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Modelling during an emergency: the 2009 H1N1 influenza pandemic

B. Y. Lee, L. A. Haidari and M. S. Lee

Public Health Computational and Operational Research (PHICOR) Group, School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA

Abstract

During the 2009 H1N1 pandemic, decision-makers had access to mathematical and computational models that were not available in previous pandemics in 1918, 1957, and 1968. How did models contribute to policy and action during the 2009 H1N1 pandemic? Modelling encountered six primary challenges: (i) expectations of modelling were not clearly defined; (ii) appropriate real-time data were not readily available; (iii) modelling results were not generated, shared, or disseminated in time; (iv) decision-makers could not always decipher the structure and assumptions of the models; (v) modelling studies varied in intervention representations and reported results; and (vi) modelling studies did not always present the results or outcomes that are useful to decision-makers. However, there were also seven general successes: (i) modelling characterized the role of social distancing measures such as school closure; (ii) modelling helped to guide data collection; (iii) modelling helped to justify the value of the vaccination programme; (iv) modelling helped to prioritize target populations for vaccination; (v) modelling addressed the use of antiviral medications; (vi) modelling helped with health system preparedness planning; and (vii) modellers and decision-makers gained a better understanding of how to work with each other. In many ways, the 2009 pandemic served as practice and a learning opportunity for both modellers and decision-makers. Modellers can continue working with decision-makers and other stakeholders to help overcome these challenges, to be better prepared when the next emergency inevitably arrives.

Keywords: Emergency, influenza, modelling, pandemic, policy-making, simulation

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Corresponding author: B. Y. Lee, Public Health Computational and Operational Research (PHICOR) Group, University of Pittsburgh, 200 Meyran Avenue, Suite 200, Pittsburgh, PA 15213, USA
E-mail: bruceleemdmba@gmail.com

Introduction

During the 2009 H1N1 pandemic, decision-makers had access to mathematical and computational models that were not available in the previous 1918, 1957 and 1968 pandemics. As soon as news about the novel influenza strain emerged from Mexico in the spring of 2009, influenza modellers around the world sprang into action. Some decision-making organizations already had in-house modelling capabilities. Others, such as the US Department of Health and Human Services, the US Centers for Disease Control and Prevention (CDC), and the World Health Organization (WHO), invited outside modellers to temporarily embed in their response operations. The use of models to assist infectious disease control strategy and policy-making was certainly not new, and many other professions and industries (e.g. meteorology, manufacturing, finance, retail, aerospace, and military) have long relied on models when making major decisions [1,2]. However, 2009 was the first time that models could contribute to a worldwide emergency response to a major infectious disease threat.

However, the question remains: how did models contribute to policy and action during the 2009 pandemic? The pandemic ended up being milder than originally anticipated, motivating some to decry the considerable money, time and resources consumed by the response. Some asked, why did the models not correctly predict the pandemic severity? Moreover, some critics blamed modellers for not providing adequate insights [3,4]. Dissatisfaction with inaccurate predictions has even led

some critics to suggest that the 'WHO's decision to declare a pandemic was at least partially influenced by a desire to boost the profits of the pharmaceutical industry' [5].

Were these criticisms on target? Should modelling not be an integral part of an epidemic emergency response, or instead was modelling mis-utilized? Did decision-makers not make full and appropriate use of modelling and simulation? Did modellers not engage the decision-makers optimally? What should the role of modelling be in future epidemics? A review of the challenges and successes of the 2009 H1N1 influenza pandemic, and the lessons learned, can help to answer these questions for future emergency epidemic control.

The Challenges

Challenge 1: expectations of modelling were not clearly defined

Prior to and during the pandemic, relatively little was stated about the expectations of modelling. Modellers may not have been clear about what models can and cannot do during an epidemic, or have been fully aware of policy-maker needs. Some previous commentaries [6,7] discussed the role and limitations of modelling in addressing infectious disease control issues, but not specifically during an emergency response, which calls for different decision-making, needs, and expectations. With limited time, decision-makers need to make rapid decisions, and may not have the time to carefully evaluate models and their results.

Was the role of modelling to accurately predict the impact and timing of the pandemic? Throughout the earlier part of the pandemic, several modellers offered estimates that were somewhat divergent and changed substantially as the pandemic progressed. For example, in late April 2009, Brockmann *et al.* [8,9] predicted that the USA would experience 1700 cases by the end of May (an estimate published by the *New York Times*). However, 8 days after their initial prediction, their estimate changed to 40 000 cases, and, 3 days later, it changed again to 90 000 cases. In September 2009, Balcan *et al.* [10] published their predictions for the timing of the pandemic peak and the daily incidence during the peak for several countries. A 2012 publication compared their predictions with available data. Although the observed peak week fell no more than 2 weeks outside of their predictions for 50% of the countries, and within 4 weeks of their predictions for 95% of the countries, the model had generally overestimated attack rates (and therefore peak incidence) derived from surveillance systems and serological studies [11]. Ultimately, none of these models predicted the exact number of cases, severity and impact of the pandemic, which proved to be milder than initially anticipated [12].

However, are accurate predictions the norm in other industries that more routinely use models for decision support? Although meteorological models can help to predict general weather trends or weather front paths, they may struggle to generate specific numbers on the inches of precipitation, the square kilometres affected by a weather pattern, the precise duration of a heat wave that will occur in 2 months, and the day on which temperatures will peak during the summer. These limitations are present despite the availability of considerably more real-time meteorological data than epidemic data. Similarly, transportation models cannot always predict traffic jams, investment models are rarely able to pinpoint the future value of an investment (e.g. stock or real estate), and military models can miss the exact location and movements of the adversary several months into the future. In general, divining the precise future tends to be challenging, especially when real-time data are limited (see Challenge 2) and the issue/problem spans large geographical areas and multiple countries.

