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Rapid Review: What is known about the duration from exposure to symptoms or diagnosis for COVID-19?

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Executive Summary

Background

The incubation period of an infectious disease is defined as the period of time between exposure to the infectious agent and onset of symptoms. An understanding of this period is important during a pandemic as it helps to inform decisions about recommended preventive measures such as self-isolation or quarantine. Early in the COVID-19 pandemic, public health bodies worldwide, including those in Canada, recommended a 14-day self-isolation period following known or suspected exposure to COVID-19. Since then, more research evidence has become available which may inform any revisions to this suggested time period.

This rapid review was produced to support public health decision makers' response to the coronavirus disease (COVID-19) pandemic. This review seeks to identify, appraise, and summarize emerging research evidence to support evidence-informed decision making.

This rapid review includes evidence available up to June 2, 2020.

In this rapid evidence service, we provide the most recent evidence to answer the question:
What is known about the duration from exposure to symptoms or diagnosis for COVID-19?

Key Points

- Across studies, estimates of mean or median incubation period were typically between four and six days. The quality of the evidence is moderate; findings are consistent.
- Within included studies, the range of incubation periods for individuals varied widely from one to 14 days; in one study researchers estimated that 1% of cases may have an incubation period of more than 14 days however the precise number is not known.
- Little is known about factors that may contribute to variation in incubation periods. One study found those 64-86 years old had a longer incubation period than those 18-64 years old; another study found that younger adults had a longer incubation period than older adults. Study quality is low, findings are inconsistent.
- Precise calculation of the incubation period was more feasible early in the pandemic, when cases were limited, and a precise exposure time was known. With widespread community transmission, accurate identification of exposure is difficult if not impossible. Given this, new evidence is unlikely to change these estimates.

Overview of Evidence and Knowledge Gaps

- Within included studies, the way that incubation period is quantified varies greatly. This likely contributes to the variability of estimates of individual incubation periods. Some studies defined incubation period as time to symptom onset (with later confirmation of infection), while some used time to positive RT-PCR test which would detect both symptomatic and asymptomatic cases.
- A number of studies estimated incubation period by serially testing household contacts of individuals with known COVID-19 over 14-day self-isolation or quarantine periods, thus incubation periods beyond 14 days may not have been detected; one study that used a longer follow-up time found that 5% of cases had incubation periods longer than 13 days, however this was based on a single study and a secondary exposure to the infection could not be ruled out.
- There are differences across studies in the way the exposure date was calculated, which also may result in imprecision in estimates. While some studies had confidence in definitive exposure, for example in the case of a super-spreader event, others used travel to a highly affected area as exposure when the specific time of exposure to the virus itself was unknown. This may underestimate or overestimate the incubation period.

Methods

Research Question

What is known about the duration from exposure to symptoms or diagnosis for COVID-19?

Search

On June 1 and 2, 2020, the following databases were searched:

- Pubmed’s curated COVID-19 literature hub: [LitCovid](#)
- [Trip Medical Database](#)
- World Health Organization’s [Global literature on coronavirus disease](#)
- Joanna Briggs Institute [COVID-19 Special Collection](#)
- [COVID-19 Evidence Alerts](#) from McMaster PLUS™ +
- [Public Health +](#)
- [COVID-19 Living Overview of the Evidence \(L·OVE\)](#)
- Cochrane Rapid Reviews [Question Bank](#)
- [Prospero Registry of Systematic Reviews](#)
- NCCMT [COVID-19 Rapid Evidence Reviews](#)
- [MedRxiv preprint server](#)

A copy of the search strategy is available on request.

Selection Criteria

The search first included recent, high-quality syntheses. Single studies were included if no syntheses were available, or if single studies were published after the search was conducted in the included syntheses. English-language, peer-reviewed sources and sources published ahead-of-print before peer review were included. Surveillance sources were excluded. When available, findings from syntheses and clinical practice guidelines are presented first, as these take into account the available body of evidence and, therefore, can be applied broadly to populations and settings.

