INTRODUCTION

PHO is actively monitoring, reviewing and assessing relevant information related to Coronavirus Disease 2019 (COVID-19). “What We Know So Far” documents are intended to provide a rapid review of the evidence related to a specific aspect or emerging issue related to COVID-19.

The development of these documents includes a systematic search of the published literature as well as scientific grey literature (e.g., ProMED, CIDRAP, Johns Hopkins Situation Reports) and media reports, where appropriate. Relevant results are reviewed and data extracted for synthesis. All “What We Know So Far” documents are reviewed by PHO subject-matter experts before posting.

As the COVID-19 outbreak continues to evolve and the scientific evidence rapidly expands, the information provided in these documents is only current as of the date of posting.

KEY POINTS

This document summarizes the evidence regarding asymptomatic infection and transmission of SARS-CoV-2, the virus that causes COVID-19, by individuals who are asymptomatic. For clarity, in this document we will use the term COVID-19 to refer to both the virus and the disease.

Asymptomatic infection:

- **There is clear evidence of asymptomatic infection with COVID-19.** Estimates of the proportion of laboratory-confirmed cases who are asymptomatic may vary by age group, study setting and study methodology, ranging from 8.2% (infants under 1 year of age),\(^1\) 18.2% (contact tracing in a conference outbreak),\(^2\) 36.7% (travellers),\(^3\) 43.2% (universal screening in a town),\(^4\) up to 87.8% (outbreak investigation in a homeless shelter)\(^5\) (see Asymptomatic Infection). The method of detection of asymptomatic cases (i.e., mass screening or testing contacts of cases), and the duration of follow-up to ensure asymptomatic individuals do not subsequently develop symptoms may influence the proportion of cases who are reported to be asymptomatic.

Asymptomatic transmission:

- There is some epidemiological and virological evidence of transmission from people who are asymptomatic and never develop symptoms. On the other hand, there is more epidemiological and virological evidence as well as inferences from modelling and statistically analyses, that
transmission can occur from presymptomatic COVID-19 patients (where transmission takes place during their incubation period). In particular, epidemiological investigations and virological findings have suggested that transmission can occur as early as six days before symptom onset and possibly even earlier, although alternative unrecognized sources of infection cannot be ruled out. Other studies have estimated the serial interval (time from onset of symptoms in one case to the onset of symptoms in the person they infect) and found that it is shorter than the length of the incubation period, suggesting transmission during the incubation period (see Modelling and Statistical Analysis below).

Background

Asymptomatic infection occurs when an individual is infected but experiences no symptoms, while asymptomatic transmission occurs when an infected individual without symptoms transmits the virus to another person. There are two mechanisms by which asymptomatic transmission can potentially occur:

1. Transmission from an individual who never develops symptoms—if the infected person is asymptomatic throughout his/her infection but nevertheless is infectious.

2. Transmission from an individual during their incubation period—if the infected person is infectious before he/she develops symptoms.

Asymptomatic Infection

Evidence of asymptomatic COVID-19 infection has been reported in studies that report on contact tracing activities, as well as in outbreak investigations and surveillance data. Asymptomatic infections have been reported in all age groups, occurring in various proportions of confirmed cases in different settings. Several studies reported that a substantial portion of COVID-19 patients remained asymptomatic at the end of their isolation period.

Asymptomatic Infections by Settings

The following highlights the proportion of asymptomatic COVID-19 cases from contact tracing activities, outbreak investigations and surveillance activities in various settings.

**HEALTH CARE SETTING**

A number of studies reported rates of asymptomatic infections after a period of isolation:

- Among the 138 cases detected in Brunei from March 5 to April 24, 2020, all were hospitalized and followed until viral clearance; 42 (30%) were presymptomatic at the time of diagnosis but later developed symptoms and 16/138 (12%) remained asymptomatic until viral clearance.\(^3\)

- 13/23 (57%) resident cases identified at a point-prevalence screening in a long-term care skilled nursing facility in Washington, United States with a COVID-19 outbreak were asymptomatic; only 3/23 (13.0%) remained asymptomatic at rescreening one week later.\(^6\)

