Epidemiological Modeling Needs New, Coherent, Federal Support for the Post-COVID-19 Era

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Introduction

Many Americans' first introduction to epidemiological modeling occurred via the media in the first months of the COVID-19 pandemic; and, like so much else associated with the pandemic response, the experience was not salutary. Although many were familiar with the idea of projecting future trends—for example the extrapolation of a company's quarterly earnings growth into future years—here was something quite different: At a time when coronavirus cases in many places were increasing exponentially, some media and politicians showed projections—models—that had the pandemic rapidly peaking and then rapidly diminishing, while others predicted a series of cycles that might continue for several years. Models varied as to the effectiveness of "flattening the curve" to keep the demand for ICU beds and respirators manageable. Many graphs in the published media showed, as a likely forecast, the disappearance of the coronavirus within a few months.[1]

It was difficult for the public to understand how, with almost all indicators trending upwards, scientists could predict a near-future peak followed by a decline. Two explanations were frequently given: "herd immunity" that might occur naturally,[2] and R_0 (the virus' "basic reproduction number") that might, by social distancing measures, be brought below the critical value of 1.0, slowing and ultimately halting virus propagation.[3]

These were difficult ideas to communicate. The dependence of the models on input data—which were scarce and often unreliable early on—was often glossed over. The models themselves were incomplete. Recognition of such real effects as asymptomatic transmission, aerosol transmission, and super-spreaders came only gradually. Scientific understanding was changing with time, communication channels to the public were cluttered with noise (not least from the Executive Branch), and the character and implications of continuing uncertainties were sometimes lost in translation.

The consequences of these shortcomings—especially the lack of clarity around genuine scientific uncertainty—are not small. The public's respect for science has been undermined in ways whose full damage has yet to manifest itself, for example, in people who will be reluctant to agree that a properly developed and tested future vaccine will be safe and effective, and who may thus refuse vaccination. It is also disheartening to see respected public health authorities

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[1] *The Economist*, "Briefing", February 29, 2020, at https://www.economist.com/briefing/2020/02/29/covid-19-is-now-in-50-countries-and-things-will-get-worse ; The New York Times, "Flattening the Coronavirus Curve", March 27, 2020, at https://www.nytimes.com/article/flatten-curve-coronavirus.html .

[2] The Guardian, "Herd immunity: will the UK's coronavirus strategy work?", March 13, 2020, at https://www.theguardian.com/world/2020/mar/13/herd-immunity-will-the-uks-coronavirus-strategy-work .

[3] Jon Cohen, "Scientists are racing to model the next moves of a coronavirus that's still hard to predict," Science (February 7, 2020) at https://www.sciencemag.org/news/2020/02/scientists-are-racing-model-next-moves-coronavirus-thats-still-hard-predict .

backing away from epidemiological modeling as a useful tool in time of pandemic crisis (even if their statements are narrowly accurate),[4] since, as we will explain, modeling is one of very few tools available for guiding policy responses.

The purpose of this report is to give our views on (i) what went right and what went wrong; (ii) what are the weaknesses in the field of epidemiological modeling, and in its federal support, that made its sub-optimal showing in time of crisis almost preordained; and (iii) what needs to be changed, so that in future crises modelers can be more effective in providing accurate models and estimates of model uncertainty, communicating more effectively to the public, and connecting more effectively to policy makers facing difficult real-time decisions. This is not a case of simply "send more money." We will show that epidemiological modeling is, in a sense, an "orphan" field;[5] and we will make specific recommendations for changes inside federal agencies and for new kinds of initiatives to support academic research on modeling.

This is not about finger-pointing. Rather, the coronavirus pandemic has exposed this deficiency (among many others) in how public health in the United States is organized, prioritized, and funded. If the nation takes necessary steps now, it will be better off during future pandemics.

Why Is Modeling Necessary?

With the goal of understanding how diseases spread in populations, epidemiology must rely on incomplete data from natural disease outbreaks—by definition such data are gathered in times when its meticulous curation may not be a high of priority. Epidemiology is an observational, not an experimental, science. Science advances by putting forth hypotheses that can be objectively evaluated. In *experimental* fields of science, for example molecular biology or accelerator particle physics, critical experiments can be designed to distinguish cleanly among new and old hypotheses. In *observational* fields, no single set of data plays the role of such experiments. Rather, there is a need for an intermediate construct—an evolving model—that, on the one hand, embodies a continuing set of hypotheses or assumptions; and, on the other hand, makes predictions that can be compared to new observational data that may become available.[6] Observational fields advance less often by single "eureka!" observations (i.e., akin to critical experiments), and more often by combining the steady acquisition of new data with the steady improvement of models. The data must be robust, timely, and granular, as addressed in a previous report by our group.[7]

Since it must make quantitative predictions, a model is, by definition, a mathematical construct. Simple models may be algebraic equations that can be solved "by hand". Somewhat more complicated models may be "ordinary differential equations" whose left-hand-sides are the rates

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[4] Dr. Anthony Fauci on Fox News: "Models are only as good as the assumptions that you put into the model…. When real data comes in, then data in my mind always trumps any model." April 10, 2020, at https://www.foxnews.com/media/fauci-coronavirus-mitigation-programs-models-china-italy

[5] Caitlin Rivers et al., "Modernizing and Expanding Outbreak Science to Support Better Decision Making During Public Health Crises: Lessons for COVID-19 and Beyond," The Johns Hopkins Center for Health Security Report (March 24, 2020) at https://www.centerforhealthsecurity.org/our-work/publications/modernizing-and-expanding-outbreak-science-to-support-better-decision-making-during-public-health-crises . These authors propose measures that, while different from ours in detail, are much in the same spirit.

