



Is SARS-CoV-2 transmitted by asymptomatic and pre-symptomatic individuals?

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KEY FINDINGS

Asymptomatic and pre-symptomatic transmission of SARS-CoV-2 may occur.

- Manifestations of COVID-19 are highly varied and may include asymptomatic cases, who do not manifest with any signs and symptoms despite testing positive for COVID-19 by viral nucleic acid tests. Pre-symptomatic cases are infected individuals who are still in their incubation period, hence do not exhibit any symptoms yet but eventually develop symptoms.
- As of June 21, 586 (2.8%) of the 20,990 active cases in the Philippines classified as asymptomatic, but it is unclear whether cases are pre-symptomatic or carriers (asymptomatic).
- Based on 36 observational studies (case reports, case series, cross-sectional and cohort studies) and 9 statistical modeling analysis, asymptomatic and pre-symptomatic transmission of SARS-CoV-2 may occur. However, 3 studies reported no transmission from pre-symptomatic and asymptomatic cases.
- Studies on viral load comparing symptomatic cases with pre-symptomatic and asymptomatic cases reported contradictory results. The duration of viral shedding was significantly longer for symptomatic patients compared to asymptomatic patients but similar for asymptomatic and pre-symptomatic patients.
- There was no difference in the transmission rates of symptomatic and asymptomatic cases. However, the estimated infectivity and probability of transmission was higher for symptomatic cases compared to asymptomatic cases, but results were imprecise due to a wide confidence interval.
- The WHO and CDC recognize the possibility of pre-symptomatic and asymptomatic transmission. According to WHO, current evidence suggests asymptomatic cases are less likely to transmit the virus than symptomatic cases.

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RESULTS

Thirty-six observational studies (2 case reports, 26 case series, 1 cross-sectional study, 3 retrospective single cohort, 4 prospective cohort) and nine statistical modelling analysis have reported that pre-symptomatic and asymptomatic transmission may occur. However, 3 studies reported no transmission from pre-symptomatic and asymptomatic cases. Characteristics of the individual studies are detailed in Appendix 1.

Pre-symptomatic Transmission (15 studies)

A study in Singapore of all 243 COVID-19 cases from January 23 to March 16 identified seven clusters with 2-5 patients each where pre-symptomatic transmission may have occurred. Ten cases (4.1%) were attributed to pre-symptomatic transmission, which accounted for 6.4% of all locally acquired cases. Transmission in four clusters occurred 1-3 days before symptom onset of the index case while exact exposure could not be determined for the rest of the clusters due to continuous exposure to the index case [7].

Another study in China on young people (aged 16-23 years old) reported 7 COVID-19 cases (31.8%) from 22 close contacts of an index case from Wuhan. Transmission occurred 1-3 days before onset of symptoms with duration of contact of 1-7 hours. [8]. A family cluster in India reported 4 index cases transmitting the infection to 26 of 43 (60%) family members during the pre-symptomatic period of 6 days [9]. In a group involving 4 clusters in China, infection was transmitted from one cluster to another during the pre-symptomatic periods of each infected case ranging from 2-9 days before symptom onset [10].

Eleven other different cluster studies in separate publications (9 in China, 1 in Taiwan, 1 in Germany) of COVID-19 cases from January to February also reported possible pre-symptomatic transmission with 1-7 secondary cases documented per cluster [11-21]. The shortest interval between close contact with the index case prior to symptom onset of index case was 1-2 days [13,18] while the longest interval was 12-14 days [11]. No computed transmission rates were reported in the 10 studies and only 5 studies reported COVID-19 negative contacts within their clusters. However, it is uncertain whether all contacts of the index case were identified on contact tracing [11-21].

Asymptomatic Transmission (11 studies and 2 statistical model)

Asymptomatic transmission was suggested by five studies in China. Each study reported 2-6 symptomatic COVID-19 secondary cases exposed to a presumed index case with travel to Hubei that tested positive for COVID-19 but remained asymptomatic with normal CT scan findings [22-26]. One study was not able to identify an index case suggesting an asymptomatic carrier may have transmitted the virus [25]. There were 18 cases of familial clustering in Chongqing, China where 9 asymptomatic cases transmitted the virus to others [31]. In Brunei, local asymptomatic transmission was documented in 1 household cluster and 1 school cluster with an attack rate of 25.7% (3 of 7 household contacts) and 3.4% (1 of 29 school contacts) respectively. Exposure to the index case ranged from 9-10 days in both clusters [27].

Surveillance data from Ningbo City, China reported 191 COVID-19 cases of which 30 (15.7%) were asymptomatic. For the asymptomatic cases, six out of the 146 (4.11%) close contacts tested positive for SARS-CoV-2 while for symptomatic cases 126 out of 2001 close contacts (6.3%) tested positive. There was no significant difference between the two groups for the risk of infection ($p = 0.288$) [28]. Exclusion of index cases with very high transmission rates also showed no significant difference in the transmission rates of the symptomatic and asymptomatic cases ($p=0.84$). [29]. The risk ratio (RR) of the infectivity (R_0) of the symptomatic group versus that of the asymptomatic group was 3.9 (95% CI:1.5-11.8) while the RR of probability of transmission per contact (p) was estimated at 1.5 (95% CI: 0.7-3.4) which showed that symptomatic cases were likely more infectious than asymptomatic cases [30].

A study in South Korea involving 97 COVID-19 cases (89 symptomatic, 4 pre-symptomatic cases and 4 asymptomatic cases) reported a household secondary attack rate of 16.2% for symptomatic cases and no

transmission from pre-symptomatic and asymptomatic cases [30]. An asymptomatic case admitted at an emergency department in China and another asymptomatic case that underwent an orthopedic surgery in Missouri, USA had no documented transmission to 455 contacts and 11 contacts respectively [33-34].

Pre-symptomatic and Asymptomatic Transmission within cluster (2 studies)

One study reported on pre-symptomatic and asymptomatic transmission within the same cluster. In a cluster of three families in China, two of the 88 close contacts (2.27%) of a pre-symptomatic patient became positive for SARS-CoV-2 while an asymptomatic case had 73 close contacts with only his son (1.37%) testing positive. [35]. In Italy, exposure to asymptomatic COVID-19 individuals was reported in 4 of 8 newly identified cases and pre-symptomatic transmission was documented in a family cluster involving 7 secondary cases [36].

Viral Shedding in Asymptomatic Cases (11 studies)

Although asymptomatic transmission was not documented in 4 case series, SARS-CoV-2 were detected with RT-PCR low cycle thresholds in the nasopharyngeal and/or throat swabs of asymptomatic cases which suggests the potential of these patients to transmit the virus. Viral shedding was documented up to 9 days in some cases and until 19 days in another case [37-40].

A nursing facility in Washington, USA reported that there was no significant difference ($p = 0.3$) in the real-time RT-PCR cycle threshold (Ct) values among residents with positive test results among the four symptom groups (symptomatic with atypical symptoms, typical symptoms, pre-symptomatic and asymptomatic) [41]. A follow-up surveillance conducted after one week reported an increase in the positive COVID-19 cases, but the median RT-PCR Ct values were still similar among the four groups. Viable virus was isolated from specimens collected 6 days before to 9 days after symptom onset. The transmission of infection from asymptomatic and pre-symptomatic residents was not quantified but evidence suggests potential for substantial viral shedding [42].

In contrast, a study in China among 31 virologically-confirmed COVID-19 patients reported Ct values for asymptomatic patients was significantly higher than those of pre-symptomatic patients, which indicated a lower viral load in asymptomatic patients [43]. A study of 71 hospitalized patients in South Korea also reported very high viral titers (CT value <20) in two of the three pre-symptomatic patients, suggesting infectious state even without symptoms [44]. In Vietnam, a study among 30 confirmed COVID-19 patients, viral loads were similar in symptomatic and asymptomatic patients ($p=0.223$). Asymptomatic transmission to up to four people was documented in 2 cases [45].

