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 based on low quality evidence.

- 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 May 14, there were 969 (11%) of the 8,825 active cases in the Philippines were classified as asymptomatic, but it is unclear whether cases are in the incubation period (pre-symptomatic) or carriers (asymptomatic). These cases are possible sources of SARS-CoV-2 transmission but may be underreported.
- Based on 30 observational studies (case reports, case series, single cohort) and 6 statistical modeling analysis, asymptomatic (carriers) and pre-symptomatic (during the incubation period) transmission of SARS-CoV-2 may occur.
- 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.
- In a cohort of nursing facility residents, 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. In contrast, another study reported significantly higher Ct values for asymptomatic cases compared to pre-symptomatic cases, which indicate lower viral load in asymptomatic cases. However, both studies have small sample size.
- The reported infectivity and probability of transmission was higher for symptomatic cases compared to asymptomatic cases; however, results were imprecise due to a wide confidence interval.
- While the WHO and CDC maintains that the risk of transmission of symptomatic cases is highest on symptom onset, the transmission rate of pre-symptomatic or asymptomatic cases compared to symptomatic cases is unclear.

RESULTS

Thirty observational studies (3 case reports, 23 case series, 2 retrospective single cohort, 2 prospective cohort) and six statistical modelling analysis have reported that pre-symptomatic and asymptomatic transmission may occur. Characteristics of the individual studies are detailed in Appendix 1.

Pre-symptomatic Transmission (12 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 [6].

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. [7].

Ten other different cluster studies in separate publications (8 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 [8-17]. The shortest interval between close contact with the index case prior to symptom onset of index case was 1-2 days [10,15] while the longest interval was 12-14 days [8]. No computed transmission rates were reported in the 10 studies and only 4 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 [8-17].

Asymptomatic Transmission (8 studies and 1 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 [18-22]. One study was not able to identify an index case suggesting an asymptomatic carrier may have transmitted the virus [21].

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 ($p = 0.288$). [23]. 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 (ρ) was estimated at 1.5 (95% CI: 0.7-3.4) which showed that symptomatic cases were likely more infectious than asymptomatic cases [24]. 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 [25]. A study in China of an asymptomatic case admitted at the emergency department also reported no transmission to 455 identified contacts [26].

Pre-symptomatic and Asymptomatic Transmission within cluster (1 study)

Two different studies 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. [22].

Viral Shedding in Asymptomatic Cases (9 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 [28-31].

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) [32]. 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 [33].

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. The similar duration of viral shedding between the two groups (7 days IQR 5-14 *vs.* 8 days IQR 5-16) suggests the possibility of transmission during the asymptomatic period [34]. 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 [35].

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 [36].

Serial interval from modelling studies (5 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. [37-41]. 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 [39,41].

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

Low-quality evidence shows that asymptomatic and pre-symptomatic transmission of SARS-CoV-2 may occur. The reported infectivity and probability of transmission was higher for symptomatic cases compared to asymptomatic cases; however, results were imprecise due to a wide confidence interval. High quality 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