- 14/19 (74%) resident cases and 4/8 (50%) staff cases identified at multiple point-prevalence screenings in a long-term care skilled nursing facility in California, United States with a COVID-19 outbreak were asymptomatic; 6/19 (31.6%) resident cases remained asymptomatic after at least 17 days of observation.\(^7\)
- 29/33 (87.9%) pregnant women who tested positive for SARS-CoV-2 at two New York obstetric centres were asymptomatic when screened at delivery; 26/33 (78.8%) remained asymptomatic until discharge. In another report from about a week before to a week after universal screening was started at these same two centres, 14/43 (32.6%) SARS-CoV-2–positive pregnant women were found to be asymptomatic on admission (two because they later developed symptoms and 12 by screening); 4/43 (9.3%) were asymptomatic throughout their postpartum courses.

- 28/131 (21.4%) COVID-19 confirmed hemodialysis patients from 65 centres in Wuhan, China remained asymptomatic throughout the course of their infection.

- 30/1,012 (3%) patients admitted during February 7-12 to a make-shift hospital for non-critically ill COVID-19 patients in Wuhan, China were asymptomatic on admission. 14/1,012 (1.4%) patients remained asymptomatic after a median duration of 24 days from exposure (interquartile range: IQR: 22-27).

- Of 31 patients who were asymptomatic on admission to a hospital in Guangzhou, China, 9/31 (29.0%) remained symptom-free during hospitalization. The viral load was higher in those who subsequently developed symptoms than in those who remained symptom-free.

- 13/328 (4.0%) adult patients admitted to a public health centre in Shanghai, China were asymptomatic; 10/328 (3.0%) remained asymptomatic from 5 to 21 days after admission, although all but one patient had radiologic abnormalities on chest CT.

- 13/71 (18.3%) admitted patients at a hospital in South Korea were asymptomatic on admission. 10/71 (14.1%) remained asymptomatic for the entire quarantine period, and the other 3 cases developed symptoms within 2 days of admission.

CONGREGATE LIVING SETTINGS

High prevalence of asymptomatic infections at the time of testing have been reported in a few congregate settings:

- 87.8% of 147 adult COVID-19 cases identified through screening at a homeless shelter in Boston.

- More than 350 of 615 (>57%) COVID-19 cases on the Theodore Roosevelt aircraft carrier.

- 3 of the 4 resident cases identified at a senior independent and assisted living community in Seattle, Washington reported feeling well between the 14 days prior to and 14-21 days after testing.

- 410/696 (58.9%) confirmed passenger and crew COVID-19 cases in the Diamond Princess cruise ship outbreak. Adjusting for the possible future development of symptoms (right censoring) using a statistical model, Mizumoto et al. estimated the asymptomatic proportion to be 17.9% (95% credible interval [CrI]: 15.5 to 20.2%).

COMMERCIAL PREMISES

Two outbreak reports identified cases that remained asymptomatic through the follow-up period:
● In a **call centre outbreak in Seoul**, 4/97 (4.1%) confirmed COVID-19 cases were presymptomatic and another 4/97 (4.1%) **remained asymptomatic throughout a 14-day isolation period**.\(^{19}\)

● In a **conference outbreak in Munich, Germany**, 2/12 (17%) infected attendees **remained asymptomatic after weeks of follow-up**.\(^{2}\)

**COMMUNITY**

There are regional and national surveillance reports on the presence of asymptomatic infection in the community:

● A national surveillance report by the **Chinese Center for Disease Control and Prevention** reported 889/45,561 (2%) of laboratory-confirmed cases as asymptomatic at the time testing as of February 11.\(^{20}\)

● 94/728 (12.9%) laboratory-confirmed children reported to the **Chinese Center for Disease Control and Prevention** during January 16-February 8, 2020 were asymptomatic (from 8.2% in children <1 year of age [7/85] to 17.6% for those 6-10 years of age [30/170]).\(^{1}\)

● **Integrated surveillance of COVID-19 in Italy** reported 28.6% of the 33,189 cases with clinical data were asymptomatic as of May 20.\(^{21}\)

● Analysis of regional surveillance data from **one day in Lombardy, Italy** found 17/380 (4.5%) cases as asymptomatic.\(^{22}\)

● 35/81 (43.2%) cases identified in two point-prevalence surveys of all inhabitants of the **municipality of Vò, Italy** were asymptomatic at the time of testing.\(^{4}\)