	Inclusion Criteria	Exclusion Criteria
Population	Individuals in the community Healthcare workers	
Intervention	Exposure to or close contact with COVID-19 cases	
Comparisons		
Outcomes	COVID-19 symptoms Positive COVID-19 test Transmission to other individuals	

Data Extraction and Synthesis

Data relevant to the research question, such as study design, setting, location, population characteristics, interventions or exposure and outcomes were extracted when reported. We synthesized the results narratively due to the variation in the methodology and outcomes for the included studies.

We evaluated the quality of included evidence using critical appraisal tools as indicated by the study design below. Quality assessment was completed by one reviewer and verified by a second reviewer. Conflicts were resolved through discussion. For some of the included evidence a suitable quality appraisal tool was not found, or the review team did not have the expertise to assess methodological quality. Studies for which quality appraisal has not been conducted are noted within the data tables.

Study Design	Critical Appraisal Tool
Synthesis	Health Evidence™ Quality Appraisal Tool
Case Series	Joanna Briggs Institute (JBI) Checklist for Case Series

Findings

Quality of Evidence

This document includes five completed syntheses, four in-progress syntheses and 11 single studies for a total of 20 publications included in this evidence review addressing two distinct questions. The quality of the evidence included in this review is as follows:

		Total	Quality of Evidence
Syntheses	Completed Reviews	5	4 Low 1 Moderate
	In Progress Reviews	4	-
Single Studies	Completed	11	1 Low 6 Moderate 4 High

Warning

Given the need to make emerging COVID-19 evidence quickly available, many emerging studies have not been peer reviewed. As such, we advise caution when using and interpreting the evidence included in this rapid review. We have provided a summary of the quality of the evidence as low, moderate, or high quality to support the process of decision making. Where possible, make decisions using the highest quality evidence available.

Table 1: Syntheses

Reference	Date Released	Description of included studies	Summary of Findings	Quality Rating: Synthesis	Quality Rating: Included Studies
He, W., Yi, G. Y., & Zhu, Y. (2020). Estimation of the basic reproduction number, average incubation time, asymptomatic infection rate, and case fatality rate for COVID-19: Meta-analysis and sensitivity analysis . <i>Journal of Medical Virology</i> . Epub ahead of print	May 29, 2020 (Search completed March 31, 2020)	This meta-analysis included 5 studies that reported incubation period (mean and standard deviation or confidence intervals) for a sample of individuals diagnosed with COVID-19 <ul style="list-style-type: none"> All included studies were from China Sample sizes, study design, and sample characteristics not reported 	Pooled incubation period = 5.08 days (95% Confidence Interval (CI): 4.77, 5.39) Incubation period in reported studies ranged from 1 to 14 days.	Low	Not reported
Zaki, N., & Mohamed, E. A. (2020). The estimations of the COVID-19 incubation period: a systematic review of the literature . <i>Preprint</i> .	May 23, 2020 (Search completed April 25, 2020)	This review included 4 studies that reported incubation periods <ul style="list-style-type: none"> All included studies from China Sample sizes of included studies ranged from 49 to 181 (not reported in one study) Study design and sample characteristics not reported 	Mean incubation periods ranged from 4.9 to 6.4 days. Incubation periods reported for individuals across studies ranged from 2.1 to >14 days. In one study, researchers estimated that 1% of cases reported symptoms >14 days after quarantine.	Low	Not reported
Izadi, N., Taherpour, N., Mokhayeri, Y., Sotoodeh Ghorbani, S., Rahmani, K., & Hashemi Nazari, S. (2020). The epidemiologic parameters for COVID-19: A Systematic Review and Meta-Analysis . <i>Preprint</i> .	May 6, 2020 (Search completed March 23, 2020)	This meta-analysis includes 22 studies reporting incubation period for COVID-19 in days <ul style="list-style-type: none"> All studies were observational but specific study designs were not reported 	Mean incubation period was 4.24 days (95% CI: 3.03, 5.44)	Low	Most studies were peer reviewed