[6] E.T. Lofgren et al. "Opinion: Mathematical models: A key tool for outbreak response", PNAS, vol. 111, no. 51 (December 23, 2014) at https://www.pnas.org/content/111/51/18095 .

[7] "Strengthening the Public Health Infrastructure: The Role of Data in Controlling the Spread of COVID-19," at http://opcast.org/OPCAST_Public_Health_Data_Report_07-28-20.pdf

of change of quantities of interest with time (infections, cases, deaths, etc.), and whose right-hand-sides embody the effects that drive such change. Nowadays, models are often expressed algorithmically, i.e., as computer programs, sometimes highly complex and computationally demanding, requiring supercomputing capabilities. An example of complexity is so-called "agent-based modeling", where the model may represent in a computer the individual daily activities of a hundred thousand or more simulated inhabitants of a city, keeping track of how often each interacts with others and infects (or is infected by) them.

Stepping back for a moment from epidemiology, the observational sciences astronomy and meteorology provide some useful perspectives on both the nature of modeling, and on how models can be practically harnessed. Models often contain a mixture of assumptions that are scientifically rigorous (like Newton's laws of motion) and assumptions that simply describe empirical regularities in the data (like the "seasonal adjustments" that are applied to retail sales figures). Both kinds of assumptions are useful. The more empirical a model is, the more likely it is to be improved by new and better data—both to tune its parameters and also to guide the improvement of underlying theory. Astronomy provides an historical example. Ptolemy's 2nd century *Almagest* expressed its geocentric model as detailed mathematical tables. Planets moved in epicycles (roughly, circles upon circles) inside the celestial sphere. The model's geocentric assumption was of course completely wrong. But its quantitative predictions—exactly where each planet would be observed in the sky on a given date—were in fact quite accurate. Not until the 17th century did observations become precise enough to show discrepancies.[8]

Another lesson, also from the history of astronomy, can be drawn from the rare transits of Venus across the solar face in 1761 and 1769. From the precise timing of these events, the absolute size of the solar system could be deduced—using a Keplerian model. Competing expeditions from multiple countries were launched. Not unlike the recent COVID-19 experience, the answers obtained were wildly discordant, and the whole enterprise was widely deemed a failure. Forty years later, the great mathematician C.F. Gauss improved the model and was able to get a single accurate result from the old, disparate data. How? Gauss invented the idea of a *statistical model*. Although Kepler's model was (nearly) exact, the observations were not. Gauss first understood that data should be viewed as one instantiation of a statistical distribution (i.e., repeated observations of the same phenomenon will never be exactly the same), and that the model must include properties of the appropriate distributions.[9] Superior models are often more sophisticated in their application of statistical theory.

Meteorology (as a basic science) and weather forecasting (as its practical application) are also relevant examples. For a long time, the limiting resources were computer power, which determines the models' smallest spatial resolution, and the availability of data. Weather prediction has improved significantly as computing power has grown and data have become more abundant. The challenge now is to master the complexity of the physics and chemistry of weather, and the ways in which even small inaccuracies in modeling present conditions are magnified as models predict further into the future. Below, we will also look to weather prediction as an example of how a field spanning basic research and operational mission can be organized at the federal level.

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[8] Interestingly, Copernicus' heliocentric model gave no more accurate predictions than Ptolemy's, because Copernicus kept the faulty assumption of circles. It was not until Kepler's introduction of elliptical orbits that the model's predictions actually improved.

[9] Fernie, Donald, *The Whisper and the Vision: The Voyages of the Astronomers*, Clarke, Irwin (1976).

Epidemiological models today span a range from more empirical to more driven by well-established biomedical science, from more mechanistic to more statistical, from models that can be run on a laptop to those requiring a supercomputer. As continuing academic research, this diversity of approaches is a good thing—*but only* if there are institutional mechanisms for evaluating models for soundness and maturity, further developing those that show promise and also evaluating models for readiness for use in practice. In time of crisis, this diversity can also be a good thing—*but only* if there are institutional mechanisms for coordinating, summarizing, and communicating the most robust predictions of the *ensemble* of models to decision-makers in real time. It is those institutional mechanisms that critically need strengthening, and on which we will make recommendations.

Types of Epidemiological Models and Their Different Uses

As a rough taxonomy, epidemiological models may be divided into three classes: *compartmental* models, *network* models, and *statistical-empirical* models—noting that individual models may have elements of more than one type.

