Asymptomatic and pre-symptomatic transmission + on surfaces

Key points

- Viral loads of people with SARS-CoV-2 (virus from 2020) peak a median of 5 days earlier than viral loads with SARS-CoV-1 (virus from 2003), meaning people that don't have symptoms can carry the virus and be infective.
- The virus replicates in the upper respiratory tract, which has implications for the containment of COVID-19.
- Studies show that anywhere between 6% to 88% of people who test positive for COVID-19 can be asymptomatic or pre-symptomatic and yet still infectious.
- With SARS-CoV-2, people can be asymptomatic throughout infection. The exact contribution of this segment to transmission is lower, but in terms of outcome whether someone is asymptomatic throughout, or pre-symptomatic before getting symptoms later on, the result is the same – i.e. people may not know they are infectious and can spread the virus.
- Transmission period can be longer than 14 days.
- The national drive using symptom-based criteria of fever and cough for testing and isolating individuals may have contributed to delays in instituting appropriate infection control measures and contributed to the large numbers of deaths observed in care homes.
- The implication of a/pre-symptomatic spread means that combination prevention measures are needed (i.e. enhanced hand hygiene, masks, testing tracing and isolation strategies, social distancing).
- Testing programmes have to include people with no symptoms.
- Environmental contamination of surfaces is a risk for spread of SARS-CoV-2 in rooms where infected patients are housed and cared for, regardless of the degree of symptoms or acuity of illness.
- SARS-CoV-3 is more stable on certain surfaces (e.g. plastic and stainless steel where viable virus was detected up to 72 hours, compared to copper and cardboard). Higher viral load has also been detected after prolonged contact (e.g. with sheets and pillow covers) compared to intermittent contact (e.g. door handle and light switch).
- Health care workers are suspected to be instrumental in spreading the virus from/to surfaces.

A. Evidence of a- or pre-symptomatic transmission

Research	Main lessons to take away
Oran, D.P.; Topol, E.J. (2020) **Prevalence of Asymptomatic SARS-CoV-2 Infection – A Narrative Review**. *Ann Intern Med.* Published online 3 June, 2020. https://www.acpjournals.org/doi/pdf/10.7326/M20-3012	*"The likelihood that approximately 40% to 45% of those infected with SARS-CoV-2 will remain asymptomatic suggests that the virus might have greater potential than previously estimated to spread silently and deeply through human populations."* *"Asymptomatic persons can transmit SARS-CoV-2 to others for an extended period, perhaps longer than 14 days."* *"The focus of testing programs for SARS-CoV-2 should be substantially broadened to include persons who do not have symptoms of COVID-19."*
Wei, W.E. *et al* (2020) **Presymptomatic Transmission of SARS-CoV-2 – Singapore, January 23 – March 16, 2020.** *Morbidity and Mortality Weekly Report*, CDC. April 10, 2020, Vol. 69, No. 14. https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6914e1-H.pdf	*"This investigation identified seven clusters of COVID-19 in Singapore in which presymptomatic transmission likely occurred. Among the 243 cases of COVID-19 reported in Singapore as of March 16, 157 were locally acquired; 10 of the 157 (6.4%) locally acquired cases are included in these clusters and were attributed to presymptomatic transmission".*
Kimball, A. *et al* (2020) **Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled Nursing Facility – King County, Washington, March 2020**. *Morbidity and Mortality Weekly Report*, CDC. April 3, 2020, Vol. 69, No. 13. https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6913e1-H.pdf	Experience from a skilled nursing facility found that 30% of those residents that were tested were positive, but of these over half (57%) did not have symptoms at the time of the test (yet 7 days after testing, 10 out of the 13 had developed symptoms). This study suggests that symptom-based screening in long-term care facilities could fail to identify approximately half of residents with COVID-19.
Arons, M.M. *et al* (2020) **Presymtomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility**. *The New England Journal of Medicine.* Published: April 24, 2020. https://www.nejm.org/doi/pdf/10.1056/NEJMoa2008457?articleTools=true	Experience from a skilled nursing facility found 63% of residents tested positive, and over half of those (57%) did not have symptoms at the time of the test. Infection control strategies solely focusing on symptomatic residents were not enough to prevent introduction of the virus into the facility.
Gandhi, M.P.H. *et al* (2020) **Asymptomatic transmission, the Achilles' Heel of Current Strategies to Control Covid-19**. *The New England Journal of Medicine.*	Viral loads with SARS-CoV-1 (virus from 2003) were associated with symptom onset, peak a median of 5 days later than viral loads with SARS-CoV-2 (virus from 2020). This is what made symptom-based detection of infection more effective in the case of SARS CoV-1.

