COVID-19 Evidence Update

COVID-19 Update from SAHMRI, Health Translation SA and the Commission on Excellence and Innovation in Health

15 June 2020

Asymptomatic and pre-symptomatic cases and transmission of SARS-COV-2

Executive Summary

Definitions:

- "Asymptomatic cases" refers to people who have SARS-CoV-2 at levels that are detectable (via positive PCR test) but are not exhibiting clinical symptoms at the time of the positive test. These people may be pre-symptomatic (about to develop symptoms), or truly asymptomatic (never develop symptoms).
- "Asymptomatic transmission" refers to the transmission of virus by people who do not yet have symptoms (pre-symptomatic transmission) or who never develop symptoms (truly asymptomatic transmission).

State of literature:

- There is a large body of scientific literature reporting on "asymptomatic cases", and a smaller body of literature reporting on "asymptomatic transmission". Much of this literature conflates truly asymptomatic cases with pre-symptomatic cases, and does not distinguish between them.
- Individual reports of the prevalence of "asymptomatic cases" vary enormously – from 1.6% [1] to 96% [2] – and are not a useful guide.
- Accurate estimates of truly asymptomatic cases and transmission are difficult to ascertain, and dedicated studies are required.

Pooled estimates: Best available data on truly asymptomatic cases and transmission comes from two separate systematic reviews and meta analyses (both pre-prints; not yet peer-reviewed) [3, 4]:

- Prevalence of truly asymptomatic cases: 15% prevalence (both papers);
- Truly asymptomatic transmission rate: 0-2% (4 observational studies) and 6% (1 modelling study).

Conclusion: The World Health Organization reports that truly asymptomatic transmission is 'rare'. This is supported by the weight of available evidence. Pre-symptomatic transmission of SARS-CoV-2 is well established, although likely to be less prevalent than symptomatic transmission.

Australian research underway: The FFX (First Few X cases) Study will measure rates of symptomatic and asymptomatic transmission in households. It will also investigate children's propensity to transmit. Further, the Australia Seroprevalence Study will estimate the prevalence of SARS-CoV-2 antibodies in the Australian population, quantifying undetected cases.

SAHMRI South Australian Health & Medical Research Institute | Health Translation SA >RESEARCH >ACTION >IMPACT | Commission on Excellence and Innovation in Health. | Government of South Australia

Context

Definitions

- (Truly) Asymptomatic – SARS-CoV-2 RNA detectable but symptoms never develop
- Pre-symptomatic – SARS-CoV-2 RNA detectable before symptom onset
- Paucisymptomatic – those with detectable SARS-CoV-2 RNA but with few symptoms
- "Asymptomatic" is often used imprecisely, in both the scientific literature and in lay settings, conflating pre-symptomatic and truly asymptomatic cases

World Health Organization Statements

- WHO Interim guidance on the use of face masks 5 June 2020 [5]: Brief summary of the literature on the possibility of transmission from people who are infected with SARS-CoV-2 but who have not yet developed symptoms. Concluded that the evidence was of low quality but suggests that asymptomatically-infected individuals are much less likely to transmit the virus than those who develop symptoms.
- WHO press briefing 8 June 2020: technical lead Maria Van Kerkhove said that asymptomatic transmission of the SARS-CoV-2 virus was "very rare".
    - This press briefing attracted considerable media attention and criticism from experts (The Scientist 10 June; STAT 9 June). It also generated articles that were widely shared on social media but were classified by experts as misinformation (Health Feedback). Its rapid spread was assisted by those who oppose physical distancing and/or promote health misinformation.
- WHO follow-up Q and A session: Van Kerkhove clarified that asymptomatic transmission was still an open question. She indicated that she was referring only to patients who never show any symptoms at all, not those who have yet to show symptoms (i.e. pre-symptomatic) or those who only show mild symptoms.