Compartmental models

Also called mass-action models, compartment models assume some degree of homogeneity within a population—for example that every infectious individual has the same probability of infecting every susceptible individual. Every individual is assigned to a "compartment". The most famous compartmental models, SEIR (for Susceptible, Exposed, Infectious, and Recovered) and SIR (lacking the Exposed component) have been taught in every graduate school of public health and with precursors dating back to the 1920s.[10] In the simplest formulations, ordinary differential equations (ODEs) describe the time history of the fraction of population in each compartment.

Compartmental models contain adjustable parameters that are different for different diseases, and can be different in different populations (e.g., Italy vs. Germany). Early, and then continuing, data for a given epidemic must be used to fit for these parameters before useful predictions can be made. If the parameters are inadequately determined, or if their changes in time due to policy interventions or other effects are not accounted for, the model predictions can be wildly wrong.

Simple compartmental models can easily be implemented on a laptop by anyone with even modest epidemiological and mathematical skill. It is by now clear that much of the confusion about modeling in early months of the coronavirus pandemic was due to haste by well-meaning individuals of varying backgrounds in implementing simple compartmental models, seeding them with incomplete data of variable quality, and putting out predictions that ranged from reassuring to apocalyptic. The confusion was magnified by the (again, well-meaning) decision of many scientific journals to publish submissions prior to peer review, albeit so labeled, and further magnified by the lack of any U.S. nationwide institutional infrastructure with an accepted role for sorting out the confusion and giving authoritative advice.

More elaborate, state-of-the-art compartmental models replace simple ODEs by sometimes complex statistical models for how individuals transition between compartments; and by

[10] E.g., W.O. Kermack, A.G. McKendrick, A contribution to the mathematical theory of epidemics, *Proc. R. Soc. London*, 115 (1927) 700. A more recent "bible" in the field is R.M. Anderson and R.M. May, *Infectious Diseases in Humans: Dynamics and Control* (Oxford, 1991).

increasing the number of compartments (or subdividing existing ones) to mitigate the assumption of absolute homogeneity. So-called metapopulation models consider sets of local populations connected by migrating individuals. Models may also differ in the sophistication with which they incorporate initial or ongoing data, for example using machine learning (ML) techniques.

A recognized world center in predominantly compartmental, mechanistic, modeling is the Medical Research Council (MRC) Centre for Global Infectious Disease Analysis (GIDA)[11] at Imperial College, London. Chartered in 2007 by the British government as a national center of excellence,[12] GIDA has come to be regarded as the U.K.'s authoritative resource on epidemiological modeling. It has been able to establish close connections to the U.K.'s national public health authorities, and has "a seat at the table" in times of crisis management. The United States has no similarly authoritative, dedicated capability. GIDA will serve as a model for some of our recommendations, below, although we recognize some of its shortcomings as a single institution (thus without the advantages of multi-institution competition) serving two distinct missions (advancing science, crisis readiness), and with a single dominant methodology (elaborated SEIR).

Network models

This class of models breaks the assumption of population homogeneity in one of several ways. Agent-based models were already mentioned. These break homogeneity all the way down to single (if simulated) individuals with heterogenous characteristics deduced from detailed census, social network, cell-phone mobility, or other fine-grained, data. Notably, these models then simulate "actual" daily lives of large numbers of these "agents" in their home-work transportation patterns, workplace densities, shopping, recreation, and so forth, in a specific, usually urban, setting, e.g., Wichita, Kansas. Multiple simulation runs may be made so as to estimate variability. Agent-based models have large numbers of parameters to set, but many of these can be set via data other than epidemiological, e.g., phone data, traffic density, retail sales, etc.

In contrast to agent-based network models, some other network models can be more abstractly statistical in construction, representing the contact patterns of individuals by a social graph whose vertices represent individuals and whose connecting lines represent, for instance, the probability that one individual will infect another. Social graphs can have multiple layers and multiple scales, embodying the nested and overlapping effects of families, friendship groups, social gathering sites, schools, socio-economic or ethnic communities, and so on. Models can be "run" by instantiating a graph with the desired statistical properties and then propagating the disease on it in simulation, or by inferring results from the underlying statistical features of the graphs using a combination of simulation and analytic methods.

In contrast to compartmental models, network models can model local outbreaks, "second waves", and other dynamics due to disease propagation from community to community. Network models can distinguish variability due to public health interventions (social distancing, masking, etc.) from variability due to underlying population inhomogeneity. The additional potential of network models, as compared to compartmental (i.e., mass-action) models, can be especially important for forecasting the later stages of an epidemic: Mass-action models must

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[11] GIDA was formerly called the Centre for Outbreak Analysis and Modeling.

[12] Centre for Outbreak Analysis and Modelling, 2008 Annual Report, at https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/2008.pdf

generally predict rapid exponential decay when R_0 falls below one. Network models can show the more complicated dynamics of complicated social networks with pockets of disease. (Metapopulation models are an intermediate case.[13]) For COVID-19, rapid exponential decay has been seen sometimes, but not always. In the United States thus far, it is the exception, not the rule.

