**Annex: Evidence that asymptomatic / pre-symptomatic transmission exists**

*Evidence suggests that a significant portion of infected individuals are asymptomatic, with some recent studies suggesting that asymptomatic/pre-symptomatic transmissions account for a substantial amount of COVID-19 cases.* Studies on different population groups currently report a wide range of asymptomatic and pre-symptomatic infections. For example, in Guanghzhou, China 4 out of 295 patients (1.4%) were asymptomatic,[[1]](#endnote-1) while another Chinese study reported asymptomatic infection in 16.7 – 66.7% of cases in 5 family clusters.[[2]](#endnote-2) A French study showed one asymptomatic case (8.3%) in a cluster of 12 cases linked to a single index case. The asymptomatic case had similar viral load as that of a symptomatic case.[[3]](#endnote-3)

*Ships provide a more contained setting to investigate asymptomatic infection*. In the Diamond Princess Cruise Ship, 17.9% of the 634 confirmed cases (95% CI: 15.5-20.2%)were confirmed as asymptomatic,[[4]](#endnote-4) another study on a US Naval ship found 60% of the over 600 US sailors who tested positive for COVID-19 were asymptomatic or pre-symptomatic.[[5]](#endnote-5)

*There is also asymptomatic infection in children but it is of unclear significance for transmission*. A study of hospitalized children in China reported 2 out of 10 (20.0%) were asymptomatic.[[6]](#endnote-6) A retrospective Chinese descriptive clinical study found 8 out of 14 children (57.1%) with confirmed COVID-19 were asymptomatic.[[7]](#endnote-7) Another hospital-based study of eight young COVID-19 confirmed patients in a cluster, aged 16-23 years, were exposed to an asymptomatic case.[[8]](#endnote-8)

Estimate of asymptomatic ratio based on a Bayesian model among Japanese nationals evacuated from Wuhan on chartered flight found 41.6% of infected evacuees were asymptomatic.The overall asymptomatic ratio is estimated to decrease to 33.3% if one of the 5 asymptomatic evacuees develop symptoms within the 14 days.[[9]](#endnote-9) A Chinese study of daily case counts in China found 78% of 166 new confirmed cases identified were asymptomatic.[[10]](#endnote-10)

*COVID-19 has also been reported among evacuated flight passengers, but unclear if this is pre-symptomatic or true asymptomatic*. A study of passengers on repatriation flights to Greece from the UK, Spain and Turkey found 36 out of 41 (87.8%) were either pre-asymptomatic or true symptomatic.[[11]](#endnote-11) Another study of 566 Japanese[[12]](#endnote-12) repatriated from China, among 503 asymptomatic passengers, entry screening PCR results were positive for 5 (1.0%), and 3 remained asymptomatic after 14 days. Two further asymptomatic individuals tested positive on day 10.

*Studies show that some asymptomatic patients eventually progress and develop symptoms*. For example, a study in a Washington care facility, among 13 out of 76 (17.1%) who are asymptomatic, after being reassessed a week after testing, 10 of them developed symptoms and were recategorized as presymptomatic.[[13]](#endnote-13)Another study of 1012 patients in China, 30 of 1012 (3.0%) patients were asymptomatic on admission, of whom 16 (53.3%) developed symptoms.[[14]](#endnote-14) 14 (32.6%) of the 43 pregnant women ultimately tested positive after initially presenting without symptoms in a New York pregnancy ward with remaining afebrile and asymptomatic.[[15]](#endnote-15) Other asymptomatic cases progress over the course of disease with CT abnormalities but remain asymptomatic.[[16]](#endnote-16)

*Studies vary on number of cases attributed to pre-symptomatic transmission from 6 to 44%*. For example, pre-symptomatic transmission was reported from a review of 243 cases in Singapore: 6.4% of the 157 locally acquired cases were attributed to pre-symptomatic transmission.[[17]](#endnote-17) A Chinese study of 94 confirmed cases, 44% (95% CI, 25–69%) of secondary cases estimated to be infected during the index cases’ pre-symptomatic stage.[[18]](#endnote-18) Another Chinese study found 12.6% of 468 transmission events across 752 cases analyzed involved pre-symptomatic transmission[[19]](#endnote-19)

Pre-symptomatic transmission rates is driven by the time post-infection to become infectious, and the time post-infection to become symptomatic. A February 2020 study of 468 transmission events across 752 cases in China show a mean serial interval (time before becoming infectious) of 3.96 days, (95% CI 3.53–4.39 days).[[20]](#endnote-20) while a March 2020 study of 181 cases in 25 countries shows median incubation period of 5.1 days (95% CI, 4.5 to 5.8 days)[[21]](#endnote-21)

A meta-analysis[[22]](#endnote-22) of 3062 participants suggests that asymptomatic are a small minority, although probably not a representative cohort. This study synthesized 38 heteregenuos studies on clinical characteristics of COVID-19 patients: 11.9% were asymptomatic.

**Current gaps in research**

* + - Research is needed on out of hospital management for asymptomatic cases. There is a need for better data to determine transmission dynamics among asymptomatic individuals and to inform screening practices.

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