REFERENCES

1. World Health Organization. Coronavirus disease 2019 (COVID-19) Situation Report 73. Retrieved on April 10, 2020 from https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200402-sitrep-73-covid-19.pdf?sfvrsn=5ae25bc7_2.
2. Dong Y, Mo X, Hu Y, et al. Epidemiological Characteristics of 2143 Pediatric Patients With 2019 Coronavirus Disease in China. *Pediatrics.* 2020.
3. Mizumoto K, Kagaya K, Zarebski A, Chowell G. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. Euro Surveill. 2020 Mar;25(10). doi: 10.2807/1560-7917.ES.2020.25.10.2000180.
4. Department of Health Beat COVID-19 Today: A COVID Philippine Situationer Issue 19. 2020 May 16. Available at https://drive.google.com/drive/folders/1YWLkmsKjVYT9DjWfIGQx3E_iBPYznjf2
5. Lai CC, Liu YH, Wang CY, Wang YH, Hsueh SC, Yen MY, Ko WC, Hsueh PR. Asymptomatic carrier state, acute respiratory disease, and pneumonia due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): Facts and myths. J Microbiol Immunol Infect. 2020 Mar 4. pii: S1684-1182(20)30040-2. doi: 10.1016/j.jmii.2020.02.012. [Epub ahead of print]
6. Wei W, Li Z, Chiew C, Yong S, Toh M, Lee V. Presymptomatic Transmission of SARS-CoV-2 — Singapore, January 23–March 16, 2020. MMWR Morb Mortal Wkly Rep 2020;69:411–415. DOI: 10.15585/mmwr.mm6914e1
7. Huang L, Zhang X, Zhang X, Wei Z, Zhang L, Xu J, Liang P, Xu Y, Zhang C, Xu A. 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. Journal of Infection (2020), doi: 10.1016/j.jinf.2020.03.006
8. Ye F, Xu S, Rong Z, Xu R, Liu X, Deng P, Liu H, Xu X. Delivery of infection from asymptomatic carriers of COVID-19 in a familial cluster. Int J Infect Dis. 2020 Apr 2. pii: S1201-9712(20)30174-0. doi: 10.1016/j.ijid.2020.03.042. [Epub ahead of print]
9. Li C, Ji F, Wang L, Wang L, Hao J, Dai M, et al. Asymptomatic and Human-to-Human Transmission of SARS-CoV-2 in a 2-Family Cluster, Xuzhou, China. Emerg Infect Dis. 2020 Mar 31;26(7). doi: 10.3201/eid2607.200718. [Epub ahead of print] Available from: https://wwwnc.cdc.gov/eid/article/26/7/20-0718_article. Accessed on 8 April 2020.
10. Qian G, Yang N, Ma AHY, Wang L, Li G, Chen X, Chen X. A COVID-19 Transmission within a family cluster by presymptomatic infectors in China. Clin Infect Dis. 2020 Mar 23. pii: ciaa316. doi: 10.1093/cid/ciaa316. [Epub ahead of print]
11. Cai J, Sun W, Huang J, Gamber M, Wu J, He G. Indirect Virus Transmission in Cluster of COVID-19 Cases, Wenzhou, China, 2020. Emerg Infect Dis. 2020 Mar 12;26(6). doi: 10.3201/eid2606.200412. [Epub ahead of print]. https://wwwnc.cdc.gov/eid/article/26/6/20-0412_article
12. Tong ZD, Tang A, Li KF, Li P, Wang HL, Yi JP, Zhang YL, Yan JB. Potential Presymptomatic Transmission of SARS-CoV-2, Zhejiang Province, China, 2020. Emerg Infect Dis. 2020 May 17;26(5). doi: 10.3201/eid2605.200198. [Epub ahead of print] https://wwwnc.cdc.gov/eid/article/26/5/20-0198_article
13. Yu P, Zhu J, Zhang Z, Han Y, Huang L. A familial cluster of infection associated with the 2019 novel coronavirus indicating potential person-to-person transmission during the incubation period. J Infect Dis. **2020** Feb 18. pii: jiaa077. doi: 10.1093/infdis/jiaa077. [Epub ahead of print]
14. Liu YC, Liao CH, Chang CF, Chou CC, Lin YR. A locally transmitted case of SARS-CoV-2 infection in Taiwan. N Engl J Med 2020 Feb 12. https://doi.org/10.1056/NEJMc2001573.
15. 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, Zwirglmaier K, Zange S, Wölfel R, Hoelscher M. Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. N Engl J Med. **2020** Mar 5;382(10):970-971. doi: 10.1056/NEJMc2001468. Epub **2020** Jan 30.
16. Jiang Y, Niu W, Wang Q, Zhao H, Meng L, Zhang C. Characteristics of a family cluster of Severe Acute Respiratory Syndrome Coronavirus 2 in Henan, China [published online ahead of print, 2020 Apr 23]. J Infect. 2020;S0163-4453(20)30239-5. doi:10.1016/j.jinf.2020.04.028
17. Li P, Fu J-Bo, Li K-Feng, Chen Y, Wang H-Ling, Liu L-Jie, Liu J-Nan, Zhang Y-Li, Liu S-Lan, Tang A, Tong Z-Dong, Yan J-Bo. Transmission of COVID-19 in the terminal stage of incubation period: a familial cluster, International Journal of Infectious Diseases (2020), doi: https://doi.org/10.1016/j.ijid.2020.03.027
18. Zhang J, Tian S, Lou J, Chen Y. Familial cluster of COVID-19 infection from an asymptomatic. Crit Care. 2020 Mar 27;24(1):119. doi: 10.1186/s13054-020-2817-7.