Statistical-empirical models

Models of this type seek to predict disease dynamics by carefully curating an ensemble of experiences at various locales—for example, the rise and subsequent fall of coronavirus cases in individual cities in China, Italy, and Spain, and then finding the best statistical matches of the current data in a place of interest (e.g., New York City) to that ensemble. Efforts at utilizing this technique by the Institute for Health Metrics and Evaluation (IHME) at the University of Washington attracted much attention early in the coronavirus pandemic, because of the model's seeming ability to make predictions without any detailed knowledge about the underlying disease—how it was transmitted, what its infectious period was, and so forth.

The model's defenders asserted that their underlying data—epidemiological curves—were more, not less, directly related to the desired predictions of cases and deaths than is the case with other model types. Unfortunately, IHME's model predictions changed greatly as new data were incorporated; and they became politicized when the Trump Administration cherry-picked the more favorable results.[14] Judgment on whether statistical-empirical models can play a useful role must thus await further research and calmer times.

Varying uses for models

In addition to there being different types of epidemiological models, each can be optimized for quite different uses. Here are four examples:

- For advancing the basic science of epidemiology, a model may be entirely retrospective, using the historical data of a past epidemic as well as properties of its disease known from basic biomedical research. Such a model need have no predictive ability at all. Data from late stages of an epidemic may shed light on its early stages—only possible after the fact.
- During an epidemic, fragmented and incomplete data are inevitable. From the raw data alone, it is hard to know what is the true, current state. Models can provide a unified situational awareness (sometimes called "nowcasting"). Here also, prediction/forecasting, other than from the immediate past to the immediate future, is not the purpose of the model.
- Forecasting is of course the most difficult application.[15] Not only does a model embody assumptions about the past and present, it makes assumptions about the future (e.g., public health policy interventions and the reaction of the population to them) that may turn out to be different from what is anticipated. Even if its disease model were perfect, epidemic forecasting would be quite different from weather forecasting: When NOAA forecasts a hurricane, authorities may tell people to take shelter—but their doing so does

[13] See, for example, a model description at https://wwwnc.cdc.gov/eid/article/26/10/20-1702-app1.pdf

[14] Sharon Begley, "Influential Covid-19 model uses flawed methods and shouldn't guide U.S. policies, critics say," STAT (April 17, 2020) at https://www.statnews.com/2020/04/17/influential-covid-19-model-uses-flawed-methods-shouldnt-guide-policies-critics-say/

[15] Yogi Berra is inevitably here quoted: "It's tough to make predictions, especially about the future."

not change the path of the hurricane! During an epidemic, the customers for forecasting include not only public health authorities, and the public at large, but also the pharmaceutical industry. Choosing the right time and place for drug and vaccine trials may rely on predictions of when and where cases are likely to occur.

- Closely related to forecasting, but distinct, is the use of models to support decision-making by federal, state, and local authorities.[16] Sometimes called "counter-factual analyses", these models are optimized for questions like, "if we do this, how many *fewer* deaths will occur". This application cares less about absolute predictions, more about differential predictions among sets of policy alternatives. In this application, a model may be embedded in a stochastic optimization program capable of answering a quantitative question like: "What combination of new case rate, testing positivity rate, and hospital ICU occupancy should be the threshold for relaxing lockdown restrictions from Stage 3 to Stage 2?"[17]

How Has Epidemiological Modeling Been Supported in the United States?

In recent years, a patchwork of federal agencies has provided resources in support of epidemiological modeling, both for research and development as well as for operational use in time of crisis. A partial list of model-supporting agencies includes: the National Institutes of Health (NIH), the National Science Foundation (NSF), the Centers for Disease Control and Prevention (CDC), the United States Agency for International Development (USAID), the Department of Homeland Security (DHS), the Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response (DHHS/ASPR), and the Defense Threat Reduction Agency (DTRA). There is little coordination among this alphabet soup of agencies. In the period leading up to COVID-19, moreover, the overall trend was towards decreasing support.

For much of the first part of the current century, NIH's National Institute of General Medical Sciences (NIGMS) was a leader among federal agencies, with its program called Models of Infectious Disease Agent Study (MIDAS). Many practitioners whom we interviewed cited MIDAS as significant in the development of the field. Indeed, MIDAS seemed poised to effectuate many of the functions that we recommend as necessary, below. MIDAS once funded centers of excellence in epidemiological modeling at universities including Harvard University, the University of Pittsburgh, the University of Chicago, the University of Washington, Yale University, the University of Virginia, and Northwestern University. Unfortunately, a combination of budget cuts and retiring staff at NIH reduced MIDAS to a pale shadow of what it was (or could have been). While the program continues in name,[18] functioning primarily as a communications hub for researchers and public health practitioners and facilitating the awarding of some small grants. Therel also exists within NIH a small effort in modeling cross-national epidemics (especially flu) in the Division of International Epidemiology and Population Studies (DIEPS) of the Fogarty International Center.

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[16] D.B. George et al., "Technology to advance infectious disease forecasting for outbreak management," *Nature Communications* 10, 3932 (2019).at https://doi.org/10.1038/s41467-019-11901-7

[17] Stochastic optimization is a methodology for trying many different parameter values until one finds an optimal set. For an example, see X. Wang et al., "Impact of Social Distancing Measures on Coronavirus Disease Healthcare Demand, Central Texas, USA," Emerg. Infect. Dis. 2020 Oct, at https://doi.org/10.3201/eid2610.201702

[18] See https://midasnetwork.us/ .