		<ul style="list-style-type: none"> The majority of studies were from China; all from Asia 			
McAloon, C. G., Collins, A., Hunt, K., Barber, A., Byrne, A., Butler, F., Casey, M., Griffin, J. M., Lane, E., McEvoy, D., Wall, P., Green, M. J., O'Grady, L., & More, S. J. (2020). The incubation period of COVID-19: A rapid systematic review and meta-analysis of observational research . <i>Preprint</i> .	April 28, 2020 (Search completed April 8, 2020)	<p>This meta-analysis included 8 studies</p> <ul style="list-style-type: none"> 7 studies from China 1 study including data from 7 countries Sample sizes ranged from 10 to 587 <p>Study design and sample characteristics not reported</p>	<p>Mean incubation period was 5.8 (95% CI: 5.01, 6.69) days</p> <p>Median incubation period was 5.1 (95% CI: 4.5, 5.8) days</p> <p>One study was removed from the analysis due to high heterogeneity</p> <p>The authors note discrepancies in the ways in which incubation time was calculated within studies.</p>	Low	Not reported
Tang, C., Zhang, K., Wang, W., Pei, Z., Liu, Z., Yuan, P., Guan, Z., & Gu, J. (2020). Clinical Characteristics of 20,662 Patients with COVID-19 in mainland China: A Systemic Review and Meta-analysis . <i>Preprint</i> .	April 23, 2020 (search completed March 15, 2020)	<p>This meta-analysis included 147 studies of fair to high quality including 20,662 patients ranging from age 1 month to 100 years.</p>	<p>Authors concluded it was inappropriate to combine data on incubation period due to the heterogeneity of studies and inconsistency in reporting of timelines of cases. No results were reported.</p>	Moderate	Moderate-High

Veillez noter que tous les renseignements ne sont pas accessibles dans les deux langues officielles, parce que la source de l'information n'est pas nécessairement assujettie à la Loi sur les langues officielles.

Table 2: In-Progress Syntheses

Title	Anticipated Release Date	Description of document
Lane, M.Y., Fregonese, F., Winters, N., Campbell, H., & Menzies, D. Asymptomatic COVID-19 carriers and time to symptom onset: a systematic review. PROSPERO 2020 CRD42020181543	May 31, 2020	This systematic review will answer the question: What is the proportion of people who are asymptomatic at the time of diagnosis with COVID-19 among contacts and general population samples? Among those asymptomatic, in how many did symptoms eventually develop and over what time period?
Da Silva, J.M.N., dos Santos, C., & Diaz-Quijano, F.A. Current evidence of the transmissibility of COVID-19: a systematic review. PROSPERO 2020 CRD42020178285	May 31, 2020	This review will calculate pooled mean, CI and range of incubation period from experimental, observational and modelling studies.
Yoon, S., Kronbichler, A., Kresse, D., Lee, K.W., Shin, J.I., & Effenberger, M. Asymptomatic patients as a source of COVID-19 infections: a systematic review and meta-analysis. PROSPERO 2020 CRD42020185789	June 10, 2020	This review will quantify the clinical, laboratory and radiologic findings of asymptomatic cases of COVID-19. Within identified studies, incubation period will be extracted as time from exposure to diagnosis.
Chakraborty, S., Sagar, S., Kirubakaran, K., Barnabas, J.P., David, T., & Tharyan, P. A rapid systematic review to determine the serial time and distance for which an infected individual with COVID-19 acts as an agent of transmission. PROSPERO 2020 CRD42020187638	June 30, 2020	This rapid review will answer the question: “What is the serial time and distance for which an infected individual with COVID-19 acts as an agent of transmission?”