● 30/112 (26.8%) cases in a **cluster of fitness dance classes in South Korea** were asymptomatic at the time of testing.\(^{23}\)

There are also studies reporting community-based infections that remained asymptomatic after a period of time:

● **50/1,015 (4.9%)** confirmed cases (41 adults and 9 children) in **Huangshi, China** were **asymptomatic throughout a quarantine period of at least 14 days**, according to publicly available disease databases of Hubei Provincial Health Committee up to March 27, 2020.\(^{24}\)

● **5/48 (10.4%)** secondary cases among close contacts in **Zhuhai, China** **remained asymptomatic through a 21-day follow-up**.\(^{25}\)

● **Wan R et al.** described 2 close contacts of confirmed patients. Case 1 was exposed at work to a COVID-19 patient and diagnosed 16 days later by reverse transcription polymerase chain reaction (RT-PCR). He **remained asymptomatic up to the end of the isolation period 25 days after exposure**; two chest radiographs taken during his isolation period were negative. Case 2 was the adult son of a COVID-19 patient. Case 2 was isolated the day after the parent’s diagnosis and he **remained asymptomatic throughout 26 days of isolation**. Two chest radiographs taken during his isolation were also negative.\(^{26}\)
TRAVELLERS
A few countries that tested their repatriated passengers or travellers from countries at high-risk of COVID-19 also reported asymptomatic infections:

- 40/783 (5.1%) repatriated passengers to Greece during March 20-25, 2020 who tested positive for SARS-CoV-2 reported no general or respiratory symptoms.\(^{27}\)
- 2/114 (1.8%) repatriated passengers to Germany on February 1 were asymptomatically infected and remained afebrile 7 days after diagnosis, although one patient developed a faint rash and minimal pharyngitis.\(^{28}\)
- Out of the 30 arrivals to Brunei who tested positive for SARS-CoV-2 between March 21 and April 24, 11 (36.7%) were presymptomatic and 3 (10%) were asymptomatic.\(^{3}\)
- In a cluster of 6 travellers and 6 secondary cases in Vietnam, 1/12 cases (8.3%) remained asymptomatic but viral RNA was detected by RT-PCR throughout the 9-day follow-up period.\(^{29}\)

Abnormal Chest Imaging
Asymptomatically infected individuals can have abnormal chest imaging.

- Hu Z et al. showed that 12/19 asymptomatic adults and children had abnormal chest CT scans.\(^{30}\)
- Chan JF et al. described an abnormal chest CT in a 10-year old asymptomatic child.\(^{31}\)
- Wang Y et al. noted pneumonia in CT findings in 37/55 of asymptomatic cases on admission. Note that all 55 cases developed symptoms during hospitalization: 14 had mild infection, 39 had ordinary symptoms and 2 had severe COVID-19.\(^{32}\)
- Zhou X et al. reported that 9/10 asymptomatic patients hospitalized at a public health centre had signs of pneumonia on their chest CT scans.\(^{13}\)
- Zhou R et al. noted bilateral abnormalities in chest CT scans typical of pneumonia in 4/9 patients who remained asymptomatic throughout hospitalization.\(^{12}\)
- Inui S et al. reported that chest CT findings consistent with pneumonia were seen in 41/76 (54%) asymptomatic passengers on Diamond Princess cruise ship.\(^{33}\)

Asymptomatic Transmission
There is some evidence of transmission from people who are asymptomatic and never develop symptoms, and more evidence of transmission from people who are in their incubation period (i.e. people who transmit infection while asymptomatic, but prior to their development of symptoms).

Transmission From People who Never Developed Symptoms
Findings from epidemiological and virological investigation have been published to support the observation that transmission can occur from people who never developed symptoms after their infection.
EPIDEMIOLOGICAL EVIDENCE FOR ASYMPTOMATIC TRANSMISSION

Several authors reported clusters of infections in China where epidemiological findings suggest the possibility of transmission by asymptomatic patients.

- **Zhou J et al.** reported two transmission events by asymptomatic patients in ZhuZhou, China.\(^3^4\)
  - A 37-year-old woman was isolated for observation after returning from Wuhan on January 22, 2020. Viral RNA was only detected in the 5th specimen taken on February 15, and she remained asymptomatic up to March 2 when her test turned negative and showed no pulmonary imaging changes. Meanwhile, her father was diagnosed of COVID-19 on February 12, 3 days before viral RNA was detected in the woman's specimen.
  - An asymptomatic patient who returned from Wuhan appears to have infected her mother-in-law and father-in-law.