19. Su L, Ma X, Yu H, Zhang Z, Bian P, Han Y, et al. The different clinical characteristics of corona virus disease cases between children and their families in China - the character of children with COVID-19. Emerg Microbes Infect. 2020 Dec;9(1):707-713. doi: 10.1080/22221751.2020.1744483.
20. 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. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. Sci China Life Sci. 2020 Mar 4. doi: 10.1007/s11427-020-1661-4. [Epub ahead of print]
21. Bai Y, Yao L, h T, Tian F, Jin DY, Chen L, Wang M. Presumed Asymptomatic Carrier Transmission of COVID-19. JAMA. 2020 Feb 21. doi: 10.1001/jama.2020.2565. [Epub ahead of print]
22. Qiu C, Deng Z, Xiao Q, et al. Transmission and clinical characteristics of coronavirus disease 2019 in 104 outside-Wuhan patients, China [published online ahead of print, 2020 May 5]. J Med Virol. 2020;10.1002/jmv.25975. doi:10.1002/jmv.25975
23. Chen Y, Wang A, Yi B, et. al. The epidemiological characteristics of infection in close contacts of COVID-19 in Ningbo city. Chin J Epidemiol 2020. doi: 10.3760/cma.j.cn112338-20200304-00251
24. He D, Zhao S, Lin Q, Zhuang Z, et. al. The relative transmissibility of asymptomatic COVID-19 infections among close contacts. Int J Infect Dis. 2020 Apr 18; 94:145–147. doi: 10.1016/j.ijid.2020.04.034
25. Park SY, Kim YM, Yi S, Lee, S, et. al. Coronavirus Disease Outbreak in Call Center, South Korea. Emerg Infect Dis. 2020 Aug. doi: 10.3201/eid2608.201274
26. Gao M, Yang L, Chen X, Deng Y, Yang S, Xu H, Chen Z, Gao X, A study on infectivity of asymptomatic SARS-CoV-2 carriers, Respiratory Medicine (2020), doi: https://doi.org/10.1016/j.rmed.2020.106026.
27. Jiang X, Zhang XL, Zhao XN, Li CB, et. al. Transmission potential of asymptomatic and paucisymptomatic SARS-CoV-2 infections: a three-family cluster study in China. J Infect Dis 2020 Apr 22. doi: 10.1093/infdis/jiaa206
28. Zou L, Ruan F, Huan M, et. al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. NEJM 2020; published February 19. DOI: 0.1056/NEJMc2001468
29. Kam KQ, Yung CF, Cui L, Lin Tzer Pin R, Mak TM, Maiwald M, Li J, Chong CY, Nadua K, Tan NWH, Thoon KC. A Well Infant with Coronavirus Disease 2019 (COVID-19) with High Viral Load. Clin Infect Dis. 2020 Feb 28. pii: ciaa201. doi: 10.1093/cid/ciaa201. [Epub ahead of print]
30. Le TQM, Takemura T, Moi ML, Nabeshima T, Nguyen LKH, Hoang VMP, et al. Severe Acute Respiratory Syndrome Coronavirus 2 Shedding by Travelers, Vietnam, 2020. Emerg Infect Dis. 2020 Apr 2;26(7). doi: 10.3201/eid2607.200591. [Epub ahead of print]
31. Mao ZQ, Wan R, He LY, Hu YC, Chen W. The enlightenment from two cases of asymptomatic infection with SARS-CoV-2: is it safe after 14 days of isolation? Int J Infect Dis 2020 Apr 3. doi: 10.1016/j.ijid.2020.03.041
32. Kimball A, Hatfield KM, Arons M, James A, Taylor J, Spicer K, et al. Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled Nursing Facility — King County, Washington, March 2020. MMWR Morb Mortal Wkly Rep. 2020 Apr 3;69(13):377-381. doi: 10.15585/mmwr.mm6913e1
33. Arons M, Hatfield KM, Reddy SC, Kimball A, et. al. Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility. N Engl J Med 2020 Apr 24. doi:10.1056/NEJMoa2008457
34. Zhou R, Li F, Chen F, Liu H, Zheng J, Lei C, Wu X. Viral dynamics in asymptomatic patients with COVID-19, International Journal of Infectious Diseases (2020), doi: https://doi.org/10.1016/j.ijid.2020.05.030
35. Kim SE, Jeong HS, Yu Y, Shin SU, Kim S, Oh TH, Kim UJ, et. al. Viral kinetics of SARS-CoV-2 in asymptomatic carriers and presymptomatic patients, International Journal of Infectious Diseases (2020), doi: https://doi.org/10.1016/j.ijid.2020.04.083
36. Jiang X, Luo M, Zuo Z, Wang X, Chen C, Qiu J. Asymptomatic SARS-CoV-2 infected case with viral detection positive in stool but negative in nasopharyngeal samples lasts for 42 days. J Med Virol 2020 Apr 24. doi: 10.1002/jmv.25941 [Online ahead of print]
37. He X, Lau EHY, Wu P, et. al. Temporal dynamics in viral shedding and transmissibility of COVID-19. medRxiv 2020. DOI: 10.1101/2020.03.15.20036707
38. Nishiura H, Linton N, Akhmetzhanov A. Serial interval of novel coronavirus (COVID-19) infection. Int J Infect Dis 2020 Mar 4; 93:284-286. doi: 10.1016/j.ijid.2020.02.060. [Epub ahead of print]
39. Du Z, Xu X, Wu Y, Wang L, Cowling BJ, Ancel Meyers L. Serial interval of COVID-19 among publicly reported confirmed cases. Emerg Infect Dis. 2020 Jun. DOI:10.3201/eid2606.200357
40. Tindale LC, Coombe M, Stockdale JE, Garlock ES, Lau WYV, Saraswat M, Yen-Hsiang BL, Zhang L, Chen D, Wallinga J, Colijn C. Transmission interval estimates suggest pre-symptomatic spread of COVID-19. medRxiv 2020. DOI: 10.1101/2020.03.03.20029983.
41. Wong J, Abdul Aziz ABZ, Chaw L, et al. High proportion of asymptomatic and presymptomatic COVID-19 infections in travelers and returning residents to Brunei [published online ahead of print, 2020 May 5]. J Travel Med. 2020;taaa066. doi:10.1093/jtm/taaa066
42. Centers for Disease Control and Prevention. Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19). Retrieved on April 10, 2020 from https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html