Determining asymptomatic case rates, transmission and the implications

- Disagreement about the level of asymptomatic SARS-CoV-2 infection is partly due to studies that report data based on a single time point. The lack of follow up data makes it difficult to determine whether people remain asymptomatic throughout or whether they go on to develop symptoms and become re-classified as pre-symptomatic [4].
- Accurate estimates of the proportion of true asymptomatic infections are needed to determine the appropriate control strategies. If transmission is predominantly via symptomatic people then the focus should be on testing and quarantining of close contacts. Conversely, if most transmission is via asymptomatic cases, then social distancing should be prioritised [4].
- Asymptomatic individuals are hard to trace, unlikely to self-isolate, and are likely to retain normal social and travel patterns [6].
- Fraser 2004 [7] (PNAS): The authors conclude that SARS-CoV-1 was easier to control (than HIV or pandemic influenza) because R0 and proportion of asymptomatic/pre-symptomatic cases was low. Conversely, influenza was difficult to control because of the high level of pre-symptomatic transmission.
- Gandhi 2020 [8], editorial (NEJM): The different trajectory of SARS-CoV-2 compared to SARS-CoV-1 suggests that asymptomatic, pre-symptomatic and/or paucisymptomatic (i.e. those with few symptoms) transmission is a contributing factor.
- South Australia is part of the national FFX (First Few X) Study which is in part designed to answer questions about asymptomatic transmission. Furthermore, the National Seroprevalence Survey is designed to give an estimate of number of South Australians with SARS-Cov-2 antibodies, which will also provide insights into undetected transmission.

Media Reporting

- Studies on asymptomatic transmission of SARS-CoV-2 have attracted media attention over the course of the pandemic (Science alert, 24 Feb 2020; CNN, 19 March 2020; The Guardian, 30 May 2020; NewsGP 2 June 2020; ABC news 4 June 2020).
- The reports indicate concern about spread from people who do not self-isolate because they show no symptoms. They also cite various studies showing a range of asymptomatic prevalence rates, suggesting that it is not yet known whether asymptomatic spread is common.

Key summary from the evidence

**Note: "asymptomatic" is used below in the same way as it is reported by each study's authors, who often do not delineate between truly asymptomatic and pre-symptomatic cases and transmission.*

Asymptomatic* cases - incidence (and transmission, if reported)

Reviews

Byambasuren 4 June 2020 [3], systematic review and meta-analysis (medRxiv PRE-PRINT):

- Identified studies that had attempted to estimate the proportion of asymptomatic COVID-19 cases and selected those with minimal or no bias. Single case/small cluster studies were excluded.
- All cases had a follow up period of at least 7 days to distinguish asymptomatic from pre-symptomatic cases.
- Primary outcome: proportion of all people with confirmed SARS-CoV-2 infection who were completely asymptomatic throughout the follow-up period.
- Results: 9 articles (5 published, 4 pre-prints) from 6 countries, tested 21,035 close contacts of at least 843 confirmed COVID-19 cases. A total of 599 were positive and 83 were asymptomatic. Note 123 studies were excluded for reasons such as no/unclear follow up period (26%) and unclear sampling frame (22%).
- Diagnosis was confirmed via RT-qPCR in all studies; testing of the study sample was generally very high, and follow-up period was mostly between 7 and 14 days.
- The Proportion of asymptomatic cases ranged from 4% to 41% (see figure below).
- **The overall estimate from the fixed effects model was 15% (95%CI 12%-18%).**

