

# COVID-19 Scientific Advisory Group Rapid Response Report

## Key Research Question: What is the evidence supporting the possibility of asymptomatic transmission of SARS-CoV-2?

### Context

- Asymptomatic transmission (including pre-symptomatic transmission) of SARS-CoV-2 could reduce the effectiveness of control measures that are related to symptom onset (isolation, face masks and enhanced hygiene for symptomatic persons, and parameters of contact tracing), particularly if routine practices, including the use of diligent hand hygiene and environmental disinfection after patient encounters are not adhered to.
- Concerns regarding asymptomatic transmission are driven by data that suggest that approximately 18% – 55.6% of people with positive RT-PCR in various populations were asymptomatic at testing, and epidemiologic modelling suggesting that asymptomatic or presymptomatic cases may be responsible for potentially significant transmission. However, this is discrepant from epidemiologic descriptions from the initial epidemic in China which did not suggest that asymptomatic transmission is driving COVID19 epidemics.

### Key Messages from the Evidence Summary

- It is biologically plausible that SARS-CoV-2 can be transmitted when patients are asymptomatic, pre-symptomatic, or mildly symptomatic (potentially from 2.5 days prior to onset of symptoms), based on the finding that RT-PCR levels are high early in infection.
- Efficiency of transmission during asymptomatic through pauci-symptomatic infection is unclear, with some conflict between epidemiologic data models and outbreak reports.
- Transmission events and their dynamics are complex, but most evidence from other respiratory viruses suggest that transmission events predominantly occur with the peak of symptoms (highest fever, levels of coughing, sneezing and rhinorrhea). which correlates with the highest RT- PCR values the highest viable viral loads.
- There is little data on cultivatable viral loads with SARS-CoV-2 in asymptomatic, pre-symptomatic, pauci-symptomatic and symptomatic infection, or on the proportion of transmission which may be attributed to these categories, which precludes definitive recommendations currently.
- Further evidence is required to elucidate the transmission dynamics of SARS-CoV-2 in multiple populations in the community, long-term care and the acute care hospital. The diligent use of routine infection prevention and control practices would be expected to reduce risk of asymptomatic transmission which is felt more likely to be related to contact than droplet spread in prolonged close contact/food sharing.
- A large proportion of pre-symptomatic transmission would limit the effectiveness of control measures that are initiated by symptom onset, including additional precautions (droplet /contact) guided by point-of-care risk assessment, self-isolation, and contact tracing. The proportion of transmission events via droplet and/or contact would be needed to inform an evidence based decision, and the evidence must be monitored.

### Recommendations for Discussion:

*The Scientific Advisory Group was unable to provide consensus recommendations, due to shortcomings in existing data, but acknowledges there are expected publications and additional guidance forthcoming that will be incorporated into an updated review once available. The Scientific Advisory Group supported consideration of ethical frameworks and the precautionary principle in decision making in the context of an evolving risk assessment.*

### Committee Discussion

The SAG did not reach a consensus recommendation based on available evidence. The data considered resulted in considerably varied opinions on the likelihood of asymptomatic transmission as a large contributor to transmission, although all acknowledged that there are credible reports of asymptomatic carriage and household asymptomatic transmission. Five committee members were in agreement with the key messages while two committee members felt that the current epidemiological situation should be treated as if asymptomatic or presymptomatic transmission is occurring, which would have implications for risk assessment screening.

### Summary of Evidence

Literature for this review was collected from a pragmatic search of the new COVID-19 literature. Key limitations of this review are related to limited inclusion of evidence from SARS and MERS and the speed with which evidence is available. In addition, some of the evidence is preprint, published as correspondence, or are observational studies, with lower rigor than formal epidemiological studies

### *Current understanding of transmission of COVID-19*

The World Health Organization (WHO) issued a scientific brief March 29, 2020 that stated the following. “According to current evidence, COVID-19 virus is transmitted between people through respiratory droplets and contact routes. Droplet transmission occurs when a person is in in close contact (within 1 m) with someone who has respiratory symptoms (e.g. coughing or sneezing,) and is therefore at risk of having his/her mucosae (mouth and nose) or conjunctiva (eyes) exposed to potentially infective respiratory droplets (which are generally considered to be > 5-10 µm in diameter). Droplet transmission may also occur through fomites in the immediate environment around the infected person. Therefore, transmission of the COVID-19 virus can occur by direct contact with infected people and indirect contact with surfaces in the immediate environment or with objects used on the infected person (e.g. stethoscope or thermometer)” (World Health Organization, 2020c).