Published: April 24, 2020 https://www.nejm.org/doi/pdf/10.1056/NEJMe2009758?articleTools=true	With the current virus (SARS-CoV-2), people that don't have symptoms can carry the virus and be infective – e.g. 17 of 24 specimens (71%) from pre-symptomatic persons had viable virus by culture 1 to 6 days before the development of symptoms.
Baggett, T. P. *et al* (2020) **Prevalence of SARS-CoV-2 Infection in Residents of a Large Homeless Shelter in Boston.** *JAMA*. Published: April 27, 2020. https://jamanetwork.com/journals/jama/fullarticle/2765378	A total of 147 participants (36.0%) had PCR test results positive for SARS-CoV-2. Among individuals with PCR test results positive for SARS-CoV-2 - cough (7.5%), shortness of breath (1.4%), and fever (0.7%) were all uncommon, and 87.8% were asymptomatic. The majority of individuals with newly identified infections had no symptoms and no fever at the time of diagnosis, suggesting that symptom screening in homeless shelters may not adequately capture the extent of disease transmission in this high-risk setting. These results support PCR testing of all asymptomatic shelter residents if a symptomatic individual with COVID-19 is identified in the same shelter.
Public Heath England – April 2020 Report not seen but referenced in the minutes of the 15th NERVTAG meeting, as well as two subsequent news articles: https://m.box.com/shared_item/https%3A%2F%2Fapp.box.com%2Fs%2F3lkcbxepqixkg4mv640dpvvg978ixjtf/view/677989903140 (date: 28 April, 2020) https://www.bbc.co.uk/news/uk-52727221 (date: 19 May, 2020) https://www.theguardian.com/world/2020/may/18/agency-staff-were-spreading-covid-19-between-care-homes-phe-found-in-april (date: 18 May, 2020)	***NERVTAG:*** *"It was found that 75% of the residents carried the virus and only 25-33% were symptomatic. Approximately 45% of the healthcare workers were also carrying the virus, with 25-33% symptomatic".* ***BBC:*** *The study, which was carried out over the Easter weekend, looked at tests of staff and residents and the results were passed to the Department of Health and Social Care before the end of the month. PHE said the results suggested there were "high numbers of asymptomatic or pre-symptomatic cases among staff and residents" and that "infection may be being imported into the homes by staff".* ***Guardian:*** *The genome tracking research by PHE into the behaviour of the virus in six care homes in London found that "Infection is spreading from care home to care home, linked to changed patterns of staffing, working across and moving between homes." The infection could be introduced by "bank staff" – floating workers used to fill temporary vacancies in different homes – it said, adding that workers were often asymptomatic so "by the time local health protection teams are informed of an outbreak substantial transmission may already have occurred".*
Du, Z. *et al* (2020) **Serial Interval of COVID-19 among Publicly Reported Confirmed Cases.** *Research Letter,* Volume 26, Number 6—June 2020. https://wwwnc.cdc.gov/eid/article/26/6/20-0357_article	*"We estimate the distribution of serial intervals for 468 confirmed cases of coronavirus disease reported in China as of February 8, 2020. The mean interval was 3.96 days (95% CI 3.53–4.39 days), SD 4.75 days (95% CI 4.46– 5.07 days); 12.6% of case reports indicated presymptomatic transmission".*

	"Fifty-nine of the 468 reports indicate that the infectee had symptoms earlier than the infector. Thus, presymptomatic transmission might be occurring".
Vetter, P. *et al* (2020) **Clinical features of covid-19: The wide array of symptoms has implications for the testing strategy.** Editorial, *BMJ* 2020;369:m1470. Published: 17 April 2020. https://www.bmj.com/content/bmj/369/bmj.m1470.full.pdf	*"Available evidence from observational and modelling reports indicates that up to 12% of transmission occurs before an index case develops symptoms. This has important implications for the effectiveness of any testing strategy and for contact tracing and containment measures. To curtail active transmission of SARS-CoV-2, testing should be extended far beyond people who fit a narrow case definition and other populations currently considered at risk. The current strategy will not capture the full picture, missing a substantial number of patients with atypical presentations or few symptoms. Worse, restrictive testing criteria could lead to unrecognised cases transmitting the virus in health care settings or the community and to delays in appropriate patient triage and management".*
He, X. *et al* (2020) **Temporal dynamics in viral shedding and transmissibility of COVID-19.** Brief Communication, *Nat Med.* 2020; 26:672–5. Epub ahead of print. Published: 15 April 2020 https://www.nature.com/articles/s41591-020-0869-5.pdf	*"We report temporal patterns of viral shedding in 94 patients with laboratory-confirmed COVID-19 and modelled COVID-19 infectiousness profiles from a separate sample of 77 infector–infectee transmission pairs. We observed the highest viral load in throat swabs at the time of symptom onset, and inferred that infectiousness peaked on or before symptom onset. We estimated that 44% (95% confidence interval, 25–69%) of secondary cases were infected during the index cases' pre-symptomatic stage, in settings with substantial household clustering, active case finding and quarantine outside the home. Disease control measures should be adjusted to account for probable substantial pre-symptomatic transmission".*
Byambasuren, O. *et al* (2020) **Estimating the extent of true asymptomatic COVID-19 and its potential for community transmission: systematic review and meta-analysis** (preprint). *medRxiv*, 2020.05.10.20097543. Published: 4 June, 2020. https://www.medrxiv.org/content/10.1101/2020.05.10.20097543v2	*"The proportion of asymptomatic cases ranged from 4% to 41%."* *"Our estimates of the prevalence of asymptomatic COVID-19 cases and asymptomatic transmission rates are lower than many highly publicized studies, but still sufficient to warrant policy attention. Further robust epidemiological evidence is urgently needed, including in sub-populations such as children, to better understand the importance of asymptomatic cases for driving spread of the pandemic."*
Wang Y. *et al* (2020) **Characterization of an asymptomatic cohort of SARS-COV-2 infected individuals outside of Wuhan, China.** *Clin Infect Dis.* 2020.	*"Between January and March, 2020, we identified and hospitalized 279 RT-PCR+ contacts of COVID-19 patients. Of these, 63 (23%) remained asymptomatic until discharge; 29 had abnormal and 34 had normal chest CT findings."*

