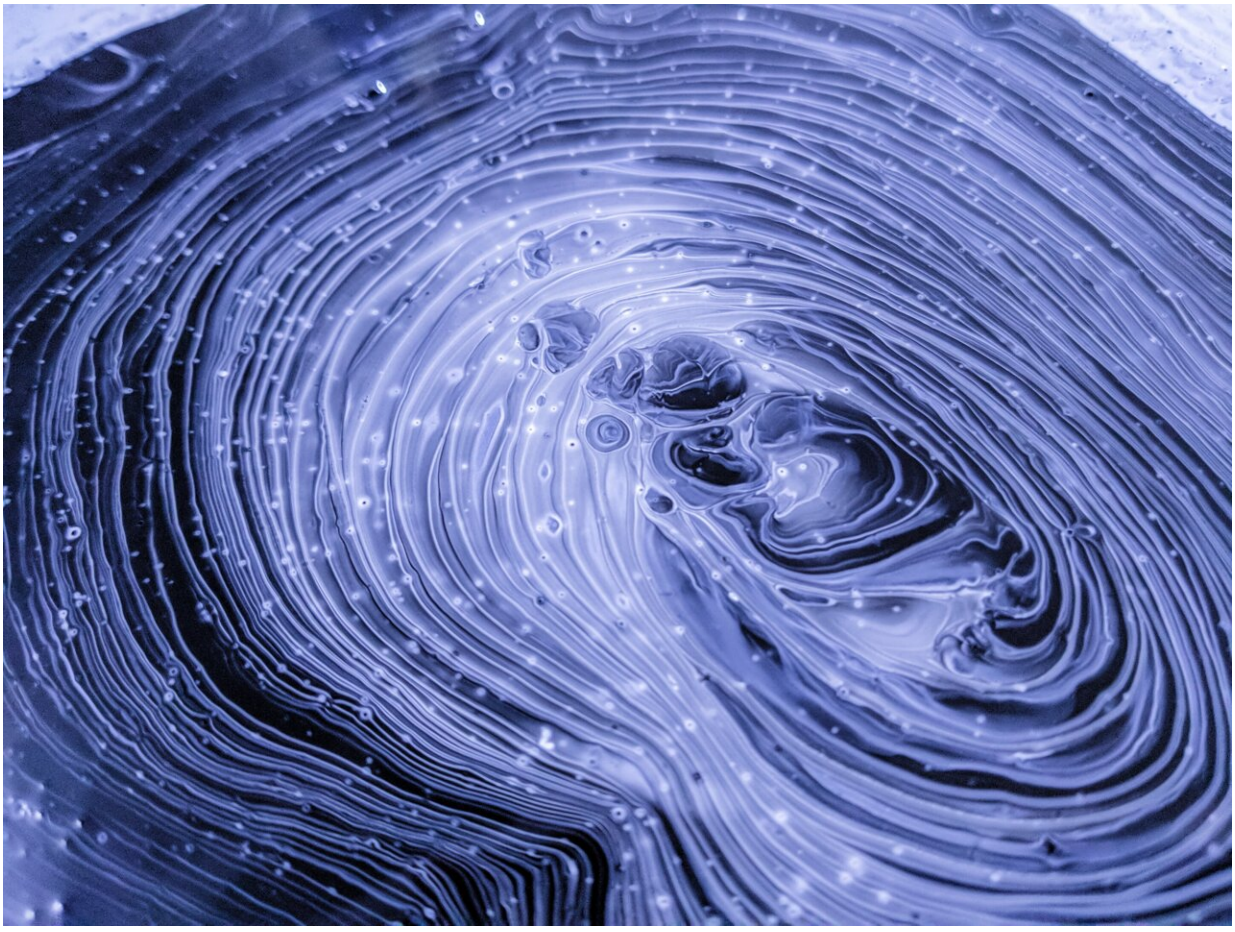
A million deaths from coronavirus: Seven experts consider key questions

September 28 2020, by Sarah L Caddy, Anne Moore, Connor Bamford, David Hunter, Derek Gatherer, Robert West, Susan Michie



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The pandemic has reached a grim milestone: 1 million people have now died of COVID-19, according to Worldometers.

