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Concise Communication

The difference in the incubation period of 2019 novel coronavirus (SARS-CoV-2) infection between travelers to Hubei and nontravelers: The need for a longer quarantine period

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Abstract

Data collected from the individual cases reported by the media were used to estimate the distribution of the incubation period of travelers to Hubei versus that of nontravelers. Because a longer and more volatile incubation period has been observed in travelers, the duration of quarantine should be extended to 3 weeks.

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An epidemic of viral pneumonia started in Wuhan, the capital of Hubei province in China, in December 2019. A new coronavirus was identified and named by the World Health Organization as SARS-CoV-2; it is genetically similar to SARS-CoV and MERS-CoV.[1] Recently, snakes have been suggested as the natural reservoirs of SARS-CoV-2, assuming that the Huanan Seafood Wholesale Market in Wuhan is the origin of the virus.[2]

Different preventive measures have been implemented by health authorities, and the 14-day quarantine is commonly used. Although previous studies have estimated the incubation period of SARS-CoV-2 to help determine the length of quarantine, recently some patients have presented with rather mild symptoms, such as cough and low-grade fever or even no symptoms,[3] indicating that the incubation period might have been 24 days,[4] which constitutes a greater threat to the effectiveness of entry screening. Against this background, in the present study, we estimated the distribution of incubation periods of patients infected within versus outside Hubei.

Methods

The details of most cases were reported by the media and were not available on the official web pages of the local health authorities in China. The first cases outside Hubei were reported on January 20, 2020. Therefore, we conducted 3 searches in Chinese for individual cases reported by the media between January 20, 2020, and February 12, 2020, with search terms "pneumonia" AND "Wuhan" AND "age" AND "new" using Google from February 7, 8, and 9. The inclusion of the search term "age" was intended to narrow the search results because the presence of this term in an article implies a description of an individual case.

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Individual cases with time of exposure and symptom onset as well as type of exposure were eligible for inclusion. There was no language restriction. Since most patients did not have complete information about the source of infection, the time of exposure was considered a time interval within which the exposure was believed to lie. In contrast, patients did recall the exact date of symptom onset. The present paper considered 2 types of exposure: (1) traveling to Hubei, China, and (2) contact with the source of infection such as an infected person or places where infectious agents stayed. For data accuracy, only confirmed cases outside Hubei province and within China were considered. The following data were collected: (1) location at which the case was confirmed, (2) gender, (3) age, (4) time of exposure, (5) time of first symptom onset, (6) type of exposure (traveler to Hubei or nontraveler), and (7) symptoms.

The incubation period distribution was estimated using maximum likelihood estimation (MLE), where the likelihood function of each observation in the data set was either exact or single-interval censored.[5] For an individual case with exact time of exposure and symptom, the likelihood function for an exact incubation period observation, T, was $f_\theta(T)$, where f and θ were the probability distribution function (PDF) of the incubation period and the set of parameters, respectively. For an individual case with exposure lying between E_1 and E_2, the likelihood function for an incubation observation was $F_\theta(S - E_1) - F_\theta(S - E_2)$, where F and S were the cumulative distribution function (CDF) of the incubation period and the time of symptom onset, respectively. Therefore, to find the maximum likelihood estimates of θ, the maxima of the sum of the individual log-likelihood functions, either $f_\theta(T)$ or $F_\theta(S - E_1) - F_\theta(S - E_2)$, depending on the data type of the observation, were computed with R software (R Foundation for Statistical Computing, Vienna, Austria).

T was assumed to follow log-normal, Weibull, and gamma distribution. To ascertain possible difference in distribution between the traveler and nontraveler group, θ was adjusted

Table 1. Maximum likelihood estimates for COVID-19 incubation periods

		Estimation results			Model selection criterion	Incubation period		
		Parameter	Standard error	p value*	AIC**		Mean	Variance
Log-normal	Location	0.44	0.24	0.063	276.183	Traveler to Hubei	1.7	0.8
	Dispersion	0.48	0.17	0.005*				
	Indicator (location)	1.34	0.26	<0.001*		Non-traveler	7.5	32.5
	Indicator (dispersion)	0.20	0.18	0.279				
Weibull	Shape	2.30	0.90	0.011*	270.727	Traveler to Hubei	1.8	0.7
	Scale	1.99	0.46	<0.001*				
	Indicator (shape)	-0.45	0.93	0.627		Non-traveler	7.2	16.2
	Indicator (scale)	6.10	0.81	<0.001*				
Gamma	Shape	4.63	3.16	0.143	271.344	Traveler to Hubei	1.7	0.7
	Rate	2.65	1.91	0.166				
	Indicator (shape)	-1.86	3.21	0.563		Non-traveler	7.2	18.5
	Indicator (rate)	-2.26	1.91	0.237				