Zhou et al. conclude that asymptomatic SARS-CoV-2 carriers can spread the virus before viral RNA was detected. It should be noted that they did not provide any information on potential alternate sources of infection or on the reliability of the testing done.

- **Zhang J et al.** reported a family cluster of 5 in Beijing. The index case was the only one in the cluster who had been to Wuhan; he returned to Beijing in January and invited his nephew (M/32) for dinner that day. This nephew became ill 3 days later and was diagnosed 2 days after symptom onset. Around that time, the index patient’s wife (F/45) had a fever and they heard of a relative in Wuhan having COVID-19. As a result, the index patient and family visited a hospital to be assessed and the index and 4 family members (including the nephew and wife) were diagnosed with COVID-19. Both the index patient and a family member remained asymptomatic throughout the observation up to the end of February. The index patient’s chest radiograph showed ground glass opacities but that of the other asymptomatic family member was normal. The authors believe the index patient passed the infection on to his family despite having no symptoms himself. However, details of other family members’ contact history were not given to rule out potential alternate sources of infection.\(^3^5\)

- A study by **Bai Y et al.** reported on an asymptomatic individual who transmitted COVID-19 to five family members in Anyang. She tested positive 18 days after her presumed exposure, with a negative test on day 16 and two negative tests on days 26 and 29. Although the authors argue that the asymptomatic individual was the source of infection for the family members, the family visited a hospital as well. Although the hospital reported no COVID-19 cases at that time, this is a potential alternative source of exposure.\(^3^6\)

- **Hu Z et al.** reported on an asymptomatic case who appears to have acquired his infection in Hubei province and transmitted his infection to his wife, son and daughter-in-law who lived with him in Nanjing. His family members denied any other known exposures to confirmed or suspect COVID-19 patients.\(^3^0\)

- **Lavezzo E et al.** reported on 3 cases who appeared to have acquired their infection based on contact with asymptomatic individuals. The cases were identified on the second of two point-prevalence surveys that took place at the end of a two-week lockdown of the municipality of Vò, Italy: case 1 had exposure to 4 infected relatives who did not have any symptoms at the time of contact; case 2 had a meeting with an asymptomatic case before the lockdown; case 3 shared
the same flat with two asymptomatic relatives. The authors noted that all the asymptomatic individuals never developed symptoms during the two-week lockdown.4

VIROLOGICAL EVIDENCE FOR ASYMPTOMATIC TRANSMISSION

Several studies reported high viral loads in asymptomatic individuals as measured by real-time RT-PCR.

- **Arons MM et al.**37 cultured the real time RT-PCR-positive specimens from two point-prevalence surveys in a skilled nursing facility as part of an outbreak investigation, as described in Kimball A et al.6 above. Viral growth was observed for 13/20 symptomatic residents, 17/24 presymptomatic residents, 1/3 asymptomatic residents. Viable virus was isolated from 6 days before to 9 days after symptom onset. In addition, high viral RNA loads were detected in all groups with median cycle threshold values at 24.8 in those with typical symptoms and 25.5 for those who were asymptomatic. This suggests the potential for substantial viral shedding in asymptomatic cases. No correlation was observed between cycle threshold values and time from symptom onset.37

- **Zou L et al.** noted that an asymptomatic individual had similar viral loads from nasal and throat swabs compared to 17 symptomatic individuals.38

- **Roxby AC et al.** noted that the viral load in 3 generally asymptomatic residents (one developed a mild cough) of an independent living community were similar to those reported among ill hospitalized patients.16

- **Kam K et al.** noted a high viral load in a nasopharyngeal specimen from a generally well baby. Nasopharyngeal specimens were positive for 16 days and one stool specimen was also positive.39

- **Hoehl S et al.** observed COVID-19 virus in cell culture in throat specimens from two repatriated passengers who tested positive by RT-PCR. One patient developed slight rash and minimal pharyngitis the day after testing but both persons remained well and afebrile during the 7 days after hospital isolation.28

- **Cereda D et al.** noted that the median viral RNA levels in nasal swabs were not statistically different between 295 symptomatic and 17 asymptomatic obstetric cases: 5.0 log_{10} RNA copies/mL (range 1.7-10.1) vs 4.7 log_{10} copies/mL (range 2.1-7.1), (P=.51).22

Transmission During the Incubation Period

There is both epidemiological and virological evidence, as well as inferences from modelling and statistical analysis, that point to transmission from people prior to their symptom onset.

