

Cycle threshold as a measure of infectivity from Covid-19 PCR tests

Alberto Boretti

Abstract

The Covid-19 polymerase-chain-reaction (PCR) test run with a cycle threshold of 40 returns as positive also cases of patients only having a small number of viral fragments in the sample. This produces an overrated number of those who are considered infected. It is suggested to always include the cycle number for positivity in the test result, as well as to lower the cycle threshold to 30-35 for more appropriate detection of those contagious.

Cycle threshold and positive Covid-19 result

The “gold standard” Covid-19 test is the Polymerase-chain-reaction (PCR) test. This test amplifies tiny amounts of DNA material to become large enough to be analyzed. While this test provides a yes-no answer to infection, it does not provide any measure of the viral load, that otherwise makes the difference between really infective patients and patients that are not. PCR tests identify as positive also patients with only a tiny amount of viral fragments making no difference vs. patients with a significant amount of viruses. The difference is that very infective patients are detected after a limited number of cycles, while patients with only viral fragments may also be detected performing more cycles. Many works raise concern over this coronavirus testing usually adopting a large number of cycles claiming it is diagnosing as positive a large number of patients who carry small amounts of viruses or even only fragments.¹⁻¹⁰ Most of the positive people from a PCR test are not likely to be contagious, and this creates significant problems in managing an outbreak overrating the threat while placing unneeded effort on some while neglecting effort on others.

A Covid-19 test “yes-no” with a cycle threshold (CT) too is simply not good enough. It is the viral load that deter-

mines who is infectious. This information is, however, already included in the test, and it is the number of cycles performed to detect the viral material.

The PCR test amplifies the genetic material in the sample performing several cycles. The smaller number of cycles required for the detection of viral matter, the greater is the number of viruses. The greater is the viral load, the greater is the patients’ infectivity. This number of amplification cycles needed to find the virus is not included in the results, although it is of paramount importance. The patients are more infectious the smaller is the number of cycles performed to produce a positive result. Thus, it should be given as part of the test results and taken into consideration.

As the current number of cycles performed before declaring a “no” is too large, there is a need to change this parameter in reporting the positive cases. In three sets of testing data that include CTs from Massachusetts, New York, and Nevada, up to 90% of the positive carried hardly any virus.¹ The CT used now to decide that a patient is infected must be adjusted. Tests with such a high threshold may detect not only live viruses but also fragments posing no risk. It is claimed that any test with a CT above 35 is too sensitive.^{2,3,4} Most of the tests were set to use 40, a few 37. The US CDC suggests that it is extremely difficult to detect any live virus in a sample above a threshold of 33 cycles.² A more reasonable cutoff would be even less than 35, at about 30, or even less than 30.⁴ If 30, the amount of viral genetic material in the sample would have to be 1,000 times larger than the current standard to produce a “yes”, as every ~3.3 increase in the CT value reflects a 10 times reduction in starting material.⁹ Lower CT values are associated with more severe infection.¹⁰ The number of people with positive results that are not infectious is concerning. The viral load of Covid-19 is an important factor in disease severity and the probability of transmission.^{3,4,5,6}

A test with a CT of up to 40 is approved for use in diagnosing Covid-19 in Melbourne, Australia. This is excessive. Many of those that are now considered infectious are practically not. According to, in the early days of the pandemic in Melbourne, “yes” were detected at a range of CT values from 19.3 to 35.6, on average closer to the lower rather than the upper limit.⁸ A CT of 40 for a “yes” is definitively excessive.

Figure 1 is the outbreak of Covid-19 in Melbourne depict-

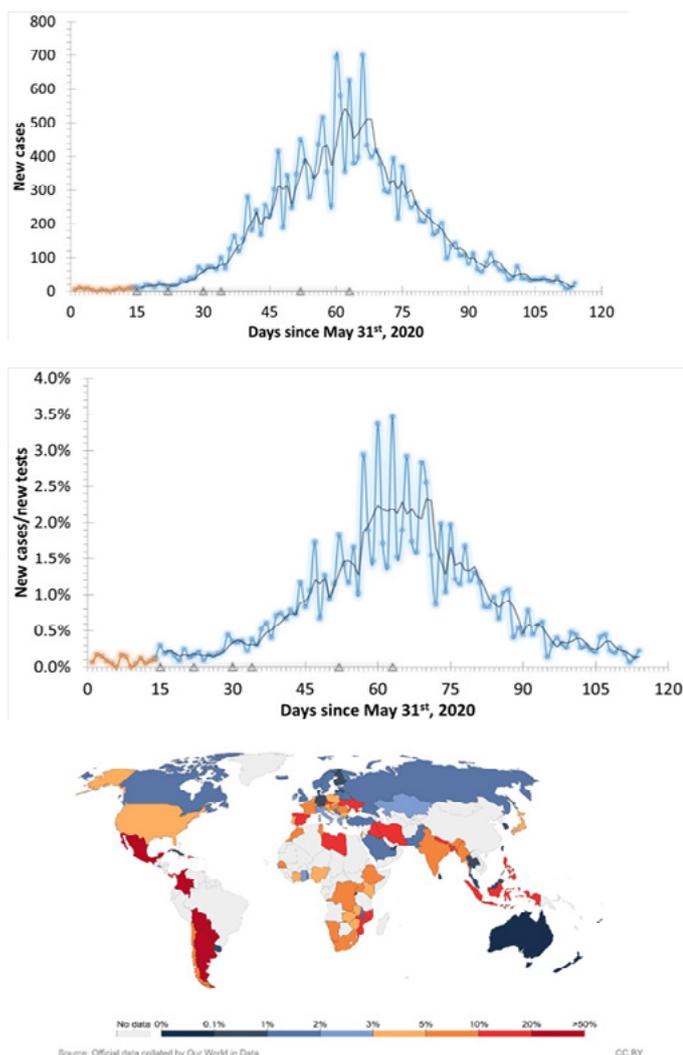
Alberto Boretti, College of Engineering, Prince Mohammad Bin Fahd University, Al Khobar, Khobar, Dhahran 34754, Saudi Arabia