In a cohort of 199 COVID-19 patients in a residential treatment center in South Korea, 53 (26.6%) were asymptomatic. The mean duration of viral shedding for all patients was 24.5 days however duration of viral shedding was significantly longer for symptomatic patients compared to asymptomatic patients (25.2 days versus 22.6 days, $p < 0.01$) [46]. Comparing the asymptomatic and pre-symptomatic groups, the duration of viral shedding was similar (7 days IQR 5-14 vs. 8 days IQR 5-16). The similar duration of viral shedding suggests the possibility of disease transmission during the asymptomatic period [43].

SARS-CoV-2 was also detected on anal swab of an asymptomatic 8-year-old girl for 42 days who had negative nasopharyngeal results. It is unknown whether asymptomatic patients positive on anal swab only can transmit the infection, but her close contact never became infected [47].

Serial interval from modelling studies (7 studies)

From four modelling studies conducted in China, Japan, Germany and Singapore, the estimated mean serial interval from onset of symptoms of the index case to onset of symptoms of the secondary case were shorter than the reported incubation period of 5-9 days which suggest pre-symptomatic transmission may occur. [49-52]. Negative serial interval was documented by *Du et. al* and *Wong et. al* in 59 of 468 reports

(12.6%) and 6 of 53 reports (11.3%) respectively suggesting the possibility of asymptomatic transmission [50,52]. The estimated pre-symptomatic transmission rate was 37% (95% CI: 16-52%) for South Korea, 48% (95% CI: 32-67%) for Singapore and 62% (95% CI: 50-76) for Tianjin, China [53-54].

Ongoing Clinical Trials

There are seven ongoing clinical trials on asymptomatic transmission of COVID-19 conducted in the USA, UK, Norway, France, Hong Kong and China. The studies are mostly observational cohorts of asymptomatic healthy individuals with known COVID-19 patient contacts who are followed up for development of COVID-19 infections. The details of the clinical trials are presented in Appendix 2.

CONCLUSION

Asymptomatic and pre-symptomatic transmission of SARS-CoV-2 may occur. Studies that compared the viral load of pre-symptomatic, asymptomatic and symptomatic cases reported contradictory results. The duration of viral shedding was significantly longer for symptomatic patients compared to asymptomatic patients but similar for asymptomatic and pre-symptomatic patients. The transmission rate of pre-symptomatic or asymptomatic cases compared to symptomatic cases is unclear with conflicting results reported by different studies. Hence, prospective cohort studies are needed to validate these findings and determine the extent of asymptomatic and pre-symptomatic transmission.

Declaration of Conflict of Interest

No conflict of interest

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Table 1. Characteristics of included studies

No.	Title/Author	Study design	Country	Population	Key findings
1	<p>Presymptomatic Transmission of SARS-CoV-2 — Singapore, January 23–March 16, 2020</p> <p>Wei W, Li Z, Chiew C, Yong S, Toh M, Lee V</p>	Case series	Singapore	COVID-19 cases (n=243)	<p>All cases in Singapore from January to March 16 were included. Seven clusters of cases were identified with pre-symptomatic transmission as most likely reason for secondary cases. 10 of 243 cases (4.1%) were identified in these clusters and accounted for 6.4% of 157 locally acquired cases.</p> <p>Limitations Other unknown source may have initiated the clusters Recall and interviewer bias Underdetection of asymptomatic illness</p>
2	<p>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</p> <p>Huang L, Zhang X, Zhang X, Wei Z, Zhang L, Xu J, Liang P, Xu Y, Zhang C, Xu A</p>	Case series	China	Contacts of index case from Wuhan	<p>22 contacts of the index case (22-year-old man from Wuhan) were identified. 7 contacts were COVID-19 positive (1 relative and 6 previous classmates)</p> <p>Patient 1 (index case): 22/M, arrived from Wuhan Jan 19, developed symptoms (fever, itchy eyes) on January 22 Patient 2 (cousin): 16/F, exposed to Px 1 on Jan 19, developed symptoms on January 26 Patient 3 (previous classmate): 22/M, exposed to Px 1 on Jan 21, developed symptoms on January 24 Patient 4 (previous classmate): 22/M, exposed to Px 1 on Jan 21, developed symptoms on January 22 Patient 5 (previous classmate): 22/M, exposed to Px 1 on Jan 21, developed symptoms on January 25 Patient 6 (previous classmate): 21/M, exposed to Px 1 on Jan 21, developed symptoms on January 23 Patient 7 (previous classmate): 22/M, exposed to Px 1 on Jan 21, developed symptoms on January 23 Patient 8 (previous classmate): 23/M, exposed to Px 1 on Jan 21, developed symptoms on January 22</p>
3	<p>Asymptomatic transmission of severe acute respiratory syndrome-coronavirus 2 within a family cluster of 26 cases: Why quarantine is important?</p> <p>Mahapure KS, Kulkarni NS</p>	Case series	India	COVID-19 cases	<p>A family of four returned from Saudi Arabia on March 13. Family was quarantined on March 19 when 3 members developed symptoms. They all tested positive on March 22. A total of 368 individuals were identified on contact tracing (43 family members and 325 non-close contacts). 26 of the 43 family members (60%) tested positive for SARS-COV-2.</p>
4	<p>A cluster of the Corona Virus Disease 2019 caused by incubation period transmission in Wuxi, China</p> <p>Gao Y, Shi C, Chen Y, Shi P, Liu J, Xiao Y, <i>et al.</i></p>	Case series (collected from Public Health Emergency Reporting Management Information System)	China	Cluster of four generations (n=15) median age of 51 years old	<p>First-generation case A transmitted to the second-generation cases (B-D) 2–7 days before the onset. The second-generation cases C and D only contacted with the third-generation cases (E-I) once and infected the third-generation 6–7 days before onset. Cases E and F of the third generation had meals at the same table with cases J-N of the fourth generation for several times, 3–8 days before the onset of the disease, and J-N were infected. Case G infected case O after spending 4 hours with him 9 days prior to onset. We analyzed 6 cases of a clear history of unique exposure and onset, with a median incubation period of 10 days (range, 3–12). None of the 15 cases involved had a history of other suspected exposures.</p> <p>In this cluster, each generational case(s) transmitted to the next generation during their incubation period and the time was 2–7 days (first-second), 6-7 days (second-third), 3–8 days and 9 days (third-fourth) before their symptom onset, respectively. This confirmed that the infection can be transmitted during the pre-symptomatic period (latency period) before the symptom onset</p>
5	<p>Delivery of infection from asymptomatic carriers of</p>	Case series	Luzhou, China	Familial cluster of five patients	<p>Patient 3/4/5 – (+) travel to Wuhan Contact of all 5 cases – Jan 23-25, 30</p>

