**Maximum incubation period for COVID-19 infection:
do we need to rethink the 14-day quarantine policy?**

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Information about the incubation period is crucial for planning containment measures in epidemics. In the case of COVID-19 infection, a maximum incubation period as 14 days has been widely accepted by WHO and other public health actors, and has been recommended as a duration of self-quarantine after the contact with infected person or after the return from epidemic areas. However, since the early February 2020 data have indicated a substantially longer incubation period in some cases. A first study initially published as preprint, reported the 24-day incubation period in one of 1,099 included patients,(1) however, the WHO objected that this single case has reflected a double exposure having first contact with infected person 24 days before the symptoms onset and second contact later. As a result, the final article accepted for publication reported the incubation period only as median and interquartile range (IQR) for the whole cohort.(2) However, since then a considerable number of preprints and published articles have identified the maximum incubation period as 15,(3) 17,(4) 19,(5) and 32(6) days. Notably, these incubation periods longer than 14 days were registered not only in sporadic cases, but in a substantial proportion reaching 1.5% out of 67,(3) 5.0% out of 339,(7) 7.7% out of 104,(6) and 9.5% out of 136(4) patients with traced contacts (see Table S1 in the Supplement). A considerable proportion of patients included in these cohorts have not been hospitalized and thus represent more generalizable population during epidemic, in contrast to some reports concerning predominantly hospitalized patients with more aggressive infection. The estimation of the incubation period could be affected by the uncertainty of the exact dates of exposure (recall bias), that was eliminated in one of the aforementioned reports(4) by selectively including patients who temporary stayed only one or two days in the Hubei province or its capital Wuhan during the early epidemic period. Reasons for differences in proportion of patients with longer incubation period between these reports remain unclear, with some data suggesting it could be related to advanced age.(4) To date only basic demographic factors were studied in some reports, but no analysis has been done to identify possible clinical or genetic factors explaining the variance in duration of COVID-19 incubation period.

Primary anonymized patient-level data containing quantitative estimation of the incubation period remain unpublished in open access, with only aggregated information most often available in the form of median and IQR. This makes it impossible to reliably conclude how often the incubation period exceeds the currently recommended 14-day threshold, or which percentage of patients develop symptoms or have a positive SARS-CoV-2 real-time polymerase chain reaction test at any given time after the proven contact with infected person. This uncertainty could be resolved by establishing a primary open data repository which would allow to perform detailed analysis of the incubation period in different subgroups that may be crucial for defining the self-managed quarantine period for travelers coming from abroad. Such analysis would be particularly important given the gradual easing of restrictive measures, reopening borders between regions and the approaching summer vacation period. Availability of these data would inform balanced decisions accounting the interests of public health and economy, and facilitate the engagement of general educated public in the decision making about approval of anti-epidemic measures. An agreement on the maximum incubation period is also important for successful contact tracing that according to the current rules is limited by 14 days.

A possibility to develop COVID-19 symptoms beyond the currently recommended 14-day quarantine in more than 5% of infected persons poses a question whether the epidemic could be halted if mass traveling between regions with different infection rates become active again. Of note, several Chinese territories have accepted a policy of longer quarantine period that seems to account for the aforementioned published data and uncertainty about the maximum incubation period. Thus, recent indications for incoming overseas travelers from the Beijing authorities require to keep 21-day quarantine (performed as a 14-day medical observation in designated facilities followed by an additional 7-day health observation at home),(8) and the mandatory home quarantine period has been increased to 28 and 35 days in several Chinese provinces bordering countries with a high number of persons with confirmed infection.(9)

The world urgently needs representative open access data about the maximum incubation period of COVID-19 infection from all trusted sources that should be collected and analyzed by an independent international consortium. While a vaccine against COVID-19 is still being developed, this would inform global policy regarding duration of quarantine to minimize the risks of further infection spread, and assist to develop sustainable individual and collective preventive measures.

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Contributors

Idea and design: BB, AB. Acquisition and analysis of data: BB. Interpretation of data: BB, AB.

Drafting of the manuscript: BB, AB.

