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Coronavirus Pandemic

Examining the incubation period distributions of COVID-19 on Chinese patients with different travel histories

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Abstract

Introduction: Current studies estimated a general incubation period distribution of COVID-19 based on early-confirmed cases in Wuhan, and have not examined whether the incubation period distribution varies across population segments with different travel histories. We aimed to examine whether patients infected by community transmission had extended incubation periods than the early generation patients who had direct exposures to Wuhan.

Methodology: Based on 4741 patient case reports from municipal centers of disease control by February 21, 2020, we calculated the incubation periods of 2555 patients with clear epidemiological survey information and illness development timeline. All patients were categorized into five groups by their travel histories. Incubation period distributions were modeled for each group by the method of the posterior Weibull distribution estimation.

Results: Adults aged 30 to 59 years had the most substantial proportion of confirmed cases in China. The incubation period distribution varied slightly across patient groups with different travel histories. Patients who regularly lived in Wuhan and left to other locations before January 23, 2020 had the shortest posterior median value of 7.57 days for the incubation period, while the incubation periods for persons affected by local community transmission had the largest posterior median of incubation periods, 9.31 days.

Conclusions: The median incubation period for all patients infected outside Wuhan was 9 days, a bit of more extended than the early estimated 5-day incubation period that was based on patients in Wuhan. Our findings may imply the decreases of virulence of the COVID-19 virus along with intergenerational transmission.

Key words: COVID-19; incubation period; travel histories; China.

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Introduction

The epidemic of novel coronavirus disease named COVID-19, an outbreak from the city of Wuhan, China, is rapidly spreading worldwide [1]. Some key epidemiological parameters of this contagious epidemic, including clinical symptoms and incubation periods, have been intensively investigated and disclosed to global communities [2-10]. The incubation period, the time gap between the date of initial contact with the transmission source and the symptoms onset date, is one of the most critical parameters for health care professionals to observe the illness development process, recognize viral virulence, and guide pathology research. However, the estimates on the incubation period are diversified, although the World Health Organization recommends the incubation period ranges from 1 to 14 days with a median of 5 days [11]. However, these studies only depicted a general incubation period distribution based on the early confirmed cases who were first found in Wuhan, the epicenter of this outbreak. These studies have not examined whether the incubation period distribution varies across different population segments with different travel histories.

The research question of this study is whether patients who were infected by community transmission have extended incubation periods than the early generation patients who have direct exposures to Wuhan. Along with the epidemic continuing, there was a growing number of patients who became infected outside Wuhan or by human-to-human transmission within local communities. These patients, to some

extent, could be viewed as at least third-or-above generation patients [12]. Whether these infected persons have expanded incubation periods compared to the early generation patients found in Wuhan is an important question that deserves intensive research. Identifying the linkage between the incubation period and intergenerational transmission could help to forecast epidemic evolution and benefits authorities outside China to make related arrangements on addressing COVID-19.

