s \mid b, e, \mathcal{D})}{\int \int f_{T,S}(t, s \mid b, e, \mathcal{D}) \, ds \, dt} = \frac{g(t)h(s - t)}{\int_b^{e-} g(t) \int_t^M h(s - t) \, ds \, dt}.
\]
where \( H(s) = \int_0^s h(x) \, dx \) is the distribution function of the incubation period. Assuming \( g(t) = \kappa \exp(rt) \) and using integration by parts, for \( r \neq 0 \),
\[
\int_b^{e_-} g(t)H(M-t) \, dt = \kappa \int_b^{e_-} \exp(rt)H(M-t) \, dt \\
= \frac{\kappa}{r} \int_b^{e_-} H(M-t) \, d\exp(rt) \\
= \frac{\kappa}{r} \left[ \exp(rt)H(M-t) \bigg|^{t=e_-}_{t=b} + \int_b^{e_-} \exp(rt)h(M-t) \, dt \right].
\]

By using \( h(\cdot) = h_{\alpha,\beta}(\cdot) \) and using Lemma 3, we have
\[
\int_b^{e_-} g(t)H_{\alpha,\beta}(M-t) \, dt = \kappa \left[ \exp(rt)H_{\alpha,\beta}(M-t) - \left( \frac{\beta}{\beta + r} \right)^\alpha \exp(rM)H_{\alpha,\beta+r}(M-t) \right]^{t=e_-}_{t=b}.
\]

Now we integrate \( t \) in (27) from \( b \) to \( e_- \) and get
\[
f_S(s | b, e, D, S \leq M) = r \left( \frac{\beta}{\beta + r} \right)^\alpha \exp(rs) \left[ H_{\alpha,\beta+r}(s-b) - H_{\alpha,\beta+r}((s-e)_+) \right] / \left[ \exp(rt)H_{\alpha,\beta}(M-t) - \left( \frac{\beta}{\beta + r} \right)^\alpha \exp(rM)H_{\alpha,\beta+r}(M-t) \right]^{t=e_-}_{t=b}.
\]

For \( r = 0 \), using integration by parts,
\[
\int_b^{e_-} g(t)H_{\alpha,\beta}(M-t) \, dt = \kappa \int_{(M-e)_+}^{M-b} H_{\alpha,\beta}(x) \, dx \\
= \kappa \left[ xH_{\alpha,\beta}(x) \bigg|^{x=M-b}_{x=(M-e)_+} - \int_{(M-e)_+}^{M-b} xh_{\alpha,\beta}(x) \, dx \right] \\
= \kappa \left[ xH_{\alpha,\beta}(x) \bigg|^{x=M-b}_{x=(M-e)_+} - \int_{(M-e)_+}^{M-b} x \cdot \frac{\beta^\alpha}{\Gamma(\alpha)} x^{\alpha-1} \exp(-\beta x) \, dx \right] \\
= \kappa \left[ xH_{\alpha,\beta}(x) \bigg|^{x=M-b}_{x=(M-e)_+} - \frac{\alpha}{\beta} \int_{(M-e)_+}^{M-b} \frac{\beta^{\alpha+1}}{\Gamma(\alpha+1)} x^\alpha \exp(-\beta x) \, dx \right] \\
= \kappa \left[ xH_{\alpha,\beta}(x) - \frac{\alpha}{\beta} H_{\alpha+1,\beta}(x) \bigg|^{x=M-b}_{x=(M-e)_+} \right].
\]

We can similarly integrate \( t \) out and obtain the full data likelihood. Details are omitted.