Estimating the Asymptomatic Proportion of 2019 Novel Coronavirus onboard the Princess Cruises Ship, 2020

Authors: Kenji Mizumoto1,2,3, Katsushi Kagaya 2,4, Alexander Zarebski5, Gerardo Chowell3

Affiliations

1. Graduate School of Advanced Integrated Studies in Human Survivability, Kyoto University Yoshida-Nakaadachi-cho, Sakyo-ku, Kyoto, Japan
2. Hakubi Center for Advanced Research, Kyoto University, Yoshidahonmachi, Sakyo-ku, Kyoto, Japan
3. Department of Population Health Sciences, School of Public Health, Georgia State University, Atlanta, Georgia, USA
4. Seto Marine Biological Laboratory, Field Science, Education and Research Center, Kyoto University, Shirahama-cho, Nishimuro-gun, Wakayama 649-2211 Japan
5. Department of Zoology, University of Oxford, UK

Corresponding author: Kenji Mizumoto
Corresponding author email: mizumoto.kenji.5a@kyoto-u.ac.jp
Abstract

The potential infectiousness of asymptomatic COVID-19 cases together with a substantial fraction of asymptomatic infections among all infections, have been highlighted in clinical studies. We conducted statistical modeling analysis to derive the delay-adjusted asymptomatic proportion of the positive COVID-19 infections onboard the Princess Cruises ship along with the timeline of infections. We estimated the asymptomatic proportion at 17.9% (95% CrI: 15.5%–20.2%), with most of the infections occurring before the start of the 2-week quarantine.

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Background

Since COVID-19 emerged in the city of Wuhan, China in December 2019, thousands of people have succumbed to the novel coronavirus especially in the Province of Hubei while hundreds of imported and secondary cases have been reported in multiple countries as of February 29, 2020 [1].

The clinical and epidemiological characteristics of COVID-19 continue to be investigated as the virus continues its march through the human population [2-3]. While reliable estimates of the reproduction number and the death risk associated with COVID-19 are crucially needed to guide public health policy, another key epidemiological parameter that could inform the intensity and range of social distancing strategies to combat COVID-19 is the asymptomatic proportion, which is broadly defined as the proportion of asymptomatic infections among all the infections of the disease. Indeed, the asymptomatic proportion is a useful quantity to gauge the true burden of the disease and better interpret estimates of the transmission potential. This proportion varies widely across infectious diseases, ranging from 8% for measles and 32% for norovirus up to 90-95% for polio [4-6]. Most importantly, it is well established that asymptomatic individuals are frequently able to transmit the virus to others [7-8].
COVID-19 is not the exception to this pattern, with accumulating evidence indicating that a substantial fraction of the infected individuals with the novel coronavirus are asymptomatic [9-11].

As an epidemic progresses over time, suspected cases are examined and tested for the infection using polymerase chain reaction (PCR) or rapid diagnostic test (RDT). Then, time-stamped counts of the test results stratified according to the presence or absence of symptoms at the time of testing are often reported to the public in near real-time.

Nevertheless, it is important to note that the estimation of the asymptomatic proportion needs to be handled carefully since real-time outbreak data are influenced by the phenomenon of right censoring, due to the time lag between the time of examination and sample collection and the development of illness.

In this paper, we conduct a statistical modeling analysis to estimate the asymptomatic proportion among infected individuals who have tested positive for COVID-19 infections onboard the Princess Cruises Ship along with their time of infections, accounting for the delay in onset of symptoms and right-censoring.
Epidemiological description and data

In Yokohama, Japan, an outbreak of COVID-19 unfolded on board the Princess Cruise Ship, which had been under quarantine orders since February 5, 2020, after a former passenger of the cruise ship tested positive for the virus after disembarking in Hong Kong. By February 21, 2020, two days after the scheduled two-week quarantine came to an end, a total of 634 people including one quarantine officer, one nurse and one administrative officer tested positive for COVID-19 out of the 3,711 passengers and crew members on board the vessel. Laboratory testing by PCR were conducted, prioritizing symptomatic or high-risk groups.

Daily time series of laboratory test results for COVID-19 (both positive and negative), including information of presence or absence of symptoms from February 5, 2020 to February 20, 2020 were extracted from secondary sources [12]. The reporting date, number of tests, number of tested positive and number of symptomatic and symptomatic cases at the time of sample collection are provided, while the time of infection and true asymptomatic proportion are not available.

A total of 634 people have tested positive among 3063 tests as of February 20, 2020. Out of 634 cases, a total of 313 cases are female and six were aged 0-19 years,
152 were aged 20-59 years and 476 were 60 years and older (Figure 1). The nationality of the cases includes Japan (270), United States (88), Philippines (54), Canada (51), Australia (49), Hong Kong (30) and China (28).