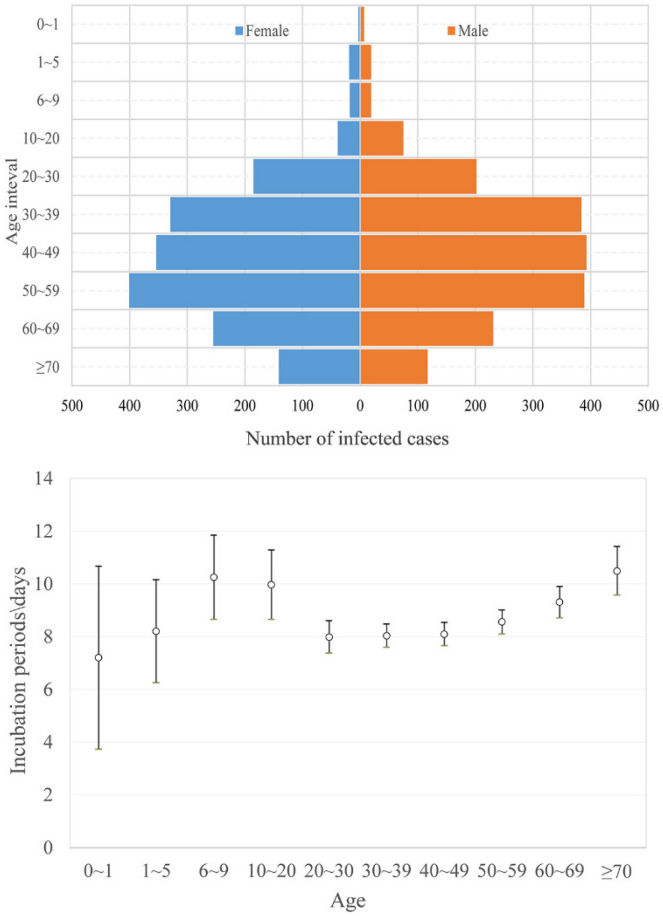
Methodology

Data and Preprocessing

The dataset used for this retrospective study was collected from the patient case records from municipal centers of disease control in Mainland of China. By February 21, 2020, we collected 4741 case records of patients outside Hubei, Qinghai, and Tibet. It accounts for 36.86% of the total infected persons in 28 provincial administration units in Mainland of China.

Although all patients had clear epidemiological survey information on the probable date and location of being infected, only approximately 50% of these patients (n = 2555) had related information on the illness development timeline, by which we identified the date of symptoms onset. Further, all 2555 patients were divided into five groups by their travel histories. The first group included persons who were infected in Wuhan, where they regularly resided in but left before January 23, 2020 when the city was closed off. The second group included persons who visited or shortly transited in Wuhan and became infected. The persons who were infected in a location that is outside Wuhan, where he or she regularly dwelled in but left, were categorized into group 3. Additionally, the persons who briefly visited but became infected in a location outside Wuhan, which was not where the patient regularly lived, were sorted into group 4. The persons who did not have travel histories and just became infected by community transmission were marked as group 5. We calculated the incubation period distribution for each group.

Figure 1. The age-sex pyramid and incubation period by age on COVID-19-infected persons in China.



Statistical Methods

Since the Weibull distribution may fit the incubation period estimation best [8], we conducted posterior estimates, by the software R.3.60, for patients from these five groups, respectively [13]. In addition, Kruskal-Wallis tests were performed to examine the significance of the intergroup variability in statistics.

Results

Infected Population and Incubation Period by Sex and Age

The age-sex pyramid of the infected population shows that the number of infected cases varies significantly across age (Figure 1). The number of infected populations increases with age interval from 10 years to 20 years and reaches a peak at the age interval from 50 to 59. After that, the number of infected persons decreases evidently. This result shows that although all population segments are vulnerable to be infected by SARS-CoV-2, adults, especially middle-aged adults, have the highest incidence ratio. The reason is that they have higher possibilities of contacting direct transmission sources in their daily life than other population segments. Regarding the incubation periods, males and females have similar incubation periods of approximately eight days. However, the incubation period varies evidently with age. The age group from 20 to 50 years old had the shortest duration, while the older age groups in this study had the most prolonged incubation periods. A U-

Table 1. Incubation periods for patients with different travel histories.

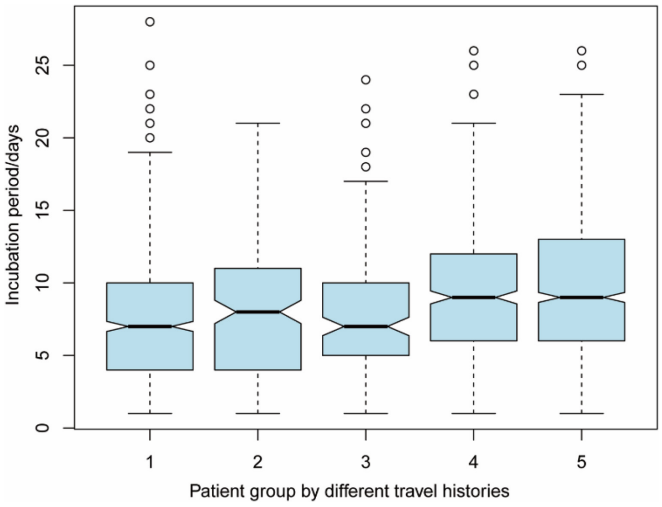
Group	Living and travel histories	N	%	Mean	95% CI	Weibull distribution estimates			
						Median	Posterior median	Shape	Scale
1	Regularly live in Wuhan and became infected	743	29.08	8.28	7.19-9.37	7	7.57	1.59	8.45
2	Visited or transited in Wuhan and became infected	188	7.36	8.34	7.41-9.27	8	8.15	1.83	9.18
3	Regularly live outside Wuhan and became infected	154	6.03	8.12	7.19-9.05	7	8.08	1.78	9.09
4	Visited or transited in a location outside Wuhan and became infected	448	17.53	9.59	8.62-10.56	9	9.11	2.18	10.29
5	No travel history and became infected by local community transmission	1022	40.00	9.44	8.49-10.38	9	9.31	2.11	10.51
Sum	All patient cases	2555	100	8.98	7.98-9.9	8	8.61	1.88	9.69