Published: 22 May, 2020. https://europepmc.org/article/med/32442265	*"Asymptomatic individuals infected with SARS-CoV-2 are an important source of transmission. Early identification of asymptomatic cases with subsequent isolation and treatment may contribute to decreased transmission and mortality."*
Roxby, A.C. *et al* (2020) **Outbreak Investigation of COVID-19 Among Residents and Staff of an Independent and Assisted Living Community for Older Adults in Seattle, Washington.** *JAMA Intern Med.* Published: 21 May, 2020. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2766448	*"Testing was performed on 80 residents; 62 were women (77%), with mean age of 86 (range, 69-102) years. SARS-CoV-2 was detected in 3 of 80 residents (3.8%); none felt ill, 1 male resident reported resolved cough and 1 loose stool during the preceding 14 days. Virus was also detected in 2 of 62 staff (3.2%); both were symptomatic. One week later, resident SARS-CoV-2 testing was repeated and 1 new infection detected (asymptomatic)."* *"In this study, symptom screening failed to identify residents with infections and all 4 residents with SARS-CoV-2 remained asymptomatic after 14 days. Although 1 asymptomatic infection was found on retesting, a widespread facility outbreak was avoided. Compared with skilled nursing settings, in assisted/independent living communities, early surveillance to identify asymptomatic persons among residents and staff, in combination with adherence to recommended preventive strategies, may reduce viral spread."* *"The findings of both asymptomatic and mild SARSCoV-2 infection in elderly persons, and in staff providing them assistance, underscore the vital importance of current recommendations for continued social distancing, strict staff screening, and visitor exclusion per current CDC guidance".*
Graham, N.S.N. *et al* (2020) **SARS-CoV-2 infection, clinical features and outcome of COVID-19 in United Kingdom nursing homes.** *medRxiv*, 2020.05.19.20105460. Published: 3 June, 2020. https://www.journalofinfection.com/action/showPdf?pii=S0163-4453%2820%2930348-0	A study that looked at 4 nursing homes affected by COVID-19 outbreaks in central London, involving 394 residents and 70 staff. *"Overall, 26% of residents died over the two-month period. All-cause mortality increased by 203%. Systematic testing identified 40% of residents as positive for SARS-CoV-2, and of these 43% were asymptomatic and 18% had only atypical symptoms; 4% of asymptomatic staff also tested positive."* *"Testing asymptomatic staff members has not been reported in previous studies. This group is likely to have been an important route for SARS-CoV-2 transmission into and within nursing homes. Viral sequencing provided evidence for multiple viral strains within a single nursing home, suggesting that there were multiple introductions into individual nursing homes."* *"The initial national drive using symptom-based criteria of fever and cough for testing and isolating individuals may,*

	therefore, have contributed to delays in instituting appropriate infection control measures and, in the nursing home setting, contributed to the large numbers of deaths observed in this highly vulnerable population." *"The SARS-CoV-2 outbreak in four UK nursing homes was associated with very high infection and mortality rates. Many residents developed either atypical or had no discernible symptoms. A number of asymptomatic staff members also tested positive, suggesting a role for regular screening of both residents and staff in mitigating future outbreaks."*
Buitrago-Garcia, D.C. *et al* (2020) **The role of asymptomatic SARS-CoV-2 infections: rapid living systematic review and meta-analysis.** *medRxiv*, 2020.04.25.20079103. Published online: 24 May, 2020. https://doi.org/10.1101/2020.04.25.20079103	Reviewed 37 studies. *"The overall estimate of the proportion of people who become infected with SARS-CoV-2 and remain asymptomatic throughout infection was 15%."* *"In modelling studies, 40-60% of all SARS-CoV-2 infections are the result of transmission from presymptomatic individuals."* *"An intermediate contribution of pre-symptomatic and asymptomatic infections to overall SARS-CoV2 transmission means that combination prevention measures, with enhanced hand and respiratory hygiene, testing tracing and isolation strategies and social distancing, will continue to be needed."*
Emery, J.C. *et al* (2020) **The contribution of asymptomatic SARS-CoV-2 infections to transmission - a model-based analysis of the Diamond Princess outbreak.** *medRxiv*, 2020.05.07.20093849. Posted: 11 May, 2020. https://doi.org/10.1101/2020.05.07.20093849	*"On the Diamond Princess 74% (70-78%) of infections proceeded asymptomatically... Despite the intense testing 53%...of infections remained undetected, most of them asymptomatic. Asymptomatic individuals were the source for 69%...of all infections."* *"Asymptomatic SARS-CoV-2 infections may contribute substantially to transmission. This is essential to consider for countries when assessing the potential effectiveness of ongoing control measures to contain COVID-19."*
Tabata, S. *et al* (2020). **Non-severe vs severe symptomatic COVID-19: 104 cases from the outbreak on the cruise ship "Diamond Princess" in Japan.** *medRxiv*, 2020.03.18.20038125. Posted: 7 April, 2020. https://doi.org/10.1101/2020.03.18.20038125	*"…76 and 28 patients were classified as non-severe (asymptomatic, mild), and severe cases, respectively. Chest CT abnormalities were found in 43 in non-severe cases and 23 in severe cases."* *"Our study highlighted the high prevalence of asymptomatic and mild cases of COVID-19 as a result of mass infection on a cruise ship."*
Ing, A.J. *et al* (2020) **COVID-19: in the footsteps of Ernest Shackleton.** *Thorax*	A study that documented the complete COVID-19 testing of all passengers and crew from an isolated cruise ship to Antarctica.

