and from onset-of-symptoms to hospital discharge to be 24·7 days (22·9–28·1). The study findings give an estimate of the overall case fatality ratio in China of 1·38% (95% CrI 1·23–1·53), which becomes higher as age increases (figure).

Estimates of case fatality ratios might vary slightly from country to country because of differences in prevention, control, and mitigation policies implemented, and because the case fatality ratio is substantially affected by the preparedness and availability of health care. Early studies[5,6] have shown that delaying the detection of infected cases not only increases the probability of spreading the virus to others (most likely family members, colleagues, and friends) but also makes the infection worse in some cases, thereby increasing the case fatality ratio.[7]

Comparisons of case fatality ratios for SARS, COVID-19, and seasonal influenza in different age groups are shown in the figure. Even though the fatality rate is low for younger people, it is very clear that any suggestion of COVID-19 being just like influenza is false: even for those aged 20–29 years, once infected with SARS-CoV-2, the case fatality ratio is around three times higher than that of seasonal influenza in people aged 18–49 years. For people aged 60 years and older, the chance of survival following SARS-CoV-2 infection is approximately 95% in the absence of comorbid conditions. However, the chance of survival will be considerably decreased if the patient has underlying health conditions, and continues to decrease with age beyond 60 years.[5,6]

Although China seems to be out of the woods now, many other countries are facing tremendous pressure from the COVID-19 pandemic. The strategies of early detection, early diagnosis, early isolation, and early treatment that were practised in China[6] are likely to be not only useful in controlling the outbreak, but also contribute to decreasing the case fatality ratio of the disease.

I declare no competing interests.

Shigui Ruan
ruan@math.miami.edu

Department of Mathematics, University of Miami, Coral Gables, FL 33146, USA

1 WHO. Update 49—SARS case fatality ratio, incubation period. May 7, 2003. https://www.who.int/csr/sars/archive/2003_05_07a/en/ (accessed March 21, 2020).

2 WHO. Middle East respiratory syndrome coronavirus (MERS-CoV): key facts. March 11, 2019. https://www.who.int/en/news-room/fact-sheets/detail/middle-east-respiratory-syndrome-coronavirus-(mers-cov) (accessed March 21, 2020).

3 WHO. Coronavirus disease 2019 (COVID-19) situation report—62. March 21, 2020. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200322-sitrep-62-covid-19.pdf?sfvrsn=f7764c46_2 (accessed March 22, 2020).

4 Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; published on Feb 28. DOI:10.1056/NEJMoa2002032.

5 The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China, 2020. *China CDC Weekly* 2020; **2:** 113–22.

6 WHO. Report of the WHO–China Joint Mission on coronavirus disease 2019 (COVID-19). February 28, 2020. https://www.who.int/publications-detail/report-of-the-who-china-joint-mission-on-coronavirus-disease-2019-(covid-19) (accessed March 25, 2020).

7 Verity R, Okell LC, Dorigatti I, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. *Lancet Infect Dis* 2020; published online March 30. https://doi.org/10.1016/S1473-3099(20)30243-7.

8 Chan-Yeung M, Xu RH. SARS: epidemiology. *Respirology* 2003; **8** (suppl)**:** S9–14.

9 Centers for Disease Control and Prevention. Estimated influenza illnesses, medical visits, hospitalizations, and deaths in the United States—2018–2019 influenza season. Jan 8, 2020. https://www.cdc.gov/flu/about/burden/2018-2019.html (accessed March 25, 2020).

Scientific and ethical basis for social-distancing interventions against COVID-19

Caia Image/Science Photo Library

Published **Online** March 23, 2020
https://doi.org/10.1016/S1473-3099(20)30190-0

See **Articles** page 678

On Dec 31, 2019, the WHO China Country Office received notice of a cluster of pneumonia cases of unknown aetiology in the Chinese city of Wuhan, Hubei province.[1] The incidence of coronavirus disease 2019 (COVID-19; caused by severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) has since risen exponentially, now affecting all WHO regions. The number of cases reported to date is likely to represent an underestimation of the true burden as a result of shortcomings in surveillance and diagnostic capacity affecting case ascertainment in both high-resource and low-resource settings.[2] By all scientifically meaningful criteria, the world is undergoing a COVID-19 pandemic.

