Medical Xpress

Will COVID-19 become a mostly childhood disease?

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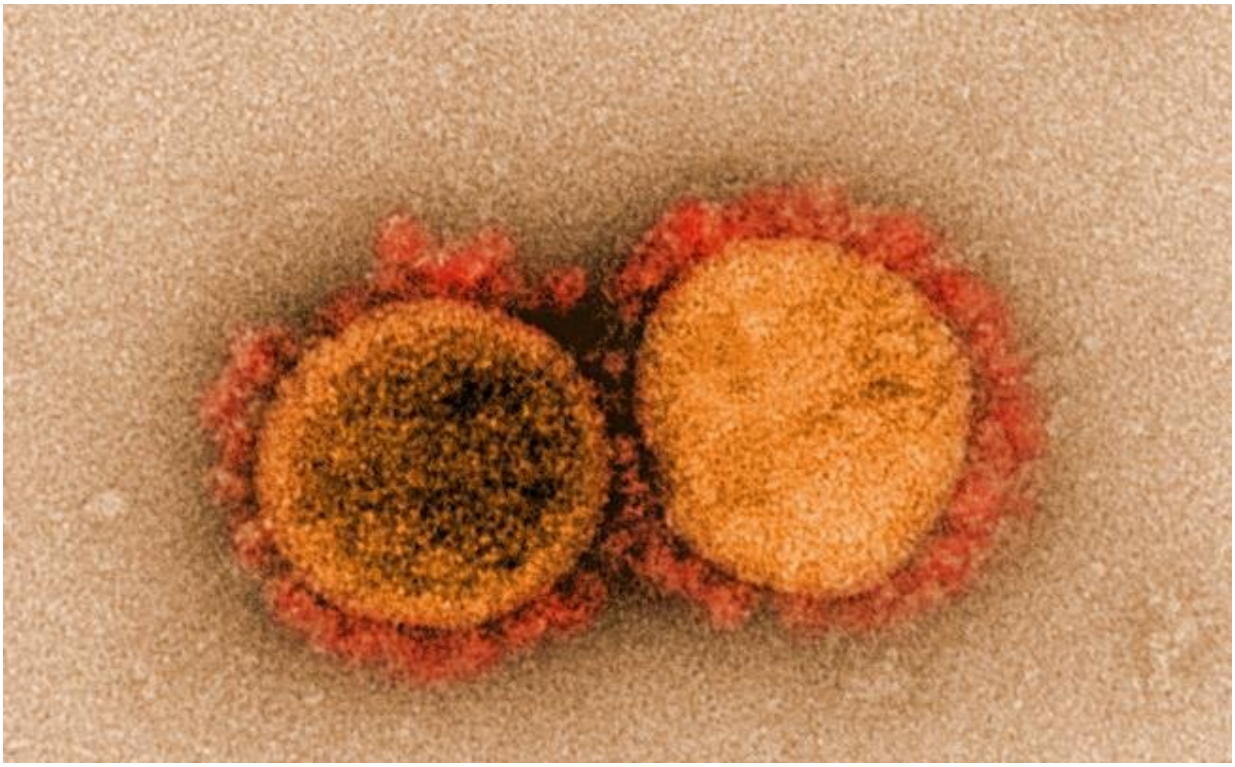

Transmission electron micrograph of SARS-CoV-2 virus particles, isolated from a patient. Image captured and color-enhanced at the NIAID Integrated Research Facility (IRF) in Fort Detrick, Maryland. Credit: NIAID

Within the next few years, as the SARS-CoV-2 virus becomes endemic in the global population, COVID-19 may behave like other common-cold coronaviruses, affecting mostly young children who have not yet

been vaccinated or exposed to the virus, according to new modeling results. Because COVID-19 severity is generally lower among children, the overall burden from this disease is expected to decline.

"Following infection by SARS-CoV-2, there has been a clear signature of increasingly severe outcomes and fatality with age," said Ottar Bjornstad. "Yet, our modeling results suggest that the risk of infection will likely shift to younger children as the adult community becomes immune either through vaccination or exposure to the virus."

Bjornstad explained that such shifts have been observed in other coronaviruses and influenza viruses as they have emerged and then become endemic.