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Table 3: Completed Single Studies

Reference	Date Released	Study Design	Setting	Index Infection Event	Number of Cases	Summary of findings	Quality Rating:
Tomie, T. (2020). Incubation period of COVID-19 in the live-house cluster of accurately known infection events and delay time from symptom onset of public reporting observed in cases in Osaka, Japan . <i>Preprint</i> .	May 26, 2020	Case series	Osaka, Japan	Live concerts at 4 venues, Feb 15-21	48	COVID-19 infections were traced back to exposure at four small concerts. Mean incubation period from exposure to onset of symptoms was 6.8 days; median 5.7 days.	Moderate
Böhmer, M. M., Buchholz, U., Corman, V. M., Hoch, M., Katz, K., Marosevic, D. V., Böhm, S., Woudenberg, T., Ackermann, N., Konrad, R., Eberle, U., Treis, B., Dangel, A., Bengs, K., Fingerle, V., Berger, A., Hörmansdorfer, S., Ippisch, S., Wicklein, B., ... Zapf, A. (2020). Investigation of a COVID-19 outbreak in Germany resulting from a single travel-associated primary case: a case series . <i>The Lancet Infectious Diseases</i> . Epub ahead of print.	May 15, 2020	Case series	Munich, Germany	Traveler returning from China attended business meeting, Jan 20	16	Employees in contact with returning traveler quarantined and tested for COVID-19. Median incubation period from exposure to onset of symptoms 4.0 days (Inter Quartile Range (IQR): 2.3-4.3). Close monitoring of contacts may have increased detection of early symptoms.	High
Bui, L. V., Nguyen, H. T., Levine, H., Nguyen, H., Nguyen, T. A., Nguyen, T. P., Nguyen, T., Do, T. T. T., Tuan, N. P., & Bui, H. M. (2020). Estimation of the incubation period of SARS-CoV-2 in Vietnam . <i>Preprint</i> .	May 15, 2020	Case series	Vietnam	No index event, all cases Jan 23-Apr 13	265	All cases available in national public health database; researchers analyzed those with clear window of possible COVID-19 exposure. Mean incubation period from exposure to onset of symptoms 6.4 days (95% Confidence Interval (CI) 4.9, 8.5); median 5.6 days.	Moderate
Wu, J., Huang, Y., Tu, C., Bi, C., Chen, Z., Luo, L., Huang, M., Chen, M., Tan, C., Wang, Z., Wang, K., Liang, Y., Huang, J., Zheng, X., & Liu, J. (2020). Household Transmission of SARS-CoV-2, Zhuhai, China, 2020 . <i>Clinical Infectious Diseases</i> . Epub ahead of print.	May 11, 2020	Case series	Zhuhai, China	No index event, Jan 17-Feb 29	48	Household members of 35 index patients admitted to hospital were monitored for symptoms and tested for COVID-19. Median incubation period from exposure to onset of symptoms was 4.3 days (95% CI 3.4, 5.3).	High

