



Q&A

COVID-19: A Global Pandemic—Two Global Perspectives

The Editor-in-Chief and editorial staff worked collaboratively to conduct 2 separate interviews that bring our readers 2 different perspectives on the novel coronavirus pandemic. Our first interview is with **Christian Lindmeier**, spokesperson for the World Health Organization (WHO). Mr Lindmeier provides a global public health perspective on the COVID-19 outbreak, describing the WHO's research agenda in this area, tactics to reduce the spread of the disease, and lessons learned from the Chinese health system.

Our second interview is with **Mirjam Kretzschmar, PhD**, a professor of dynamics of infectious diseases at the University Medical Centre Utrecht, The Netherlands. Her research focuses on developing individual-based modeling approaches to study contact patterns and their relationship with transmission of infection. In the interview, Dr Kretzschmar addresses the uncertainties in modeling and predicting the spread of the coronavirus and discusses ways the HEOR community can contribute to public health decision making about this disease.

Their responses to our questions about the COVID-19 outbreak on the following pages provides unique views from a public health and an outcomes researcher's (namely disease modelling) perspective.



Interview With Christian Lindmeier Spokesperson for the World Health Organization, Geneva, Switzerland

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VOS: How reliable are the data regarding overall infection rates reported by countries that traditionally keep information close to the vest and that do not usually seek help from outside organizations such as WHO? In light of the epidemiological data on hand to date, do you have any insight into why this disease has spread more rapidly in some countries versus others?

Lindmeier: The WHO requests that national authorities report probable and confirmed cases of novel coronavirus COVID-19 infection within 48 hours of identification, through the National Focal Point and the Regional Contact Point for International Health Regulations at the appropriate WHO regional office. Reporting of case-based reports is requested as long as it is feasible for the country. When it is not feasible to report case-based data, countries are requested to provide daily and weekly aggregated data.

We fully recognize that affected countries are under great pressure to respond to the outbreak and the WHO continues to encourage them to share the data we need, but this is not because of a lack of transparency from their side. It is directly linked to the emergency situation and the logistical challenges countries face to collect those data.

We’re communicating with ministers directly and we urge all countries to share these data with the WHO immediately.

VOS: What does it take to classify a disease outbreak as a pandemic, and what is the impact to the global community?

Lindmeier: A pandemic is the worldwide spread of a new disease. An influenza pandemic occurs when a new influenza virus emerges and spreads around the world, and most people do not have immunity. Viruses that have caused past pandemics typically originated from animal influenza viruses.

For both seasonal and pandemic influenza, the total number of people who get severely ill can vary. However, the impact or severity tends to be higher in pandemics in part because of the much larger number of people in the population who lack pre-existing immunity to the new virus. When a large portion of the population is infected, even if the proportion of those infected that go on to develop severe disease is small, the total number of severe cases can be quite large.

VOS: Can you provide examples of recent tactics that the WHO has employed to help control the spread of the virus and to help educate healthcare workers and the public to prevent further transmissions?

Lindmeier: Since the beginning of the outbreak, the WHO continues to coordinate the global response, through country and regional offices and headquarters, by shedding light continuously on the following key areas:

- Increasing understanding of the disease. The WHO is constantly analyzing data as we receive it and working closely with global experts on a range of topics. WHO is proposing specific studies to better understand transmission, risk factors, and source of the infection. Some of these studies are already underway.
- Providing advice to countries on critical preparedness, readiness and response actions for COVID-19, and to individuals on how to protect themselves and others, including on the safe home care for patients with suspected COVID-19 infection. The advice includes protecting others from coughs and sneezes, hand cleaning, food safety, and best practices at markets. We are also covering travel and international traffic in relation to the outbreak of the novel coronavirus COVID-19. Finally, we are advising businesses and employers to make sure they implement containment measures at workplaces.
- Keeping countries and the general public informed. The WHO is informing the public through daily situation reports and dashboards, such as the WHO Health Emergency Dashboard, and the WHO Novel Coronavirus (COVID-19) Situation Dashboard, that are displaying data in real time.
- Coordinating with partners. The WHO is working with our networks of researchers and other experts to coordinate global work on surveillance, epidemiology, forecasting, diagnostics, clinical care and treatment, and other ways to identify and manage the disease and limit onward transmission.
- Healthcare workers are at the front line of any outbreak response and as such are exposed to hazards that put them at risk of infection with an outbreak pathogen (in this case COVID-19). Hazards include pathogen exposure, long working hours, psychological distress, fatigue, occupational burnout, stigma, and physical and psychological violence. Facilities should familiarize personnel with technical updates on COVID-19 and provide appropriate tools to assess, triage, test, and treat patients and to share infection prevention and control information with patients and the public.