Epub ahead of print: [accessed 29 June]. Published: 24 June, 2020. https://thorax.bmj.com/content/early/2020/06/09/thoraxjnl-2020-215091	*"Of the 217 passengers and crew on board, 128 tested positive for COVID-19 on reverse transcription–PCR (59%). Of the COVID-19-positive patients, 19% (24) were symptomatic; 6.2% (8) required medical evacuation; 3.1% (4) were intubated and ventilated; and the mortality was 0.8% (1). The majority of COVID-19-positive patients were asymptomatic (81%, 104 patients). We conclude that the prevalence of COVID-19 on affected cruise ships is likely to be significantly underestimated, and strategies are needed to assess and monitor all passengers to prevent community transmission after disembarkation."*
Bigelow, B.F. *et al* (2020) **Outcomes of Universal COVID-19 Testing Following Detection of Incident Cases in 11 Long-term Care Facilities.** *JAMA Intern Med.* Published: July 14, 2020. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2768377	A report from universal testing of untested residents across 11 Maryland long-term care facilities. *"… universal screening increased the total number of detected COVID-19 cases across all sites from 153 to 507; of these, 281 (55.4%) were asymptomatic."* *"In this study of 11 Maryland long-term care facilities, an additional 354 cases (39.6% of those tested) were identified with universal testing, despite initial targeted, symptom-based testing. These results underscore the importance of universal testing because symptom-based approaches may miss a substantial number of cases. Unrecognized asymptomatic cases among residents could perpetuate transmission within facilities."* *"Using symptom-based testing alone to identify positive residents is not adequate to assess case burden and inform outbreak-control efforts in these settings. Additional testing resources are urgently needed to identify the true burden of COVID-19 and curb transmission in long-term care settings."*
Wells, P.M. *et al* (2020) **Estimates of the rate of infection and asymptomatic COVID-19 disease in a population sample from SE England.** *medRxiv*, 2020.07.29.20162701. Posted online: 30 July, 2020 https://www.medrxiv.org/content/10.1101/2020.07.29.20162701v1	*"Of 48 seropositive individuals with full symptom data, nine (19%) were fully asymptomatic, and 16 (27%) were asymptomatic for core COVID-19 symptoms: fever, cough or anosmia. Specificity of anosmia for seropositivity was 95%, compared to 88% for fever cough and anosmia combined."*
Lee, S. *et al* (2020) **Clinical Course and Molecular Viral Shedding Among Asymptomatic and Symptomatic Patients With SARS-CoV-2 Infection in a Community Treatment Center in the Republic of Korea.** *JAMA Intern Med.* Published online: 6 August, 2020.	A study showing that the viral load for symptomatic and asymptomatic people is similar. *"In this cohort study of symptomatic and asymptomatic patients with SARS-CoV-2 infection who were isolated in a community treatment center in Cheonan, Republic of Korea, the Ct values in asymptomatic patients were similar to those in symptomatic patients. Isolation of*

https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2769235	*asymptomatic patients may be necessary to control the spread of SARS-CoV-2."*

B. Smaller case studies of pre- or asymptomatic transmission

Wölfel, R. *et al* (2020) **Virological assessment of hospitalized patients with COVID-2019.** *Nature.* 2020 Epub ahead of print. Published: 1 April 2020 https://www.nature.com/articles/s41586-020-2196-x	*"Coronavirus disease 2019 (COVID-19) is an acute infection of the respiratory tract that emerged in late 2019. Initial outbreaks in China involved 13.8% of cases with severe courses, and 6.1% of cases with critical courses. This severe presentation may result from the virus using a virus receptor that is expressed predominantly in the lung; the same receptor tropism is thought to have determined the pathogenicity—but also aided in the control—of severe acute respiratory syndrome (SARS) in 2003.* *However, there are reports of cases of COVID-19 in which the patient shows mild upper respiratory tract symptoms, which suggests the potential for pre- or oligosymptomatic transmission. There is an urgent need for information on virus replication, immunity and infectivity in specific sites of the body.* *Here we report a detailed virological analysis of nine cases of COVID-19 that provides proof of active virus replication in tissues of the upper respiratory tract. Pharyngeal virus shedding was very high during the first week of symptoms, with a peak at 7.11 × 10^8 RNA copies per throat swab on day 4. Infectious virus was readily isolated from samples derived from the throat or lung, but not from stool samples—in spite of high concentrations of virus RNA. Blood and urine samples never yielded virus.* *Active replication in the throat was confirmed by the presence of viral replicative RNA intermediates in the throat samples. We consistently detected sequence-distinct virus populations in throat and lung samples from one patient, proving independent replication. The shedding of viral RNA from sputum outlasted the end of symptoms.* *Seroconversion occurred after 7 days in 50% of patients (and by day 14 in all patients), but was not followed by a rapid decline in viral load. COVID-19 can present as a mild illness of the upper respiratory tract. The confirmation of active virus replication in the upper respiratory tract has implications for the containment of COVID-19".*
Jiang, F.C. *et al* (2020) **Detection of Severe Acute Respiratory Syndrome Coronavirus 2 RNA on Surfaces in**	*"We investigated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) environmental contamination in 2 rooms of a quarantine hotel after 2 pre-symptomatic persons who stayed there were laboratory-confirmed as having coronavirus disease. We detected SARS-CoV-2 RNA*

