INFECTIOUS DISEASES

A pandemic's trajectory using PCR testing

Science **373**, eabh0635 (2021)

One of the first steps when responding to a pandemic involves monitoring the spread of the disease in real time. The reproductive number, R_t, inferred using the time series of observed case counts, hospitalizations or deaths, has been extensively used as a measure of the spread of COVID-19. However, the use of R_t as an epidemiological parameter is hindered by limited test availability and reporting delays. As an alternative, James Hay and colleagues propose the use of the cycle threshold (Ct) values obtained from RT-qPCR (reverse transcription quantitative polymerase chain reaction) testing and show that, even with a limited number of samples, they can be used to effectively measure the pandemic's trajectory.

Testing for COVID-19 through RT-qPCR involves an amplification step where copies of the virus' genetic material are made by running multiple cycles of denaturation, annealing and elongation. This step allows for detection of even the smallest amount of genetic material in the sample. The Ct value is the number of cycles it takes for the RT-qPCR test to detect the virus. A higher viral load (that is, a higher amount of virus in an infected person's blood) requires a smaller number of cycles, thus leading to smaller Ct values. The main intuition put forth by Hay et al. is that a growing increase in the spread of the pandemic leads to a higher number of newly infected individuals, and thus, to higher viral loads among tested individuals; a decrease in the spread of the pandemic has the opposite effect.

To estimate the spread of COVID-19 from the Ct values, the authors combine two models: a Bayesian model to estimate the days since infection for an individual based on their Ct values, and an epidemic transmission model. The authors show the scope of this method by performing extensive simulation-recovery experiments in a finite population using a single random cross section of virologic testing among patients. The trajectory obtained from the Ct-based models was similar to the baseline estimate (a standard compartmental modeling approach) but, using a smaller sample size, the Ct-based models accurately distinguished whether the samples were taken soon or long after the onset of the pandemic. To further test the predicted epidemic spread using a Ct-based model, the method was applied to data obtained from the Brigham and Women's Hospital in Boston, Massachusetts between 15 April and 10 November 2020. The results showed that the median and skewness of the detectable Ct distribution were correlated with R_t and that the model could reproduce observed epidemic trajectories and the growth or decline of cases using only positive Ct values. The authors' approach is an important contribution to science as it uses a measure already available through routine testing to predict the spread of a pandemic, and it provides a good agreement with observed infected numbers while using a smaller testing sample.

Ananya Rastogi

Published online: 13 August 2021
https://doi.org/10.1038/s43588-021-00121-z