Figure 1 – Age distribution of reported 2019 Novel Coronavirus cases by gender onboard the Princess Cruises ship (Female = 313, Male = 321)

Out of the 634 confirmed cases, a total of 306 and 328 were reported to be symptomatic and asymptomatic, respectively. The proportion of asymptomatic individuals appears to be 16.1% (35/218) before February 13, 25.6% (73/285) on February 15, 31.2% (111/355) on February 16, 39.9% (181/454) on February 17, 45.4% (246/542) on February 18, 51.9% (322/621) on February 19 and 51.7% (328/634) on February 20 (Table 1). Soon after identification of the first infections, both symptomatic and asymptomatic cases were transported to designated medical facilities specialized in infectious diseases in Japan. However, these patients were treated as external (imported) cases, and a detailed description of their clinical progression is not publicly available.

The asymptomatic proportion was defined as the proportion of asymptotically infected individuals among the total number of infected individuals.
Statistical modelling

Here, we describe the statistical model that was employed to estimate the asymptomatic proportion using the time-series dataset described above.

The reported asymptomatic cases consists of both true asymptomatic infections and symptomatic cases that had not yet developed symptoms at the time of data collection, i.e., the data is right-censored. Each datum consists of an interval of time during which the individual may have been infected and a binary variable indicating whether they were symptomatic as of the 18th of February.

For individual $i$ let $[a_i, b_i]$ denote the interval during which they may have been infected and $c$ represents the censor date of observation of being symptomatic. The (unknown) time at which individual $i$ was infected is denoted $X_i$ and, if they develop symptoms, let $D_i$ denote the delay from the time of infection until the time they are symptomatic, with cumulative density function (CDF), $F_D$. The asymptomatic proportion, $p$, is the probability an individual will never develop symptoms.

Given an individual was exposed during the interval $[a_i, b_i]$ the probability for them being asymptomatic at time $c$ is

$$g(x, p) = \begin{cases} 
    p + (1 - p)(1 - F_D(c - x)), & \text{if they do not have symptoms,} \\
    F_D(c - x), & \text{if they do have symptoms,}
\end{cases}$$
Given they were infected at time $x$ for some $a \leq x \leq b$. Since the natural history of each individual’s infection is independent, the likelihood function is just the product of the $g(X_i, p)$ for each individual. Previous work on COVID-19 suggests that the distribution of the delay, $D$, between infection and onset of symptomatic infections follows a Weibull distribution, with the mean and SD at 6.4 and 2.3 days [3].

The observations were treated as survival data with right-censoring. The probability of being asymptomatic along with the infection time of each individual where estimated in a Bayesian framework using Hamiltonian Monte Carlo (HMC). A detailed description of the model used and the computation is provided in a Technical Appendix.

**Findings from the real-time outbreak analysis**

Posterior median estimates of true asymptomatic proportion among the reported asymptomatic cases is at 0.35 (95% CrI: 0.30–0.39), with the estimated total number of the true asymptomatic cases at 113.3 (95% CrI: 98.2-128.3) and the estimated asymptomatic proportion at 17.9% (95% CrI: 15.5%–20.2%).

We conducted sensitivity analyses to examine how varying the mean incubation period between 5.5 and 9.5 days affects our estimates of the true asymptomatic proportion. Estimates of the true asymptomatic proportion among the reported asymptomatic cases are somewhat sensitive to changes in the mean incubation period, ranging from 0.28 (95% CrI: 0.23–0.33) to 0.40 (95% CrI: 0.36–0.44), while the
estimated total number of true asymptomatic cases range from 91.9 (95% CrI: 75.2–108.7) to 130.8 (95% CrI: 117.1–144.5) and the estimated asymptomatic proportion ranges from 20.6% (95% CrI: 18.5%–22.8%) to 39.9% (95% CrI: 35.7%–44.1%).

Heat maps were used to display the density distribution of infection timing by individuals (Figure S1) where the vertical line corresponds to the date of February 5, 2020. Among the symptomatic cases, the infection timing appears to have occurred just before or around the start of the quarantine period, while the infection timing for asymptomatic cases appears to have occurred well before the start of the quarantine period.

**Discussion**

We have conducted statistical modeling analyses on publicly available data to elucidate the asymptomatic proportion, along with the time of infection among the COVID-19 infected cases onboard the Princess Cruises ship.

