Pandemic Surge Models in the Time of Severe Acute Respiratory Syndrome Coronavirus-2: Wrong or Useful?

With 2 million confirmed cases and more than 100 000 deaths worldwide, the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic has generated fear, uncertainty, and doubt as the world has witnessed COVID-19-related deaths and overwhelmed hospitals in Wuhan, China; Italy; and New York City. With no preexisting herd immunity, vaccine, or proven antiviral treatment, public health decision making must rely on mitigation through social distancing. Such public health decisions cannot be answered by simple epidemiologic methods, because they involve “tradeoffs, uncertainty, and values,” leading to the use of models to inform administrative and policy decision makers (1). At the behest of decision makers at the local, regional, hospital system, and national levels, all the models discussed herein have been designed to forecast demand for hospital resources—namely acute and critical care beds and mechanical ventilators—to understand hospital capacity constraints and to determine when peak demand will occur. Rapidly developed to be fit for purpose and user-friendly, these models all inform local decision makers but have been used worldwide and continue to evolve. However, they differ fundamentally in their methodological approaches and the degree to which their projections can be customized to local context. They also are all exemplars of British statistician George E.P. Box's famous aphorism, “All models are wrong, but some are useful.”

The Institute for Health Metrics and Evaluation (IHME) COVID-19 hospital forecasting project at the University of Washington has gained much media exposure. Initially based on observed mortality in Wuhan City, the IHME model has been augmented by 8 (on 5 April) and then 19 cities (on 10 April) in Italy and Spain and supplemented by French data on older persons in hospitals and nursing homes on 13 April (2). The IHME's mortality curve-fitting approach echoes that of William Farr, a British statistician and epidemiologist: “The death rate is a fact; anything beyond this is an inference.” Seeking to identify a “natural law of epidemics,” Farr fit curves through epidemic mortality data in 1840 and found that epidemics could be described as bell-shaped curves (normal distributions) (3). His approach preceded the discovery of viruses and the acceptance of the germ theory of diseases, so it contained no mechanistic understanding of disease transmission (3). Likewise, on the basis of observed mortality curves in cities that have already reached their peak during the pandemic, the IHME approach uses the observed mortality curves in cities that have already reached their peak during the pandemic to predict

deaths in other areas that have not yet had their peaks and derives hospitalization rates from hospitalization-to-death ratios, from which it predicts intensive care unit (ICU) and mechanical ventilator use (2). Originally starting with 4 interventions equally weighted for effectiveness, since 5 April the IHME has included the effects of only 3 social distancing measures (school closures, stay-at-home orders, and nonessential business closures [now excluding travel restrictions]) by using 3 different models (short-term day 5, long-term day 20, and a time-dependent weighting of these predictions) (2). The IHME's approach to curve fitting mortality assumes that the shape of the curve (with adjustments for the timing of policy interventions) incorporates infectious disease transmission.

In contrast, the University of Pennsylvania's COVID-19 Hospital Impact Model for Epidemics (CHIME) is a dynamic transmission or mechanistic model (4). In 1908, John Brownlee explored the then-established germ theory concept of infection transmission and recognized the need to incorporate the host population into epidemic modeling on the basis of infectiousness: “If there be given a number of susceptible persons in a community, and if one, say, infect three, the whole body of the susceptible persons will become involved, and the last remaining few finally swept off. Even when allowance is made, on various hypotheses, for the chance of infection being small, because of dilution of the susceptibility by the insusceptibility only lengthened, not changed in form” (3). His research pioneered susceptible-exposed-infected-recovered infectious disease models (SEIR, or simply SIR when excluding exposures) that rely on a population of susceptible persons who may become exposed to the infectious agent and which may result in transmission of infection from which they may recover (such as influenza) with or without immunity or develop chronic disease (such as hepatitis C virus). Data inputs to such models include specification of such concepts as basic reproductive number (R_0), the number of additional cases that 1 infection will generate (2.3 in Wuhan) (in the absence of mitigation, $1 - 1/R_0$ = the proportion of the population likely to be infected, or approximately 60% [for $R_0 = 2.3$] [5], and mitigation or vaccination that reduces the doubling time to <1 leads to resolution of the epidemic); doubling time, the number of days for the epidemic to double in cases (7.4 days in Wuhan); incubation period, the number of days from infection to symptoms (5.2 days in Wuhan); and serial interval, the number days between illness onset in the initial infection and onset in secondary transmissions (7.5 days in Wuhan) (6). Exposure details might include duration and degree of infectious-

ness before and during symptom onset; population density on the basis of contacts at school, at work, or randomly in the community; heterogeneity in infection transmission (such as superspreaders); and asymptomatic or mild infections that do not lead to hospital evaluation but might be transmissible.

To facilitate tailored predictions by administrators and policymakers to their local circumstances, the CHIME model simplifies these disease inputs into regional population at risk, where the number infected depends on the regional population size, hospital market share, and currently hospitalized census (7). CHIME calculates the basic reproductive number (R_0) from inputs for the doubling time and recovery (infectiousness) in days with a constant mitigation reduction from social distancing at the date of implementation (7). The severity impact of infection includes the proportion of acute and ICU hospitalization and mechanical ventilation and the average length of stay (LOS) in the hospital and the ICU with or without a ventilator. The CHIME model assumes uniform or homogeneous susceptibility to infection risk, regardless of population density, contact location, or heterogeneity in infectivity (4), and calculates R_0 on the basis of a predetermined relationship to input specifications. It can incorporate asymptomatic or mild infections by accounting for such persons when estimating proportions of need for hospitalization, ICU care, and mechanical ventilation. Of importance, the investigators compare their projections with those of other existing models (cross-validation) (4).