	<p>COVID-19 in a familial cluster (Pre-print)</p> <p>Ye F, Xu S, Rong Z, Xu R, Liu X, Deng P, Liu H, Xu X</p>				<p>Patient 1 – 50/F, mother of Case 2, severe pneumonia, mild symptoms of cough and fever Feb 1 then became better. Feb 3 had fever recurrence, dizziness, non-productive cough and shortness of breath</p> <p>Patient 2 – 28/M, nephew of Case 3, 4 cousin of Case 5, asymptomatic</p> <p>Patient 3 – 50/M, uncle of Case 2, had contact with Case 1 and 2, 14 days prior to her symptoms fever and cough on Feb 7</p> <p>Patient 4 – 51/F, aunt of Case 2, had contact with Case 1 and 2, 12 days prior to her symptoms on Feb 5 diarrhea and throat pain after admission but without radiographic abnormalities</p> <p>Patient 5 – 23/M, cousin of Case 2, had contact with Case 1 and 2, 14 days prior to her symptoms of fever and cough on Feb 7</p> <p>Before Case 1 presented with symptoms, Case 2-5 were asymptomatic. Case 2 did not present with signs and symptoms of infection despite COVID positive RT-PCR result, hence is an asymptomatic carrier. COVID-19 can be transmitted by asymptomatic carriers during the incubation period.</p>
6	<p>Asymptomatic and Human-to-Human Transmission of SARS-CoV-2 in a 2-Family Cluster, Xuzhou, China</p> <p>Li C, Ji F, Wang L, Wang L, Hao J, Dai M, et al.</p>	Case series	Xuzhou, China	2 family clusters (n = 7)	<p>Patient 1 (index): 56 yo/M stayed at the Hankou station in Wuhan on route to Xuzhou, China (Jan 14). Index case was confirmed with COVID 19 on Jan 25 with symptoms of fever, cough and sore throat. All the six patients who he was in contact with tested positive for COVID 19 between Jan 26-31.</p> <p>Close contact (Jan 14 -22)</p> <p>Patient 2: 32/F pregnant daughter, had contact with index case 6 days before index case presented with symptoms</p> <p>Patient 3: 21/F daughter, had contact with index case 6 days before index case presented with symptoms</p> <p>Patient 4: 42/M, son-in-law, hospitalized, had contact with index case 5 days before index case presented with symptoms</p> <p>Patient 5: 62/M, shared same ward with Px 4, had contact with index case Jan 15-18 while index case was asymptomatic, had contact with index case 5 days before index case presented with symptoms</p> <p>Patient 6: 34/M, son of Px 5, had contact with index case Jan 15-18 while index case was asymptomatic, had contact with index case 5 days before index case presented with symptoms</p> <p>Patient 7: 56/F, wife of Px 5, had contact with Px 5, 2 days before Px 4 presented with fever</p> <p>The study confirms asymptomatic and human-to-human transmission through close contacts in familial and hospital settings.</p>
7	<p>A COVID-19 Transmission within a family cluster by presymptomatic infectors in China</p> <p>Qian G, Yang N, Ma AHY, Wang L, Li G, Chen X, Chen X.</p>	Case series	Zhejiang China	Nine family members	<p>Index patients were a couple who participated in a temple activity on Jan 19. Patient 3-6 stayed with the index patients prior to index patients' onset of symptoms. Patient 3-6 had dinner with Case 5-7 while they were still asymptomatic. Except for Patient 5, all the family members with direct and indirect contact with the index cases became COVID positive. Index 2 and Case 4 remained asymptomatic.</p> <p>Patient 1 (index 1): 58/F, had fever, fatigue and headache on Jan 24, diagnosed COVID-19 on Jan 29</p> <p>Patient 2 (index 2): 60/M, remained asymptomatic, diagnosed on Feb 1 with COVID-19</p> <p>Patient 3: 32/F, daughter of index patients, had contact with Index 1 and 2 between Jan 20-23 (4 days before Index 1 had symptoms), had fever and cough on Jan 27</p> <p>Patient 4: 32/M, son in law, had contact with Index 1 and 2 between Jan 20-23 (4 days before Index 1 had symptoms), had fever on Feb 1</p> <p>Patient 5: 6/F, grandchild, asymptomatic, COVID negative, had contact with Index 1 and 2 between Jan 20-23 (4 days before Index 1 had symptoms)</p> <p>Patient 6: 13m/F, grandchild, asymptomatic, COVID positive, had contact with Index 1 and 2 between Jan 20-23 (4 days before Index 1 had symptoms)</p> <p>Patient 7: 57/F, mother of Patient 4, had dinner with Patient 3-6 on Jan 23 (4 days before Patient 3 had symptoms)</p>

					Patient 8: 57/M, father of Patient 4, had dinner with Patient 3-6 on Jan 23 (4 days before Patient 3 had symptoms) Patient 9: 76/F, grandmother of Patient 4, had dinner with Patient 3-6 on Jan 23 (4 days before Patient 3 had symptoms)
8	Indirect Virus Transmission in Cluster of COVID-19 Cases, Wenzhou, China Cai J, Sun W, Huang J, Gamber M, Wu J, He G.	Case series	China	Cluster of COVID-19 cases in a shopping mall (n=35)	7 people with close contact working in the same office tested positive with the virus. Possible index case has history of travel to Wuhan - returned in December 18, exhibited mild symptoms in January 15. Symptoms of other 6 officemates started between January 1 to 14. Additional 28 people were diagnosed with COVID-19 (7 mall staff, 10 mall customers, 11 close contacts). Only 16 patients had direct contact with case patients but other positive cases shared facilities (restrooms, elevators).
9	Potential Presymptomatic Transmission of SARS-CoV-2 Tong ZD, Tang A, Li KF, Li P, Wang HL, Yi JP, Zhang YL, Yan JB	Case series	China	Family cluster of COVID-19 cases	2 cases of COVID-19 both attended the same conference and had dinner with a teacher from Wuhan who was later found out to have COVID-19 as well. Teacher claimed he had no symptoms during the conference and dinner. No other known potential exposures to COVID were noted. The family members of the 2 cases were later positive with COVID-19 but did not have symptoms.
10	A familial cluster of infection associated with the 2019 novel coronavirus indicating potential person-to-person transmission during the incubation period Yu P, Zhu J, Zhang Z, Han Y, Huang L.	Case series	China	Family cluster of COVID-19 cases (n=4)	4 COVID-19 cases from one family unit The first case who developed symptoms had limited mobility and did not leave the house in 2 weeks prior to illness. He only had contact with the other 3 cases (2 of which arrived 5 days earlier from Wuhan) who developed symptoms after him.
11	A locally transmitted case of SARS-CoV-2 infection in Taiwan Liu YC, Liao CH, Chang CF, Chou CC, Lin YR	Case report	Taiwan	52-year-old woman from Taiwan with travel history to Wuhan, China and her 50-year-old husband	The index case presented with fever and myalgia 5 days after her arrival from China. At the same time, her husband presented with rhinorrhea and both sought medical consult. Both tested positive for COVID-19. The study suggests transmission of the disease while the index case was asymptomatic. Patient 1 (Index case): 52/F, travelled from Wuhan, China, had fever and myalgia on Jan 25 Patient 2: 50/M, husband of index case, had contact with index case on Jan 21, 4 days before index case had symptoms, presented with rhinorrhea on Jan 25
12	Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, Zimmer T, Thiel V, Janke C, Guggemos W, Seilmaier M, Drosten C, Vollmar P, Zwirgmaier K, Zange S, Wölfel R, Hoelscher M.	Case series	Germany	COVID-19 cases (n=4)	2 cases (Patient 1&2) met with a Shanghai business partner who did not exhibit symptoms during her stay in Germany. However, she became ill on her flight back to China. The other 2 cases (Patient 3&4) had contact with Patient 1 while he was still asymptomatic.
13	Characteristics of a family cluster of Severe Acute Respiratory Syndrome	Case series	China	Family cluster of COVID-19 cases	The index patient (38-year-old, female) visiting from Hangzhou from January 23-February 2 and transmitted the disease to her family members while she was in the pre-symptomatic phase.