### *What is the evidence supporting the possibility of asymptomatic transmission or SARS-CoV-2?*

Viral load data (humans and animal models): Small studies have demonstrated very early high viral loads (by PCR) in presymptomatic, asymptomatic, and mildly symptomatic patients, making this a plausible concern. In a study of 18 patients, patients with early symptoms had high viral loads as did 1 asymptomatic patient (as distinguished from SARS-CoV, which had higher loads later in illness (Zou et al., 2020; World Health Organization, 2020b). It is unclear whether infectivity via droplet spread of virus from asymptomatic persons in the absence of strongly droplet generating events such as cough or sneeze is a driver of transmission, but droplet generation by talking is a theoretic concern. In experimental SARS-CoV-2 infection of macaques, early and prolonged virus excretion from the nose and throat in the absence of clinical disease was seen. (Rockx et al., preprint)

## Asymptomatic Transmission of SARS-CoV-2 • 3

Data from human COVID-19 clusters: Reported rates of asymptomatic infection detected by PCR based screening range from 15.8% in children with infection (Lu et al, 2020), to 17.9% (95% CI 15.5% - 20.2%) in a cruise ship cluster in which ½ of the cases were asymptomatic at the time of diagnosis (Mizumoto et al., 2020) and 33.3% (95% CI 8.3% - 58.3%) in a study of Japanese evacuees (Nishiura et al., preprint). However, in this latter event, 50% (12/24) of asymptomatic patients had characteristic CT findings, and 25% (5/20) developed fever. Therefore patients reporting no significant symptoms may have objective indicators of infection and may also be “presymptomatic.” However, in the absence of a rapid turnaround screening test, this group is still of concern for possible transmission. Another rapid release published in MMWR indicates that in a residential long-term care facility experiencing rapid transmission of COVID-19 infection, 13/23 (56.5%) of COVID19 positive residents were asymptomatic at the time of the test (Kimball et al, 2020) with 10 going on to develop symptoms within 7 days.

Epidemiologic modelling: If the mean interval estimate (the time between symptoms developing in the infector and infectee) is shorter than the mean incubation period, presymptomatic transmission is suggested, as it would support that transmission can occur early after infection and possibly before symptoms. Modelling the serial interval estimate (efficiency of propagation) suggests that the serial interval estimate for SARS-COV2 is 3.96 days (95% CI 3.53 – 4.39) which is significantly shorter than SARS-COV1 (8.4 days) or MERS-COV (14.6 days) (Zhao et al., preprint; Nishiura, Linton & Akmetzhanov, 2020), suggesting earlier transmission. However, estimates of the serial interval vary. In a description of 468 confirmed cases in China, 12.6% of the serial intervals were negative (the infectee developed symptoms before the infector) suggestive of pre-symptomatic transmission (Du et al., 2020). In another preprint article that described viral shedding and modelled transmission chain data, the mean interval estimate was longer at 5.8 days, with infectiousness estimated to start at -2.5 days before symptom onset, and peak at -0.6 days before symptom onset with decline over 7 days. The proportion of transmission before symptom onset was estimated at 44%, noting that the relative proportion of post symptom transmission was reduced by isolation (He et al 2020). Other cases and series of asymptomatic transmission have been reported in familial and non-familial settings, with one case study suggesting transmission may occur 1-2 days prior to development of symptoms.(Chan et al., 2020; Bai et al., 2020; He et al., preprint; Rothe et al., 2020). An additional publication reviewing undocumented cases in China (with a presumption that many were asymptomatic) suggested undocumented cases may account for 79% of documented cases (Li et al., 2020). A March 30, 2020 report from the Imperial College COVID-19 Response Team also estimated that the percentage of total population infected is orders of magnitude higher than case counts, related to mild and asymptomatic infections as well as limited testing capacity, with the model suggesting attack rates ranging from 0.7% of the population in Germany through to 15% in Spain. The relative proportion of asymptomatic infection was not modelled (Flaxman et al., 2020).