At NSF, some epidemiological modeling is supported by the program on Ecology and Evolution of Infectious Diseases (EEID) within the Directorate for Biological Sciences. The scope of this support is limited by two realities apart from budget: First, since NSF does not in general support the study of human disease (that being considered NIH's domain), NSF's program must focus on other useful but arguably peripheral aspects, for example the evolution of zoonotic diseases in animals. Second, as a matter of policy, NSF limits its salary support of most principal investigators to two months annually;[19] but much of the research on epidemiological modeling (not NSF-funded) is conducted in medical schools and schools of public health that expect their faculty to bring in twelve-month salary support. NIH does allow twelve-month salaries (but with a cap on salary levels). Previously, there existed a level of cooperation between NSF/EEID and NIH/MIDAS, allowing for coordinated funding to some researchers; but apparently this cooperation has decayed with the decline of MIDAS.

Within DHS, there previously existed a pandemic response effort in the National Infrastructure Simulation and Analysis Center (NISAC). NISAC was started in 1999 as a collaboration between the Los Alamos and Sandia National Laboratories. Its oversight was later moved to DHS, but it continues to have access to DOE supercomputing facilities. NISAC's scope included pandemic response as well as other kinds of natural disasters (hurricanes, earthquakes, etc.). NISAC's Incident Response Fast Analysis and Simulation Team (FAST) connected policy-makers to the national labs for immediate situational analyses.[20] In 2016-2017, however, at the direction of senior DHS officials, NISAC's effort in pandemic response was largely dismantled, with a sudden shift of priority to cyber-threat machine learning. A news report quoted a former official: "They've allowed a lot of capability to decay, including the pandemic models and transportation models and a whole bunch of other stuff in favor of chasing the soccer ball on different cyber things."[21]

Since 2013, CDC has supported the real-time curation of seasonal flu forecasts from multiple academic and private industry researchers. Twenty-four different teams participated in the flu forecasting initiative during the 2018-2019 flu season, and winners were declared, providing motivation for the cross-fertilization of best practices.[22] Separately, the Intelligence Advanced Research Project Agency, IARPA, also sponsors a flu forecasting competition.[23] With the onset of the COVID-19 pandemic, CDC has partnered closely with the volunteer COVID-19 ForecastHub effort at the University of Massachusetts Amherst[24] to maintain a COVID-19 Mathematical Modeling portal.[25] The portal curates and displays the model predictions of dozens of geographically and methodologically scattered forecasting efforts with respect to deaths,

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[19] NSF Grant Proposal Guide section II.C.2g(i)(a) at https://www.nsf.gov/pubs/policydocs/pappguide/nsf09_1/gpg_2.jsp

[20] DHS, "About the National Infrastructure Simulation and Analysis Center" at https://www.dhs.gov/about-national-infrastructure-simulation-and-analysis-center (page last updated June, 2016).

[21] Daniel Lippman, "DHS wound down pandemic models before coronavirus struck," *Politico* (03/24/2020) at https://www.politico.com/news/2020/03/24/dhs-pandemic-coronavirus-146884 .

[22] "FluSight: Flu Forecasting" at https://www.cdc.gov/flu/weekly/flusight/index.html . "Los Alamos National Laboratory, led by Dr. Dave Osthus, provided the most accurate national-, regional-, and state-level influenza-like illness forecasts. … The Delphi group at Carnegie Mellon University, led by Dr. Roni Rosenfeld, provided the most accurate national-level hospitalization forecasts."

[23] P. Chakraborty et al., "What to know before forecasting the flu," *PLOS Computational Biology* (October 12, 2018) at https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1005964 .

[24] "The COVID-19 Forecast Hub" at https://covid19forecasthub.org/

[25] "COVID-19 Mathematical Modeling" at https://www.cdc.gov/coronavirus/2019-ncov/covid-data/mathematical-modeling.html .

hospitalizations, and cases. This effort is a fruitful example of academic-government partnership, especially for the speed in which it has been stood up under crisis conditions. Such "ensemble modeling" is, in other fields, a proven method for getting more accurate predictions, and also for advancing state-of-the-art.[26]

Noteworthy, however, is that the "data" for this useful effort, namely the outputs from the multiple models, flow from outside CDC to inside. Historically, relations between CDC and the academic forecasting/modeling community have been difficult at times, because the necessary data flow to advance the field of epidemiological modeling is in the other direction, from CDC to outside research groups; and CDC has not been seen as being supportive of that. In the case of flu, CDC is the recipient of vast amounts of data from state and local public health authorities. The data are (or can easily be) aggregated so as to avoid patient privacy issues. Several leading academic investigators expressed to us their frustration at being unable to obtain these data for retrospective research purposes at city level of aggregation. The problem appears to be less the existence of any formal policy forbidding it, and more that the support of basic epidemiological research in this way is not seen by CDC as a mission priority. That needs to be changed.

Within the Department of Defense, DTRA's Technical Reachback program provides 24/7/365 capabilities for combatant commanders to get immediate technical advice relating to battlefield environmental hazards, including biological releases.[27] The program has funded some research in epidemiological modeling.