	<p>Coronavirus 2 in Henan, China</p> <p>Jiang Y, Niu W, Wang Q, Zhao H, Meng L, Zhang C</p>				<p>Patient 1 – index case, 38/F, symptoms and positive on Feb 3</p> <p>Patient 2 – 87/F, grandmother of Px 1, lived with Px 1, symptoms on Feb 2, positive test on Feb 8</p> <p>Patient 3 – 66/M, father of Px 1, lived with Px 1, symptoms on Feb 3, radiologic change but negative test</p> <p>Patient 4 – 68/F, mother of Px 1, lived with Px 1, symptoms on Feb 4, radiologic change but negative test</p> <p>Patient 5 – 58/M, uncle of Px 1, exposure Jan 24 & 27, positive test on Feb 8, asymptomatic</p> <p>Patient 6 – 59/F, aunt of Px 1, exposure Jan 24 & 27, positive test on Feb 8, asymptomatic</p> <p>Patient 7 – 55/M, uncle of Px 1, exposure Jan 24 & 27, symptoms and radiologic change Feb 8, negative test</p> <p>Patient 8 – 34/F cousin of Px 1, exposure Jan 24, symptoms on Feb 2, radiologic change but negative test</p> <p>Patient 9 – 34/M, husband of Px 8, exposure Jan 27, symptoms on Feb 8, positive test on Feb 11</p> <p>Patient 10 – 56/M, Father of Px 9, exposure Jan 27, symptoms on Feb 2, positive test on Feb 5</p> <p>Patient 11 -57/F, mother of Px 9, exposure Jan 27, positive test on Feb 10, asymptomatic</p> <p>Patient 12 – 34/F, exposure Jan 27, sister of Px 9, symptoms Feb 6, positive test on Feb 8</p> <p>Patient 13 – 9/M, son of Px 12, symptoms and positive test Feb 10</p>
14	<p>Transmission of COVID-19 in the terminal stage of incubation period: a familial cluster, International Journal of Infectious Diseases</p> <p>Li P, Fu JB, Li KF, Chen Y, et al.</p>	Case series	China	Family cluster of COVID-19 cases (n=6_	<p>Patient A (56-year-old, male) was identified as a close contact of COVID-19 case (a relative diagnosed on Feb 4 and lived with him from January 26-28). He tested positive on Feb 6 and developed symptoms on Feb 7. Close contacts of Patient A were 5 family members he visited and lived with in Zhoushan on Jan 31-Feb 3. Of the 5 family members, 4 (80%) tested positive for SARS-COV-2.</p> <p>Patient A – 56/M, index patient, positive on Feb 6, symptoms on Feb 7</p> <p>Patient B – 66/M, father-in-law of Px A, symptoms and positive test on Feb 9</p> <p>Patient C – 64/F, mother-in-law of Px A, symptoms and positive test on Feb 9</p> <p>Patient D – 42/F, sister-in-law of Px A, symptoms and positive test on Feb 9</p> <p>Patient E – 7/F, daughter of Px A, positive test on Feb 9, asymptomatic</p> <p>Patient F – 41/F, wife of Px A, negative test and asymptomatic</p>
15	<p>A SARS-CoV-2 familial cluster infection reveals asymptomatic transmission to children</p> <p>Chen M, Fan P, Liu Z, et al.</p>	Case series	China	A cluster of COVID-9 cases	<p>A 34-year-old, woman, spent a few days in Wuhan and returned to Xianyang on January 22. Routine examination was done on January 30 when here daughter presented with COVID symptoms and tested positive. The index case had negative RT-PCR but showed ground-glass opacities in right lower lobe and was quarantined. She developed symptoms on February 6 and tested positive on Feb 9. She was exposed to her two children who developed the disease from Jan 22 to Jan 30.</p> <p>Patient 1 – index case, 34/F, CT scan findings on Jan 30, symptoms on Feb 6, positive test on Feb 9</p> <p>Patient 2 – 8/F, daughter of Px 1, symptoms and positive test on Jan 30</p> <p>Patient 3 – 9/M, son of Px 1, symptoms and positive test on Jan 31</p> <p>Patient 4 – husband of Px 1, negative test on Jan 31</p>
16	<p>Familial cluster of COVID-19 infection from an asymptomatic</p> <p>Zhang J, Tian S, Lou J, Chen Y.</p>	Case series	China	Familial cluster of five patients (index patient and 4 close contacts)	<p>Patient 1 (index case) was a 48-year-old male who went to Wuhan, China came back to Beijing on Jan 19. He did not have signs and symptoms of the disease before his family members each became sick. He went to hospital for assessment on Jan 23. All 5 patients (index + 4 contacts) tested positive for COVID 19. Index case and Px 2 remained asymptomatic.</p> <p>Patient 2: 45/F, wife of index case, had fever on Jan 23, had contact with index case since Jan 19</p> <p>Patient 3: asymptomatic, had contact with index case since Jan 19</p> <p>Patient 4: 38/M, nephew of index case, started to have fever and fatigue on Jan 22 after meeting his uncle on Jan 19</p> <p>Patient 5: mother of Px 3, had fever and joint pain on Jan 27, had contact with Px 3 since Jan 19</p> <p>Asymptomatic cases should be identified and isolated appropriately to prevent disease spread to close contacts.</p>

17	The different clinical characteristics of corona virus disease cases between children and their families in China - the character of children with COVID-19 Su L, Ma X, Yu H, Zhang Z, Bian P, Han Y, et al.	Case series	Jinan, China	Nine children and their families with COVID-19 infection	There were 2 adult COVID-19 patients without clear epidemiologic source of possible contact with anyone diagnosed with COVID-19, no known contact with someone who came back from Wuhan, or any person with respiratory symptoms. The study suggest that asymptomatic carriers may infect other people.
18	Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. Hu Z, Song C, Xu C, Jin G, Chen Y, Xu X, Ma H, Chen W, Lin Y, Zheng Y, Wang J, Hu Z, Yi Y, Shen H.	Case series	China	Asymptomatic COVID-19 cases (no symptoms on testing) screened from close contacts (n=24)	24 cases: 5 developed symptoms, 7 showed no symptoms and normal CT scan findings CT scan findings: 12 had ground glass opacities, 5 strip shadowing 3 family members of Case 13 (no symptoms and normal CT scan findings) were diagnosed with COVID-19 and exhibited symptoms. All 3 denied history of travel or contact with confirmed or suspected COVID-19 patient apart from Case 13. Relative 1 (Wife of Case 13): Fever, cough, fatigue, vomiting (8 days after return of Case 13 from Hubei) Relative 2 (Son of Case 13): Fever, cough (5 days after return of Case 13 from Hubei) Relative 3 (Daughter-in-law of Case 13): Fever, cough, fatigue, arthralgia (4 days after return of case 13 from Hubei)
19	Presumed Asymptomatic Carrier Transmission of COVID-19 Bai Y, Yao L, Wei T, Tian F, Jin DY, Chen L, Wang M.	Case series	China	Family cluster of COVID-19 cases (n=6)	5 COVID-19 patients were exposed to an asymptomatic COVID (+) case who had history of travel from Wuhan. All 5 patients were symptomatic with characteristic CT scan findings. Patient 2 met the primary case on January 10 and 13 while Patient 3-6 met Patient 1 on January 13. None of the patients had travel to Wuhan or contact with anyone else from Wuhan. However, initial COVID test of the asymptomatic case was negative and was only positive on repeat testing which was about 19 days after contact with the patients. Patient 1: primary case traveled from Wuhan on January 10 Patient 2: developed symptoms January 23 Patient 3: developed symptoms January 25 Patient 4: developed symptoms January 26 Patient 5: developed symptoms January 25 Patient 6: developed symptoms January 17 Incubation period: 4-13 days
20	Transmission and clinical characteristics of coronavirus disease 2019 in 104 outside-Wuhan patients, China Qiu C, Deng Z, Xiao Q, et al.	Case series	China	COVID-19 cases admitted at hospitals in Hunan province from Jan 23-Feb 23 and their contacts	Of 104 COVID-19 patients admitted, 1 was asymptomatic (0.96%) with no documented transmission. 4 asymptomatic cases were identified on contact tracing with 2 cases transmitting the infection to 3 relatives each. However, one of the 4 cases were not tested for SARS-CoV-2 but was assumed to be an asymptomatic carrier because he was identified as the index case of three of his relatives who tested positive.
21	Asymptomatic transmission of SARS-CoV-2 and implications for mass gatherings Wong J, et al.	Case series	Brunei	Asymptomatic COVID-19 cases and their contacts	A religious event in Malaysia on February 28 to March 2 attended by 16,000 people became an international super-spreader event (SSE). Nineteen of the 75 people (25.3%) who attended tested positive for SARS-CoV-2 upon return to Brunei. Two clusters connected to this super-spreader event showed local asymptomatic transmission. Cluster A (household cluster) Patient 1 – 30/M, index patient, traveled to Malaysia on Feb 27 for SSE and returned March 3, positive March 10 Patient 2 – 32/F, wife of Px 1, symptoms Mar 9, positive Mar 12 Patient 3 – 10mo/F, daughter of Px 1, symptoms Mar 11, positive Mar 12 Patient 4-8 – other household contacts of Px 1, negative for SARS-CoV-2