In their report for *Annals*, Giannakeas and colleagues use their COVID-19 Acute and Intensive Care Resource Tool (CAIC-RT) to examine the steady-state consequences of constrained hospital resources on patient throughput (8). In contrast to the other models described here, CAIC-RT ignores the epidemic and focuses on capacity imposed by resource limitations. This type of model originates in an engineering field called operations research, which seeks to maximize outputs given constraints and to identify queues and bottlenecks that may benefit from additional resources, such as those in factory production. The CAIC-RT can be tailored to their local age distribution of patients with SARS-CoV-2 infection presenting to a health care system or hospital and to the age-stratified proportion requiring hospitalization, critical care, and mechanical ventilation (9). At the beginning of the epidemic, the system has sufficient resource capacity to care for all patients with SARS-CoV-2 infection. Eventually, with full use, the steady-state assumption becomes necessary. On the basis of the number of acute care and ICU beds and mechanical ventilators (potentially supplemented by surge capacity or by shifting non-COVID-19 beds to COVID-19 ones as user inputs), as well as mean LOS for each, CAIC-RT calculates the maximum number of patients moving in and out of each of those resources on a daily basis due to admissions, discharges, deaths, or

transfers from one resource to another or from or to another health care facility. By setting inputs equal to outputs (on the basis of LOS), CAIC-RT determines the maximum daily patient flows and assumes that as soon as a patient leaves a resource, that resource is filled by another; therefore, it does not explicitly account for day-to-day variation resulting in queues or bottlenecks, as typically occur during epidemics.

The aforementioned models differ in their approaches, data needs, reproducibility, methodological complexity, and transparency, as well as in their assessment of face validity, uncertainty, verification, cross-model validity, and external validity (10). As with hurricane-tracking models, they make varying projections; yet in the face of uncertainty, they provide useful real-time forecasts to prepare for the pandemic, as evidenced by their broad use. Of note, 2 of the models consider mitigation of basic reproductive number, but only 1 permits user input. Any reduction in R_0 through mitigation results in a flatter curve, delaying the peak and lowering the likelihood of exceeding resource capacity, but would also reduce herd immunity, because more persons remain susceptible. In the absence of a vaccine, this reduced herd immunity leads to a higher risk for subsequent resurgent epidemic waves. Beyond its mortality impact, this pandemic has triggered a substantial worldwide economic downturn, particularly for economically vulnerable persons and small businesses (5). With tradeoffs between economic recovery and health objectives (5), these models make useful predictions that inform timely health care system preparations but also decision making by policymakers who seek to minimize mortality and not overwhelm the health care system, yet also seek to manage the economy, while awaiting development of safe and effective vaccines and antiviral treatments. Regardless of the model, the SARS-CoV-2 pandemic will end.

John B. Wong, MD
Tufts Medical Center
Boston, Massachusetts

Disclosures: Author has disclosed no conflicts of interest. The form can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M20-1956.

Corresponding Author: John B. Wong, MD, Division of Clinical Decision Making, Tufts Medical Center, 800 Washington Street #302, Boston, MA 02111; e-mail, jwong@tuftsmedicalcenter.org.

Ann Intern Med. 2020. doi:10.7326/M20-1956

References

1. Owens DK. Analytic tools for public health decision making. *Med Decis Making.* 2002 Sep-Oct;22:S3-10. [PMID: 12369229]
2. Institute for Health Metrics and Evaluation. COVID-19 estimation updates. Accessed at www.healthdata.org/covid/updates on 14 April 2020.

3. **Fine PEM.** John Brownlee and the measurement of infectiousness: an historical study in epidemic theory. *Journal of the Royal Statistical Society Series A (Statistics in Society)*. 1979;142:347-62.
4. **Weissman GE, Crane-Droesch A, Chivers C, et al.** Locally informed simulation to predict hospital capacity needs during the COVID-19 pandemic. *Ann Intern Med*. 2020. [PMID: 32259197] doi:10.7326/M20-1260
5. **Anderson RM, Heesterbeek H, Klinkenberg D, et al.** How will country-based mitigation measures influence the course of the COVID-19 epidemic? *Lancet*. 2020;395:931-934. [PMID: 32164834] doi:10.1016/S0140-6736(20)30567-5
6. **Li Q, Guan X, Wu P, et al.** Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med*. 2020; 382:1199-1207. [PMID: 31995857] doi:10.1056/NEJMoa2001316
7. **Penn Medicine.** The CHIME App. Accessed at <https://code-for-philly.gitbook.io/chime> on 14 April 2020.
8. **Giannakeas V, Bhatia D, Warkentin MT, et al.** Estimating the maximum capacity of COVID-19 cases manageable per day given a health care system's constrained resources. *Ann Intern Med*. 16 April 2020. [Epub ahead of print]. doi:10.7326/M20-1169.
9. **Giannakeas V, Bhatia D, Warkentin MT, et al.** CAIC-RT: COVID-19 Acute and Intensive Care Resource Tool. Accessed at <https://caic-rt.shinyapps.io/CAIC-RT> on 14 April 2020.
10. **Eddy DM, Hollingworth W, Caro JJ, et al; ISPOR-SMDM Modeling Good Research Practices Task Force.** Model transparency and validation: a report of the ISPOR-SMDM modeling good research practices task force-7. *Med Decis Making*. 2012 Sep-Oct;32:733-43. [PMID: 22990088]