USAID's PREDICT program of epidemiological research, while not specifically aimed at modeling, supplied large amounts of data of value to epidemiological modeling, including the identification of more than 160 novel coronaviruses. The program was curtailed in 2019 by the Trump administration and terminated in March, 2020. In response to criticism from Senators Angus King and Elizabeth Warren, the program was then extended for six months with a small amount of funding.[28]

The coronavirus pandemic has prompted increased interest in modeling by the pharmaceutical industry. Clinical trials of drugs require that there be enough diagnosed cases of the disease to enroll a statistically sufficient number in the trial. Trials of vaccines require enough natural cases of disease in the unvaccinated control group. Forecasts of when and where outbreaks may occur are thus important. In the present pandemic, as one example, Johnson & Johnson systematically reached out to a number of academic and other modeling groups to create, in effect, its own ensemble model, which it is using to guide decisions about when and where to activate trial sites and set enrollment levels.[29] It is salient that this was an impromptu effort within one company—that there was no pre-existing government or academic infrastructure in place to support this important application.

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[26] V. Kotu and B. Deshpande, *Data Science (Second Edition) Concepts and Practice* 2019, pp. 19-37 at https://www.sciencedirect.com/science/article/pii/B9780128147610000022 .

[27] "ARA Wins DTRA Contract" at https://www.ara.com/news/ara-wins-dtra-contract .

[28] Wikipedia, "PREDICT (USAID)" at https://en.wikipedia.org/wiki/PREDICT_(USAID) .

[29] Peter Loftus, "For Covid-19 Vaccine, J&J Plans 60,000-Subject Pivotal Trial," *The Wall Street Journal* (August 20, 2020) at https://www.wsj.com/articles/for-covid-19-vaccine-j-j-plans-60-000-subject-pivotal-trial-11597936496

What needs to be done?

Two points should by now be evident: (i) that epidemiological modeling can and must play an important role in pandemic response, and (ii) that, within the federal government, it is an orphan field. Before we suggest remedies, let us step back and consider a quite different, yet in many ways analogous field, namely weather forecasting and the fundamental research behind it.

Meteorology, and closely-related climate science, are, like astronomy and epidemiology, observational sciences, relying on the fusion of data and models to advance. Meteorology relies on an undergirding foundation of basic science, but (unlike most astronomy, say) the field also has a critical operational mission. The nation (and world) depend on timely, accurate weather forecasts. The economic value of such forecasts, some tens of billions of dollars annually,[30] justifies government and private investment in an entire value chain consisting of (i) basic atmospheric research, (ii) the development of large-scale (supercomputer) climate and weather models for research, (iii) the operationalization of those models (and combining ensembles of independent models) for 24/7 weather forecasting and longer-term forecasts of climate-change impact, (iv) the distribution of forecasts, in formats of practical utility, to policy-makers, private-sector companies, and consumers.

In the United States, this value chain is predominantly coordinated by two federal agencies. A somewhat simplified description is this: NSF supports basic science as the lead *research* agency, in large part through its National Center for Atmospheric Research (NCAR) in Boulder, Colorado. Managed by a consortium of universities, NCAR integrates model development, observations, and supercomputer facilities. The National Oceanic and Atmospheric Administration (NOAA), as the lead *mission* agency, conducts more-applied scientific research and operates weather and other environmental satellites and their data flows. Then, NOAA's National Weather Service (NWS) operationalizes forecast codes, ingests voluminous data, produces forecasts, and particularizes these forecasts to user needs through 120 local weather-forecast offices.

The analogies are clear. In times of pandemic, the economic value of good epidemiological forecasts would be large—potentially saving trillions of dollars. Even in the case of annual flu epidemics, savings in the billions might be attainable with targeted public health measures. Advancing the state-of-the-art of epidemiological modeling requires long-term, robust basic research (NCAR-like). It also requires coordinated mechanisms for operationalizing and communicating this research to decision makers, the public, and the private sector (NWS-like). Above all, it requires a clear assignment of responsibility to appropriate federal agencies, along with budgets that allow them to meet those responsibilities.

Recommendations

We make three high-level and then four more-specific recommendations. *Our high-level recommendations are these:*

1. The National Science Foundation should be the lead *research* agency with primary responsibility for supporting basic and initial translational research in epidemiological modeling, with new Congressionally appropriated funding.

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[30] National Weather Service Enterprise Analysis Report (2017) at https://www.weather.gov/media/about/Final_NWS%20Enterprise%20Analysis%20Report_June%202017.pdf

NSF, especially through NCAR, has extensive experience in large-scale modeling in support of basic research. It also operates national supercomputer centers. In addition to basic biological sciences, NSF has outreach into fields necessary for the success of the interdisciplinary field of epidemiological modeling, for example, evolutionary and environmental biology, computer and computational science, and data science. No other basic science agency has this scope.

2. The Centers for Disease Control and Prevention should be the lead *mission* agency, with primary responsibility for operationalizing the research results of NSF's research program.

CDC would be the epidemiological analog to NOAA and NWS.[31] Only CDC has the ability to gather data from state and local public health agencies and to distribute back to them actionable recommendations. We define this role further below.