					<p>Cluster B (school cluster)</p> <p>Patient 1 – 13/F, father attended SSE and tested positive on Mar 11, positive on Mar 11</p> <p>Patient 2 – 39/F, teacher of Px 1, exposed to Px 1 from Mar 3 to 12, positive on Mar 13, symptoms on Mar 16</p> <p>Patient 3-30 – other school contacts of Px 1, negative for SARS-CoV-2</p>
22	<p>The epidemiological characteristics of infection in close contacts of COVID-19 in Ningbo city</p> <p>Chen Y, Wang A, Yi B, et. al.</p>	Case series	China	COVID-19 cases in Ningbo, China and their close contacts	<p>Surveillance data from January 20 to March 6 in Ningbo City identified 191 COVID-19 primary/index cases (161 symptomatic, 30 asymptomatic). The symptomatic cases had 2001 close contacts with 126 testing positive for SARS-CoV-2 while asymptomatic cases had 146 close contacts with 6 testing positive. The infection rate of close contacts (number of cases per contact) was calculated at 6.30% for symptomatic cases and 4.11% for asymptomatic cases. The difference was not statistically significant ($\chi^2 = 1.128, P > 0.05$).</p> <p>Timing of contact with symptomatic cases to determine if pre-symptomatic transmission occurred was not investigated.</p>
23	<p>The relative transmissibility of asymptomatic COVID-19 infections among close contacts.</p> <p>He D, Zhao S, Lin Q, Zhuang Z, et. al.</p>	Statistical modelling analysis	Hong Kong	COVID-19 cases and their contacts	<p>Based on data from study of Chen et. al., the reproduction number (ratio of the case counts in the first generation divided by those in the second generation) was calculated as 0.76 (126/161) and 0.20 (6/30) for the symptomatic and asymptomatic groups respectively with RR of 3.9 (95%CI: 1.5-11.8).</p> <p>From the classic 'SEIR' modelling framework, the RR of the risk (probability) of transmission per contact of the symptomatic group against the asymptomatic group was estimated at 1.5 (95%CI: 0.7-3.4). Symptomatic cases may be more likely to be infectious, but the difference is not statistically significant.</p> <p>Results may be due to difference in the contact tracing surveillance scheme implemented on the two groups of the primary cases. In such case, the RR estimate may be higher than its true value.</p>
24	<p>Comparison of transmissibility of coronavirus between symptomatic and asymptomatic patients: Reanalysis of the Ningbo COVID-19 data</p> <p>Yin G, Jin H</p>	Statistical modelling analysis	China	COVID-19 cases and their contacts	<p>After excluding cases associated with super-spreaders from the data of Chen et. al., the odds ratio and difference in transmission rates were not statistically significant by Fisher's exact test between symptomatic and asymptomatic cases. The odds ratio of transmission rates of coronavirus between the symptomatic and asymptomatic patients is 1.2 with a 95% confidence interval [0.5, 2.8].</p>
25	<p>Characterization of an asymptomatic cohort of SARS-COV-2 infected individuals outside of Wuhan, China</p> <p>Wang Y, Tong J, Qin Y, et. al.</p>	Retrospective cohort	China	Asymptomatic COVID-19 cases	<p>Of the 279 COVID-positive contacts of COVID-19 cases identified between January to March 2020, 63 (23%) were asymptomatic. Among the asymptomatic cases, there were 18 cases of familial clustering in which 9 cases transmitted the virus to others.</p>
26	<p>Coronavirus Disease Outbreak in Call Center, South Korea</p> <p>Park SY, Kim YM, Yi S, Lee, S, et. al.</p>	Case series	South Korea	Residents, employees and visitors in a building in Seoul, South Korea and their household contacts	<p>In a building in Seoul, 97 of 1,143 tested positive for SARS-CoV-2. Among the 97 patients, 89 (91.7%) were symptomatic, 4 (4.1%) were pre-symptomatic and 4 (4.1%) were asymptomatic. A total of 225 household contacts were identified from the positive cases. COVID-19 occurred in 34 household contacts of symptomatic cases. None of the 11 household contacts of pre-symptomatic cases and 4 household contacts of asymptomatic cases tested positive for SARS-CoV-2.</p> <p>The actual transmissibility of pre-symptomatic cases or asymptomatic cases may have not been detected due to mass testing, self-quarantine and isolation measures.</p>
27	<p>A study on infectivity of asymptomatic SARS-CoV-2 carriers</p>	Case Report	China	Asymptomatic COVID-19 case and her contacts	<p>An asymptomatic COVID-19 case admitted for worsening congenital heart disease had a total of 455 contacts (224 hospital staff, 196 family members, 35 patients) who were either exposed to the index patient or was around the emergency department observation unit (EDOU).</p>