*Corresponding author: Alberto Boretti
E-mail: a.a.boretti@gmail.com*

ed by using a CT of 40. In (a) are the new Covid-19 cases reported for Melbourne, Australia. The second outbreak was declared on June 15, 2020 (day 15). In (b) is the positive rate obtained by dividing the number of new cases by the number of new tests. The triangles along the x-axis indicate the introduction of novel restrictions to limit the spread. A trend line of period 3 added. In (c) is the 7 days rolling average of the share of positive cases computed by ourworldindata.org for the different world countries. The positive rate is much larger where for different reasons those tested are mostly medium-to-severe cases.

In the case of Victoria, Australia were also asymptomatic people are tested; the number of contagious people is likely largely overestimated.

Figure 1: (a) New Covid19 cases reported for Melbourne, Australia. The start of the second outbreak was declared June 15, 2020 (day 15). (b) The positive rate obtained by dividing the number of new cases by the number of new tests. The triangles along the x-axis indicate the introduction of novel restrictions to limit the spread. The trend line of period 3 added. (c) Are the 7 days rolling average of the share of positive cases computed by ourworldindata.org.



A lower CT of 30 vs. 40 would have translated into a reduced number of infected cases. Apart from the reporting in day x of the positive cases of tests performed 1 to 3 days before, and the strongly variable number of tests performed per day, variable from a few thousand to forty thousand, the positive rate also suffers from unreported tests disclosed only later. As an example, on 3 September, 82,309 new tests were reported, including a data correction of 47,962 tests conducted before 1 August, plus 17,249 delayed tests from one laboratory; and the 17,098 received in the previous 24 hours. Positive rate is 0.1-0.2% day 1 to 15. It is 0.2-0.4% day 16 to day 27 as a result of the increased focus on the most disadvantaged sectors of the population. Then it starts growing as an indication of an outbreak from day 28. The positive rate stops growing and becomes flat a few days before the introduction of the harsher stay-at-home restrictions of day 63.

Conclusion

The Covid-19 PCR test is a “yes-no” test that is not qualitative and therefore is misleading. The CT of 40 presently adopted is excessive and should be drastically revised downwards. The CT for detection should be mentioned for every positive case. Different measures should take into account the CT. Those detected positive with CT more than the new upper limit of 30-35 cycles should be considered not infectious such as Victoria, Australia. This problem is relevant in cases where not only the very sick are tested. The official figures of the Covid-19 outbreak for Victoria, Australia should be revised downwards accordingly. Most of those positive are very likely not contagious.

References

1. Mandavilli, A., 2020. Your Coronavirus Test Is Positive. Maybe It Shouldn't Be.
2. Centers for disease control and prevention, 2020. Duration of isolation and precautions for adults with COVID-19.
3. S N Rao, D Manissero, V Steele et al, 2020. Clinical utility of cycle threshold values in the context of COVID-19.
4. M R Tom, Mina M J. To interpret the SARS-CoV-2 test, consider the cycle threshold value. Clinical Infectious Diseases. p. ciaa619 2020.
5. G M Joynt, W K Wu. Understanding COVID-19: What does viral RNA load really mean? The Lancet Infectious Diseases 2020; 20(6), pp.635-636.
6. L Geddes. Puzzle over viral load. New Scientist 2020; 245(3276):8.
7. Chuter R. COVID-19: To test or not to test. 2020.

Short Communication

8. BS Chong, T Tran. Sample pooling is a viable strategy for SARS-CoV-2 detection in low-Prevalence settings. medRxiv 2020.
9. MR Tom MJ Mina. To interpret the SARS-CoV-2 test, consider the cycle threshold value. *Clin Infect Dis* 2020.
10. T Jefferson, C Heneghan. COVID-19: Clinical utility of cycle threshold values. 2020.