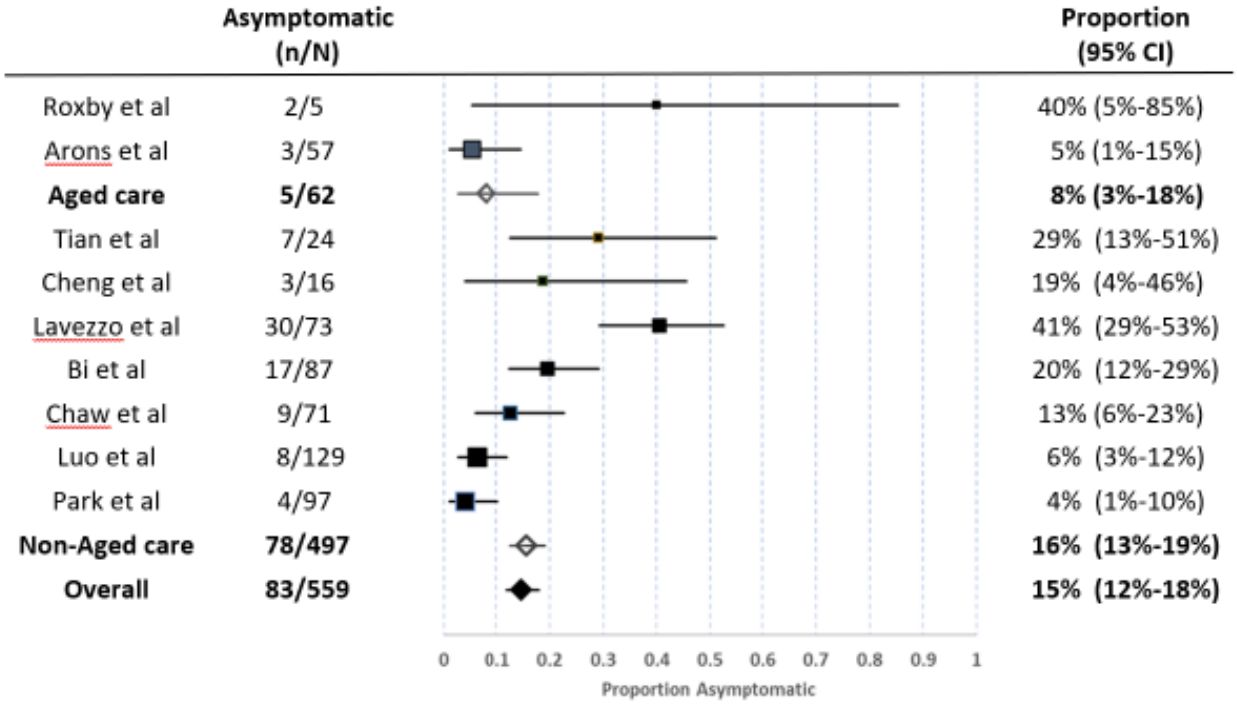


Figure 3. Fixed effects pooled estimates of proportion of asymptomatic carriers by subpopulations. N - positive cases; n - asymptomatic cases.

- Secondary outcome: 4 studies reported the estimate of community spread from asymptomatic cases. **Asymptomatic transmission rates** ranged from **0 to 2.2%** (see Table below). The C_t from RT-PCR assays reported in three studies did not differ between asymptomatic and symptomatic individuals.

