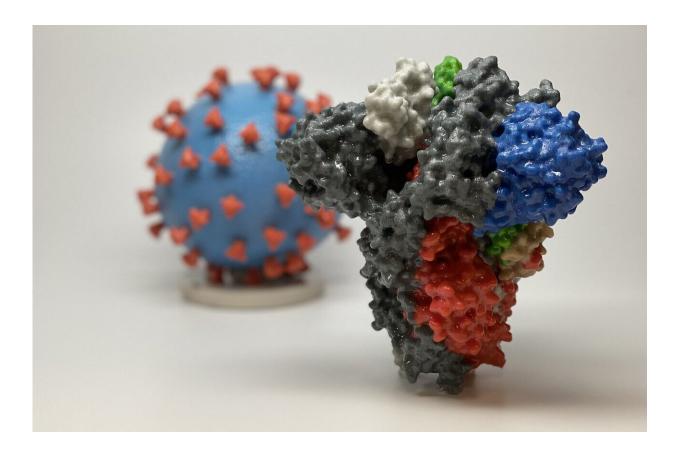


Focus on COVID-19 deaths in under-65s for better insights into infection rates across populations, say researchers

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3D print of a spike protein of SARS-CoV-2, the virus that causes COVID-19—in front of a 3D print of a SARS-CoV-2 virus particle. The spike protein (foreground) enables the virus to enter and infect human cells. On the virus model, the virus surface (blue) is covered with spike proteins (red) that enable the virus to enter and infect human cells. Credit: NIH



Simply comparing the total number of deaths across countries may provide a misleading representation of the underlying level of transmission of SARS-CoV-2, the virus that causes COVID-19, because of large differences in reported COVID-19 death rates in elderly populations in different countries.

The research, conducted by scientists at the University of Cambridge and the Institut Pasteur, was published today in the leading journal *Nature*. It highlights how large COVID-19 outbreaks in European nursing homes, and the potential for missing deaths in some Asian and South American countries, have skewed COVID-19 death data for older age groups, rendering cross-country comparisons of the scale of the pandemic inaccurate.

The researchers say that reporting of deaths from COVID-19 among those under the age of 65 is likely to be far more reliable, and can therefore give clearer insights into the underlying transmission of the virus and enable better comparisons between countries—crucial in guiding government strategies to try to get COVID-19 under control.

"Simply comparing the total number of deaths across countries can be misleading as a representation of the underlying level of transmission of SARS-CoV-2. Most deaths are in older people, but they are the least comparable across countries," said Megan O'Driscoll, a Ph.D. researcher in the University of Cambridge's Department of Genetics and first author of the paper.

In countries including the UK, Canada and Sweden, the COVID-19 pandemic has disproportionately affected nursing home residents, who account for over 20% of all reported COVID-19 deaths. The level of SARS-CoV-2 transmission among the general population can be difficult to disentangle from these large outbreaks.



By contrast, some countries in Asia and South America have far fewer reported COVID-19 deaths in older people than expected. One potential explanation for these missing deaths is that causes of deaths in elderly populations may be less likely to be investigated and reported as countries struggle to contain the epidemic.

"Nursing homes are enclosed communities of people, and once the virus gets in it can spread quickly resulting in higher levels of <u>infection</u> than in the general population. We're seeing an excessively large number of deaths from COVID-19 in this older age group, particularly in countries that have many nursing homes," said Dr. Henrik Salje in the University of Cambridge's Department of Genetics, the senior author of the report.

He added: "It's not just that residents are older than the general population, they are also generally more frail, so a 70-year old living in a nursing home is often more likely to die of COVID-19 than a 70-year old in the general population. To reduce the overall number of COVID-19 deaths it is vital to protect vulnerable elderly communities."

In their new model, the researchers integrated age-specific COVID-19 death data from 45 countries with 22 national-level seroprevalence surveys. Governments of many countries are using seroprevalence surveys to estimate the number of people in a population with antibodies against the <u>coronavirus</u>. Antibodies indicate if a person has been infected with SARS-CoV-2 at some point, so are a good indicator of population-wide infection rates.

"Our model shows that the number of COVID-19 deaths by age, in people under 65 years old, is highly consistent across countries and likely to be a reliable indicator of the number of infections in the population. This is of critical use in a context where most infections are unobserved," said O'Driscoll.



The model can be used at a country-wide level to predict a person's likelihood of dying from COVID-19 following infection, depending on their age. It also works in reverse, to estimate a country's total number of infections given its number of COVID-19 deaths in an age group, which is particularly useful in places where seroprevalence studies have not been conducted.

Using death data from under-65 age groups only, which is most representative of transmission in the whole population, it shows that by the 1 September this year an average of 5% of the population of a country had been infected with SARS-CoV-2. However, in some places it was much higher, especially South America.

For example, using Peru's COVID-19 death figures, which equate to 0.01% of the country's population, the model suggests that over half of the <u>population</u> of Peru has now been infected with SARS-CoV-2—a figure far higher than expected. This indicates particularly high rates of transmission of the virus in Peru.

But even after excluding data from the over 65's, the model shows that COVID-19 death rates cannot be compared between some countries, because the relationship between infections and deaths is not consistent when other widespread 'co-morbidity' factors are involved.

"It seems that people living in places such as Slovenia and Denmark have a low probability of death following infection with SARS-CoV-2, even after accounting for the ages of their populations, which is very different to what we've seen in New York, for example. There are likely to be fundamental differences in the populations across countries, which might include their underlying health," said Salje.

The model also revealed a strong pattern across countries in the 5-9 year age group, which consistently has the lowest probability of death



following SARS-CoV-2 infection.

The work demonstrates how age-specific death data alone can be used to reconstruct the underlying level of SARS-CoV-2 infection in a country and how it has changed over time. The researchers say this approach could be applied at sub-national scale, and may be of particular use in settings where large seroprevalence studies might not be feasible.

More information: Megan O'Driscoll et al. Age-specific mortality and immunity patterns of SARS-CoV-2, *Nature* (2020). DOI: 10.1038/s41586-020-2918-0

Provided by University of Cambridge

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