Improving the definition of COVID-19-related deaths

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Accurate measurements of the mortality associated with COVID-19 in different regions of the United States and the World document the ultimate impact of the SARS-CoV-2 pandemic and reflect the effectiveness of local health systems. Mortality figures can identify regions that require greater resources and allow individuals in each geographic region to realistically assess their risk of dying from COVID-19. These data can motivate residents to take additional precautions such as sheltering in place, avoiding large gatherings and enclosed public spaces, and wearing face masks. Reliable mortality figures may also encourage those who are hesitant to seek SARS-CoV-2 vaccination.

The World Health Organization defines a COVID-19 death as "a death resulting from a clinically compatible illness in a probable or confirmed COVID-19 case."[1] The United Kingdom has modified this definition, requiring that a positive RTPCR test to have been performed within 28 days of death.[2] This revised definition has significantly lowered case fatality rates. In the United States, the Center for Disease Control has created two categories: a confirmed case or death defined by meeting confirmatory laboratory evidence of COVID-19 and a probable case or death that has epidemiologic and/or clinical criteria consistent with COVID-19 but is lacking confirmatory laboratory evidence for COVID-19. A number of states and regions are not reporting probable cases, thereby lowering the number of reported COVID-19 deaths.[3]

Some infectious disease experts have expressed concern that the number of COVID-19 related deaths has been underestimated in the United States[4] and the World.[5] Differences in the availability of RTPCR testing, delays in the interval between testing and reporting results [6] as well as unexplained deaths outside of the hospital can all contribute to underdiagnosis. To work around the problem of insufficient testing, investigators have used excess all-cause mortality as a surrogate marker for U.S. COVID-19 deaths. Observations from March 1 to March 30, 2020 revealed the number of excess all-cause deaths was 28% higher than the official reports of COVID-19 deaths during the same period, supporting concerns that the COVID-19 death toll is underestimated.[6]

Hall et. al. in this issue of the *Journal of Infectious Disease* have described a more sensitive and specific diagnostic approach that has the potential to improve the accuracy of COVID-19 death reports. The investigators created a data set that linked all individuals in England who had received more than one nasal or throat swab RTPCR for SARS-CoV-2 to a mortality register that included bodies that had undergone postmortem upper respiratory track sampling for the coronavirus. The study identified 1,665 deceased persons with a suitable test both before and after death. To determine postmortem RTPCR sensitivity (the proportion of people with COVID-19 who had a positive post-mortem result) all those with a positive test before death were analyzed. Among those individuals with a positive test within a week of death and a post-mortem test 0-6 days after death 96.8% (61/63) of post-mortem tests were positive. Sensitivity declined when either the time interval for testing before and/or after death exceeded these intervals. To test specificity (the proportion of people without COVID-19 who had a negative post-mortem test), those with a negative test before death were evaluated and 5.8% (20/313) had a positive post-mortem test, giving a specificity of 94.2%. The time of post-mortem sampling did not affect specificity. A small number of individuals with a negative premortem test were suspected of having COVID-19 (28 cases) and this diagnosis was included on their death certificate. If these individuals were excluded from the analysis specificity increased to 97.5%.

Although this study has some limitations (absence of systematic postmortem testing, small numbers, different RTPCR test kits, and variations in nasopharyngeal sampling), these results are important and provide a more systematic approach for accurately measuring COVID-19 deaths. Postmortem RTPCR testing within 6 days of death is feasible and cost-effective and has the potential to eliminate the category of probable COVID-19 deaths. Postmortem testing will be particularly helpful for detecting COVID-19 deaths that take place outside of the hospital. Nursing home patients are a particular concern because COVID-19 manifestations are more difficult to detect. Increasing age is associated with a less robust immune response, blunting fever[7] and other manifestations of infection.[8] Impaired cognition may limit the ability to obtain an accurate history and clinical

deterioration may be inadvertently attributed to underlying chronic diseases, rather than COVID-19. Postmortem testing for COVID-19 should be strongly considered in this population.

As the pandemic recedes in the U.S.A., testing programs are likely to be dismantled and although postmortem coronavirus testing is a delayed measure of disease activity, consistent postmortem testing could serve as a backup method for detecting an unexpected surge in cases. Given the high sensitivity and specificity of this approach, the WHO and CDC should strongly consider including postmortem RTPCR SARS-CoV-2 testing as one of the key criteria for reporting COVID-19 deaths.

References

1. WHO. Estimating mortality from COVID-19: Scientific Brief August 4, 2020 Available at:

https://www.who.int/news-room/commentaries/detail/estimating-mortality-from-covid-

19.

2. Griffin S. Covid-19: England comes into line with rest of UK on recording deaths. BMJ

2020; 370:m3220.

3. CDC. About CDC COVID-19 Data, March 23, 2021. Available at:

https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/about-us-cases-deaths.html.

4. Bowden J. Fauci: 'No doubt' US has undercounted COVID-19 deaths. The Hill **2021**.

5. Lin TPH, Wan KH, Huang SS, Jonas JB, Hui DSC, Lam DSC. Death tolls of COVID-19: Where

come the fallacies and ways to make them more accurate. Glob Public Health **2020**;

15:1582-7.

6. Weinberger DM, Chen J, Cohen T, et al. Estimation of Excess Deaths Associated With the

COVID-19 Pandemic in the United States, March to May 2020. JAMA Intern Med **2020**;

180:1336-44.

7. McConeghy KW, White E, Panagiotou OA, et al. Temperature Screening for SARS-CoV-2 in

Nursing Homes: Evidence from Two National Cohorts. J Am Geriatr Soc **2020**; 68:2716-20.

8. Arons MM, Hatfield KM, Reddy SC, et al. Presymptomatic SARS-CoV-2 Infections and

Transmission in a Skilled Nursing Facility. N Engl J Med **2020**; 382:2081-90.