The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Competing interests

None

References

1. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical characteristics of 2019 novel coronavirus infection in China. *MedRxiv*. 2020; DOI: 10.1101/2020.02.06.20020974.
2. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*. 2020 Feb 28;382:1708–20. DOI: 10.1056/NEJMoa2002032.
3. Tan W, Lu Y, Zhang J, Wang J, Dan Y, Tan Z, et al. Viral Kinetics and Antibody Responses in Patients with COVID-19. *medRxiv*. 2020 Jan 1;2020.03.24.20042382. DOI: 10.1101/2020.03.24.20042382.
4. Jiang AB, Lieu R, Quenby S. Significantly longer Covid-19 incubation times for the elderly, from a case study of 136 patients throughout China. *medRxiv*. 2020 Jan 1;2020.04.14.20065896. DOI: 10.1101/2020.04.14.20065896.
5. Bai Y, Yao L, Wei T, Tian F, Jin D-Y, Chen L, et al. Presumed Asymptomatic Carrier Transmission of COVID-19. *JAMA*. 2020 Feb;323(14):1406–7. DOI: 10.1001/jama.2020.2565.
6. Qiu C, Xiao Q, Liao X, Deng Z, Liu H, Shu Y, et al. Transmission and clinical characteristics of coronavirus disease 2019 in 104 outside-Wuhan patients, China. *J Med Virol*. 2020; DOI: 10.1002/jmv.25975.
7. Bi Q, Wu Y, Mei S, Ye C, Zou X, Zhang Z, et al. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. *Lancet Infect Dis*. 2020;3099(20):1–9. DOI: 10.1016/S1473-3099(20)30287-5.
8. Beijing has lowered Public Health Emergency Response Level. Beijing Foreign Affairs Office [Internet]. http://www.ebeijing.gov.cn/feature_2/MultilingualInfoonNCP/Policies/t1627615.htm
9. Chinese Regions Extend Quarantine Periods Up to 35 Days. Caixin [Internet]. 2020. <https://www.caixinglobal.com/2020-04-24/chinese-regions-extend-quarantine-periods-up-to-35-days-101546956.html>

Supplementary appendix to the article
**“Maximum incubation period for COVID-19 infection:
do we need to rethink the 14-day quarantine policy?”**

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Table S1. Detailed data on the incubation period extracted from the reports cited in the main article.

Data excluded from analysis

References

Table S1. Detailed data on the incubation period extracted from the reports cited in the main article.

Reference	Reference in the main article	Total studied population	Persons having incubation period >14 days	Median incubation period, days	Maximal incubation period, days	Exact phrase from the manuscript describing incubation period	Methodology of incubation period measurement	Factors responsible to the variability of the incubation period	Other details
[1]	3	67	1	6	15	“We estimated the median incubation period was 6.0 days (range 1-15 days).” Individual data on incubation periods are plotted at Supplementary Figure 3.	“The incubation period was defined as the time from exposure to the onset of illness. We constructed epidemic curves for date of exposure to illness onset and other key dates relating to epidemic identification and disease process by R software.”	“The mean incubation duration for male was 7.3±3.1 days, and that was 5.7 ±3.0 for female (p=0.054). The mean incubation duration for 10-18 yrs, 19-45 yrs, 46-65 yrs and 66-77 yrs group were 12.0±2.7, 6.3±3.0, 6.8±3.0 and 5.6±2.5 days, respectively.” (Supplementary Figure 3)	-
[2]	4	136	13	Reported only by age groups, not for the whole cohort	17	The incubation periods are plotted at figures 1 and 2 for 15-64 and 65-86 age groups, respectively. Incubation period longer than 14 days had 7 out of 110 patients in 15-64 years and 6 out of 22 patients in 65-86 age groups. Exact data for 4 patients under 15 years are not reported.	“The incubation period for each COVID-19 patient is inferred as the number of days between exposure and symptom onset.”	“For the 15-64 age group, the median incubation time of 7 days, for the 65-90 age group the median 10 days is statistically significantly longer.”	“We included only those COVID-19 patients who stayed in Hubei for at most two calendar days. The day of exposure was taken as the first day to Hubei if the patient stayed in Hubei for one calendar day; or as the middle of the first and second day in Hubei if the patient stayed for two calendar days. By excluding COVID-19 patients who stayed in Hubei for more than two days, one can better define the day of exposure.”
[3]	5	5	1	Not reported	19	“The incubation period for patient 1 was 19 days”.	Not reported	Not reported	Familial cluster of 5 patients.
[4]	6	104	8	6	32	“8 patients got more longer incubation duration (18, 19, 20, 21, 23, 24, 24 and 32 days) that more than 14 days”	“We carefully surveyed the contact history of every patients, including whether he or she ever lived in or travelled to Wuhan, or had closely contacted with people returning from Wuhan during two months before their illness onset. In addition, the history of contacting with animals and eating game meat was also screened. If necessary, we directly communicated with the attending physician, patients or their family members.” “Standard questionnaire and form were used for contact investigation and data collection. The data were independently reviewed by two trained physicians and checked by another two physicians respectively.”	Not reported	“Of the 104 patients, 93 (89.42%) patients had a clear contact history with the infections, 11 (10.53%) were sporadic cases that hardly identified a definite contact history.” “Family clusters accounted the most infections of COVID-19 in this study population. Cluster 6 (2 cases) and 14 (7 cases) infected via taking the same public vehicle together. Nosocomial transmission did not happen so far in the two centers. Six clusters (Table 1, cluster 2, 12, 14, 15, 18 and 19) demonstrated the existing of transmission chain of 3 “generation” (index case of one cluster identified as an infector who originally contracted the COVID-19 from Wuhan and then infected someone else, who infected another individual). Of note, 5 asymptomatic cases (C’1, C’2, C’3, C’4 and C102) were found in this study.” “As an asymptomatic patient, C’4 infected C92 (C’4’s mother), C94 (C’4’ s father-in-law) and C102 (C’4’ s daughter)”
[6]	7	391	Not reported	4.8	Not reported	“We estimated that about 5·0% of cases who develop symptoms would	“We defined symptom-based surveillance to include	Not reported	“Household contacts and those travelling with a case were at higher risk of infection (odds ratio