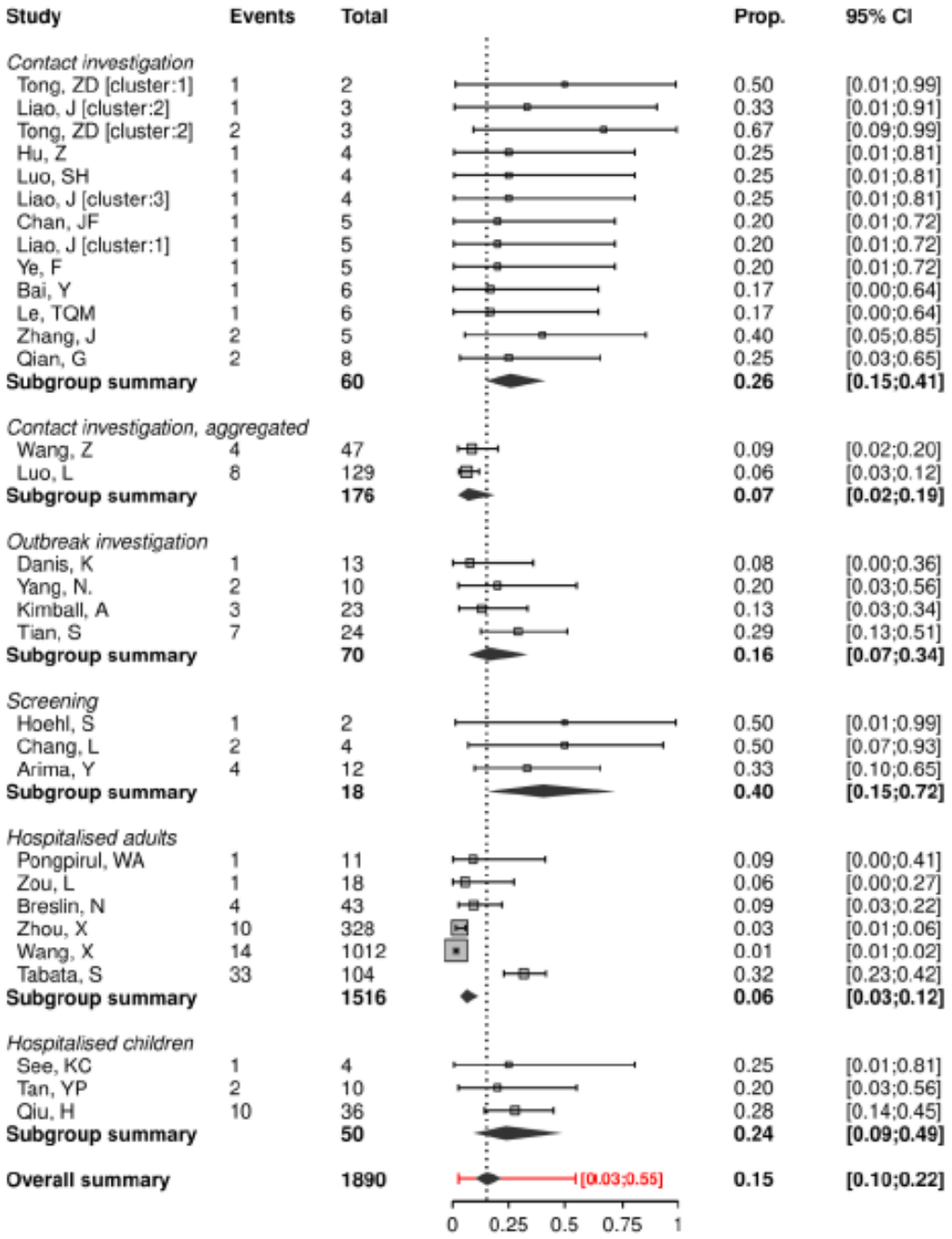
Table 2. Comparison of secondary transmission rates

Study ID	Asymptomatic transmission rate	Symptomatic transmission rate	Relative risk
Chaw et al	15/691 (2.2%)	28/1010 (2.8%)	0.79
Cheng et al	0/91 (0%)	22/2644 (0.8%)	0.0
Luo et al	1/305 (0.3%)	117/2305 (5.1%)	0.06
Park et al	0/4 (0%)	34/221 (15.4%)	0.0

- Other noteworthy findings: there was some risk of bias in 7 of the 9 studies and several well publicized studies did not meet the inclusion criteria. These included the Diamond Princess cruise ship [9] which did not meet the criteria for follow-up and the Icelandic study which could not differentiate asymptomatic from pre-symptomatic and excluded symptomatic people [10].

Buitrago-Garcia 24 May 2020 [4], systematic review and meta-analysis (medRxiv PRE-PRINT):

- Included studies with confirmed SARS-CoV-2 infection and that documented follow-up and start and end symptom status, or that investigated transmission. Single patient case reports were excluded.
- Results: 37 reports were included (31 published, 6 pre-prints).
- Primary outcome 1: Proportion of people with **asymptomatic SARS-CoV-2 infection** – 28 studies with empirical data and 1 modelling study. The main risk of bias was the sampling frame. The results are displayed in the figure below. The **overall estimate was 15%** (95%CI=10% to 22%). The estimate differed according to study methods and setting.



- Primary outcome 2: Proportion of people with **pre-symptomatic SARS-CoV-2 infection** – 15 studies with heterogeneous findings so a summary estimate was **not calculated**.
- Primary outcome 3: Contribution of asymptomatic and pre-symptomatic infection to SARS-CoV-2 transmission – **4 modelling studies,** but only 1 reported on **asymptomatic transmission** [11]. This study estimated asymptomatic transmission as **6%** (95%CI 0 to 57%) of the total transmission, based on the fraction of asymptomatic infections on the Diamond Princess cruise (46%). Conversely, **pre-symptomatic** patients were estimated to account for **47%** (11 to 58%) of the total. Transmission estimates for pre-symptomatic patients in the remaining modelling studies was between **40% and 60%**.
- Many studies were assessed as having risk of bias.