Our estimated asymptomatic proportion is at 17.9% (95% CrI: 15.5%–20.2%), which overlaps with a recently derived estimate of 33.3% (95% CI: 8.3%–58.3%) from data of Japanese citizens evacuated from Wuhan [13]. Considering the similarity in viral loads and the high possibility of potent transmission potential, the high proportion of asymptomatic infections has significant public health implications [14]. For instance, self-isolation for 14-day periods are also recommended for contacts with asymptomatic cases [15].
Most of the infections appear to have occurred before or around the start of the 2-week quarantine that started on February 5, 2020, which further highlights the potent transmissibility of the SARS-CoV-2 virus, especially in confined settings. To further mitigate transmission of COVID-19 and bring the epidemic under control in areas with active transmission, it may be necessary to minimize the number of gatherings in confined settings.

Our study is not free from limitations. First, laboratory tests by PCR were conducted focusing on symptomatic cases especially at the early phase of the quarantine. If asymptomatic cases where missed as a result of this, it would mean we have underestimated the asymptomatic proportion. Second, it is worth noting that the data of passengers and crews employed in our analysis is not a random sample from the general population. Considering that most of the passengers are 60 years and older, the nature of this age distribution may lead to underestimation if older individuals tend to experience more symptoms. An age standardized asymptomatic proportion would be more appropriate in that case. Third, the presence of symptoms in cases with COVID-19 may correlate with other factors unrelated to age including prior health conditions such as cardiovascular disease, diabetes, immunosuppression. Therefore, more detailed data documenting the baseline health of the individuals including the presence of underlying diseases or comorbidities would be useful to remove the bias in estimates of the asymptomatic proportion.

In summary, we have estimated the proportion of asymptomatic cases among individuals who have tested positive for novel COVID-19 along with the times of
infection of confirmed cases onboard the Princess Cruises Ship after adjusting for the
delay in symptom onset and right-censoring of the observations.

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Additional files

Additional file 1: Supplementary document

Additional file 2: Figure S1. Heat maps of the density distribution of infection timing by individuals

A) Symptomatic cases (N= 306), B) Asymptomatic cases (N= 328). Vertical axis represents each individual from 1 to N. Cases disembarked after testing positive for the disease. Day 1 corresponds to January 20, 2020, when the first symptomatic case embarked. The vertical line corresponds to February 5, 2020 when the quarantine period started.
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Table 1 – Test results for Passengers and crews of the Diamond Princess cruise (N = 3711)

| Date  | No of passengers and crew members on board | No. of test (cumulative) | No. of test | Positive (cumulative) | No. of symptomatic cases | No. of asymptomatic cases | No. of asymptomatic cases (cumulative) |
|-------|------------------------------------------|--------------------------|-------------|-----------------------|--------------------------|--------------------------|---------------------------------------|
| Feb/5 | 3711                                     | 31                       | 31          | 10                    | 10                       |                          |                                       |
| Feb/6 | 71                                       | 102                      | 10          | 10                    | 20                       |                          |                                       |
| Feb/7 | 171                                      | 273                      | 41          | 61                    |                          |                          |                                       |
| Feb/8 | 6                                        | 279                      | 3           | 64                    |                          |                          |                                       |
| Feb/9 | 57                                       | 336                      | 6           | 70                    |                          |                          |                                       |
| Feb/10| 103                                      | 439                      | 65          | 135                   |                          |                          |                                       |
| Feb/11|                                          |                          |             |                       |                          |                          |                                       |
| Feb/12|                                          |                          |             |                       |                          |                          |                                       |
| Feb/13|                                          |                          |             |                       |                          |                          |                                       |
| Feb/14| 3451                                     | 260‡                     | 73‡         |                       |                          |                          |                                       |
| Feb/15| 217                                      | 930                      | 67          | 285                   | 29                       | 38                       | 73‡                                   |
| Feb/16|                                          |                          |             |                       |                          |                          |                                       |
| Feb/17| 3183                                     | 528‡                     | 73‡         |                       |                          |                          |                                       |
| Feb/18|                                          |                          |             |                       |                          |                          |                                       |
| Feb/19|                                          |                          |             |                       |                          |                          |                                       |
| Feb/20|                                          |                          |             |                       |                          |                          |                                       |

§Reported date

‡As this is a cumulative number, the exact date of disembarkation is unavailable.

¶As this is a cumulative number, the reported date for 35 asymptomatic cases are unavailable.
Age distribution by gender

| Age group | Male | Female |
|-----------|------|--------|
| <20       |      |        |
| 20-       |      |        |
| 30-       |      |        |
| 40-       |      |        |
| 50-       |      |        |
| 60-       |      |        |
| 70-       | 125  | 100    |
| 80-       | 25   |        |
| 90-       |      |        |