3. The National Institutes of Health and the Department of Energy should have defined (and funded) partnering roles with NSF and CDC in epidemiological modeling.

Both NIH and DOE have experience in operationalizing translational research that augments that of NSF and CDC. In addition, both agencies bring necessary subject-matter strengths.

NSF is not, by charter, well-suited for emergency response, while both DOE and NIH are combined research and mission agencies able to meet operational needs in real time. Among all science agencies, DOE leads in the use of large-scale modeling in support of its missions. DOE has a long history of expertise in and support for supercomputing, primarily through many of its national laboratories, which provide the most powerful U.S. supercomputing capabilities in the public sector. DOE's national laboratories can play a crucial role in the computational aspects of epidemiological modeling. NIH has primary responsibility for the study of specific disease states and supports the scientists most knowledgeable about those diseases. Both NIH and NSF have previously successfully partnered with DOE.[32] A "blueprint" for such collaborations in biomedical areas, and testimony as to their success, was recently briefed to Congress.[33]

Involving DOE in the provisioning of computing and data resources (especially surge and operational capacity) across research needs (partnering with NSF) and operational needs (partnering with CDC) will facilitate the translation of research models to operational use.

Since NSF lacks a mandate in human health science, its partnering with NIH in supporting the basic biomedical science of modeled diseases is essential. NIH engagement will help to tether the work of modelers to the biological realities of the particular disease being modeled. NIH also has the benefit of the experience of its previous MIDAS program. While NIH lacks a well-developed culture in mathematical modeling in general, and in the provision of supercomputing facilities for modeling in particular, partnering between NSF and NIH will help to build such a culture, so that successor efforts to MIDAS can be more sustainable.

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[31] Caitlin Rivers and Dylan George, "How to Forecast Outbreaks and Pandemics: America Needs the Contagion Equivalent of the National Weather Service," Foreign Affairs (June 29,2020) at https://www.foreignaffairs.com/articles/united-states/2020-06-29/how-forecast-outbreaks-and-pandemics

[32] In Congress, on the House side, DOE has the same authorization committee (Energy and Commerce) as NIH. On the Senate side, it is overseen by the Committee on Energy and Natural Resources.

[33] U.S. Congress, "Oversight Hearing on DOE's Role in Advancing Biomedical Sciences" (February 5, 2020) at https://docs.house.gov/Committee/Calendar/ByEvent.aspx?EventID=110447 .

Both DOE and NIH are able to fund the twelve-month academic salaries of individual principal investigators, and they should commit to co-funding epidemiological modeling researchers in institutions requiring twelve-month salary funding.

Our more specific recommendations are these:

4. Starting immediately, the National Academies of Science, Engineering, and Medicine (NASEM), with funding from NSF and NIH, should establish a series of workshop conferences on modeling, with the aims of creating a community of modeling researchers, benchmarking the field, and facilitating the transition of models from research to operational settings.

These workshops should bring together practitioners from different modeling communities, including the private sector, representing a wide range of model types and applications as well as a range from basic research to operational use and decision support. The workshops should explore such themes as how to benchmark models against each other and against data, both in real time and retrospectively; how to transition models from research to operational settings; how model results can best be communicated to the public; what kinds of products are most useful for decision-makers; and so forth.

Currently, the remaining parts of the MIDAS program perform some similar functions; but the greater convening power and influence of NASEM is now warranted. It is time to create a broad community of modeling researchers who can cross-pollinate advances in modeling research.

5. Approximately five university-based national centers for epidemiological modeling research should be chartered by NSF by competitive selection, with funding funded from a new Congressional appropriation at approximately $10-$15 million per year each for five years.

These centers collectively would be the analog of NCAR. In today's world, however, it makes more sense to have a larger number of distributed centers, not a single one. It is important to get the selection criteria right. Each center should have an empowered director, an external advisory committee, and a coherent program for research, education, and outreach. The U.K.'s GIDA (discussed above), with strong collaborations between modelers and disease experts, is a useful model; but our centers should not take on the roles that we describe as better suited for CDC as the lead mission agency.

A center should not be a loose association of principal investigators pursuing their own unrelated programs, and it will be essential to enforce this requirement during the selection process. Each center should have a specific focus and a coherent program of research, without unduly constraining the creative exploration of individual researchers. Because public health is a state and local responsibility, the centers should be geographically diverse. Partnering relationships with state and local public health organizations, as well as partnering with researchers at other universities should be an essential requirement, as should be programs for training the next generation of modelers and receptive decision-makers, for example, at summer institutes.

Centers should be free to use part of their funding to support collaborating researchers at other institutions. Collaborations with the private sector should be encouraged. An understanding of the ways epidemiological modeling is used in industry should help to inform the modeling topics addressed by the Center. Models of use to industry may be different from other models. A vaccine trial may, for example, have as a defined endpoint reduction of "moderate to severe infection," which is different from the more-often modeled reductions of "cases" or "deaths".

Within their universities, the centers should be interdisciplinary organizations able to draw on expertise in departments spanning biomedical science, evolutionary and environmental biology, computer and data science, etc. Siting a center wholly within a school of public health would not, in our view, harness broad enough perspectives and thinking "outside the box".