Oran 2020 [2], narrative review (Annals of Internal Medicine):

- Aimed to synthesise studies reporting the prevalence of “asymptomatic SARS-CoV-2".
- 16 cohort studies were included in the review but **only 5 included longitudinal data**, making it difficult to distinguish truly asymptomatic from pre-symptomatic cases. The summary of studies is provided in the table below. Reported “positive but asymptomatic” rates varied from 6.3% to 96.0%.
- The authors suggest, based on the 3 largest/most representative samples (Iceland, Indiana (USA), and Vo (Italy)) that the prevalence of “asymptomatic infection” was around **40-45%.**

Table. Summary of SARS-CoV-2 Testing Studies

Cohort	Tested, *n*	SARS-CoV-2 Positive, *n* (%)	Positive but Asymptomatic, *n* (%)	Notes*
Iceland residents (6)	13 080	100 (0.8)	43 (43.0)	R
Vo', Italy, residents (7)	5155	102 (2.0)	43 (42.2)	R, L
Diamond Princess cruise ship passengers and crew (8)	3711	712 (19.2)	331 (46.5)	–
Boston homeless shelter occupants (9)	408	147 (36.0)	129 (87.8)	–
New York City obstetric patients (11)	214	33 (15.4)	29 (87.9)	L
U.S.S. *Theodore Roosevelt* aircraft carrier crew (12)	4954	856 (17.3)	~500 (58.4)	E
Japanese citizens evacuated from Wuhan, China (2)	565	13 (2.3)	4 (30.8)	L
Greek citizens evacuated from the United Kingdom, Spain, and Turkey (14)†	783	40 (5.1)	35 (87.5)	L
Charles de Gaulle aircraft carrier crew (13)	1760	1046 (59.4)	~500 (47.8)	E
Los Angeles homeless shelter occupants (10)	178	43 (24.2)	27 (62.8)	–
King County, Washington, nursing facility residents (15)	76	48 (63.2)	3 (6.3)	L
Arkansas, North Carolina, Ohio, and Virginia inmates (16)	4693	3277 (69.8)	3146 (96.0)	–
New Jersey university and hospital employees (17)	829	41 (4.9)	27 (65.9)	–
Indiana residents (18)	4611	78 (1.7)	35 (44.8)	R
Argentine cruise ship passengers and crew (19)	217	128 (59.0)	104 (81.3)	–
San Francisco residents (29)	4160	74 (1.8)	39 (52.7)	–

E = estimated from incomplete source data; L = longitudinal data collected; R = representative sample.
* A dash indicates that the study did not have a representative sample, collected no longitudinal data, and did not require estimation of missing data.
† Clarified via e-mail communication with coauthor.

Gao 2020 [1], narrative review (J Microbiol Immunol Infect):

- reports incidence rate of “asymptomatic infections” from a selection of studies (overlaps with Oran review).
- Reported “incidence of asymptomatic infections” ranged from **1.6% to 56.5%.**
- Authors noted that each study had shortcomings so it is difficult to know the true incidence rate.

Table 2 The incidence of asymptomatic infections with COVID-19 in different studies.

	China[8] (n = 72,314)	Japan[9] (n = 565)	Diamond Princess[10] (n = 3711)	Korea[11] (n = 28)	Washington[12] (n = 76)	Wuhan Children[13] (n = 1391)
RT-PCR positive cases	56,128	13	634	28	23	171
Asymptomatic cases	889	4	328	3	13	27
Incidence rate (%)[a]	1.6	30.8	51.7	10.7	56.5	15.8

[a] As of the data published in the literature, the proportion of asymptomatic infections in the population with positive nucleic acid test.

Lee 2020 [12], narrative review (Can J Anesth):

- **Cases**: reporting on 5 studies (overlaps with Oran review) suggested that **“asymptomatic and pre-symptomatic”** rates ranged from **17.9% to 57%** of those who test positive to COVID-19. When factoring population prevalence and population infection rate, point prevalence of asymptomatic cases was **0.34% in Iceland** (low population infection rate) and **10% on the Diamond Princess** cruise ship (high population infection rate).
- **Transmission**: reporting on 4 studies, the authors suggest that there is a window of time when the patient is infectious but not yet exhibiting symptoms. One study suggested that viral transmission occurring 2-3 days prior to symptom onset in **up to 44% of patients**. Another study suggested that **6.4%** of infections occurred prior to symptom onset in the index case.