EPIDEMIOLOGICAL EVIDENCE FOR PRESYMPTOMATIC TRANSMISSION

Several studies describe potential transmission prior to symptom onset, i.e., in the incubation period. In most instances, the contacts who acquired the infection reported no other known sources of exposure other than a case who was in their incubation or early symptomatic period.

- **Hijnen D et al.** reported an outbreak amongst at least 11/13 attendees (one attendee was not tested) from seven countries at a 2-day conference in Munich, Germany in February, when under 20 cases of COVID-19 had been diagnosed in the country. The index patient (a physician
was believed to have been infected when examining a patient in Italy two days before the start of the conference) **developed symptoms only after he had left the conference.**

- **Rothe C et al.** reported an outbreak in Germany resulting from a business meeting in late January. Böhmer MM et al. reconstructed the transmission events with epidemiological findings and whole genome sequencing of 13 of the 16 subsequent cases. The index case was a Chinese resident from Shanghai who had had contact with her parents from Wuhan before visiting Germany in January for work reasons. Presymptomatic transmission likely occurred from patient 4 (symptom onset on January 24) to patient 5, as patient 5 did not meet the index case but had encounters with patient 4 on January 22 when they sat back to back in the canteen and patient 5 turned to ask patient 4 to borrow the salt shaker from their table. Böhmer MM et al. noted that **presymptomatic transmission is strongly supported by virus sequence analysis.** In addition, presymptomatic transmission could possibly have occurred for 5 more cases.

- **Jang S et al.** reported on the active surveillance results of a COVID-19 cluster associated with fitness dance classes. On February 15, 2020, a 4-hour workshop for 27 fitness instructors took place in Cheonan, South Korea (approximately 200 km from Daegu where an outbreak was emerging). After discovering cases in Cheonan linked to fitness dance classes, the workshop was investigated. Eight of the 27 instructors at the workshop were found to be infected with SARS-CoV-2. One of these instructors was from Daegu, and therefore was the presumed source case for the outbreak, and developed symptoms on February 18, 2020, three days after the workshop.

- **Cheng HY et al.** conducted a prospective study that enrolled all the initial 100 confirmed cases in Taiwan from January 15 to March 18, 2020 and their 2,761 close contacts. All close contacts were quarantined at home for 14 days after their last exposure to the index case, and any typical symptoms triggered testing. High-risk contacts (e.g., household and hospital contacts) were tested regardless of symptoms. No secondary clinical cases were detected from all 91 close contacts of the 9 asymptomatic patients. Cheng et al. identified 22 secondary cases, 18 of whom had symptoms. They determined a secondary clinical infection risk of 0.7% (95% confidence interval (CI): 0.4% - 1.0%) among 2,761 close contacts. **For the 299 contacts with exclusive presymptomatic exposures to the index case, the secondary clinical attack rate was 0.7% (95% CI, 0.2%-2.4%).** The authors noted that the actual contribution of early transmission could be greater as they did not completely identify contacts before symptom onset of the index cases.

- **Wei WE et al.** reviewed the clinical and epidemiological records of all 243 cases in Singapore to determine whether presymptomatic transmission might have occurred. Of these cases, 157 were locally acquired with 10 (6.4%) attributed to presymptomatic transmission within 7 clusters, where investigation did not identify any other potential sources of infection. The authors noted that although an unknown source might have caused some of these infections, given that COVID-19 prevalence was very low during the period under investigation and strong surveillance systems were in place, presymptomatic transmission was deemed the most likely mode of transmission. The authors also note that recall bias related the onset date of symptoms might add uncertainty to the duration of the presymptomatic period.