Quarantine Rooms. *Dispatch*, Volume 26, Number 9, Sept 2020. https://wwwnc.cdc.gov/eid/article/26/9/20-1435_article	*on 8 (36%) of 22 surfaces, as well as on the pillow cover, sheet, and duvet cover".* *"Our study demonstrates extensive environmental contamination of SARS-CoV-2 RNA in a relatively short time (<24 hours) in occupied rooms of 2 persons who were pre-symptomatic".* *"Our results also indicate a higher viral load detected after prolonged contact with sheets and pillow covers than with intermittent contact with the door handle and light switch. The detection of SARS-CoV-2 RNA in the surface samples of the sheet, duvet cover, and pillow cover highlights the importance of proper handling procedures when changing or laundering used linens of SARS-CoV-2 patients. Thus, to minimize the possibility of dispersing virus through the air, we recommend that used linens not be shaken upon removal and that laundered items be thoroughly cleaned and dried to prevent additional spread".*
Jiang, X.L. *et al* (2020) **Transmission potential of asymptomatic and pauci-symptomatic SARS-CoV-2 infections: a three-family cluster study in China**. *J Infect Dis.* 2020; jiaa206 Epub ahead of print. Published: 22 April, 2020. https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiaa206/5823691	*"We report a 3-family cluster of infections involving asymptomatic and paucisymptomatic transmission. Eight of 15 (53%) members from 3 families were confirmed with SARS-CoV-2 infection. Of 8 patients, 3 were asymptomatic and 1 was paucisymptomatic. An asymptomatic mother transmitted the virus to her son, and a paucisymptomatic father transmitted the virus to his 3-monthold daughter. SARS-CoV-2 was detected in the environment of 1 household. The complete genomes of SARS-CoV-2 from the patients were > 99.9% identical and were clustered with other SARS-CoV-2 sequences reported from China and other countries".*
Cai J, Sun W, Huang J, Gamber M, Wu J, He G. (2020) **Indirect virus transmission in cluster of COVID-19 cases, Wenzhou, China, 2020.** *Emerg Infect Dis*. 2020; Vol. 26 (6). Epub ahead of print. Published: 12 March, 2020. https://wwwnc.cdc.gov/eid/article/26/6/20-0412_article	*"To determine possible modes of virus transmission, we investigated a cluster of coronavirus disease cases associated with a shopping mall in Wenzhou, China. Data indicated that indirect transmission of the causative virus occurred, perhaps resulting from virus contamination of common objects, virus aerosolization in a confined space, or spread from asymptomatic infected persons".*
Rothe, C. *et al* (2020) **Transmission of 2019-nCoV infection from an asymptomatic contact in Germany**. *N Engl J Med*. 2020; 382:970–1.	*"A 33-year-old otherwise healthy German businessman (Patient 1) became ill with a sore throat, chills, and myalgias on January 24, 2020. The following day, a fever of 39.1°C (102.4°F) developed, along with a productive*

Published: 5 March, 2020. https://www.nejm.org/doi/pdf/10.1056/NEJMc2001468?articleTools=true	*cough. By the evening of the next day, he started feeling better and went back to work on January 27".* *"Before the onset of symptoms, he had attended meetings with a Chinese business partner at his company near Munich on January 20 and 21. The business partner, a Shanghai resident, had visited Germany between January 19 and 22. During her stay, she had been well with no signs or symptoms of infection but had become ill on her flight back to China, where she tested positive for 2019-nCoV on January 26"*
Yu, P. *et al* (2020) **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; 221:1757–61. Published: 18 February, 2020. https://academic.oup.com/jid/article/221/11/1757/5739751	*"We report the epidemiological features of a familial cluster of 4 patients in Shanghai, including an 88-year-old man with limited mobility who was exposed only to asymptomatic family members whose symptoms developed later. The epidemiological evidence has shown possible transmission of 2019 novel coronavirus during the incubation period".*
Tong, Z.D. *et al* **Potential presymptomatic transmission of SARS-CoV-2, Zhejiang province, China, 2020**. *Emerg Infect Dis*. 2020; 26:1052–4. Published: 9 March, 2020. https://wwwnc.cdc.gov/eid/article/26/5/20-0198_article	*"In summary, we identified 2 persons with confirmed cases of symptomatic COVID-19 after their exposure to a potentially presymptomatic person who was later diagnosed with laboratory-confirmed COVID-19. These 2 persons later transmitted SARS-CoV-2 to 3 family members, who did not report symptoms at the time their SARS-CoV-2 infections were detected".*
Wei, W.E. *et al* (2020) **Presymptomatic Transmission of SARS-CoV-2 — Singapore, January 23–March 16, 2020**. *Morbidity and Mortality Weekly Report* 49: 411-416. Published: 10 April, 2020. https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e1.htm	*"Among the 243 cases of COVID-19 reported in Singapore as of March 16, 157 were locally acquired; 10 of the 157 (6.4%) locally acquired cases are included in these clusters and were attributed to presymptomatic transmission. These findings are supported by other studies that suggest that presymptomatic transmission of COVID-19 can occur"*
Qian, G. *et al* (2020) **COVID-19 Transmission Within a Family Cluster by Presymptomatic Carriers in China**. *Clin Infect Diseases*, 2020. Published: 23 March, 2020. https://academic.oup.com/cid/advance-	*"The clinical features were diverse across patients; in particular, there were 2 asymptomatic patients and 1 patient whose symptoms were so severe that he had to be transferred to ICU. Second, this cluster demonstrated that COVID-19 is transmittable during the incubation period, as the daughter and her family caught the disease during the incubation period of index 1 and index 2. Third, patients can stay asymptomatic, such as index 2 and case 4 in this cluster. Given that Zou et al found that the viral load of*