						<p>not show symptoms until 14 days after infection.”</p> <p>“95% of secondary cases were expected to develop symptoms within 14·3 days (95% CI 11·1–17·6) of their infector”.</p>	<p>symptomatic screening at airport and train stations, community fever monitoring, home observation of recent travellers to Hubei, and testing of patients admitted to hospital. Contact-based surveillance is the identification of cases through monitoring and testing of close contacts of confirmed cases, independently of their symptom presentation. By protocol, those in the contact-based group were tested for SARS-CoV-2 infection regardless of symptoms, whereas those in the other categories were tested only if they showed signs or symptoms of disease.”</p> <p>“Distributions were fit to the timing of key events in each confirmed case’s course of infection and treatment. The time from infection to symptom onset (incubation period) was assumed to be log-normally distributed and estimated as previously described. We determined the left and right boundaries on the possible exposure and symptom onset times. Cases who recently travelled to Hubei were assumed to have been exposed while there. Cases without a recent travel history but with exposure to a confirmed case were assumed to be exposed from the time of earliest to latest possible contact with that case. Only cases for whom we could identify the earliest and latest possible time of exposure and who had a date of symptom onset were included in the analysis.”</p> <p>“Transmission was characterised by examining the relationship between confirmed cases and their infected and uninfected close contacts. The household secondary attack rate was calculated as the percentage of household contacts (those sharing a room, apartment, or other sleeping arrangement) who were later confirmed to have SARS-CoV-2 infection. The distribution of serial intervals (the time between symptom onset in the confirmed case and their infected contacts) was calculated by fitting parametric distributions to the time of symptom onset in clear case–contact pairs.”</p>		<p>6·27 [95% CI 1·49–26·33] for household contacts and 7·06 [1·43–34·91] for those travelling with a case) than other close contacts.”</p> <p>“The household secondary attack rate was 11·2% (95% CI 9·1–13·8), and children were as likely to be infected as adults (infection rate 7·4% in children <10 years vs population average of 6·6%).”</p> <p>“At the time of the first clinical assessment, 25 (29%) of 87 cases in the contact-based surveillance group did not have fever, and 17 (20%) of 87 had no symptoms. By contrast, 258 (88%) of 292 in the symptom-based surveillance group had fever, and only eight reported no symptoms.”</p>
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							“When assessing the impact of characteristics of infected individuals, we only included risk sets where a single potential infected individual was clearly identifiable.”		
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Data excluded from analysis

We also identified the manuscript “Jiang X, Niu Y, Li X, et al. Is a 14-day quarantine period optimal for effectively controlling coronavirus disease 2019 (COVID-19)? medRxiv. 2020. doi:10.1101/2020.03.15.20036533” that indicates incubation period longer than 14 days in 11.5% out of 2015 individuals. It has been excluded from our analysis because it assumes “gastrointestinal tract infection through oral transmission” in some patients that is not recognized as a transmission route for COVID-19 infection.

References

1. Tan W, Lu Y, Zhang J, Wang J, Dan Y, Tan Z, et al. Viral Kinetics and Antibody Responses in Patients with COVID-19. medRxiv. 2020. DOI: 10.1101/2020.03.24.20042382.
2. Jiang AB, Lieu R, Quenby S. Significantly longer Covid-19 incubation times for the elderly, from a case study of 136 patients throughout China. medRxiv. 2020. DOI: 10.1101/2020.04.14.20065896.
3. Bai Y, Yao L, Wei T, Tian F, Jin D-Y, Chen L, et al. Presumed Asymptomatic Carrier Transmission of COVID-19. JAMA. 2020 Feb;323(14):1406–7. DOI: 10.1001/jama.2020.2565.
4. Qiu C, Xiao Q, Liao X, Deng Z, Liu H, Shu Y, et al. Transmission and clinical characteristics of coronavirus disease 2019 in 104 outside-Wuhan patients, China. J Med Virol. 2020; DOI: 10.1002/jmv.25975.
5. Jiang X, Niu Y, Li X, Li L, Cai W, Chen Y, et al. Is a 14-day quarantine period optimal for effectively controlling coronavirus disease 2019 (COVID-19)? medRxiv. 2020; DOI: 10.1101/2020.03.15.20036533.
6. Bi Q, Wu Y, Mei S, Ye C, Zou X, Zhang Z, et al. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. Lancet Infect Dis. 2020;3099(20):1–9. DOI: 10.1016/S1473-3099(20)30287-5.