In the absence of any pharmaceutical intervention, the only strategy against COVID-19 is to reduce mixing of susceptible and infectious people through early ascertainment of cases or reduction of contact. In *The Lancet Infectious Diseases*, Joel Koo and colleagues[3] assessed the potential effect of such social distancing interventions on SARS-CoV-2 spread and COVID-19 burden in Singapore. The context is worthy of study, since Singapore was among the first settings to report imported cases, and has so far succeeded in preventing community spread. During the 2003 severe acute respiratory syndrome coronavirus (SARS-CoV) outbreak in Singapore, numerous non-pharmaceutical interventions were implemented successfully, including effective triage and infection control measures in health-care settings, isolation and quarantine of patients with SARS and their contacts, and mass screening of school-aged children for febrile illness.[4] Each of these measures represented an escalation of typical public health action. However, the scale and disruptive impact of these interventions were small compared with the measures that have been implemented in China in response to COVID-19, including closure of schools, workplaces, roads, and transit systems; cancellation of public gatherings; mandatory quarantine of uninfected people without known exposure to SARS-CoV-2; and large-scale electronic surveillance.[5,6] Although these actions have been praised by WHO,[5] the possibility of imposing similar measures in other countries raises important questions. Populations for whom social-distancing interventions have been implemented require and deserve assurance that the decision to enact these measures is informed by the best attainable evidence.

For a novel pathogen such as SARS-CoV-2, mathematical modelling of transmission under differing scenarios is the only viable and timely method to generate such evidence. Koo and colleagues[3] adapted an existing influenza epidemic simulation model[7] using granular data on the composition and behaviour of the population of Singapore to assess the potential consequences of specific social-distancing interventions on the transmission dynamics of SARS-CoV-2. The authors considered three infectivity scenarios (basic reproduction number [R_0] of 1·5, 2·0, or 2·5) and assumed between 7·5% and 50·0% of infections were asymptomatic. The interventions were quarantine with or without school closure and workplace distancing (whereby 50% of workers telecommute). Although the complexity of the model makes it difficult to understand the impact of each parameter, the primary conclusions were robust to sensitivity analyses. The combined intervention, in which quarantine, school closure, and workplace distancing were implemented, was the most effective: compared with the baseline scenario of no interventions, the combined intervention reduced the estimated median number of infections by 99·3% (IQR 92·6–99·9) when R_0 was 1·5, by 93·0% (81·5–99·7) when R_0 was 2·0, and by 78·2% (59·0–94·4) when R_0 was 2·5. The observation that the greatest reduction in COVID-19 cases was achieved under the combined intervention is not surprising. However, the assessment of the additional benefit of each intervention, when implemented in combination, offers valuable insight. Since each approach individually will result in considerable societal disruption, it is important to understand the extent of intervention needed to reduce transmission and disease burden.

New findings emerge daily about transmission routes and the clinical profile of SARS-CoV-2, including the substantially underestimated rate of infection among children.[8] The implications of such findings with regard to the authors' conclusions about school closure remain unclear. Additionally, reproductive number estimates for Singapore are not yet available. The authors estimated that 7·5% of infections are clinically asymptomatic, although data on the proportion of infections that are asymptomatic are scarce; as shown by Koo and colleagues in sensitivity analyses with higher asymptomatic proportions, this value will influence the effectiveness of social-distancing interventions. Additionally, the analysis assumes high compliance of the general population, which is not guaranteed.

Although the scientific basis for these interventions might be robust, ethical considerations are multifaceted.[9] Importantly, political leaders must enact quarantine and social-distancing policies that do not bias against any population group. The legacies of social and economic injustices perpetrated in the name of public health have lasting repercussions.[10] Interventions might pose risks of reduced income and even job loss, disproportionately affecting the most disadvantaged populations: policies to lessen such risks are urgently needed. Special attention should be given to protections for vulnerable populations, such as homeless, incarcerated, older, or disabled individuals, and undocumented migrants. Similarly, exceptions might be necessary for certain groups, including people who are reliant on ongoing medical treatment.

The effectiveness and societal impact of quarantine and social distancing will depend on the credibility of public health authorities, political leaders, and institutions. It is important that policy makers maintain the public's trust through use of evidence-based interventions and fully transparent, fact-based communication.

We declare no competing interests.