VOS: Can you summarize the discussions and overall direction from the WHO's recent forum in plotting a research agenda for the virus? How can the HEOR community contribute to the research agenda and to the WHO's R&D Blueprint?

Lindmeier: Following the recommendations of the Emergency Committee, Tedros Adhanom Ghebreyesus, PhD, MSc, the WHO Director-General, met with world scientists at WHO's Geneva headquarters from 11-12 February 2020 to assess the current level of knowledge about the new COVID-19 virus, agree on critical research questions that need to be answered urgently, and ways to work together to accelerate and fund priority research that can contribute to curtail this outbreak and prepare for future outbreaks.

There are currently over 200 clinical trials registered on the Chinese clinical trials registry, testing a variety of interventions with a variety of endpoints. Outside of China, there is a global data platform facilitated by the WHO with the goal of producing a global cohort of hospitalized patients. Clinical characterization protocols are available to inform sampling strategies and sharing. A number of large-scale randomized trials are being planned, both inside and outside China. Epidemiologic studies

as conducted by public health authorities have been conducted by the relevant groups in the United States, Europe, and other regions with exported cases.

Prioritization activities for which interventions to study, so as to optimize the outcome of individual patients, from antivirals to immunomodulators to supportive care interventions, are ongoing. In addition, work to coordinate research is ongoing, with the hoped-for standard data variable and outcome collection by a variety of international networks. Most importantly is ensuring adequate coordination of these efforts to achieve useable results across regions.

See R&D roadmap for more information on R&D priorities: <https://www.who.int/blueprint/priority-diseases/key-action/Roadmap-version-FINAL-for-WEB.pdf?ua=1>.

VOS: Please discuss the progress in developing a vaccine for COVID-19. Because so many companies are scrambling to develop and test vaccines, is there concern that the vaccine may not be clinically effective in the treatment of the disease? What are some of the risks to the public with vaccines developed under this kind of accelerated schedule?

Lindmeier: The WHO has received applications for review and approval of more than 40 diagnostic tests. More than 41 vaccines are in development and many clinical trials of therapeutics are underway. We expect the initial results within a few weeks.

A master global clinical trial protocol for research and prioritization of therapeutics is ongoing at the WHO. The WHO is preparing a landscape analysis of the vaccine and therapeutic investigational candidates that could be used against COVID-19 and will work on an evidence-based framework to transparently select the most promising/advanced therapeutics and vaccines candidates to move forward for clinical evaluation. We will convene meetings to discuss all critical steps that are required (eg proof-of-concept, preliminary safety data, regulatory expectations) ahead of planning for efficacy trials as well as key epidemiological and clinical aspects that we must learn and that will help enlighten vaccine and treatment development.

VOS: Overall, what can we learn from the way the affected countries have reacted to the COVID-19 epidemic?

Lindmeier: I quote WHO Director-General, Dr Tedros Adhanom Ghebreyesus, who said, "China and other countries are demonstrating that spread of the virus can be slowed and impact reduced through the use of universally applicable actions, such as working across society to identify people who are sick, bringing them to care, following up on contacts, preparing hospitals and clinics to manage a surge in patients, and training health workers. WHO calls on all countries to continue efforts that have been effective in limiting the number of cases and slowing the spread of the virus. Every effort to contain the virus and slow the spread saves lives. These efforts give health systems and all of society much-needed time to prepare, and researchers more time to identify effective treatments and develop vaccines. Allowing uncontrolled spread should not be a choice of any government, as it will harm not only the citizens of that country but affect other countries as well."

Interview With Mirjam Kretzschmar, PhD Infectious Disease Modeler, University Medical Centre Utrecht, The Netherlands



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VOS: Can you briefly explain what the COVID-19 virus is and how it relates to SAR-CoV2 or to influenza type A, particularly with respect to its transmission rate and probability of having severe outcomes?

Kretzschmar: COVID-19 is the disease caused by the new coronavirus SARS-CoV-2. The virus emerged at the end of 2019 in Wuhan, China, and has since spread all over the world. It is believed that the virus was transmitted from animals to humans and was then able to spread from human to human. It is related to the SARS-CoV virus, which caused the outbreak of SARS in 2003. However, it is less lethal than SARS, but has a higher transmissibility. At this time, it is not yet possible to give a reliable estimate of the probability of having a severe outcome due to limited testing and limited knowledge of the extent of transmission in populations. We do know, however, that risk of severe outcomes increases with age. The influenza virus is a different virus, not related to coronavirus. Epidemiologically, the situation for influenza is different, because most people have at least some partial immunity, there is a vaccine, and medication available for treatment.

