

# Asymptomatic and Presymptomatic Spread of COVID-19: A Literature Review as of September 9, 2020

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A troubling finding that has emerged during the COVID-19 pandemic is the ability to spread SARS-Cov-2 before showing symptoms of COVID-19. This can increase difficulty in containing spread, contact tracing after diagnosis, and estimating the prevalence of COVID-19 in the population.

## *Prevalence of Asymptomatic and Presymptomatic COVID-19*

A unique challenge exists in trying to estimate the prevalence of positive COVID-19 cases that are asymptomatic, or never show symptoms. These individuals likely will not voluntarily seek testing simply because they may not believe they have COVID-19. Therefore, the estimated count may be a conservative estimate. Some studies have conducted universal testing on specific populations such as those in shelters or receiving elective surgeries, but these people differ from the general population and estimates may not be generalizable. Some reports estimate the proportion of positive COVID-19 cases that are asymptomatic to be high, with more than half of those testing positive being asymptomatic at the time. These studies have ranges of asymptomatic, positive COVID-19 cases from 56% - 88%.<sup>1-4</sup> Other longitudinal studies find a much lower prevalence of truly asymptomatic individuals with positive COVID-19 tests. Following positive cases for 14 days finds prevalence of those who remain asymptomatic between 2 – 30%.<sup>5, 6</sup> One study found that over a third of patients confirmed as positive cases (110/303) were initially asymptomatic, but nearly 20% of that third developed symptoms during isolation.<sup>7</sup>

Thus, the best way to estimate the true prevalence of asymptomatic COVID-19 cases is through carefully constructed random samples of the population or by combining many study estimates via meta-analysis. This has been done on a small number of occasions. The state of Indiana conducted a random sample at the end of April to estimate prevalence of COVID-19. In this survey they found a prevalence of COVID-19 of 2.79%. Of those who tested positive, 44.2% reported being asymptomatic.<sup>8</sup> Another study in Indianapolis in April and May utilized a survey of residents without COVID-19 symptoms. This study found a prevalence of COVID-19 of 3.1%. Since the sample was only residents not showing symptoms, this equates to 3.1% being asymptomatic or presymptomatic.<sup>9</sup>

Reviews that have been published have tried to combine estimates of the prevalence of asymptomatic cases as well. One review, using only case series of COVID-19 patients, estimates an average of 24% of cases as asymptomatic.<sup>10</sup> Another review, using estimates from samples greater than 1000 people estimates the overall prevalence of asymptomatic cases to be 2-13%.<sup>11</sup> A third “living systematic review” included all study types with no limits on sample size or design estimates 20% of COVID-19 patients remain asymptomatic throughout.<sup>12</sup> And, a

review of case series of children, found that approximately 26% were asymptomatic.<sup>13</sup> As can be seen, estimating a true prevalence of asymptomatic COVID-19 cases is difficult. Even with these estimates from cross-sectional surveys, an asymptomatic case could present symptoms days after testing and this would present a differential misclassification.

A key takeaway among studies of COVID-19 positive patients is that there may be a high percentage of asymptomatic cases, even if they present with symptoms after the study has concluded. But, when looking at the entire population, the proportion of individuals that are currently COVID-19 positive and asymptomatic still remains small. It is important to recognize that asymptomatic COVID-19 occurs and these patients are able to transmit SARS-Cov-2 without knowing that they have COVID-19.

### *Temporal Dynamics*

Asymptomatic cases are especially problematic because they are able to spread the SARS-Cov-2 virus without knowing they are infected. Viral load in asymptomatic cases is high enough at approximately 2-3 days before symptoms start to spread to others and peaks, on average, about 1 day before symptom onset.<sup>14</sup> The period of viral shedding is relatively similar between those who remain asymptomatic (median: 7 days) and those who show symptoms of COVID-19 (median: 8 days).<sup>15</sup> Therefore, universal precautions (ie: masking) help to prevent spread as transmission can occur even when symptoms never appear.

### *Proportion of Infection from Asymptomatic and Presymptomatic*

Since asymptomatic and pre-symptomatic (i.e. have not developed symptoms yet) individuals are able to spread SARS-Cov-2, it is important to know the proportion of infections attributable to them. This is also a difficult estimate to obtain because contact tracing becomes less effective when there are high proportions of asymptomatic spread.<sup>16</sup> One study that used 77 transmission pairs estimated the proportion of infection from asymptomatic or presymptomatic cases to be 44%.<sup>14</sup> Another model, using publicly available data from Singapore and Tianjin, estimates the proportion of presymptomatic spread in these cities to be greater than 50%.<sup>17</sup> And a review of cohorts tested for COVID-19 estimates approximately 40-45% of SARS-Cov-2 infections can be accounted by those that are currently asymptomatic.<sup>18</sup> Hence, it would seem that just under half of all new cases of COVID-19 are attributable to spread from someone, who at the time, was not showing any symptoms.

### *Conclusion*

The number of asymptomatic COVID-19 cases is not accurately known at this time; however, available studies suggest significantly large numbers of COVID-19 patients may be asymptomatic. These positive cases are able to spread SARS-Cov-2 for nearly as long as a symptomatic case and may account for 40% or more of the spread of the disease. While studies have tried to identify prevalence, many challenges remain to accurately define the size of this population. Therefore, wearing of masks and physical distancing should continue to be

encouraged to help slow the spread of COVID-19 from those who may not realize they are infectious.

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