article/doi/10.1093/cid/ciaa316/5810900	*symptomatic and asymptomatic patients were similar, asymptomatic patients can still infect others. These "silent patients" may remain undiagnosed and be able to spread the disease to large numbers of people. Last, it appears that children may not be as susceptible to this new virus as adults and elderly persons, and they may fare better when they have contracted the virus. As reported in this family cluster, the 6-year-old child was not infected and the 13-month-old was infected but stayed asymptomatic."* *"In summary, there are variations across individuals in the clinical manifestations of COVID-19, indicating that we should pay attention to how to prevent people from being infected by asymptomatic patients and patients who are in the incubation period."*
Zou, L. *et al* (2020) **SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients**. New England Journal of Medicine, 2020. Published: 19 March, 2020. https://www.nejm.org/doi/pdf/10.1056/NEJMc2001737	*"The viral load that was detected in the asymptomatic patient was similar to that in the symptomatic patients, which suggests the transmission potential of asymptomatic or minimally symptomatic patients. These findings are in concordance with reports that transmission may occur early in the course of infection and suggest that case detection and isolation may require strategies different from those required for the control of SARS-CoV. How SARS-CoV-2 viral load correlates with culturable virus needs to be determined. Identification of patients with few or no symptoms and with modest levels of detectable viral RNA in the oropharynx for at least 5 days suggests that we need better data to determine transmission dynamics and inform our screening practices."*
Bai, Y. *et al* (2020) **Presumed asymptomatic carrier transmission of COVID-19**. *JAMA*, 2020, 323 (14) 1406-1407. Published: 21 February, 2020. https://jamanetwork.com/journals/jama/fullarticle/2762028	A study of a family cluster of 5 people indicating that transmission may have been from an asymptomatic carrier.
Tong, Z.D. *et al* (2020) **Potential Presymptomatic Transmission of SARS-CoV-2, Zhejiang Province, China, 2020.** Emerging Infectious Diseases 26 (5). Published: 9 March, 2020. https://wwwnc.cdc.gov/eid/article/26/5/20-0198_article	*"We identified 2 persons with confirmed cases of symptomatic COVID-19 after their exposure to a potentially presymptomatic person who was later diagnosed with laboratory-confirmed COVID-19. These 2 persons later transmitted SARS-CoV-2 to 3 family members, who did not report symptoms at the time their SARS-CoV-2 infections were detected".*

Luo, L. *et al* (2020) **Modes of contact and risk of transmission in COVID-19 among close contacts.** *medRxiv*, 2020.03.24.20042606. Published: 26 March, 2020. https://www.medrxiv.org/content/10.1101/2020.03.24.20042606v1	*"…the proportion of asymptomatic and mild infections account for almost half of the confirmed cases among close contacts. The household contacts were the main transmission mode, and clinically more severe cases were more likely to pass the infection to their close contacts."*
Hu, Z. *et al* (2020) **Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China.** *Sci. China Life Sci.* 63, 706–711 (2020). Published: 4 March, 2020. https://link.springer.com/article/10.1007/s11427-020-1661-4	*"This study aims to present the clinical characteristics of 24 cases with asymptomatic infection screened from close contacts..."* *"Five cases (20.8%) developed symptoms (fever, cough, fatigue, etc.) during hospitalization. Twelve (50.0%) cases showed typical CT images of ground-glass chest and 5 (20.8%) presented stripe shadowing in the lungs. The remaining 7 (29.2%) cases showed normal CT image and had no symptoms during hospitalization. These 7 cases were younger (median age: 14.0 years;P=0.012) than the rest."*
Huang, R *et al* (2020) **A family cluster of SARS-CoV-2 infection involving 11 patients in Nanjing, China.** *Lancet Infect Dis.* 2020;20(5):534-5. Published: 28 February, 2020. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7159019/	*"…the family cluster of patients we describe provides evidence that asymptomatic people can be potential sources of SARS-CoV-2 infection."*
Pan, X. *et al* (2020) **Asymptomatic cases in a family cluster with SARS-CoV-2 infection.** *Lancet Infect Dis.* 2020;20(4):410-1. Published: 19 February, 2020. https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(20)30114-6.pdf	*"In this family cluster, although all individuals tested positive for SARS-CoV-2 infection on qRT-PCR, only patient 1 showed clinical symptoms, decreased lymphocyte count, and abnormal chest CT images. However, any of the three individuals could have been the first one to become infected and thus transmitted the virus to the other two family members. Importantly, asymptomatic patients (such as patients 2 and 3) might be unaware of their disease and therefore not isolate themselves or seek treatment, or they might be overlooked by health-care professionals and thus unknowingly transmit the virus to others."*
Chan, J.F.W et al (2020) **A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster.** *Lancet* 2020; 395: 514–23.	Testing of a family cluster of 7 people showed 5 of the 7 were positive for SARS-CoV-2 and 1 of these 5 (a 10 year old child) was asymptomatic.