Oxford Centre for Evidence-based medicine 6 April 2020, non-peer review summary (online):

- Literature search returned 21 reports for analysis. Results indicated that between 5% and 80% of people testing positive for SARS-CoV-2 may be asymptomatic, although some may go on to develop symptoms and become reclassified as pre-symptomatic. The quality of evidence was reported as low.

Primary studies (not already included in review studies)

- Huang 2020 [13] (Journal of Infection): index patient was pre-symptomatic 22yo male. Before symptom onset he closely contacted 22 people. All were subsequently quarantined and of these 7 tested positive for SARS-CoV-2. The median time from exposure to symptom onset in secondary cases was 2 days.
- Gao 2020 [14] (Respir Med): index case was 22yo female already in hospital receiving treatment for other health condition. The authors suggested that she was "asymptomatic" (for COVID-19 related symptoms) but tested positive for SARS-CoV-2. None of the 455 contacts who had been exposed tested positive.
- Cohort testing of hospital patients:
  - Gruskay 2020 [15] (J Bone Joint Surg Am): 9 out of 16 (**56%**) preoperative patients who tested positive for SARS-CoV-2 were "asymptomatic at baseline"; there were no demographic differences between asymptomatic and symptomatic patients.
  - Yang 2020 [16] (JAMA Network Open): 33 out of 78 (**42%**) patients were "asymptomatic". Compared to symptomatic patients, asymptomatic patients were **younger**, female, shorter duration of viral shedding, faster lung recovery, and more stable SARS-CoV-2 testing results.
  - Mays 2020 [17] (J Clin Microbiol): 2056 "asymptomatic patients" were screened; 9 tested positive and 2 were inconclusive for SARS-CoV-2; in comparison 137 of 1336 (**10.3%**) of patients showing symptoms tested positive.
  - Al-Shamsi 2020 [18] (JAMA Oncol): 7 out of 85 cancer patients who were screened were asymptomatic with COVID-19; all subsequently developed symptoms.
  - Ochiai 2020 [19] (Int J Gynaecol Obstet): 2 confirmed and 1 suspected case of COVID-19 in a cohort of 52 obstetric patients; none presented with symptoms.
- Additional case reports: Chen 2020 [20] (J Infect Public Health); Jiang 2020 [21] (J Infect Dis); Samsami 2020 [22] (Arch Acad Emerg Med); Corman 2020 [23] (Transfusion).

Asymptomatic* transmission

Reviews

Furukawa 2020 [24], narrative review (Emerg Infect Dis):
Searched PubMed for articles published from Jan 1 to April 2, 2020. Search terms included SARS-CoV-2, COVID-19, asymptomatic, pre-symptomatic, and transmission.

- Epidemiologic evidence:
  - Pre-symptomatic transmission: 6 studies, 4 in China (1 case/family/couple per study), 1 in Germany (1 case), 1 in Singapore (6 cases, 1 couple);
  - Asymptomatic transmission: 3 studies, all single cases in China; and
  - Either pre-symptomatic or asymptomatic: 2 studies, 1 case and 1 couple in China.
  - Reported secondary transmission from asymptomatic/pre-symptomatic cases occurred within families or households (8 studies), during shared meals (2 studies) or when visiting family in hospital (2 studies).
  - A limitation of the reports from China is the inability to rule out alternative exposure in the community when community transmission was potentially occurring undetected. The authors state that this limitation is not applicable for the cases in Germany and Singapore as there was limited/no community spread at the time.
- Virologic evidence:
  - Infectiousness can be inferred from cycle threshold (C_t) values; the RT-PCR C_t value represents the number of PCR cycles required to detect SARS-CoV-2 RNA where lower values=higher viral load and imply higher infectiousness.