*Joseph A Lewnard, Nathan C Lo
jlewnard@berkeley.edu

Division of Epidemiology, School of Public Health and Center for Computational Biology, College of Engineering, University of California, Berkeley, CA 94720, USA (JAL); and Department of Medicine, University of California, San Francisco, CA, USA (NCL)

1. WHO. Pneumonia of unknown cause—China. https://www.who.int/csr/don/05-january-2020-pneumonia-of-unkown-cause-china/en/ (accessed March 5, 2020).
2. Cohen J, Kupferschmidt K. Labs scramble to produce new coronavirus diagnostics. *Science* 2020; **367:** 727.
3. Koo JR, Cook AR, Park M, et al. Interventions to mitigate early spread of COVID-19 in Singapore: a modelling study. *Lancet Infect Dis* 2020; published online March 23. https://doi.org/10.1016/S1473-3099(20)30162-6.
4. Tan CC. SARS in Singapore—key lessons from an epidemic. *Ann Acad Med Singapore* 2006; **35:** 345–49.
5. Kupferschmidt K, Cohen J. China's aggressive measures have slowed the coronavirus. They may not work in other countries. March 2, 2020. https://www.sciencemag.org/news/2020/03/china-s-aggressive-measures-have-slowed-coronavirus-they-may-not-work-other-countries (accessed March 9, 2020).
6. Kupferschmidt K, Cohen J. Can China's COVID-19 strategy work elsewhere? March 6, 2020. https://science.sciencemag.org/content/367/6482/1061?rss%253D1= (accessed March 11, 2020).
7. Chao DL, Halloran ME, Obenchain VJ, Longini IM. FluTE, a publicly available stochastic influenza epidemic simulation model. *PLoS Comput Biol* 2010; **6:** e1000656.
8. Bi Q, Wu Y, Mei S, et al. Epidemiology and transmission of COVID-19 in Shenzhen, China: analysis of 391 cases and 1286 of their close contacts. *medRxiv* 2020; published online March 4. DOI:10.1101/2020.03.03.20028423 (preprint).
9. Gonsalves GS, Kapczynski A, Ko AI, et al. Achieving a fair and effective COVID-19 response: an open letter to Vice-President Mike Pence, and other federal, state, and local leaders from public health and legal experts in the United States. https://docs.google.com/document/d/1NVOSECOEp8deYnmJfO0uKtRHcNcbmNrk7dW752dzMeE/edit (accessed March 5, 2020).
10. Kass NE. An ethics framework for public health. *Am J Pub Heal* 2001; **91:** 1776–82.

COVID-19 in children: the link in the transmission chain

iStock/yaoinlove

Published **Online**
March 25, 2020
https://doi.org/10.1016/S1473-3099(20)30236-X

See **Articles** page 689

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), emerged from Wuhan, Hubei province, China, in late 2019 and has now reached pandemic status.[1] Coronaviruses typically cause mild upper respiratory tract infections;[2] however, SARS-CoV-2,[3] severe acute respiratory syndrome coronavirus (SARS-CoV),[4] and Middle East respiratory syndrome coronavirus (MERS-CoV)[5] have all been associated with severe illness and death. Common symptoms reported in adults with COVID-19 are fever, dry cough, and fatigue; severe cases have been associated with dyspnoea and bilateral ground-glass opacities on chest CT.[3] In China, the SARS-CoV-2 reproductive number is estimated at 2.[6] The combined case-fatality rate is 2% in China,[7] and the risk of death is increased significantly in older people (approximately 15%).[7] It is noteworthy that infants and children have not been featured prominently in COVID-19 case statistics. An analysis from China has shown that children younger than 10 years account for only 1% of COVID-19 cases,[7] similar to the proportion for SARS-CoV and MERS-CoV epidemics.[4,5]

Infants and young children are typically at high risk for admission to hospital after respiratory tract infection with viruses such as respiratory syncytial virus and influenza virus.[8] Immaturity of the respiratory tract and immune system is thought to contribute to severe viral respiratory disease in this age group.[8] Therefore, the absence of paediatric patients with COVID-19 has perplexed clinicians, epidemiologists, and scientists. Case definitions and management strategies for children are absent because of the limited number of paediatric patients with COVID-19. In *The Lancet Infectious Diseases*, Haiyan Qiu and colleagues[9] have shed light on this under-represented population with a clinical report of 36 paediatric patients (aged 1–16 years) with PCR-confirmed COVID-19. Their analyses have important implications for clinical management of younger people with SARS-CoV-2 infection and social distancing policies to prevent virus transmission.

The patients in this study[9] were being treated at three hospitals located in Zhejiang province, China, which is 900 km from Wuhan. The children accounted for roughly 5% of total patients with COVID-19. Patients were stratified by disease severity and were assessed in hospital (mean duration of hospitalisation, 14 [SD 3] days) for secondary bacterial and fungal infection, sepsis, immune responses, and organ dysfunction (lung, liver, heart, and kidney). All children underwent CT examination for diagnosis of pneumonia.