### *Discussion*

There are consistent laboratory data supporting early high levels of virus (generally inferred by RT-PCR) before or at the time of symptom development, and in some persistently asymptomatic cases. The key practical question is whether this finding actually results in significant spread of infection, compared to spread from individuals with “droplet generating” symptoms such as cough and sneeze. It may be more plausible that asymptomatic spread would be most likely to occur via contact (nasal secretion contamination of hands and fomites) in closer quarters, as is observed in family cluster case reports. However, epidemiologic modelling flags concern for potentially significant transmission, but the assumptions made and the accuracy of epidemiologic symptom onset data (determination of any symptoms versus symptoms that limited activity, for example) are a potential weaknesses in these analysis, as potentially reflected in the serial intervals differing by > 1.5 days in different reports. Further, the nature of the contacts in the transmission chains used in modelling studies is not well described

## Asymptomatic Transmission of SARS-CoV-2 • 4

(specifically if there was prolonged household contact or food sharing). It is noted, however that for containment control strategies the definition of contacts covered 2-3 days prior to symptom onset of the index case in these reports (in Hong Kong since 22 February and in mainland China since 21 February 2020.) These epidemiologic models seem to contradict the finding that close household contacts made up the majority of identified clusters in the initial epidemic, with droplet and fomite transmission suggested as the major driver of the initial SARS-CoV-2 epidemic in China (World Health Organization, 2020a). It will be crucial to follow evolving evidence to resolve these discrepancies and support appropriate precautions if a significant role of asymptomatic spread is suggested.

### *Why the evolution of evidence in this area matters*

**Implications for Personal Protective Equipment (PPE) Recommendations:** The possibility of asymptomatic spread of SARS-CoV-2 may affect recommendations for universal mask use in COVID-19 exposed healthcare workers (HCW) (to reduce the risk of nosocomial spread) and recommendations for HCW protection in direct patient care of patients who do not have a positive screen for COVID-19 symptoms in higher risk areas. However, defining the nature and duration of contact that would be considered “higher risk” in a health care setting with asymptomatic COVID-19 positive patients remains unclear. It is acknowledged that in some areas PPE shortages are a practical issue, and there is a possibility of worsening the degree of overall HCW risk over the course of the epidemic if PPE supplies are not targeted appropriately. The Scientific Advisory Group (SAG) supports the use of both the precautionary principle and ethical framework to aid in application of decisions made on the basis of the best possible evidence (Bean et al.)

**Implications for Public Health Control Strategies:** Social distancing strategies, which are not predicated on symptom development, remain a cornerstone control measure. Contact tracing could include presymptomatic phase contacts, and possibly public notification of areas of potential risk in the community due to presymptomatic/asymptomatic case interactions (with attention to avoidance of stigmatization). Isolation of COVID-19 contacts, for example in the context of long term care, is supported. Enhanced community surveillance of representative groups (by rapid implementation of approved viral testing and validated serologic tests once available) in the community will need to be prioritized to guide application of public health measures.

The evidence for this topic is changing very rapidly. It is necessary to monitor the literature for new estimates of spread from asymptomatic persons, information around rapid potential screening of asymptomatic persons, efficacy of face shields, masks, and cloth masks, alone and in combination. This brief should be re-visited weekly to ensure all evidence is accounted for.

Date question received by advisory group: started by previous group (before 24 March 2020)

Date report submitted to committee: March 27, 2020

Date of first assessment: April 2, 2020

(If applicable) Date of re-assessment: N/A

## Authorship & Committee Members

This report was written by Lynora Saxinger (co-chair), building on an initial report drafted by Ranjani Somyani. . The full Scientific Advisory Group was involved in discussion and revision of the document: Braden Manns (co-chair), John Conly, Alexander Doroshenko, Shelley Duggan, Jing Hu, Nelson Lee, Andrew McRae, Jeremy Slobodan, Brandie Walker, and Nathan Zelyas. External reviewers included Joseph Kim, Uma Chandran, and Michael Parsons.