Multiple authors also reported clusters of infections in China where the transmission histories suggest the occurrence of presymptomatic transmission. It should be noted that due to circulation of COVID-19 in China during that time, it is possible that there was another unrecognized source of infection, in addition to the cases reported.
• **Gao Y et al.** reported a 15-person cluster with 4 generations of transmission and 6 asymptomatic cases in Wuxi. Except the index case, none of the other 14 cases had any history of suspicious exposure except for contact with the previous generation case(s). In this cluster, infections are believed to have spread to the next generation before onset in the previous generation as follows: 2-7 days before onset (1st to 2nd generation), 6-7 days before onset (2nd to 3rd generation), and 3-8 days and 9 days before onset (3rd to 4th generation). The authors noted that generation 2 might also have been infected from other sources while touring in Japan. However, the transmission history of the other generations support the idea of presymptomatic transmission.44

• **Luo SH et al.** reported a cluster of 4 adults in Anqing. Epidemiological evidence suggests that one patient was infected by her husband during the presymptomatic stage of his infection. Neither the wife nor husband had travelled to Wuhan or adjacent areas or had recent exposure to wild animals. However, the husband likely acquired his infection from a relative while the relative was symptomatic.45

• **Huang L et al.** reported a cluster of 8 teenagers and young adults aged 16-23 years in Hefei, originating from a 22-year-old male returning from Wuhan. Six secondary cases became infected after contact of several hours duration with the index case one day before his symptom onset; another secondary case was likely exposed 3 days before the index case’s symptom onset. None of the secondary cases had visited Wuhan or had any exposure to wet markets, wild animals, or medical institutes within the previous 3 months.46

• **Li C et al.** described transmission in a familial and hospital settings in Xuzhou. The source case is believed to have acquired his infection on January 14, 2020 during a 6-hour transfer in a train station in Wuhan when travelling to Xuzhou and developed symptoms on January 19, 2020. While caring for his son-in-law in hospital he interacted with another patient and that patient’s son from January 15 to 18 (1 to 4 days before the source patient’s onset of symptoms); both the other patient and his son became infected. The source case also infected several members of his family whom he was with both before and after the onset of symptoms. Other source(s) of infection, particularly in the hospital setting may also be possible, although were not mentioned by the authors.47

• **Li P et al.** describe a familial cluster of 4 in Zhoushan, who had close contact with a presymptomatic family member 4 to 7 days before the index case’s symptom onset. Other than the index case, the family reported no contact with people with fever or respiratory symptoms in Wuhan or other areas with persistent local COVID-19 transmission in the 14 days prior to their symptom onset, and no history of contact with wild animals or poultry.48

• **Ye F et al.** reported a cluster of 5 people from 2 families in Luzhou. The three members of Family 1 traveled from Wuhan to Luzhou on January 22, and met with the two members of Family 2 between January 23 and 25 and on January 30. Family 2 had not left Luzhou and their only contact with anyone from Wuhan was Family 1. The first and last contact between Family 1 and 2 was 13 and 6 days before the first case in Family 1 developed symptoms on February 5. All five family members developed symptoms and the symptoms in the first case in Family 2 started on February 1, 2020, 4 day before the symptoms in Family 1.49

• **Yu P et al.** described an 88-year-old man from Shanghai who developed symptoms 5 days after the arrival of two visitors from Wuhan. The two visitors developed symptoms after the man,
with the earliest symptom onset among the two visitors occurring 11 hours after the man’s first symptoms. This suggests that at least one of the visitors had spread infection in their incubation period. Assuming the visitor with the earliest symptom onset transmitted infection to the man, the earliest the infection could have occurred is from 5 days before onset of illness in that visitor, based on the date of the visitors’ arrival.\textsuperscript{50}

- **Huang R et al.** described a patient from near Wuhan who visited her family in Nanjing and did not develop symptoms until 4 days after leaving Nanjing. She infected six family members, some of whom she lived with and some with whom she attended one or more dinners with, including one on the day before her departure. Two family members, who appear to have been infected at the family dinner with the visiting woman the day before her departure, attended another family dinner with three different relatives. This occurred on the day after the dinner with the visiting woman, and 3 and 4 days before the onset of symptoms. The three relatives subsequently developed symptoms and were found to be infected with COVID-19. This suggests that transmission can occur at least 5 days before symptom onset and that transmission may occur as early as 1 day following exposure.\textsuperscript{51}