Note: *Significantly different from zero under 5% **the lower the better fit to the data

Table 2. Estimated incubation periods for SARS-CoV-2 from different studies

			Incubation period	
	n	Distribution estimated	Mean (days)	95th percentile (days)
Li et al. (2020) [7]	10	Log-normal	5.2 (4.1, 7)	12.5 (9.2, 18)
Backer et al. (2020) [8]	88	Weibull	6.4 (5.6, 7.7)	10.3 (8.6, 14.1)
Backer et al. (2020) [8]	88	Gamma	6.5 (5.6, 7.9)	11.3 (9.1, 15.7)
Backer et al. (2020) [8]	88	Log-normal	6.8 (5.7, 8.8)	13.3 (9.9, 20.5)
This study (Travelers to Hubei)	175	Weibull	1.8 (1.0, 2.7)	3.2 (1.0, 3.8)
This study (Non-travelers)	175	Weibull	7.2 (6.1, 8.4)	14.6 (12.1, 17.1)

by including additional parameters and indicator variables that took the value 0 or 1 to indicate the type of exposure. For example, the θ for a log-normal distribution is given by $(\mu + D\mu_D, \sigma + D\,\sigma_D)$, where D is the indicator variable.

Results

In total, 1,457 results were generated by Google, and 175 cases from 64 web pages were eligible for inclusion. All patients could recall the data of symptom onset, and 51 patients were able to recall the exact date of exposure. Many of these patients stayed in Hubei for a day or had a friend or family gathering on a particular day. The remaining 124 patients could only recall the time interval of exposure and largely went to Hubei for sightseeing, work, or family visiting, or lived with an infected family member.

Of the 151 cases with gender data, 93 were male (61.6%, 95% confidence interval [CI], 53.3%–69.4%). The average age was 41.2 years (95% CI, 38.8–43.5). Travelers to Hubei accounted for 59.8% (95% CI, 49.3%–69.6%). With the exception of chill ($P = .04997$), there was no difference in clinical characteristics between the 2 groups. Fever (81.6% for travelers and 82.8 for nontravelers) and cough (40.6% for travelers and 44.8 for nontravelers) were the most common symptoms regardless of type of exposure.

The results of maximum likelihood estimation are shown in Table 1. The Akaike information criterion (AIC) suggested that the Weibull distribution provided the best fit with the data. Both indicator variables of the shape and scale parameters were significant in the Weibull model, suggesting different incubation period distributions between the 2 groups of patients.

Discussion

The very first observation of the incubation period of SARS-CoV-2 came from the National Health Commission of China, which reported an incubation time between 1 and 14 days.[6] Statistical estimation of the distribution of incubation periods has been done in 2 other studies.[7,8] In the present study, we further explored the difference in incubation periods among different groups of patients. Clinical data were collected from the individual cases reported by the media because they were not fully available on the official web pages of the Chinese health authorities. Maximum likelihood estimation was used to estimate the distributions of the incubation period.

We found significant difference in the distribution of the incubation period between travelers to Hubei and nontravelers. The difference was due to both the location and variability, as indicated by the means of 1.8 and 7.2 days and the variances of 0.7 and 16.2 in the Weibull model. Such a difference might be due to the difference in infectious dose; travelers to Hubei might have been exposed to different sources of infection multiple times during their stay in

Hubei. In contrast, patients with no travel history to Hubei were temporarily exposed to their infected relatives, friends, or colleagues and showed mild or even no symptoms.

The incubation period of nontravelers may have been highly volatile, as suggested by the higher variance in the gamma model that provided slightly poorer fit. This feature could potentially pose a threat to the effectiveness of the existing preventive measures. The duration of quarantine period must be considered with caution.

For comparison, previous studies on the incubation period for SARS-CoV-2 are shown in Table 2. The 95th percentiles reported in previous studies varied between 10.3 and 13.3 days, consistent with the current practice of quarantine period of 2 weeks. However, in the present study, the 95th percentile of the incubation period for SARS-CoV-2 in nontravelers could be 14.6 days and up to 17.1 days under 95% level of confidence. Coupled with the high variability of the incubation period, the duration of the quarantine period of 3 weeks is more suitable.

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