shaped relationship possibly exists in incubation period distributions across ages.

Incubation Period Distribution Variations by Travel Histories

The patients from group 1 who regularly lived in Wuhan and left to other locations before January 23, 2020 had the shortest median of seven days for the incubation period (Table 1 and Figure 2). The posterior median of the Weibull distribution estimation for patients from group 1 was 7.57 days, which was the shortest one among all patient groups. The incubation period for persons who visited or shortly transited in the city of Wuhan and became infected on average was eight days. These two groups of patients were believed to be directly affected by the early generations of transmission sources. In contrast, persons who became infected in a location that they regularly resided in that was outside of Wuhan and left to another site (e.g., hometown) had a posterior median incubation period of 8.08 days. The incubation periods for patients who visited or shortly transited in a location outside Wuhan and became infected on average were 9.11 days. Notably, the incubation periods for persons affected by the transmission within local communities had the largest posterior median of incubation periods, 9.31 days. The Kruskal-Wallis testing results further show that patients from group 5 have statistically significant variances with patients from groups 1, 2, and 3. Additionally, variations between groups 1 and 4 and variances between groups 4 and 3 are significant at the confidence level of 99% and 95%, respectively.

Figure 2. Incubation period distributions of COVID-19 on Chinese patients with different travel histories.



1: Live in Wuhan; 2: Visited/transited in Wuhan; 3: Live outside Wuhan; 4: Visited/transited in a location outside Wuhan and became infected; 5: No travel history and became infected by local community transmission.