Table 1. Characteristics of included studies

No.	Title/Author	Study design	Country	Population	Key findings
1	Presymptomatic Transmission of SARS-CoV-2 — Singapore, January 23–March 16, 2020 Wei W, Li Z, Chiew C, Yong S, Toh M, Lee V	Case series	Singapore	COVID-19 cases (n=243)	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. Limitations Other unknown source may have initiated the clusters Recall and interviewer bias Underdetection of asymptomatic illness
2	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 Huang L, Zhang X, Zhang X, Wei Z, Zhang L, Xu J, Liang P, Xu Y, Zhang C, Xu A	Case series	China	Contacts of index case from Wuhan	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) 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
3	Delivery of infection from asymptomatic carriers of COVID-19 in a familial cluster (Pre-print) Ye F, Xu S, Rong Z, Xu R, Liu X, Deng P, Liu H, Xu X	Case series	Luzhou, China	Familial cluster of five patients	Patient 3/4/5 – (+) travel to Wuhan Contact of all 5 cases – Jan 23-25, 30 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 Patient 2 – 28/M, nephew of Case 3,4 cousin of Case 5, asymptomatic 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 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 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 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.
4	Asymptomatic and Human-to-Human Transmission of SARS-CoV-2 in a 2-Family Cluster, Xuzhou, China Li C, Ji F, Wang L, Wang L, Hao J, Dai M, et al.	Case series	Xuzhou, China	2 family clusters (n = 7)	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. Close contact (Jan 14 -22) Patient 2: 32/F pregnant daughter, had contact with index case 6 days before index case presented with symptoms