On January 13, we published "Mystery China pneumonia outbreak likely caused by new human coronavirus" by Connor Bamford, a virologist at Queen's University Belfast. Since then, we have published more than 3,500 articles on the now not-so-novel coronavirus, officially named SARS-CoV-2. Despite this huge output from the world's leading experts, we have merely skimmed the surface of all there is to know about this perplexing pathogen. So much remains a mystery.

At this important juncture, we asked several experts from different fields what their burning question about the coronavirus is. Here is what they said:

Connor Bamford, Research Fellow, Virology, Queen's University Belfast

How did SARS-CoV-2 enter the human population?

We must understand how SARS-CoV-2-like viruses jump into humans if we are to stop the next pandemic, as we do for influenza. Although originally thought to have emerged in the Huanan Seafood Wholesale Market in December 2019, the earliest patient had no link to the market suggesting the virus had emerged before then. How did this happen?

Since the original investigations into the beginnings of SARS coronaviruses in 2002, horseshoe bats in south-east Asia have been implicated as the reservoir hosts, and a virus (RmYN02) that is extremely similar to SARS-CoV-2 has already been found in bats. However, similar viruses have also been found in pangolins, raising the possibility that SARS-CoV-2 may not have jumped directly from a bat.

Also, SARS-CoV-2 has already spread to cats, dogs, tigers and mink, and for SARS-CoV-1 (the virus that caused the 2002-04 SARS epidemic), farmed civet cats and raccoon dogs acted as intermediate hosts, bringing a bat virus into proximity to humans. It is possible that SARS-CoV-2 is a generalist virus, capable of spreading through a wide range of species.

With the increase in contact between humans and wildlife, zoonoses are becoming an ever-growing threat. We must be vigilant. An important step now is to figure out the events that led SARS-CoV-2 to go from bat to human.

Sarah Caddy, Clinical Research Fellow, Viral Immunology, University of Cambridge

How can we tell if someone is protected from SARS-CoV-2?

The immune response to SARS-CoV-2 infection aims to eliminate the virus from the body. Many studies have carefully described the various stages of the immune response after initial infection, but we do not know which aspects of immunity are essential for preventing repeat infections. What are the relative roles of different types of antibodies, or the importance of different T cell subsets?

An important goal of SARS-CoV-2 immunological research is, therefore, to identify which immune component (or components) can show a person is protected from future infection. Such a marker would be termed a "correlate of protection."

The ability to measure an accurate correlate of protection would be valuable for two reasons. First, it could tell us whether someone who has

recovered from COVID-19 is likely to get re-infected. Second, identifying an easily measurable correlate of protection would be helpful for vaccine trials—it could speed up the evaluation of vaccine efficacy.

However, identifying good correlates of protection for other coronaviruses has proven notoriously difficult. Useful results have previously only been generated when volunteers were experimentally infected with viruses. The first human SARS-Cov-2 challenge studies are now due to begin early next year, so it is hoped that this will enable correlates of protection to be found more rapidly.

Derek Gatherer, Lecturer and Fellow of the Institute for Social Futures, Lancaster University

How can we explain the extreme geographical variation in COVID-19 mortality rates?

Cumulative deaths from COVID-19 per million of population (dpm), are very unevenly distributed across Europe (see map below) ranging from 7dpm in Slovakia to 856dpm in Belgium. A wedge of relatively lightly affected countries extends from Finland southwards to the northern Balkans.

There are similar pockets of low COVID-19 mortality on other continents, notably south-east Asian countries. Could the populations of low mortality countries have some cross-immunity to SARS-CoV-2 generated by recent exposure to another coronavirus—the obvious candidates being the milder "common cold" coronaviruses: 229E, NL63, OC43 or HKU1?

Deaths per million (dpm) of population in Europe and surrounding countries, as of mid-September 2020. Red: >200dpm; Blue: 100-200dpm; Black