Published: 24 January, 2020. https://www.thelancet.com/action/showPdf?pii=S0140-6736%2820%2930154-9	
Zhao, H. *et al* (2020) **COVID-19: Asymptomatic carrier transmission is an underestimated problem.** *Epidemiology and Infection*, 148, E116. Published: 4 June, 2020. doi:10.1017/S0950268820001235	*"So far, people have not paid enough attention to asymptomatic carriers. The asymptomatic carriers discussed in this study are recessive infections, that is, those who have never shown symptoms after onset of infection."* *"Because the proportion of the asymptomatic cases is underestimated and the infectiousness and prevention measures of the asymptomatic have not attracted enough attention, there will be a critical flaw in prevention and control of COVID-19."*

C. CDC Guidance recognising a- or pre-symptomatic transmission

CDC Guidance: https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/how-covid-spreads.html	*"COVID-19 may be spread by people who are not showing symptoms"*
CDC Guidance: **Key Strategies to Prepare for COVID-19 in Long-Term Care Facilities (LTCFs)** https://www.cdc.gov/coronavirus/2019-ncov/hcp/long-term-care-strategies.html	*"If COVID-19 is identified in the facility, restrict all residents to their rooms and have HCP wear all recommended PPE for care of all residents (regardless of symptoms) on the affected unit (or facility-wide depending on the situation). This includes: an N95 or higher-level respirator (or facemask if a respirator is not available), eye protection, gloves, and gown. HCP should be trained on PPE use including putting it on and taking it off".* *"This approach is recommended because of the high risk of unrecognized infection among residents. Recent experience suggests that a substantial proportion of residents could have COVID-19 without reporting symptoms or before symptoms develop".* *"When a case is identified, public health can help inform decisions about testing asymptomatic residents on the unit or in the facility".*

D. Transmission through environment and on PPE

Jiang, F.C. *et al* (2020) **Detection of Severe Acute Respiratory Syndrome Coronavirus 2 RNA on Surfaces in**	*"We investigated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) environmental contamination in 2 rooms of a quarantine hotel after 2 pre-symptomatic persons who stayed there were laboratory-confirmed as*

Quarantine Rooms. *Dispatch*, Volume 26, Number 9, Sept 2020. Published: 18 May, 2020. https://wwwnc.cdc.gov/eid/article/26/9/20-1435_article	*having coronavirus disease. We detected SARS-CoV-2 RNA on 8 (36%) of 22 surfaces, as well as on the pillow cover, sheet, and duvet cover".* *"Our study demonstrates extensive environmental contamination of SARS-CoV-2 RNA in a relatively short time (<24 hours) in occupied rooms of 2 persons who were pre-symptomatic".* *"Our results also indicate a higher viral load detected after prolonged contact with sheets and pillow covers than with intermittent contact with the door handle and light switch. The detection of SARS-CoV-2 RNA in the surface samples of the sheet, duvet cover, and pillow cover highlights the importance of proper handling procedures when changing or laundering used linens of SARS-CoV-2 patients. Thus, to minimize the possibility of dispersing virus through the air, we recommend that used linens not be shaken upon removal and that laundered items be thoroughly cleaned and dried to prevent additional spread".*
Yung, C.F. *et al* (2020) **Environment and Personal Protective Equipment Tests for SARS-CoV-2 in the Isolation Room of an Infant With Infection.** *Annals of Internal Medicine*, 2020 American College of Physicians. Published: 1 April, 2020. https://www.acpjournals.org/doi/10.7326/M20-0942	*"A 6-month-old infant was admitted for isolation in our hospital because both parents were in the isolation units of other hospitals for confirmed COVID-19. On admission, the infant was asymptomatic, but nasopharyngeal swabs confirmed COVID-19 infection with very high viral load".* *"The infant was generally well throughout admission, with only a single measured temperature of 38.5 °C on day 2 of admission. There were no respiratory symptoms, results of physical examination were normal and no other abnormal vital signs were noted throughout the infant's stay".* *"Our investigation confirmed that a generally well infant with COVID-19 can contaminate the environment with PCR-detectable virus. Although we cannot be certain of virus viability, other coronaviruses have been reported to re-main viable on surfaces for up to 9 days (4). Despite close physical contact with the infant during feeding, we did not detect any evidence of SARS–CoV-2 on the gown of the HCW.A study of mobile adults with COVID-19 who had symptoms found widespread environmental contamination but negative PPE swabs (5).* *Although our infant had no respiratory symptoms, the nearby environment could have been contaminated with SARS–CoV-2 through crying or drooling.* *There was a downward trend of viral load with increasing distance from the infant (from bedding to cot rail). However, the Ct values at the table 1 meter away from the cot indicated higher viral load. For droplet transmission, one would expect the viral load in the environment to fall with increasing distance from the immobile infant.*