6. CDC should create, and Congress should fund, a new "Office of Epidemic Forecasting and Analytics" (or an equivalent name) responsible for implementation of CDC's role as the lead mission agency.

This office would be responsible for operationalizing the research result of the university-based centers, developing epidemiological data streams to be fed back to researchers on a continuing basis, preparing for epidemic crises, and, in time of crisis, generating and authoritatively communicating model forecasts and their uncertainties to federal, state, and local decision-makers, to the public, and to industry. By policy, this office would be represented ("have a seat at the table") in the specific incident command structures activated by CDC for particular emergencies.[34]

An analysis by C. Rivers and D. George[35] suggests a budget level of about $80 million per year for this office.

Patterning on NSF's so-called "rotators",[36] the office should make use of hiring authorities under the Intergovernmental Personnel Act of 1970 (IPA) to bring into CDC members of the research community for periods of up to two years. It should partner with DOE for the provision of supercomputer resources.

The office should have engagement with the Association of State and Territorial Health Officials (ASTHO) and the Council of State and Territorial Epidemiologists (CSTE), and work to build key capacity—specifically, the ability to integrate model results into decisions—at state and local levels. The office should also develop, in advance of any epidemic, protocols for the rapid use of its ensemble of models by pharmaceutical companies in their planning and executing of clinical trials and other time-critical applications.

7. DOE, with new funding from Congress, should create a new subprogram of its Advanced Scientific Computing Research (ASCR) program [37] and assign it responsibility for supporting the missions of both the NSF and CDC in epidemiological modeling.

DOE and ASCR should consider how best to be the "bridge" between research and operations (including emergency operations). We view this as a crucial role that only DOE can fill. Beyond supplying bulk computer capacity (as, for example, at its Oak Ridge Leadership Computing Facility), DOE should actively engage researchers at its national laboratories in

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[34] "CDC Emergency Operations Center (EOC)" at https://www.cdc.gov/cpr/eoc/eoc.htm .

[35] Ref. 31 above and additional unpublished communication.

[36] American Institute of Physics, "NSF Reviewing Use of Rotating Scientists, May Seek New Hiring Authorities" (19 August 2016) at https://www.aip.org/fyi/2016/nsf-reviewing-use-rotating-scientists-may-seek-new-hiring-authorities

[37] "ASCR Subprograms," at https://www.energy.gov/science/ascr/advanced-scientific-computing-research

support of this mission, including preparing them to be rapidly available scientific resources in time of emergency.

Conclusion

Epidemiological modeling is an important but under-supported field of science that lacks a clear home among the federal science-funding agencies. Additional basic research and translational work in the field is needed between pandemics, and greater operational capabilities are needed during epidemics. We have identified here a series of actions that can strengthen modeling efforts and their operationalization, to make the country better prepared for the next pandemic.

The Ad Hoc Group

The authors are a subset of the members of President Obama's Council of Advisors on Science and Technology (OPCAST) who were involved in producing the six reports dealing with issues related to viral pandemics that his PCAST delivered between 2009 and 2016. In alphabetical order, the members of the Group are:

Christine Cassel, University of California, San Francisco
Christopher Chyba, Princeton University
Susan L. Graham, University of California, Berkeley
John P. Holdren, Harvard University (OPCAST Co-Chair, Subgroup Convenor)
Eric S. Lander, Broad Institute of MIT and Harvard (OPCAST Co-Chair)
Richard Levin, Yale University
Ed Penhoet, University of California, Berkeley
William Press, University of Texas, Austin (OPCAST Vice Chair)
Maxine Savitz, National Academy of Engineering (OPCAST Vice Chair)
Harold Varmus, Weill Cornell Medicine (OPCAST Co-Chair)

The authors have contributed to this effort as individuals working on their own time, not as representatives of their institutions. The effort has no sponsors and no budget.

The six reports relevant to pandemics that were issued by the Obama PCAST are:

U.S. Preparations for 2009-H1N1 Influenza, 88 pp, August 2009
https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/pcast-h1n1-report-final2.pdf

Reengineering the Influenza Vaccine Production Enterprise to Meet the Challenges of Pandemic Influenza, 87 pp, August 2010
https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/PCAST-Influenza-Vaccinology-Report.pdf

Realizing the Full Potential of Health Information Technology to Improve Healthcare for Americans: The Path Forward, 108 pp, December 2010
https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/pcast-health-it-report.pdf

Propelling Innovation in Drug Discovery, Development, and Evaluation, 110 pp, September 2012 https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/pcast-fda-final.pdf

Better Health Care and Lower Costs: Accelerating Improvement through Systems Engineering, 66 pp, May 2014
https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/PCAST/pcast_biodefense_letter_report_final.pdf

Preparing for Biological Threats, 18 pp, November 2016
https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/PCAST/pcast_biodefense_letter_report_final.pdf

The six reports issued by the Ad Hoc Group to date—addressing pandemic stockpiles, testing, contact tracing, data issues in pandemic management, tasks for a COVID-19 Commission, and epidemiological modeling—have drawn on these Obama PCAST studies and research and observations since. They can all be found at http://opcast.org.