	Gao M, Yang L, Chen X, Deng Y, Yang S, Xu H, Chen Z, Gao X				<p>Of the 35 patients, none tested positive for SARS-CoV-2 despite multiple tests. Median contact time was four days and longest was 21 days. All patients wore masks and were admitted at the infectious ward for medical isolation. Patient bed in the EDOU are placed 1.2 meters apart.</p> <p>None of the 196 family members who visited the ED tested positive for COVID-19. All contacts were quarantined for 14 days. Family members also wore masks while visiting the ED.</p> <p>Of the 224 hospital staff identified, 59 (26.3%) were doctors and 101 (45.1%) were nurses. Others were security guards, cleaners, transportation personnel, etc. All personnel in the ED were required to wear PPE such as N95 masks, isolation gowns and googles. None of the hospital staff tested positive or developed symptoms.</p>
28	Healthcare Personnel Exposure to a Patient with Asymptomatic SARS-CoV2 Infection during a Prolonged Surgical Intervention Lucar J, Navalkele, B., et al.	Case report	USA	Asymptomatic COVID-19 case	<p>A 17-year-old male with no medical problems underwent an orthopedic surgery in March 2020 after being in a vehicular accident. Duration of general anesthesia was 6 hours and 5 minutes. When the procedure was almost completed, the lead surgeon was informed of ground glass opacities on the patient's chest CT-scan. On consultation with the COVID response team, OR staff changed their attire to COVID-19 PPE. Post-op, the patient was placed on contact and droplet precautions. The patient was tested for COVID-19 on post-op day 2 due to brief post-operative cough which came out positive. Out of the 11 healthcare workers, staff exposed during the surgery, only one was tested for COVID due to symptoms of dry cough and result was negative. The rest of the team did not develop any symptoms. No nosocomial transmission of SARS-CoV-2 was detected in the institution up to 32 days after exposure event.</p>
29	Transmission potential of asymptomatic and paucisymptomatic SARS-CoV-2 infections: a three-family cluster study in China. Jiang X, Zhang XL, Zhao XN, Li CB, et al.	Case series	China	3 family clusters	<p>Patient 1 and 2 had travel to Xiaogan, a city adjacent to Wuhan, from Dec 29, 2019 to Jan 15, 2020. They had changed trains in Wuhan. No other patients had known travel history.</p> <p>Patient 1 – 62/F, Jan 12 had cough and rhinorrhea, confirmed SARS-CoV-2 Jan 21 Patient 2 – 65/M, husband of patient 1, Jan 17 had symptoms, confirmed SARS-CoV-2 Jan 21 Patient 3 – 37/M, son, household contact initially asymptomatic, confirmed SARS-CoV-2 and developed cough and itchy throat on Jan 23 Patient 4 – 35/F, daughter-in-law, household contact initially negative but confirmed SARS-CoV-2 on repeat swab on Jan 25, asymptomatic</p> <p>Patient 5 – 53/F, mother of patient 4, close contact of patient 3 & 4 and stayed for 1 night at the house of Patient 1-4 on Jan 21. She was asymptomatic, confirmed SARS-CoV-2 Jan 24 Patient 6 – 28/M, son of Patient 5, had fever and was hospitalized on Jan 25, confirmed SARS-CoV-2</p> <p>Patient 7 – 35/M, close contact of patient 3 at the factory and dined with Patient 3 on Jan 18, confirmed SARS-CoV-2 Jan 25, only had occasional cough Patient 8 – 3m/F, daughter of patient 7, asymptomatic, confirmed SARS-CoV-2 Jan 29</p> <p>A total of 88 contacts of Patient 3 were identified before he became symptomatic, and two contacts (Patients 5 and 7) tested positive for SARS-CoV-2. Seventy-three close contacts of Patient 5 were identified, and one contact (Patient 6) tested positive for SARS-CoV-2. The crude estimate of attack rate is 2.27% (2/88) during the pre-symptomatic phase of Patient 3 and 1.37% (1/73) for asymptomatic Patient 5.</p>
30	Suppression of COVID-19 outbreak in the municipality of Vo', Italy Lavezzo E, Franchin E, Ciavarella C, et al.	Cross-sectional	Italy	Residents of Vo, Italy (n=2812, 2343)	<p>At the first survey, 73 of 2812 subjects tested positive (2.6%). The second survey reported 29 of 2,343 subjects were positive (1.2%). Asymptomatic infection was 41.1% and 44.8% in the first and second survey respectively. 8 new cases were identified in the second survey, 4 of which were exposed to asymptomatic cases. Pre-symptomatic transmission was also documented in a family cluster with 7 secondary cases (3 living in the same household, 4 attended a gathering four days prior to symptom onset).</p>

31	SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients Zou L, Ruan F, Huan M, et al.	Case series	China	COVID-19 cases (n=17)	One of the 17 cases monitored was asymptomatic. However, viral load detected from RT-PCR of throat and nasopharyngeal swabs were similar with symptomatic cases.
32	A Well Infant with Coronavirus Disease 2019 (COVID-19) with High Viral Load Kam KQ, Yung CF, Cui L, Lin Tzer Pin R, Mak TM, Maiwald M, Li J, Chong CY, Nadua K, Tan NWH, Thoon KC.	Case report	Singapore	6 month old COVID (+) infant	Aside from 1 episode of fever, infant was asymptomatic but nasopharyngeal swabs were positive for COVID-19 up to 16 days after admission. Stool was also positive for COVID-19 but infant had no gastrointestinal symptoms. No asymptomatic transmission was recorded.
33	Severe Acute Respiratory Syndrome Coronavirus 2 Shedding by Travelers, Vietnam, 2020 Le TQM, Takemura T, Moi ML, Nabeshima T, Nguyen LKH, Hoang VMP, et al.	Case series	Vietnam	2 clusters of patients 1 st cluster: travelers 2 nd cluster: patients with close contact with the travelers (age range 3 months – 55 years old)	In the 1 st cluster, eight employees were sent to Wuhan, China for training for 2 months. 6/8 travelers developed signs and symptoms within 10 days of their return to Vietnam and were diagnosed with COVID 19. The remaining 2 were quarantined and turned out negative. In the 2 nd cluster, 11/12 patients had signs and symptoms and tested positive for COVID-19. Clinical signs, including fever and cough, were demonstrated by 11 patients an average of 9.9 (± 5.4) days after travel or close contact with COVID-19 patients, indicating an incubation period of 1–2 weeks after exposure. Virus shedding was detected from day 1 after illness onset through day 19 (4.6 days) after potential initial exposure. There was one asymptomatic patient (55 yo/M) who demonstrated virus shedding up to 9 days. This indicates potential virus transmission in the absence of clinical signs and symptoms.
34	The enlightenment from two cases of asymptomatic infection with SARS-CoV-2: is it safe after 14 days of isolation? Mao ZQ, Wan R, He LY, Hu YC, Chen W	Case series	China	COVID-19 cases	2 asymptomatic infections were identified from 78 laboratory confirmed cases. These cases were identified from contact tracing. Both never developed any symptoms. They were discharged after 9 days and 25 days respectively after 2 consecutive negative RT-PCR tests. Patient 1: 36-year-old radiology technician performed chest CT scan on a COVID-19 patient on January 2. He tested positive on RT-PCR but did not have any symptoms. He was isolated on February 7 and discharged after 2 negative COVID-19 test results on February 14 and 16. Patient 2: The 19-year-old son of a 45-year-old woman who had COVID-19 after having dinner with a business partner from Wuhan 10 days ago tested positive for COVID-19. He was isolated on January 27 and discharged on February 21 after two negative test results.
35	Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled Nursing Facility — King County, Washington, March 2020. Kimball A, Hatfield KM, Arons M, James A, Taylor J, Spicer K, et al.	Prospective single cohort	King County, Washington, USA	Residents of a long-term care skilled nursing facility (SNF) in King County, Washington (n = 76)	There were 23 (30.3%) residents who tested positive by RT-PCR of which 13 (56.5%) were asymptomatic. The asymptomatic patients were reassessed after one week, of which 10 developed symptoms and were categorized as pre-symptomatic during the initial testing. Three remained asymptomatic. The mean interval from testing to symptom onset in the pre-symptomatic residents was 3 days. Real-time RT-PCR Ct values for both genetic markers among residents with positive test results for SARS-CoV-2 ranged from 18.6 to 29.2 (symptomatic [typical symptoms]), 24.3 to 26.3 (symptomatic [atypical symptoms only]), 15.3 to 37.9 (pre-symptomatic), and 21.9 to 31.0 (asymptomatic). There were no significant differences between the mean Ct values in the four symptom status groups (p = 0.3).

