When the Foundations Are Wobbling, Part I

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The Denominator of Death Rates

D. Joy Riley, M.D., M.A.
Executive Director

How many people in the U.S. have died of SARS-CoV-2 infection, or COVID-19? That is difficult to say, and not for lack of numbers on the website of the Centers for Disease Control and Prevention (CDC). The case fatality rate for a particular disease is, basically, the number of persons dying of a disease, divided by the number of persons who have the disease, and multiplied by 100, to give an answer in terms of percentage:

$$\frac{\text{\# persons dying of COVID-19 disease X 100}}{\text{\# persons infected with SARS-CoV-2}}$$

How is this complicated? It turns out, in several ways. I asked two people, skilled in dealing with people, disease, and statistics to help us understand the difficulties inherent in interpreting fatality rates. (Their comments have been lightly edited.)

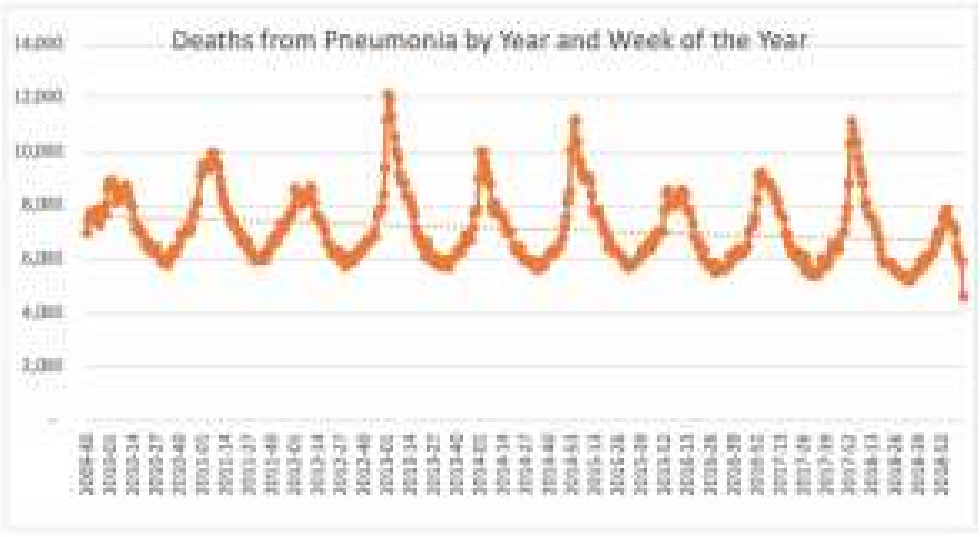
Cathy Jenkins is a biostatistician who has worked for 15 years with infectious disease researchers studying the HIV epidemic, and emergency medicine physicians whose focus is heart failure research. She explained:

> *In order to calculate the true fatality rate, we need to know the number who have or have had the disease. At the moment—with limited availability of tests—we are only able to test those who satisfy certain criteria, namely those who are exhibiting some of the more common symptoms of COVID-19. We know that there are some who develop the disease without showing any symptoms; however, we have no way of knowing how many people fall into this category without either testing everyone in the population (cost and labor prohibitive) or estimating this prevalence by carefully selecting a sample of people from the population to test.*

Richard Lachiver, M.D., M.P.H., has worked in population and occupational health for more than 30 years, and has been engaging with employers and payers extensively during this COVID-19 pandemic. Regarding the case fatality rate calculation, he said, “Simply put, you cannot have a meaningful rate without a meaningful denominator.” Some of the factors affecting the denominator in the case of COVID-19 that Lachiver enumerated include:

1. *timeliness and lag of data, perhaps due to interruptions of provider workflow processes, such as staffing problems or work from home orders;*
2. *current serology is limited by unknown and probably insufficient sensitivity and specificity;*
3. *epidemiology and population dynamics are complex: for instance, overall death rates in the U.S. were down (less than predicted) for more than two months prior to the peak of COVID-19; and*
4. *there is considerable seasonal ebb and flow and statistical variation we sometimes forget or conversely, to which we overreact.*

He gave an example of the ebb and flow of pneumonia in the U.S., in a graph he made using data from the CDC:



Regarding sensitivity and specificity, Jenkins had particular concerns, stating:

> *An accurate denominator relies on a test that correctly identifies true positives and true negatives—in other words, the ‘gold standard’. Using the ‘gold standard’ comes with a price, however, both in money and time. Therefore, there has been a push to develop diagnostic tests with lower costs and shorter processing times. What is not clear is what the test characteristics of these diagnostics are. These characteristics give insight into how often the test will identify false positives/negatives. A test that tends to report higher numbers of false positives is beneficial in identifying as many people as possible who have the disease, which helps in preventing it from spreading, but in turn, it artificially inflates the prevalence of the disease, or denominator, and therefore results in an inaccurately low fatality rate.*

How close to a “gold standard” are the varied tests we currently use for SARS-CoV-2, the virus that causes COVID-19? The answer is unclear. That fact notwithstanding, we continue to tally numbers for “positive” cases, and deaths attributed to COVID-19 for the state of Tennessee and for the U.S.

How death certificates are completed affects the denominator also. That will be the subject of our next post.