Lou, B., Li, T.D., Zheng, S.F., Su, Y.Y., Li, Z.Y., Liu, W., Yu, F., Ge, S.X., Zou, Q.D., Yuan, Q., Lin, S., Hong, C.M., Yao, X.Y., Zhang, X.J., Wu, D.H., Zhou, G.L., Hou, W.H., Li, T.T., Zhang, Y.L., ... Chen, Y. (2020). Serology characteristics of SARS-CoV-2 infection since exposure and post symptom onset . <i>European Respiratory Journal</i> . Epub ahead of print.	May 8, 2020	Case series	Hangzhou, China	No index event, Jan 19-Feb 9	80	Patients admitted to hospital were enrolled in study. It is not clear how date of exposure was established. Median incubation period from exposure to onset of symptoms was 5.0 days (IQR 2.0-10.0).	Moderate
Cheng, H.Y., Jian, S.-W., Liu, D.P., Ng, T.C., Huang, W.T., & Lin, H.H. (2020). Contact Tracing Assessment of COVID-19 Transmission Dynamics in Taiwan and Risk at Different Exposure Periods Before and After Symptom Onset . <i>JAMA Internal Medicine</i> . Epub ahead of print.	May 1, 2020	Case series	Taiwan	No index event, Jan 15-Mar 18	22	Close contacts of confirmed cases in the community were quarantined and monitored for COVID-19 symptoms. Median incubation period from exposure to onset of symptoms was 4.1 days (95% CI: 0.4, 15.8).	High
Song, R., Han, B., Song, M., Wang, L., Conlon, C. P., Dong, T., Tian, D., Zhang, W., Chen, Z., Zhang, F., Shi, M., & Li, X. (2020). Clinical and epidemiological features of COVID-19 family clusters in Beijing, China . <i>Journal of Infection</i> . Epub ahead of print.	April 28, 2020	Case series	Beijing, China	Direct or indirect contact to Wuhan region, Jan 16-Mar 6	22	Clusters of cases in four families in the community were tracked. Mean and median incubation period was 8.2 and 8 days respectively.	Moderate
Nie, X., Fan, L., Mu, G., Tan, Q., Wang, M., Xie, Y., Cao, L., Zhou, M., Zhang, Z., & Chen, W. (2020). Epidemiological Characteristics and Incubation Period of 7015 Confirmed Cases With Coronavirus Disease 2019 Outside Hubei Province in China . <i>The Journal of Infectious Diseases</i> . Epub ahead of print.	April 27, 2020	Case series	China, excluding Hubei province	No index event, Jan 19-Feb 8	2907	Retrospective analysis of COVID-19 cases in China using data from the Chinese National Health Commission. Hubei province, which contains the Wuhan region, was excluded. Median incubation period from exposure to onset of symptoms was 5.0 days (IQR 2.0-8.0). The longest observed incubation period was 24 days. More than 95% of cases had an incubation period of less than 13 days. There were no differences in incubation period between males and females or imported vs. local cases.	Moderate
Jiang, A. B., Lieu, R., & Quenby, S. (2020). Significantly longer Covid-19	April 18, 2020	Case series	China, excluding	Travel to Hubei	110 aged 15-64;	Retrospective analysis of COVID-19 cases in China, who traveled to Hubei	Low

incubation times for the elderly, from a case study of 136 patients throughout China. Preprint.			Hubei province	province, Jan 5- Jan 31	22 aged 65-86	<p>province, for <48 hours, as recorded by the Chinese National Health Commission.</p> <p>For cases aged 15-64, median incubation period from exposure to onset of symptoms was 7.00 days (95% CI 6.10, 8.10). For cases aged 65-86, median incubation period from exposure to onset of symptoms was 10.9 days (95% CL 8.9, 12.6).</p> <p>Authors do not suggest why incubation periods may differ between age groups.</p>	
Huang, L., Zhang, X., Zhang, X., Wei, Z., Zhang, L., Xu, J., Liang, P., Xu, Y., Zhang, C., & Xu, A. (2020). Rapid asymptomatic transmission of COVID-19 during the incubation period demonstrating strong infectivity in a cluster of youngsters aged 16-23 years outside Wuhan and characteristics of young patients with COVID-19: A prospective contact-tracing study. <i>Journal of Infection, 80(6)</i>, e1-e13.	April 14, 2020	Case series	Anhui, China	Traveler from Wuhan to Anhui, Jan 23	8	<p>Close contacts of a case returning to Anhui, China from Wuhan, China were monitored for COVID-19 symptoms.</p> <p>Median incubation period from exposure to onset of symptoms was 2 days (IQR 1-4 days).</p>	High
Han, Y., Feng, Z., Sun, L., Ren, X., Wang, H., Xue, Y., Wang, Y., & Fang, Y. (2020). A comparative-descriptive analysis of clinical characteristics in 2019-coronavirus-infected children and adults. <i>Journal of Medical Virology.</i> Epub ahead of print.	April 6, 2020	Case series	Shaanxi, China	No index event, Jan 31-Feb 16	7 children (aged <18 years) and 25 adults	<p>Patients admitted to hospital were enrolled in study. It is not clear how date of exposure was established.</p> <p>For children (age <18 years), the median incubation period from exposure to onset of symptoms was 5 days (IQR 3-12 days). For adults (age >18 years), the median incubation period from exposure to onset of symptoms was 4 days (IQR 2-12 days).</p>	Moderate

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