					<p>Transmission from asymptomatic and pre-symptomatic residents, who were not recognized as having SARS-CoV-2 infection prior to the testing were not isolated. Unrecognized asymptomatic and pre-symptomatic infections may contribute to further spread.</p> <p>Study was limited by the possible inaccuracy of symptom ascertainment among residents with cognitive impairment and other disabilities. The population involves the older age group with underlying medical conditions. Results may not hold true for general population.</p>
36	<p>Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility</p> <p>Arons M, Hatfield KM, Reddy SC, Kimball A, et. al.</p>	Prospective single cohort	King County, Washington, USA	Residents of a long-term care skilled nursing facility (SNF) in King County, Washington (n = 89)	<p>In a nursing facility in Washington, USA, 48 of the 89 residents tested positive for SARS-CoV-2 of which 17 (35%) had typical symptoms, 4 (8%) had atypical symptoms, and 27 (56%) had no new symptoms.</p> <p>Eighty nine percent (24/27) who were initially asymptomatic developed symptoms within the next 7 days (median 4 days, IQR 3-5 days) and were reclassified as pre-symptomatic. The median RT-PCR cycle threshold (Ct) values for the four symptom status groups were similar (asymptomatic residents, 25.5; pre-symptomatic residents, 23.1; residents with atypical symptoms, 24.2; and residents with typical symptoms, 24.8). Viral growth was observed for specimens obtained from 62.5% of residents with typical symptoms (10/16), 75% with atypical symptoms (3/4), 71% of pre-symptomatic residents (17/24), and 33% of asymptomatic residents (1/3).</p> <p>Ct values consistent with a high viral load were identified among residents who tested positive before typical symptom onset (median Ct value among 26 observations, 24.0, IQR 20.4 to 28.5) and those who tested positive 7 or more days after typical symptom onset (median Ct value among 8 observations, 25.0; IQR, 21.3 to 28.2). Viable virus was isolated from specimens collected 6 days before to 9 days after symptom onset.</p> <p>The transmission of infection from asymptomatic and pre-symptomatic residents was not quantified but evidence suggests potential for substantial viral shedding.</p>
37	<p>Viral dynamics in asymptomatic patients with COVID-19</p> <p>Zhou R, Li F, Chen F, Liu H, Zheng J, Lei C, Wu X.</p>	Prospective cohort	China	Virologically confirmed to have COVID-19 but were asymptomatic on admission (n=31)	<p>22/31 (71%) developed symptoms after admission, 9 (29%) remained asymptomatic during hospitalization</p> <p>Cycle threshold (Ct) values of asymptomatic patients (39.0, IQR 37.5-39.5) was significantly higher than those of presymptomatic patients (34.5, IQR 32.2-37.0), which indicated a lower viral load in asymptomatic patients.</p> <p>Viral load of asymptomatic patients peaked within the 1st week of admission while for presymptomatic patients peaked during the 2nd week of hospitalization.</p> <p>Duration of viral shedding remained similar between the two groups (7 days IQR 5-14 vs. 8 days IQR 5-16).</p>
38	<p>Viral kinetics of SARS-CoV-2 in asymptomatic carriers and presymptomatic patients</p> <p>Kim SE, Jeong HS, Yu Y, Shin SU, Kim S, Oh TH, Kim UJ, et. al.</p>	Prospective cohort	South Korea	Laboratory-confirmed COVID-19 cases admitted at a university hospital (n=71)	<p>From 71 hospitalized patients, three presymptomatic patients developed symptoms within 14 days of quarantine while 10 remained asymptomatic patients</p> <p>In two of the three incubation period patients, the viral titer in the presymptomatic period was very high (Ct value <20), which may indicate that patients who have COVID-19 may already be infectious when there were no symptoms yet.</p> <p>The median days to first negative RT-PCR in the entirely asymptomatic carriers was 4.5 (range 2.0–8.5) days and all asymptomatic carriers reached a first Ct>35 RT-PCR within 14 days after diagnosis. Although the presence of viral RNA in specimens does not distinguish between infective and non-infective viruses, live virus could not be detected by culture in Ct >35.</p>
39	<p>The natural history and transmission potential of asymptomatic SARS-CoV-2 infection</p>	Prospective cohort	Vietnam	COVID-19 patients admitted to Cu Chi Hospital (n=30)	<p>Of the 30 patients, 17 had mild respiratory disease and 13 were asymptomatic. No progression of symptoms was noted in both groups. Demographic and laboratory characteristics of both groups were similar on enrollment.</p> <p>Viral detection in NPS samples on enrollment were more likely in the symptomatic group (62% in asymptomatic vs 100% in symptomatic, p=0.02) but similar for both groups in saliva samples (64% in</p>

	Nguyen VVC, Vo TL, et al.				asymptomatic group vs 81% in symptomatic group, $p=0.56$). Among those who tested positive on enrollment, viral loads in both NPS and saliva samples were similar in symptomatic and asymptomatic patients ($p=0.223$). During follow-up, asymptomatic patients were found to have lower viral loads than symptomatic patients ($p=0.027$ for difference over first 19 days) and were less likely to test positive for the RT-PCR test ($p<0.001$ for difference over first 19 days) with the difference most pronounced during the first week of follow-up. Two asymptomatic cases transmitted the infection to up to four people.
40	Asymptomatic infection and atypical manifestations of COVID-19: Comparison of viral shedding duration. Noh JY, Yoon JG, Seong H, Choi WS, Sohn JW, Cheong HJ, et al.	observational cohort	South Korea	Patients with COVID-19 in a residential treatment center (n=199)	Among the 199 patients, 53 (26.6%) were asymptomatic Among the study population, mean duration of viral shedding was 24.5 days. Duration of viral shedding was longer in symptomatic patients than in asymptomatic patients (25.2 days versus 22.6 days, $p < 0.01$) Among symptomatic patients, patients with chest pain had significantly longer viral shedding (30.0 days versus 25.0 days, $p = 0.01$). Prolonged viral shedding was also found in patients who complained of sputum (26.8 days versus 24.6 days, $p = 0.03$).
41	Asymptomatic SARS-CoV-2 infected case with viral detection positive in stool but negative in nasopharyngeal samples lasts for 42 days Jiang X, Luo M, Zuo Z, Wang X, Chen C, Qiu J.	Case series	China	Familial cluster	Patient 1 – 8/F, travelled from Wuhan to Bishan district with her mother and 5 others, nasopharyngeal swab negative for SARS-CoV-2 on Feb 9, anal swab was positive but the nasopharyngeal swab was negative Feb 19, anal swab became negative on March 31 Patient 2 – 31/M, father of patient 1, symptoms on Jan 20, confirmed Jan 25 Patient 3 – mother of patient 1, COVID negative Patient 4 – 39/F, co-traveler, symptoms started Jan 18, confirmed on Jan 24 Patient 5 – co-traveler, healthy Patient 6 – co-traveler, healthy Patient 7 – co-traveler, healthy Patient 8 – co-traveler, healthy
42	Temporal dynamics in viral shedding and transmissibility of COVID-19. He X, Lau EHY, Wu P, et. al.	Statistical modeling analysis	China	Laboratory confirmed COVID-19 (94 cases)	Serial interval estimated to have mean of 5.8 days and median of 5.2 days. Infectiousness started from 2.5 days before symptom onset and reached its peak 0.6 days before symptom onset. Proportion of transmission before symptom onset was 44%. Infectiousness was estimated to decline relatively quickly within 7 days of illness onset. Viral shedding may begin 2-3 days before symptoms. But no data on viral shedding before symptom onset because samples were taken on day of onset of illness.
43	Serial interval of novel coronavirus (COVID-19) infection Nishiura H, Linton N, Akhmetzhanov A.	Statistical modeling analysis	Japan, China, Germany	Primary and secondary cases of COVID-19 (n=28 infected-infectee pairs)	Serial interval: median of 4 days, mean of 4.7 days with SD of 2.9 days. The estimated median serial interval is shorter than initial estimated incubation period of 5 days reported by studies. Pre-symptomatic transmission is likely to occur and may even be more frequent when serial interval is shorter than incubation period.
44	The serial interval of COVID-19 from publicly reported confirmed cases Du Z, Xu X, Wu Y, Wang L, Cowling BJ, Meyers LA	Statistical modeling analysis	China	COVID-19 cases (n=468)	Mean serial interval of 3.96 with SD of 4.75. 59/468 reports (12.6%) noted that the infectee developed symptoms earlier than the infector yielding negative serial intervals. Negative serial intervals suggest possibility of transmission of asymptomatic or mildly symptomatic cases. Potential source bias:

