

On RT-PCR testing and rates of SARS-CoV2 detection in asymptomatic individuals

Asymptomatic individuals testing positive for SARS-CoV2 by RT-PCR is common and represents a large proportion of disease transmission. Between 5 and 80% of people who do test positive for SARS-CoV2 are asymptomatic and symptomatic-only based screening will miss cases, as outlined by a consolidated review of evidence by the University of Oxford's Centre for Evidence Based Medicine [1]. This is consistent with evidence consolidated by the CDC [2]. These consolidations include a recent analysis of >2000 SARS-CoV2-infected children in China where 13% of RT-PCR confirmed cases were asymptomatic [3]. Rates of asymptomatic infection the elderly are also high, as shown during epidemiological investigation of an outbreak in a US nursing home where 50% of RT-PCR confirmed cases were asymptomatic [4]. One study across all age groups supported high rates of asymptomatic PCR-positives in young and elderly age groups (both ~30%), as well as showed equivalent rates for intermediate age groups of between 5 and 15% [5].

The contribution of asymptomatic transmission to the epidemic is likely significant as viral shedding (and thus risk of transmission) peaks at, or before, symptom onset [5,6]. A study combining molecular testing with detailed epidemiological contact information inferred that the proportion of transmission occurring before symptom onset was 44% [5]. This fits with larger modelling studies of the outbreak in China that suggest that 85% of infections are undocumented and that this has contributed to the rapid spread of the virus [7].

I could only find one study that attempted to estimate false negatives in asymptomatic individuals (as most are focused on the false negative rates in symptomatic individuals [e.g. 10, 6]). This study was a fitted statistical model that estimated higher rates of false negative tests in pre-symptomatic phases of disease. Specifically, the false negative rate was 100% on day 1 post exposure (95% Confidence Interval [CI] ranged between 69 – 100%) to a false negative rate on day 4 post exposure of 61% (95% CI 18 – 98%). Notably, the false negative rate during infection is also not ideal [10], decreasing from 39% (95%CI 16 – 77%) on day of symptom onset to 61% (95%CI 54 – 67%) on day 9 of symptom onset [9]. This is consistent with an Italian study that showed comparable viral loads in symptomatic and asymptomatic individuals [11] and with viral load peaking at symptom onset.

How is testing of asymptomatic individuals being used?

PCR screening of asymptomatic individuals is an important wing of testing for the control of COVID19. This was recommended at least as early as the 2nd of March 2020 in the World Health Organisation's interim guidance on Laboratory testing for COVID19 [8]. In other countries, antigen testing of asymptomatic individuals is being used extensively for: preventing reintroduction of the virus; contact tracing; and quarantine measures. For example, in China from the 1st of April all passengers entering the country through air, water and land board have nucleic acid testing; Shanghai and Beijing are also back-testing international arrivals that are still in the quarantine period; nucleic acid testing is also being used to determine the length of centralised quarantine (i.e. isolation) of asymptomatic cases (must have 2 consecutive negative PCRs separated by 24 hours - this is similarly the case in Singapore). In fact, the role of pre-symptomatic and asymptomatic transmission is now firmly recognised in China such that the contact tracing guidelines have been extended to include close contacts that occurred in the two days prior to symptom onset or detection of an asymptomatic case (Francis Hooper, Foreign Office). Intensive track-and-trace testing efforts, including of asymptomatic individuals, are thought to be core to the successful

disease control efforts in South Korea, Hong Kong and Singapore, particularly the latter where drive-through community testing is ubiquitous (Annex A, country summaries international comparators).

References

- [1] University of Oxford's Centre for Evidence Based Medicine Key take homes:
- That between 5% and 80% of people testing positive for SARS-CoV-2 may be asymptomatic
 - That symptom-based screening will miss cases, perhaps a lot of them
 - That some asymptomatic cases will become symptomatic over the next week (sometimes known as "pre-symptomatics")
 - That children and young adults can be asymptomatic
- [2] Evidence consolidation done by the CDC
- [3] Dong Y, Mo X, Hu Y, et al. Epidemiological Characteristics of 2143 Pediatric Patients With 2019 Coronavirus Disease in China. *Pediatrics*. 2020
- [4] Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled Nursing Facility — King County, Washington, March 2020 (Kimball et al) MMWR CDC 2020
- [5] High incidence of asymptomatic SARS-CoV2 infection, Chongqing, China (Tao et al) 16th March
- [6] Temporal transmission dynamics in viral shedding and transmissibility of COVID-19 (He et al)
- [7] Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-Cov2)
- [8] Laboratory testing for coronavirus disease 2019 (COVID-19) in suspected human cases: interim guidance, 2 March 2020 World Health Organisation
- [9] Variation in False Negative rate of RT-PCR based SARS-CoV2 Tests by time since exposure (Kucikra et al 2020)
- [10] Estimating false-negative detection rate of SARS-CoV-2 by RT-PCR (Wikramaratna et al)
- [11] The early phase of the COVID-19 outbreak in Lombardy, Italy (Cereda et al)