© 2020, Alberta Health Services, COVID-19 Scientific Advisory Group

This copyright work is licensed under the [Creative Commons Attribution-NonCommercial-NoDerivative 4.0 International license](https://creativecommons.org/licenses/by-nc-nd/4.0/). You are free to copy and distribute the work including in other media and formats for non-commercial purposes, as long as you attribute the work to Alberta Health Services, do not adapt the work, and abide by the other licence terms. To view a copy of this licence, see <https://creativecommons.org/licenses/by-nc-nd/4.0/>. The licence does not apply to AHS trademarks, logos or content for which Alberta Health Services is not the copyright owner

**Disclaimer:** This material is intended for general information only and is provided on an "as is", "where is" basis. Although reasonable efforts were made to confirm the accuracy of the information, Alberta Health Services does not make any representation or warranty, express, implied or statutory, as to the accuracy, reliability, completeness, applicability or fitness for a particular purpose of such information. This material is not a substitute for the advice of a qualified health professional. Alberta Health Services expressly disclaims all liability for the use of these materials, and for any claims, actions, demands or suits arising from such use.

# COVID-19 Scientific Advisory Group Rapid Response Report

## Appendix

### List of Abbreviations

CoV: Coronavirus

COVID-19: Coronavirus Disease 2019

CT: Computed Tomography Scan

MERS: Middle East Respiratory Syndrome

PCR: Polymerase Chain Reaction

PPE: Personal protective equipment

RT-PCR: Reverse Transcriptase Polymerase Chain Reaction

SAG: Scientific Advisory Group

SARS: Severe Acute Respiratory Syndrome

SARS-CoV-2: Severe Acute Respiratory Syndrome – Coronavirus – 2

WHO: World Health Organization

### Reference List

Bai, Y., Yao, L., Wei, T., Tian, F., Jin, D. Y., Chen, L., & Wang, M. (2020). Presumed asymptomatic carrier transmission of COVID-19. *Jama*. Retrieved from: <https://jamanetwork.com/journals/jama/article-abstract/2762028>. Accessed 26 March 2020

Bean, S. Reel, K., Smith, M.S., Henry, B. & McDonald, M. (2020). Ethical Framework for the Allocation of Personal Protective Equipment (during COVID-19) Retrieved from <http://jcb.utoronto.ca/news/documents/Ethical-Framework-for-the-Allocation-of-Personal-Protective-Equipment-2020.pdf>. Accessed March 28, 2020.

Chan, J. F. W., Yuan, S., Kok, K. H., To, K. K. W., Chu, H., Yang, J., ... & Tsoi, H. W. (2020). A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *The Lancet*, 395(10223), 514-523. Retrieved from: [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30154-9/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30154-9/fulltext). Accessed 26 March 2020

Du Z, Xu X, Wu Y, Wang L, Cowling BJ, Ancel Meyers L. (2020). Serial interval of COVID-19 among publicly reported confirmed cases. *Emerg Infect Dis*. Retrieved from: [https://wwwnc.cdc.gov/eid/article/26/6/20-0357\\_article](https://wwwnc.cdc.gov/eid/article/26/6/20-0357_article). Accessed 26 March 2020.

Feng, S., Shen, C., Xia, N., Song, W., Fan, M., & Cowling, B. J. (2020). Rational use of face masks in the COVID-19 pandemic. *The Lancet Respiratory Medicine*. Retrieved from [https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(20\)30134-X/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30134-X/fulltext). Accessed 26 March 2020