					<p>Data restricted to online reports of confirmed cases – rapid isolation may prevent longer serial intervals Distribution of serial intervals varies throughout an epidemic – estimates were based of reports on the outset of outbreak Identity of infector and timing of events were based on an individual's recall of events Travel related delays in transmission</p> <p>Findings should be interpreted as working hypotheses regarding the infectiousness of COVID-19 requiring further validation as more data become available.</p>
45	<p>Transmission interval estimates suggest pre-symptomatic spread of COVID-19</p> <p>Tindale LC, Coombe M, Stockdale JE, Garlock ES, Lau WYV, Saraswat M, Yen-Hsiang BL, Zhang L, Chen D, Wallinga J, Colijn C</p>	Statistical modelling analysis	Singapore Tianjin, China	<p>COVID-19 clusters n = 228 (93 Singapore, 135 Tianjin)</p>	<p>Mean incubation period: Singapore – 7.1 days (6.13, 8.25) Tianjin – 9 days (7.92, 10.2)</p> <p>Mean serial interval: Singapore – 4.56 (2.69, 9.42) Tianjin – 4.22 (3.43, 5.01)</p> <p>Early in outbreak, transmission of infection was on the average 2.55 days and 2.89 days before onset of symptoms for Singapore and Tianjin respectively.</p> <p>Estimated serial intervals are shorter than incubation period suggesting that pre-symptomatic transmission is happening.</p> <p>Limitations: Times of exposure and the presumed infectors are uncertain All possible transmission configurations not captured No adjustment for truncation (shorter serial intervals are likely to be observed first)</p>
46	<p>High proportion of asymptomatic and presymptomatic COVID-19 infections in travelers and returning residents to Brunei</p> <p>Wong J, Abdul Aziz ABZ, Chaw L, et al.</p>	Rapid Communication/ Modeling study	Brunei	COVID-19 cases	<p>From the 138 local cases of COVID-19 in Brunei, 16 (12%) were asymptomatic while 42 (30%) were presymptomatic.</p> <p>All local transmission had contact history and the short serial intervals between the infector-infectee pairs suggest possible presymptomatic transmission.</p> <p>International arrivals to Brunei were tested and quarantined for 14 days from which 30 were positive for COVID-19 (11 presymptomatic and 3 asymptomatic), which suggest that almost half of the imported cases did not present with clinical signs and symptoms upon arrival. These cases would be missed by symptom-based screening at points of entry.</p>
47	<p>Transmission onset distribution of COVID-19 in South Korea</p> <p>Chun JY, Baek G, Kim Y.</p>	Serial model (Bayesian methods)	South Korea	Inferred transmission onset time from 89 infector-infectee pairs, 72 pairs were included in the analysis	<p>Estimated the median transmission onset to be 1.31 days (standard deviation, 2.64 days) after symptom onset with peak at 0.72 days before symptom onset.</p> <p>The pre-symptomatic transmission proportion was 37% (95% credible interval [CI], 16–52%).</p> <p>The median incubation period was estimated to be 2.87 days (95% CI, 2.33–3.50 days)</p> <p>Median serial interval to be 3.56 days (95% CI, 2.72–4.44 days).</p> <p>Results showed that the transmission of COVID-19 could start before the symptom onset, and the probability peaked as the symptom start.</p>

					Among the 89 infectors, 4 cases (4.5%) were asymptomatic when diagnosed, but out of 89 infectees, 16 cases (18.0%) were asymptomatic when diagnosed.
48	Estimating the generation interval for COVID-19 based on symptom onset data Ganyani T, Kremer C, Chen D, et al.	Statistical modelling analysis	Singapore Tianjin, China	Clusters of confirmed cases in Singapore and Tianjin, China	The mean generation interval was 5.20 (95%CI 3.78-6.78) days for Singapore and 3.95 (95%CI 3.01-4.91) days for Tianjin, China based on previously reported incubation period with mean 5.2 and SD 2.8 days. The proportion of pre-symptomatic transmission was 48% (95%CI 32-67%) for Singapore and 62% (95%CI 50-76%) for Tianjin, China.

Table 2. Characteristics of clinical trials

No.	Clinical Trial ID / Title	Status	Start and estimated primary completion date	Study design	Country	Population	Intervention Group(s)	Comparison Group(s)	Outcomes
No.	Clinical Trial ID / Title	Status	Start and estimated primary completion date	Study design	Country	Population	Intervention Group(s)	Comparison Group(s)	Outcomes
1	NCT04318431 Prevalence of SARS -Cov2 Carriage in Asymptomatic and mildly-symptomatic Children (COVILLE)	Not yet recruiting	April 2020 – June 2020	Cross-sectional, Prospective, Multicentre, Observational Study	France	Asymptomatic children 6 months to 15 years old (n = 600)	Diagnostic Test: Data collection and rhinopharyngeal swab	None	Proportion of asymptomatic children or children with mild respiratory symptoms within 14 days Secondary: Confirmed Cov2-SARS cases by age Confirmed Cov2-SARS cases by symptoms Viral load Other respiratory viruses
2	NCT04328129 Household Transmission Investigation Study for COVID-19 in French Guiana (EPI-COVID-19)	Recruiting	3/23/20 – 3/23/22	Prospective cohort	French Guiana	Primary case and family household contacts (n = 450) Exclusion: pregnant women or breastfeeding	Diagnostic test: blood sample, nasopharyngeal swab	None	Evaluation of the extent of the virus transmission within households in 2 years Secondary

									Characterization of the secondary cases
3	NCT04336215 Cohort Study of SARS-CoV-2 Incidence, Transmission, and Disease Severity in Healthcare Workers	Recruiting	3/28/20 – 9/1/20	Prospective longitudinal cohort study	New Jersey, USA	Adults 20 years old and above 500 health care workers, 250 non-health care workers and household members of participants who develop SARS-CoV-2 infection during study period Exclusion: previous COVID-19 diagnosis, pregnant, medical condition, hospitalization in the past 30 days, fever on 1 st visit	Diagnostic test: nasopharyngeal/throat swabs, saliva, and blood collection	None	Prevalence and incidence of COVID-19 infections
4	NCT04318314 COVID-19: Healthcare Worker Bioresource: Immune Protection and Pathogenesis in SARS-CoV-2	Recruiting	3/18/20 – 12/31/20	Prospective observational cohort	London, United Kingdom	Healthy and asymptomatic healthcare workers 18 years old and above (n = 400) Exclusion: SARS-CoV-2 positive or symptomatic healthcare workers	Diagnostic Test: COPAN swabbing and blood sample collection	None	Seroconversion to SARS-CoV-2 positivity within 6 months
5	NCT04320732 Risk Factors for Community- and Workplace Transmission of COVID-19	Recruiting	3/27/20 – 3/27/22	Prospective Case-Control study	Oslo, Norway	Adults, Hospitalized and non-hospitalized patients/persons with COVID-19 at all stages of the disease and after the disease Healthcare personal or other groups with an increased risk of COVID-19 Exclusion: SARS-CoV-2 positive or symptomatic healthcare workers	No intervention, only prospective observation of behavior will be conducted by questionnaire	Hospitalized patients without COVID-19 Healthy volunteers	Rate of COVID-19 infection in 1 year
6	ChiCTR2000031252 Outcomes and infectivity of patients with asymptomatic novel coronavirus (COVID-19) infection	Completed recruitment No results available	1/29/20 – 6/30/20	Multi-center Observational cohort study	Chongqing, China	Patients with a clear history of contact with confirmed cases with two consecutive positive nucleic acid tests but no clinically relevant symptoms	Diagnostic: blood, throat swab and anal swab	None	Clinical Outcomes of Asymptomatic Coronavirus Infected Patients Proportion of second-generation cases and time of diagnosis among those who have close contact

									with asymptomatic infection
7	ChiCTR2000030901 Retrospective analysis of epidemiology and transmission dynamics of patients confirmed with Coronavirus Disease (COVID-19) in Hong Kong	Completed recruitment No results available	3/9/20 – 3/14/20	Case series	Hong Kong	All patients with laboratory confirmed diagnosis of COVID-19 and are listed in the Centre for Health Protection (CHP) database will be included in the study	None	None	Transmission dynamics of COVID-19 Characteristics of super-spreading events Effectiveness of public health measures

