Now that the 2009 H1N1 flu epidemic has passed, it’s possible to feel some relief. It could have been much worse. Nevertheless, despite this novel virus strain turning out to be fairly mild relative to initial fears and prior flu pandemics such as 1918, which was 100 times more lethal, 2009 H1N1 was a major infectious disease outbreak — 12,000 deaths in the United States alone and thousands more worldwide.

Realistically, it’s a question of “when?” not “if” another virus will emerge as a far more serious public-health threat. And in that respect, part of the good news from 2009 is that epidemiological modeling, a powerful tool to assist decision makers, stepped onto the fray. “Our models are a virtual laboratory to ask questions you can’t ask with real populations,” says Shawn Brown, PSC scientist and assistant professor in the University of Pittsburgh Department of Biostatistics. “We build a population, infect them with the flu, and then look at mitigation strategies, such as vaccinations or school closure, and see what effect it has.”

Through the National Institutes of Health MIDAS (Models of Infectious Disease Agent Study) Center of Excellence, led by Donald Burke of the University of Pittsburgh Graduate School of Public Health (GSPH), Brown and collaborators from GSPH and other places used PSC’s shared memory system, Pople, to model the spread of H1N1 on a regional basis, both in Allegheny County (which includes Pittsburgh) and in the Washington, D.C. metropolitan area. They did this modeling during 2009, developing results in real time, in response to requests from health officials and policy makers, as the severity of the H1N1 outbreak remained in question.

They shared their findings with the Allegheny County Health Department and officials for the state of Pennsylvania as well as the U.S. Biomedical Advanced Research and Development Authority (BARDA), the U.S. Department of Homeland Security, and the President’s Council of Advisors on Science and Technology (PCAST). For three weeks in the fall of 2009, Brown and his GSPH colleague Bruce Lee were in effect embedded with BARDA. “They presented us with scenarios,” says Brown, “and we did the modeling. Supercomputing really helped. We were able to get rapid response to complex scenarios. We’re still doing that today.”

They found, for instance — in a study published in the Journal of Public Health Management and Practice (December 2009) — that to close schools less than two weeks may slightly increase infection rates, and that (contrary to Center for Disease Control recommendations) schools may need to be closed eight weeks or longer to have a significant impact.

They also used their model to investigate questions about vaccination priorities. Their findings — Vaccine (May 2010) — support recommendations by the U.S. Advisory Committee on Immunization Practices (ACIP) that priority be given to people at risk for severe complications. Prioritizing at-risk individuals, rather than only high transmitters (i.e., children), the modeling showed, may lead to slightly more cases of flu, but it reduces serious disease and death, and overall economic cost.

This picture provides a 3D graphical representation of a pandemic influenza virus’s structure, and is reprinted with permission from the Centers for Disease Control and Prevention, Atlanta, GA.
Epidemiological modeling goes back to early 20th-century mathematical formulations that attempt to quantify the spread of epidemics by identifying the susceptible proportion of a population and specifying a rate of transmissibility. As susceptible people become infected and recover (or not), enough of the population eventually becomes immune and the epidemic passes. This fairly crude tool to estimate the length and severity of a disease outbreak has over the past two decades, with powerful computing and sophisticated software methods, gained complexity and greatly improved ability to reflect the reality of how infectious disease spreads.

Increased complexity is especially the case with “agent-based modeling” (ABM) — a relatively new approach that Brown and his colleagues used for their 2009 work on H1N1. ABM represents virtual persons as autonomous “agents” within a synthetic population built from the most accurate available data (such as the U.S. Census). As agents become infected with disease, their individual movements within the population — to work, school, cultural events, etc. — result in the virus being transmitted to other susceptible agents. Disease spread is based on algorithms that incorporate randomness, or stochastic processes.

“Disease spread is a stochastic process,” says Brown. “It’s not deterministic; you can’t say with certainty when contact between an infected and susceptible agent will lead to infection. It’s a statistical based outcome.”

Other forms of epidemiological modeling, which include compartmental modeling and network modeling, are less detailed than ABM, and approximate certain aspects of a population and their interactions — making it possible to model larger populations and geographic regions, such as an entire nation. “All these models are valid,” says Brown, “and all of them are useful. It just depends on what type of question you want to answer.”

The Pittsburgh MIDAS group’s ABM modeling incorporates disease data (how long infections last and recovery time), surveillance data (best available information on how many people are getting sick in real time) plus social and behavioral data. Families are assigned to households, children to schools, and agents to workplaces with commuting distance, location of hospitals and other demographic factors — developed from census data.

Because ABM represents an entire population inside the computer, it requires large amounts of memory. For the DC metropolitan area, MIDAS’s ABM included 4.3 million people, requiring seven gigabytes of memory. “This is a shared-memory problem,” says Brown, referring to massively parallel systems, such as PSC’s Pople, that allow each processor to access all the memory without message passing.

SCHOOL CLOSURES & VACCINE PRIORITIES

It might seem obvious that to close schools would help to contain a flu outbreak — since children in contact with other children, who then bring it home to their families, is one of the primary ways that flu spreads through a community. Still, it’s a step that imposes burdens on parents and, over time, economic costs on a community, as workers must either stay away from jobs or provide childcare. So, if you close schools to mitigate the spread of H1N1 (or some other flu), how long — in order to have optimum impact — should they remain closed?

This question arose during consultations with health officials of Allegheny County in the fall of 2009, and the MIDAS team addressed it with their ABM model. Their detailed simulations produced the unexpected finding that closing schools less than two weeks may actually prolong an epidemic. Short-duration school closures, they found, can increase transmission by returning susceptible students back to school in the middle of an epidemic when they are most vulnerable to infection.

“The study also found that identifying sick students individually and holding them away from school had minimal impact. And they found no significant differences in mitigating an epidemic between individual school closures and system-wide closures.”

Later in 2009, spurred on by the initial limited availability of H1N1 vaccine, Brown and Lee, in collaboration with officials at PCAST and elsewhere, mounted a series of simulations looking in close detail at vaccine prioritization. With limited amounts of vaccine, what groups of people — children, elderly, caregivers, etc. — should be vaccinated first?

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