    - 4 studies report low C_t values in asymptomatic and pre-symptomatic cases. Actual transmission was not reported, but the studies provide plausible virologic evidence for asymptomatic transmission.
- Modelling evidence:
    - 2 studies used models to estimate the serial interval and found that it was shorter than the estimated median incubation period, suggesting that infections may be transmitted during the pre-symptomatic period of illness, although the results may be limited by recall bias.
    - 2 studies estimated the number of infections caused by asymptomatic, pre-symptomatic or mildly symptomatic infected persons. One study suggested that up to half of infections were transmitted from pre-symptomatic cases whereas the other study suggested that up to 4/5 of infections were transmitted by asymptomatic or mild symptom cases.
- Conclusions: Each approach has limitations but together the results suggest that transmission via pre-symptomatic or asymptomatic cases is likely. However, further research is needed to ascertain the proportion of infections that are truly asymptomatic.

Wang 2020 [25], narrative review/commentary (J of Med Virology): reports results from 4 studies indicating "asymptomatic spread" of COVID-19 – 2 studies reported transmission among family members and 2 studies suggested that the viral load was similar between "asymptomatic" and symptomatic patients.

Aguirre-Duarte 16 April 2020 [26], review (medRxiv PRE-PRINT): narrative summary of 9 studies reporting primary data on "asymptomatic or pre-symptomatic" patients who were considered to have passed on COVID-19 infection – all but two studies were reporting on single cases.

Modelling

He 2020 [27] (Int J of Infect Dis):

- Background: Positive RT-PCT results only imply infectivity. It is important to study the patterns of viral shedding and live virus isolation. This study was a reanalysis of data produced by Chen et al. 2020 [28] [published in Chinese] who found that there was no statistical difference in the transmissibility of asymptomatic versus symptomatic cases. The summary of transmission is reported in the table below:

Table 1
Summary of the COVID-19 transmission and contact tracing in Ningbo from January 21 to March 6, 2020. The data are obtained from Chen et al. (2020).

	First generation	Close contacts	Second generation		
			Symptomatic	Asymptomatic	Sub-total
Symptomatic	161	2001	107	19	126
Asymptomatic	30	146	3	3	6
Total	191	2147	110	22	132

- According to Chen et al., the number of cases per contacts for symptomatic cases is (126/2001 =) 0.063 and for asymptomatic cases is (6/146 =) 0.041.
- Theoretically, the transmissibility (of an infectious disease) can be quantified by the reproduction number (R). Hence, by definition, the Rs can be calculated as (126/161 =) 0.78 and (6/30 =) 0.20 for the symptomatic and asymptomatic groups respectively. Therefore, the risk ratio (RR) of infectivity of a symptomatic group against that of the asymptomatic group is estimated at 3.9 (95%CI: 1.5–11.8). If focusing on symptomatic secondary infections, the RR is estimated at 6.6 (95% CI: 2.0–34.7). An alternative modelling framework produces as RR of 1.5 (95% CI: 0.7-3.4) which was not statistically significant.
- The authors conclude that the results should be interpreted with caution due to limitations in the dataset, however, the relative transmissibility of asymptomatic cases could be significantly smaller than symptomatic cases.

Yin 2020 [29] (JMIR Public Health Surveill):

- Background: Also comments on and reanalyses data from Chen et al. [28] who found no statistically significant difference in the transmission rates of asymptomatic and symptomatic patients. The authors did note that Chen

et al. also concluded that the closer the contact is with the infected patient, the higher the chance of infection. Criticisms of the Chen et al. study included the inappropriate use of chi-square tests and the inclusion of a super-spreader who should be regarded as an outlier and excluded.

- The authors used a permutation test to determine the difference in average numbers of contacts by the symptomatic and asymptomatic cases. The results indicated that the average number of close contacts was 13 for symptomatic cases and 5 for asymptomatic cases ($p<0.001$).
- They also used Fisher Exact tests to investigate the difference in transmission rates. The overall difference between symptomatic and asymptomatic transmission rates was not significant, however, there were subgroup differences.
- The authors state that the conclusion remains the same as Chen et al. – no significant difference in rates of transmission between asymptomatic and symptomatic cases.