					Patient 3: 21/F daughter, had contact with index case 6 days before index case presented with symptoms Patient 4: 42/M, son-in-law, hospitalized, had contact with index case 5 days before index case presented with symptoms 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 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 Patient 7: 56/F, wife of Px 5, had contact with Px 5, 2 days before Px 4 presented with fever The study confirms asymptomatic and human-to-human transmission through close contacts in familial and hospital settings.
5	A COVID-19 Transmission within a family cluster by presymptomatic infectors in China Qian G, Yang N, Ma AHY, Wang L, Li G, Chen X, Chen X.	Case series	Zhejiang China	Nine family members	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. Patient 1 (index 1): 58/F, had fever, fatigue and headache on Jan 24, diagnosed COVID-19 on Jan 29 Patient 2 (index 2): 60/M, remained asymptomatic, diagnosed on Feb 1 with COVID-19 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 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 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) 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) Patient 7: 57/F, mother of Patient 4, had dinner with Patient 3-6 on Jan 23 (4 days before Patient 3 had symptoms) 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)
6	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).
7	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.
8	A familial cluster of infection associated with the 2019 novel coronavirus indicating potential person-to-person	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.

	transmission during the incubation period Yu P, Zhu J, Zhang Z, Han Y, Huang L.				
9	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
10	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, Zwirglmaier 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.
11	Transmission of COVID-19 in the terminal stage of incubation period: a familial cluster, International Journal of Infectious Diseases Li P, Fu JB, Li KF, Chen Y, et al.	Case series	China	Family cluster of COVID-19 cases (n=6_	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. Patient A – 56/M, index patient, positive on Feb 6, symptoms on Feb 7 Patient B – 66/M, father-in-law of Px A, symptoms and positive test on Feb 9 Patient C – 64/F, mother-in-law of Px A, symptoms and positive test on Feb 9 Patient D – 42/F, sister-in-law of Px A, symptoms and positive test on Feb 9 Patient E – 7/F, daughter of Px A, positive test on Feb 9, asymptomatic Patient F – 41/F, wife of Px A, negative test and asymptomatic
12	Transmission of COVID-19 in the terminal stage of incubation period: a familial cluster, International Journal of Infectious Diseases Li P, Fu JB, Li KF, Chen Y, et al.	Case series	China	Family cluster of COVID-19 cases (n=6_	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. Patient A – 56/M, index patient, positive on Feb 6, symptoms on Feb 7 Patient B – 66/M, father-in-law of Px A, symptoms and positive test on Feb 9 Patient C – 64/F, mother-in-law of Px A, symptoms and positive test on Feb 9 Patient D – 42/F, sister-in-law of Px A, symptoms and positive test on Feb 9 Patient E – 7/F, daughter of Px A, positive test on Feb 9, asymptomatic Patient F – 41/F, wife of Px A, negative test and asymptomatic
13	Familial cluster of COVID-19 infection from an asymptomatic	Case series	China	Familial cluster of five patients (index patient and 4 close contacts)	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.

	Zhang J, Tian S, Lou J, Chen Y.				Patient 2: 45/F, wife of index case, had fever on Jan 23, had contact with index case since Jan 19 Patient 3: asymptomatic, had contact with index case since Jan 19 Patient 4: 38/M, nephew of index case, started to have fever and fatigue on Jan 22 after meeting his uncle on Jan 19 Patient 5: mother of Px 3, had fever and joint pain on Jan 27, had contact with Px 3 since Jan 19 Asymptomatic cases should be identified and isolated appropriately to prevent disease spread to close contacts.
14	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.
15	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)
16	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
17	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.
18	The epidemiological characteristics of infection in	Case series	China	COVID-19 cases in Ningbo, China and their close contacts	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