"Historical records of respiratory diseases indicate that age-incidence patterns during virgin epidemics can be very different from endemic circulation," he said. "For example, ongoing genomic work suggests that the 1889-1890 pandemic, sometimes known as the Asiatic or Russian flu—which killed one million people, primarily adults over age 70—may have been caused by the emergence of HCoV-OC43 virus, which is now an endemic, mild, repeat-infecting cold virus affecting mostly children ages 7-12 months old."

Bjornstad cautioned, however, that if immunity to reinfection by SARS-CoV-2 wanes among adults, disease burden could remain high in that group, although previous exposure to the virus would lessen the severity of disease.

"Empirical evidence from seasonal coronaviruses indicates that prior exposure may only confer short-term immunity to reinfection, allowing recurrent outbreaks, this prior exposure may prime the immune system to provide some protection against severe disease," said Bjornstad. "However, research on COVID-19 shows that vaccination provides

stronger protection than exposure to the SARS-CoV-2 virus, so we encourage everyone to get vaccinated as soon as possible."

The U.S.-Norwegian team developed what is known as a "realistic age-structured (RAS) mathematical model" that integrates demography, degree of social mixing, and duration of infection-blocking and disease-reducing immunity to examine potential future scenarios for age-incidence and burden of mortality for COVID-19.

Specifically, the researchers examined disease burden over immediate, medium and long terms—1, 10 and 20 years, respectively. They also examined disease burden for 11 different countries—including China, Japan, South Korea, Europe, Spain, United Kingdom, France, Germany, Italy, United States, Brazil and South Africa—that differed widely in their demographics. They used data from the United Nations for each of these countries to parameterize the model.

"Regardless of immunity and mixing, the population-level burden of mortality may differ among countries because of varying demographics," said Ruiyun Li, postdoctoral fellow, University of Oslo. "Our general model framework allows for robust predictions of age-dependent risk in the face of either short or long-term protective immunity, reduction of severity of disease given previous exposure, and consideration of the range of countries with their different demographics and social mixing patterns."

According to Li, social distancing is well documented to affect transmissibility, and many countries implemented interventions, such as "shelter in place," during the build-up of the virgin COVID-19 epidemic. Therefore, the team's model assumes that the reproduction number (R_0)—or the level of transmissibility—on any given day is linked to the amount of mobility on that day. The model also incorporates a variety of scenarios for immunity, including both independence and dependence of

disease severity on prior exposure, as well as short- (either three months or one year) and long-term (either 10 years or permanent) immunity.

The team's results appear today (August 11) in the journal *Science Advances*.

"For many infectious respiratory diseases, prevalence in the population surges during a virgin epidemic but then recedes in a diminishing wave pattern as the spread of the infection unfolds over time toward an endemic equilibrium," said Li. "Depending on immunity and demography, our RAS model supports this observed trajectory; it predicts a strikingly different age-structure at the start of the COVID-19 epidemic compared to the eventual endemic situation. In a scenario of long-lasting immunity, either permanent or at least 10 years, the young are predicted to have the highest rates of infection as older individuals are protected from new infections by prior infection."

Jessica Metcalf, associate professor of ecology, evolutionary biology and public affairs, Princeton University, noted that this prediction is likely to hold only if reinfections produce only mild disease. However, she said, the burden of mortality over time may remain unchanged if primary infections do not prevent reinfections or mitigate severe disease among the elderly.

"In this bleakest scenario, excess deaths due to continual severe reinfections that result from waning immunity will continue until more effective pharmaceutical tools are available," she said.

Interestingly, due to variations in demographics, the model predicts different outcomes for different countries.

"Given the marked increase of the infection-fatality ratio with age, countries with older population structures would be expected to have a

larger fraction of deaths than those with relatively younger population structures," said Nils Chr. Stenseth, professor of ecology and evolution, University of Oslo. "Consistent with this, for example, South Africa—likely due, in part, to its younger population structure—has a lower number of deaths compared to older populations such as Italy. We found that such 'death disparities' are heavily influenced by demographics. However, regardless of demographics, we predict a consistent shift of the risk to the young."

The researchers said that they designed their model so that health authorities will have a powerful and flexible tool to examine future age-circulation of COVID-19 for use in strengthening preparedness and deployment of interventions.

Bjornstad said, "The mathematical framework we built is flexible and can help in tailoring mitigation strategies for countries worldwide with varying demographics and social mixing patterns, thus providing a critical tool for policy decision making."

More information: A general model for the demographic signatures of the transition from pandemic emergence to endemicity, *Science Advances* (2021). DOI: 10.1126/sciadv.abf9040

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