Park 2020 [30] (Epidemics):

- Background: If asymptomatic cases are important for transmission, they have the potential to affect estimates of the basic reproduction number R_0 (i.e. the expected number of secondary cases generated by an average primary case in a fully susceptible population). The study investigates the relationship between individual-level features of asymptomatic cases to dynamics at the population scale during the exponential phase of an epidemic.
- Results indicate that if asymptomatic cases have a shorter generation interval than symptomatic cases, R_0 will be over-estimated, and if they have a longer generation interval, R_0 will be under-estimated.
- The authors note that cases do not have to be completely asymptomatic for our qualitative results to apply. People with mild symptoms unlikely to be diagnosed in a particular time and place (sometimes referred to as subclinical cases) are expected to affect transmission patterns in the same way.

Graham 2020 [31] (Ann Surg):

- Developed a decision-support tool for hospital leadership to understand the community exposure risk (i.e. probability of transmission from an asymptomatic community-dwelling patient) for healthcare workers. It was hypothesised that the probability of transmission is the product of the prevalence of asymptomatic cases in the community and probability of transmission per contact. The assumption for transmission was held constant at 5%, based on research estimating rates to be between 2% and 20%. Estimates of the prevalence of asymptomatic infections in the community were allowed to vary from 0 to 40% given the uncertainty.
- As expected, when prevalence of asymptomatic cases is low, the probability of transmission from an asymptomatic community case is low. Without PPE or social distancing, there is a 0.05% increase in the probability of transmission from an asymptomatic community infection for every 1% increase in asymptomatic prevalence in the community. With PPE there was a 0.0007% increase.
- Note that that model assumes random missing with patients who are equally at risk and does not account for unique clustering and networks of contacts and repeated exposure.

Grassly [32] 23 April 2020 (Imperial College COVID-19 response team; Report 16: Role of testing in COVID-19 control):

- Used a simple mathematical model to investigate the potential effectiveness of alternative testing strategies. Weekly screening of healthcare workers and other at-risk groups using PCR or point-of-care tests for infection irrespective of symptoms is estimated to reduce their contribution to transmission by 25-33% (if results immediately available; rate is 16-23% if results available 24 hours later), on top of reductions achieved by self-isolation following symptoms. The effectiveness of this strategy depends on the sensitivity and specificity of the test, frequency of testing and the timeliness of test results.
- Concluded that widespread PCR testing in the general population is unlikely to limit transmission more than contact-tracing and quarantine based on symptoms alone.

Ali 2020 [33] (J Biol Dyn):

- Formulated a deterministic epidemic model for the spread of COVID-19 that included asymptomatic transmission in the model as well as the effects of quarantine of the healthy population and isolation of infected individuals.

- The most important parameters were the contact rate (as expected) and the quarantine and isolation rates. The analysis showed that a high rate of quarantine of health people along with isolation of infected individuals is needed to control the disease.

Viral load/shedding

- Zhou 2020 [34] (Int J Infect Dis): followed up 31 adult patients with confirmed SARS-CoV-2 infection who were asymptomatic on admission. 22 presented with symptoms after admission while the remaining 9 patients were asymptomatic during hospitalisation. C_t values were available for 19 patients; viral load was significantly lower in the asymptomatic than in the pre-symptomatic patients. Furthermore, viral load peaked during the first week of admission for asymptomatic patients and during the second week for pre-symptomatic patients. However, the duration of viral shedding was similar between groups.

- Han 2020 [35] (Emerg Infect Dis): Along with positive SARS-CoV-2 RNA in nasopharyngeal swabs, viral RNA was detectable at high concentration for >3 weeks in fecal samples from 9 mildly symptomatic and 3 asymptomatic children with COVID-19. Viral RNA load in the nasopharyngeal swabs peaked early and decreased over time; symptomatic children had higher initial viral load than asymptomatic children.

- Zou 2020 [36] (NEJM): monitored viral shedding for 18 patients (1 asymptomatic, 14 mild/moderate, 3 severe). The authors concluded that 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.

- Kimball 2020 [37] (MMWR): Cycle threshold (C_t) values were assessed in 23 residents who had tested positive for SARS-CoV-2. The results 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 ($p = 0.3$).

- Lavezzo 2020 [38] (medRxiv): Found no statistically significant difference in the viral load of symptomatic vs asymptomatic SARS-CoV-2 infections.

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