Discussion

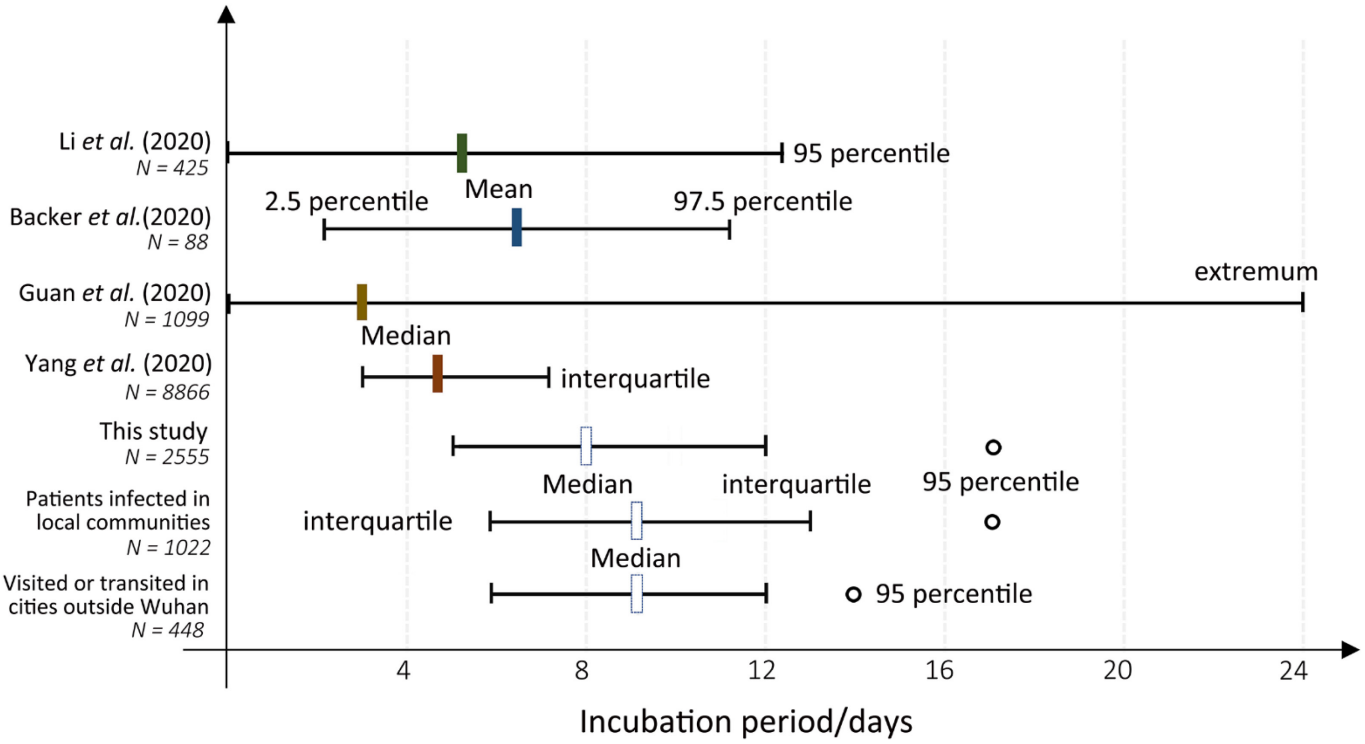
Estimating the incubation period is critical to address the COVID-19 epidemic. The estimates on the incubation period are being updated continually as an increasing number of clinical case studies are published (Figure 3). Two early studies with early infected cases in Wuhan concluded that the mean incubation periods were 5.2 and 6.4 days [4,8]. Guan *et al*. summarized that the incubation period ranged from 0 to 24 days, while the median was three days [9]. Yang *et al*. [14], using 8866 patients, found that the median incubation period was 4.75 days, with an interquartile range from 3.0 to 7.2 days. Comparatively, the estimated median value on the incubation period in this study is longer than that in other studies. The reason probably lies in the patients used in this study are patients from outside Hubei Province rather than the early infected patients first found in Wuhan.

The above comparison leads to another issue of whether the incubation period of COVID-19 virus changes with intergenerational transmissions. Investigating this issue needs profiling the incubation period distributions across infected persons with different epidemiological experiences [15]. According to this study, patients infected by local community transmission outside Wuhan had extended incubation periods. This finding is consistent with Liu *et al*. [16] that revealed the cases infected by community transmission in the city of Shenzhen (n = 33) had a slightly larger median value of longer incubation period than 5 days that were derived from the infected cases with direct travel exposure to Wuhan (n = 25). Therefore, it seems that the incubation periods for third- or above-generation patients were more extended than those of first- or second-generation patients. The possible reason is that the virulence of this novel coronavirus may decrease with intergenerational transmission, although this hypothesis needs intensive laboratory research at the pathogenicity level. At the same time, we should note that no evidence currently demonstrates that the virulence of this virus may peter out. This study not only supports the policy of determining the quarantine duration up to 14 days [9,17], but also suggests the necessity of regulating the different self-isolation duration for different regions.

Conclusion

By analyzing 4741 case reports released by China's health authorities, this retrospective research confirms that adults aged 30 to 59 years, who usually have priorities in immunity and are easily considered to be insusceptible populations, actually have the most substantial proportion of COVID-19 infected cases confirmed in China. Moreover, the incubation periods of the SARS-COV-2 virus in these population segments are not longer than that on their counterparts, e.g., adolescents and elderly populations. The international communities then should pay sufficient attention to this highly contagious epidemic for all populations. Besides, the incubation period distribution of COVID-19 may vary slightly among patients with different travel histories. The median incubation period for all patients infected outside Wuhan was nine days, a bit of more extended than the early estimated 5-day incubation period that was based on patients in Wuhan. It may suggest that the incubation period of COVID-19 may prolong along with the intergenerational transmission. Understanding the variability of incubation periods across different people could help to identify the linkage between and intergenerational transmission. Both could facilitate to make appropriate epidemiological policies on addressing the global pandemic of COVID-19.

Figure 3. Estimated incubation periods for COVID-19 virus from different studies.



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