	However, baby formula and other items, such as baby wipes, were placed on it. Therefore, it seems more likely that the contamination was due to indirect contact via HCW hands between baby and table. *These findings suggests that even generally well infants positive for SARS–COV-2 with no respiratory symptoms can easily contaminate nearby environments. Our data also reaffirm the importance of hand hygiene when caring for infants with COVID-19 and potentially in helping to reduce environmental virus contamination.*
van Doremalen, N. *et al* (2020) **Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1.** Letter, *N Engl J Med*. 2020; 382:1564–7. Published: March 17, 2020. https://www.nejm.org/doi/pdf/10.1056/NEJMc2004973?articleTools=true	*"SARS-CoV-2 remained viable in aerosols throughout the duration of our experiment (3hours), with a reduction in infectious titer from 103.5 to 102.7 TCID50 per liter of air. This reduction was similar to that observed with SARS-CoV-1, from 104.3 to 103.5 TCID50 per milli-liter (Fig. 1A). SARS-CoV-2 was more stable on plastic and stainless steel than on copper and cardboard, and viable virus was detected up to 72 hours after application to these surfaces (Fig. 1A), al-though the virus titer was greatly reduced (from 103.7 to 100.6 TCID50 per milliliter of medium after 72 hours on plastic and from 103.7 to 100.6 TCID50per milliliter after 48 hours on stainless steel)".*
Chin, A.W.H. *et al* (2020) **Stability of SARS-CoV-2 in different environmental conditions.** *Lancet Microbe*. 2020;1:e10. Published: 2 April, 2020. https://www.thelancet.com/pdfs/journals/lanmic/PIIS2666-5247(20)30003-3.pdf	*"No infectious virus could be recovered from printing and tissue papers after a 3-hour incubation, whereas no infectious virus could be detected from treated wood and cloth on day 2. By contrast, SARS-CoV-2 was more stable on smooth surfaces. No infectious virus could be detected from treated smooth surfaces on day 4 (glass and banknote) or day 7 (stainless steel and plastic). Strikingly, a detectable level of infectious virus could still be present on the outer layer of a surgical mask on day 7 (~0·1% of the original inoculum)."* *"Overall, SARS-CoV-2 can be highly stable in a favourable environment,4 but it is also susceptible to standard disinfection methods."*
Ong, S.W.X. *et al* (2020) **Air, surface environmental, and personal protective equipment contamination by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from a symptomatic patient.** *JAMA.* 2020;323:1610. Published: 4 March, 2020. https://jamanetwork.com/journals/jama/fullarticle/2762692	*"There was extensive environmental contamination by 1 SARS-CoV-2 patient with mild upper respiratory tract involvement. Toilet bowl and sink samples were positive, suggesting that viral shedding in stool could be a potential route of transmission. Post cleaning samples were negative, suggesting that current decontamination measures are sufficient".* *"Only 1 PPE swab, from the surface of a shoe front, was positive. All other PPE swabs were negative. All air samples were negative".*

Ye, G. *et al* (2020) **Environmental contamination of the SARS-CoV-2 in healthcare premises: An urgent call for protection for healthcare workers.** *medRxiv*, 2020.03.11.20034546. Published: 16 March, 2020. https://doi.org/10.1101/2020.03.11.20034546	A study looking into the most contaminated objects and PPE items in a Chinese hospital. *"The most contaminated objects and PPE are self-service printers (20.0%), hand sanitizer dispensers (20.3%), and gloves (15.4%)."*
Santarpia, J.L. *et al* (2020) **Aerosol and Surface Transmission Potential of SARS-CoV-2.** *medRxiv*, 2020.03.23.20039446. Published: 3 June, 2020. https://www.medrxiv.org/content/10.1101/2020.03.23.20039446v3	*"Overall, 70.6% of all personal items sampled were determined to be positive for SARS-CoV-2 by PCR. Of these samples, 75.0% of the miscellaneous personal items were positive by PCR, with a mean concentration of 0.22 copies/µL. Samples of cellular phones were 77.8% positive for viral RNA (0.17 copies/µL mean concentration) and remote controls for in-room televisions were 55.6% percent positive (mean of 0.22 copies/µL). Samples of the toilets in the room were 81.0% positive, with a mean concentration of 0.25 copies/µL. Of all room surfaces sampled, 75.0% were positive for SARS-CoV-2 RNA. 70.8% of the bedside tables and bed rails indicated the presence of viral RNA (mean concentration 0.26 copies/µL), as did 72.7% of the window ledges (mean concentration 0.22 copies/µL) sampled in each room. The floor beneath patients' beds and the ventilation grates in the NBU were also sampled. All five floor samples, as well as 4 of the 5 ventilation grate samples tested positive by RT-PCR, with mean concentrations of 0.45 and 0.82 copies/µL, respectively."* *"Taken together, these data indicate significant environmental contamination in rooms where patients infected with SARS-CoV-2 are housed and cared for, regardless of the degree of symptoms or acuity of illness. Contamination exists in all types of samples: high and low-volume air samples, as well as surface samples including personal items, room surfaces, and toilets."* *"Our study suggests that SARS-CoV-2 environmental contamination around COVID-19 patients is extensive, and hospital IPC procedures should account for the risk of fomite, and potentially airborne, transmission of the virus."*