VOS: How reliable are the data regarding overall infection rates reported by countries that traditionally keep information close to the vest and that do not usually seek help from outside organizations such as WHO? In light of the epidemiological data on hand to

date, do you have any insight into why this disease has spread more rapidly in some countries versus others?

Kretzschmar: That is hard to say. Even in countries that do report openly, there is a large uncertainty due to limited testing. More reliable at the moment are hospitalization data and numbers of patients needing treatment in an intensive care unit. It is unclear why there seem to be differences between countries in epidemic spread. Possible reasons are differences in contact patterns, but also differences in testing and reporting due to different healthcare systems may play a role. Finally, the epidemics in various countries were seeded at different moments in time and might therefore be at different points in the exponential growth curve.

VOS: What are the key parameters affecting the rate at which the disease spreads across a population? What determines when the rate of occurrence of new cases starts to decline?

Kretzschmar: The key parameters are contact rates and intervention effectiveness (eg, time to diagnosis and isolation of cases, effectiveness of contact tracing). The effectiveness of interventions is influenced by the proportion of cases who remain asymptomatic or who have only mild symptoms. These persons do not get diagnosed and reported to the healthcare

system, but they might contribute to further transmission, although we do not yet know what their infectivity may be. Given the importance of contact rates for epidemic spread, the most important intervention at present is social distancing. If social distancing is effective in reducing contacts to a minimum, transmission can be reduced to very low levels. It will then take around 1 to 2 weeks before effects can be seen in the numbers of new cases. Alternatively, once a substantial proportion of the population is immune, numbers of cases will start to decline.

VOS: Are there still some key uncertainties in modeling or predicting the spread of the coronavirus? If so, what are they, and do you think we will have better information about them soon?

There are many uncertainties: Proportion of asymptomatic and mild infections, how much transmission takes place before symptom onset, how much do asymptomatic persons contribute to transmission, is there immunity after recovery and how long does it last, how effective is social distancing in reducing transmission, all these factors are uncertain. In mathematical models, we need to use assumptions based on insights gained from the outbreak in China and other studies that are now published daily in scientific journals or on preprint servers. The time up to now has been too short for conducting rigorous clinical and epidemiological studies.

VOS: Do you know how much, and in what ways, the HEOR community has been able to contribute to public health decision making about this disease?

Kretzschmar: Up to now, decisions have been mainly based on the aims of outbreak containment and mitigation. These decisions to implement rigorous measures of social distancing have major economic impact, which will have implications on a longer time scale. There is a big challenge here for the HEOR community to analyze the economic aspects of this crisis and to contribute with insight about the economic impact and societal costs of this crisis. Much more work on these aspects needs to be done in the future, also for supporting decision makers once the epidemiological urgency has subsided.

VOS: Is there anything that I haven't asked you that you feel our readers should know?

Kretzschmar: Last week [Ferguson, et al](#) from the Imperial College in London, England, published a paper where they predicted the implications of the COVID-19 outbreak for the United Kingdom and the United States based on a modelling study. They used a very detailed individual-based model that took many factors such as geographic and demographic distributions into account. They analyzed the possible impact of a variety of intervention scenarios and came to the conclusion that the only possible strategy at present is suppression of further transmission if we want to prevent an overload of the health system capacities. Although many uncertainties remain, this modelling study is at present one of the best we have for assessing the possible impact of interventions. The results of Ferguson's study are in line with other modelling studies published to date. As new data become available to improve parameter estimates, better predictions may be possible. We now need better data on some of the key clinical parameters, but also on the effectiveness of social distancing measures as applied in many countries. •

Prevention starts with 10 basic things people can do:

- 1 Clean your hands regularly with an alcohol-based hand rub or wash them with soap and water.
- 2 Clean surfaces (eg, kitchen benches and work desks) regularly with disinfectant.
- 3 Educate yourself about COVID-19. Make sure your information comes from reliable sources.
- 4 Avoid traveling if you have a fever or cough, and if you become sick while on a flight, inform the crew immediately. Once you get home, contact a health professional and tell them about where you have been.
- 5 Cough or sneeze into your sleeve or use a tissue. Dispose of the tissue immediately into a closed rubbish bin, and then clean your hands.
- 6 Take extra precautions to avoid crowded areas if you are over 60 years old, or if you have an underlying condition.
- 7 If you feel unwell, stay at home and call your doctor or local health professional.
- 8 If you are sick, stay at home, and eat and sleep separately from your family. Use different utensils and cutlery to eat.
- 9 If you develop shortness of breath, call your doctor and seek care immediately.
- 10 It's normal and understandable to feel anxious, especially if you live in a country or community that has been affected. Find out what you can do in your community. Discuss how to stay safe with your workplace, school, or place of worship.