## Asymptomatic Transmission of SARS-CoV-2 • 7

- Flaxman, S., Mishra, S., Gandy, A., et al. (2020) Estimating the number of infections and the impact of nonpharmaceutical interventions on COVID-19 in 11 European countries. Imperial College London. Retrieved from: <https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gida-fellowships/Imperial-College-COVID19-Europe-estimates-and-NPI-impact-30-03-2020.pdf>. Accessed 1 April 2020.
- He, X., Lau, E. H., Wu, P., Deng, X., Wang, J., Hao, X., ... & Mo, X. (2020). Temporal dynamics in viral shedding and transmissibility of COVID-19. medRxiv. Preprint. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.03.15.20036707v2>. Accessed 26 March 2020.
- Li R, Pei S, Chen B, et al. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2) [published online ahead of print, 2020 Mar 16]. *Science* 2020;eabb3221. doi:10.1126/science.abb3221. Retrieved from: [https://pubmed.ncbi.nlm.nih.gov/32179701/?from\\_single\\_result=10.1126%2Fscience.abb3221](https://pubmed.ncbi.nlm.nih.gov/32179701/?from_single_result=10.1126%2Fscience.abb3221). Accessed 27 March 2020.
- Lu et al. (2020). SARS-CoV-2 Infection in Children. *New England Journal of Medicine*. Retrieved from: <https://www.nejm.org/doi/full/10.1056/NEJMc2005073?query=TOC>. Accessed 26 March 2020.
- Kimball A, Hatfield KM, Arons M, et al. (2020). Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled Nursing Facility — King County, Washington, March 2020. *MMWR Morb Mortal Wkly Rep*. ePub: 27 March 2020. Retrieved from: [https://www.cdc.gov/mmwr/volumes/69/wr/mm6913e1.htm?s\\_cid=mm6913e1\\_w](https://www.cdc.gov/mmwr/volumes/69/wr/mm6913e1.htm?s_cid=mm6913e1_w). Accessed 1 April 2020.
- Nishiura et al. (2020). Estimation of the asymptomatic ratio of novel coronavirus infections (COVID-19). medRxiv. Preprint. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.02.03.20020248v2.full.pdf>. Accessed 26 March 2020
- Nishiura H., Linton, N.M., Akhmetzhanov, A.R. (2020). Serial Interval of novel coronavirus (COVID-19) infections. *Int J Infect Dis*. 93 (2020). Retrieved from: [https://www.ijidonline.com/article/S1201-9712\(20\)30119-3/pdf](https://www.ijidonline.com/article/S1201-9712(20)30119-3/pdf). Accessed 26 March 2020.
- Mizumoto, K., Kagaya, K., Zarebski, A., & Chowell, G. (2020). Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*, 25(10), 2000180. <https://doi.org/10.2807/1560-7917.ES.2020.25.10.2000180>
- Rockx, B., Kuiken, T., Herfst, S., Bestebroer, T., Lamers, M., de Meulder, D., ... & van Run, P. (2020). Comparative Pathogenesis Of COVID-19, MERS And SARS In A Non-Human Primate Model. bioRxiv. Preprint. Retrieved from: <https://www.biorxiv.org/content/10.1101/2020.03.17.995639v1>. Accessed 26 March 2020.
- Rothe, C., Schunk, M., Sothmann, P., Bretzel, G., Froeschl, G., Wallrauch, C., ... & Seilmaier, M. (2020). Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. *New England Journal of Medicine*. Retrieved from <https://www.nejm.org/doi/full/10.1056/NEJMc2001468>. Accessed 26 March 2020
- World Health Organization. (2020a). Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). Retrieved from: <https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf>. Accessed 27 March 2020.

World Health Organization. (2020b). Q&A: Similarities and differences – COVID-19 and Influenza. Retrieved from: <https://www.who.int/news-room/q-a-detail/q-a-similarities-and-differences-covid-19-and-influenza>. Accessed 26 March 2020.

World Health Organization. (2020c). Modes of transmission of virus causing COVID-19: implications for IPC precaution recommendations. Retrieved from: <https://www.who.int/publications-detail/modes-of-transmission-of-virus-causing-covid-19-implications-for-ipc-precaution-recommendations>. Accessed 28 March 2020.

Zhao, S., Gao, D., Chong, M., Cai, Y., Ran, J., Cao, P., Wang, K., Lou, Y., Wang, W., Yang, L., He, D., Wang, M. (2020). Estimating the serial interval of the novel coronavirus disease (COVID-19): A statistical analysis using the public data in Hong Kong from January 16 to February 15, 2020. medRxiv. Preprint. Retrieved from: <https://www.medrxiv.org/content/10.1101/2020.02.21.20026559v1>. Accessed 26 March 2020.

Zou, L., Ruan, F., Huang, M., Liang, L., Huang, H., Hong, Z., & Guo, Q. (2020). SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *New England Journal of Medicine*, 382(12), 1177-1179. Retrieved from: <https://www.nejm.org/doi/full/10.1056/NEJMc2001737?query=TOC>. Accessed 26 March 2020.