- **Tong ZD et al.** reported a case of COVID-19 from Wuhan who attended a conference in Zhoushan three days before illness onset. Two colleagues from Zhoushan also attended the conference and dined with the case the following day (2 days before illness onset), sharing the same serving plates. The two colleagues were subsequently confirmed to be infected. This suggests that the source patient likely infected his two colleagues at least 2 days prior to symptom onset.\textsuperscript{52}

**VIROLOGICAL EVIDENCE FOR PRESYMPTOMATIC TRANSMISSION**

In addition to epidemiological reports that attribute the source of infection to presymptomatic COVID-19 patients, we found an article that reports on finding viable COVID-19 virus in specimens from patients prior to their symptom onset. Another two studies reported high viral loads in presymptomatic individuals as measured by real-time RT-PCR.

- **Arons MM et al.** cultured the real time RT-PCR-positive specimens from two point-prevalence surveys in a skilled nursing facility as part of an outbreak investigation (see also Virological Evidence for Asymptomatic Transmission). Viable virus was isolated from 6 days before to 9 days after symptom onset. In addition, high viral RNA loads were detected in all groups with median cycle threshold values at 24.8 in those with typical symptoms and 23.1 for the presymptomatic. This suggests the potential for substantial viral shedding in presymptomatic cases. No correlation was observed between cycle threshold values and time from symptom onset.\textsuperscript{37}

- **Kim SE et al.** noted very high viral loads (cycle threshold values <20) in specimens from 2 presymptomatic patients two days before symptom onset.\textsuperscript{14}

- **Zhou R et al.** noted significantly higher viral load in nasopharyngeal specimens from presymptomatic patients (median cycle threshold value: 34.5 [IQR 32.2-37.0]) than those from asymptomatic patients (median cycle threshold value: 39.0 [IQR 37.5-39.5]).\textsuperscript{12}
MODELLING AND STATISTICAL ANALYSIS

We found a modelling study which estimated that infectiousness started from 2.3 days (95% CI: 0.8-3.0 days) before symptom onset and peaked at 0.7 days (95% CI: 2.0 days before symptom onset to 0.2 days after onset). In addition, a number of authors have compared the incubation period with the serial interval of COVID-19. The serial interval is the time from onset of symptoms in one case to the time of symptom onset in the case(s) they infect. When the serial interval is shorter than the incubation period, some transmission is likely to have occurred in the incubation period.

- **He X et al.** assessed viral RNA load from 414 throat swabs of 94 patients from symptom onset up to 32 days after onset. Viral load based on RT-PCR was observed to be high soon after symptom onset and then declined. The authors then identified 77 transmission pairs from publicly available international sources. Using a mean incubation period of 5.2 days, the serial interval was estimated to have a median of 5.2 days (95% CI: 4.1-6.4 days), with 7.6% having negative serial intervals (which occur when the secondary case’s symptom onset precedes that of the primary case). The estimated proportion of presymptomatic transmission was 44% (95% CI: 25-69%).\(^{53}\)

- From 22 transmission pairs out of 100 confirmed cases in Taiwan, **Cheng HY et al.** estimated a median incubation period of 4.1 days (95% credible interval, 0.4-15.8) and a median serial interval of 4.1 days (95% credible interval, 0.1-27.8).\(^{42}\)

- Analyzing published data of 18 transmission pairs with onset dates clearly defined in published articles, **Nishiura H et al.** estimated a median serial interval of 4.6 days (95% CrI: 3.5-5.9), which was shorter than a mean incubation of approximately 5 days from other published sources.\(^{54}\)

- Analyzing 16 cases in four transmission generations, **Böhmer MM et al.** estimated a median incubation period of 4.0 days (IQR 2.3-4.3) and a median serial interval of 4.0 days (IQR 3.0-5.0).\(^{41}\)

- Assuming a single source of infection for each household, **Wu J et al.** analyzed 48 secondary cases from index cases in 35 households in Zhuhai, China and estimated a median incubation period of 4.3 days (95% CI: 3.4-5.3) and a serial interval of 5.1 days (95% CI: 4.3-6.2).\(^{25}\)

- From a cluster of seven people (1 teenager, 6 young adults) infected by a 22 year-old in Hefei, China, **Huang L et al.** estimated a median incubation period of 2 days (range 1-4) and a median serial interval of 1 day (range 0-4).\(^{36}\)
References


Citation

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