	close contacts of COVID-19 in Ningbo city Chen Y, Wang A, Yi B, et. al.				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 (χ 2 = 1.128, P > 0.05). Timing of contact with symptomatic cases to determine if pre-symptomatic transmission occurred was not investigated.
19	The relative transmissibility of asymptomatic COVID-19 infections among close contacts. He D, Zhao S, Lin Q, Zhuang Z, et. al.	Statistical modelling analysis	Hong Kong	COVID-19 cases and their contacts	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). 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. 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.
20	Coronavirus Disease Outbreak in Call Center, South Korea Park SY, Kim YM, Yi S, Lee, S, et. al.	Case series	South Korea	Residents, employees and visitors in a building in Seoul, South Korea and their household contacts	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. The actual transmissibility of pre-symptomatic cases or asymptomatic cases may have not been detected due to mass testing, self-quarantine and isolation measures.
21	A study on infectivity of asymptomatic SARS-CoV-2 carriers Gao M, Yang L, Chen X, Deng Y, Yang S, Xu H, Chen Z, Gao X	Case Report	China	Asymptomatic COVID-19 case and her contacts	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). 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. 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. 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.
22	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	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. 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 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

					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 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.
23	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.
24	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.
25	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 1st cluster: travelers 2nd cluster: patients with close contact with the travelers (age range 3 months – 55 years old)	In the 1st 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 2nd 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.
26	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.
27	Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled	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.

	Nursing Facility — King County, Washington, March 2020. Kimball A, Hatfield KM, Arons M, James A, Taylor J, Spicer K, et al.				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). 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. 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.
28	Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility Arons M, Hatfield KM, Reddy SC, Kimball A, et. al.	Prospective single cohort	King County, Washington, USA	Residents of a long-term care skilled nursing facility (SNF) in King County, Washington (n = 89)	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. 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). 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. The transmission of infection from asymptomatic and pre-symptomatic residents was not quantified but evidence suggests potential for substantial viral shedding.
29	Viral dynamics in asymptomatic patients with COVID-19 Zhou R, Li F, Chen F, Liu H, Zheng J, Lei C, Wu X.	Prospective cohort	China	virologically confirmed to have COVID-19 but were asymptomatic on admission (n=31)	22/31 (71%) developed symptoms after admission, 9 (29%) remained asymptomatic during hospitalization 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. Viral load of asymptomatic patients peaked within the 1st week of admission while for presymptomatic patients peaked during the 2nd week of hospitalization. Duration of viral shedding remained similar between the two groups (7 days IQR 5-14 *vs.* 8 days IQR 5-16).
30	Viral kinetics of SARS-CoV-2 in asymptomatic carriers and presymptomatic patients Kim SE, Jeong HS, Yu Y, Shin SU, Kim S, Oh TH, Kim UJ, et. al.	Prospective cohort	South Korea	Laboratory-confirmed COVID-19 cases admitted at a university hospital (n=71)	From 71 hospitalized patients, three presymptomatic patients developed symptoms within 14 days of quarantine while 10 remained asymptomatic patients 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. 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.
31	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
32	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.
33	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.
34	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: 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 Findings should be interpreted as working hypotheses regarding the infectiousness of COVID-19 requiring further validation as more data become available.
35	Transmission interval estimates suggest pre-symptomatic spread of COVID-19 Tindale LC, Coombe M, Stockdale JE, Garlock ES,	Statistical modelling analysis	Singapore Tianjin, China	COVID-19 clusters n = 228 (93 Singapore, 135 Tianjin)	Mean incubation period: Singapore – 7.1 days (6.13, 8.25) Tianjin – 9 days (7.92, 10.2) Mean serial interval: Singapore – 4.56 (2.69, 9.42) Tianjin – 4.22 (3.43, 5.01)

	Lau WYV, Saraswat M, Yen-Hsiang BL, Zhang L, Chen D, Wallinga J, Colijn C				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. Estimated serial intervals are shorter than incubation period suggesting that pre-symptomatic transmission is happening. 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)
36	High proportion of asymptomatic and presymptomatic COVID-19 infections in travelers and returning residents to Brunei Wong J, Abdul Aziz ABZ, Chaw L, et al.	Rapid Communication/ Modeling study	Brunei	COVID-19 cases	From the 138 local cases of COVID-19 in Brunei, 16 (12%) were asymptomatic while 42 (30%) were presymptomatic. All local transmission had contact history and the short serial intervals between the infector-infectee pairs suggest possible presymptomatic transmission. International arrivals to Brunei were tested and quarantined for 14 days from which 30 were positive for COVID-19 (11 preesymptomatic 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.

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 1st 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	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

						Exclusion: SARS-CoV-2 positive or symptomatic healthcare workers			
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