As Table 1 shows, modellers need to communicate more clearly what models can and cannot do. Modelling may be the only method for studying certain situations, such as when prospective studies are not feasible and when retrospective data may not be generalizable to the current situation. Much

TABLE 1. Challenges in H1N1 pandemic modelling and lessons learned

	Challenge	Lessons learned
1	Expectations of modelling were not clearly defined	Establish and disseminate the expectations and limitations of modelling (e.g. help plan interventions to accommodate different possibilities vs. forecast exact course of epidemic)
2	Appropriate real-time data were not readily available	Establish national and international surveillance and information systems Determine the data needed to help models make better predictions
3	Modelling results were not generated, shared, or disseminated in time	Begin working with decision-makers routinely before the epidemic occurs Expedite journal review and publication cycles during the emergency situation Establish other venues for disseminating results that also protect the work of the investigators Provide career-advancement incentives to modellers who perform public service
4	Decision-makers could not always decipher the structure and assumptions of the models	Increase the transparency of model construction and assumptions for decision-makers Avoid utilizing unnecessarily complex models Do not try to use one model to address all questions Clearly state the strengths and weaknesses of each model
5	Models varied in representing interventions	Increase the transparency of intervention representation Utilize extensive sensitivity analyses Work with decision-makers to make intervention representations relevant and realistic
6	Modelling varied in the results or outcome measures reported	Work with decision-makers to identify what outcomes they would be interested in

like weather, financial, military, educational and other forecasts, models are good at examining different possibilities and helping to prepare strategies that can accommodate these possibilities. However, models in many fields may struggle to serve as crystal balls that can make accurate predictions further than several weeks into the future. Too many uncertainties and chance elements could shift an epidemic. This is not to say that predictions should not be attempted. As with weather and financial forecasts, better available real-time data could lead to better predictions in the future.

Challenge 2: appropriate real-time data were not readily available

Just as meteorological models depend on real-time data on wind currents, temperature, barometric pressure, cloud patterns, and other important parameters, epidemic models require real-time data on disease incidence and prevalence, morbidity, mortality, prior exposure, healthcare-seeking behaviour and the implementation of countermeasures such as vaccination to have a chance of accurately predicting the course of the epidemic. However, without a central data repository and integrated national information system, most of these disease data either were not readily available or had to be pieced together from various disparate sources. In some cases, estimates and approximate calculations had to be used to transform available data into useful measures. For instance, converting influenza-like illness counts from sentinel surveillance sites into actual influenza cases necessitated estimates of the percentage of influenza-like illness cases that were actually influenza [13]. Additional delays occurred between data being gathered and made available to modellers. Different healthcare facilities and organizations did not always readily share data, for reasons ranging from patient privacy protection concerns to information system limitations to cost to competitive concerns [14,15].

The dearth of real-time data led many modellers to make assumptions that, in turn, limited the ability of the models to accurately forecast the course of the pandemic. For example, a number of modellers used data from previous pandemics or influenza seasons to calibrate their models [16,17]. However, the course of the 2009 pandemic did not parallel that of previous pandemics (each of which has been unique in its progression) or influenza seasons. In fact, morbidity and mortality estimates for the 2009 H1N1 pandemic changed dramatically from the beginning of the pandemic, leading to wide variations in critical-care demand projections [18]. Moreover, much of the available data came from particular limited geographical regions, forcing modellers to use data from one location to represent another location. For instance, Australian modellers employing the CDC's FluSurge model with US data from previous pandemics found the model to overestimate the severity of the H1N1 pandemic until it was updated with more current data on attack rates, hospitalization incidence, and mortality rates [19]. Indeed, the basic reproduction numbers (R_0) varied across different countries, highlighting the need for real-time data collection across many different locations and environments [20].

As Table 1 shows, installing worldwide surveillance networks and information systems to provide real-time data on the progress of a pandemic could greatly enhance the ability of modelling to assist decision-makers. Identifying the type of data needed to make better predictions and the impact or value of having this information could enable modelling to play an important role in guiding the development and implementation of such networks, systems, and associated tools.

Challenge 3: modelling results were not generated, shared, or disseminated in time

Fig. 1 shows how the timing of modelling publications (gleaned from a MEDLINE search over the dates 1 April 2009 to 31 August 2010, with combinations of the following keywords: model, modeling, modelling, simulation, H1N1, pandemic, and influenza) corresponded to the epidemic curve in the US (which was not too dissimilar from the curves in other parts of the world). As can be seen, the publication (and thus dissemination) of most studies occurred well after the early part of the pandemic (and, in the majority of cases, after the pandemic peak), often too late to influence decision-making. When H1N1 activity in the US peaked in October 2009, fewer than 40 modelling articles had been published. Although some of these study authors may have shared their results with decision-makers well before publication, many may not have done so, especially as academic career advancement may be tied more closely to publication in journals than to public service.

Fig. 1 also reveals that full-scale modelling activities did not start until a month or two into the pandemic, after news of the new strain emerged from Mexico in April 2009. Prior to the pandemic, many investigators had not been actively working with decision-makers, and therefore needed time to establish working relationships and ramp up activities. For example, extensive interactions between the National Institute of General Medical Sciences Models of Infectious Disease Agent Study network and Office of the Assistant Secretary of Preparedness and Response, US Department of Health and Human Services and Department of Homeland Security did not begin until late spring and early summer. For example, the embedding of investigators (Bruce Y. Lee of the University of Pittsburgh and Shawn T. Brown of the Pittsburgh Supercomputing Center) in the Office of the Assistant Secretary of Preparedness and Response did not occur until September 2009 [27].

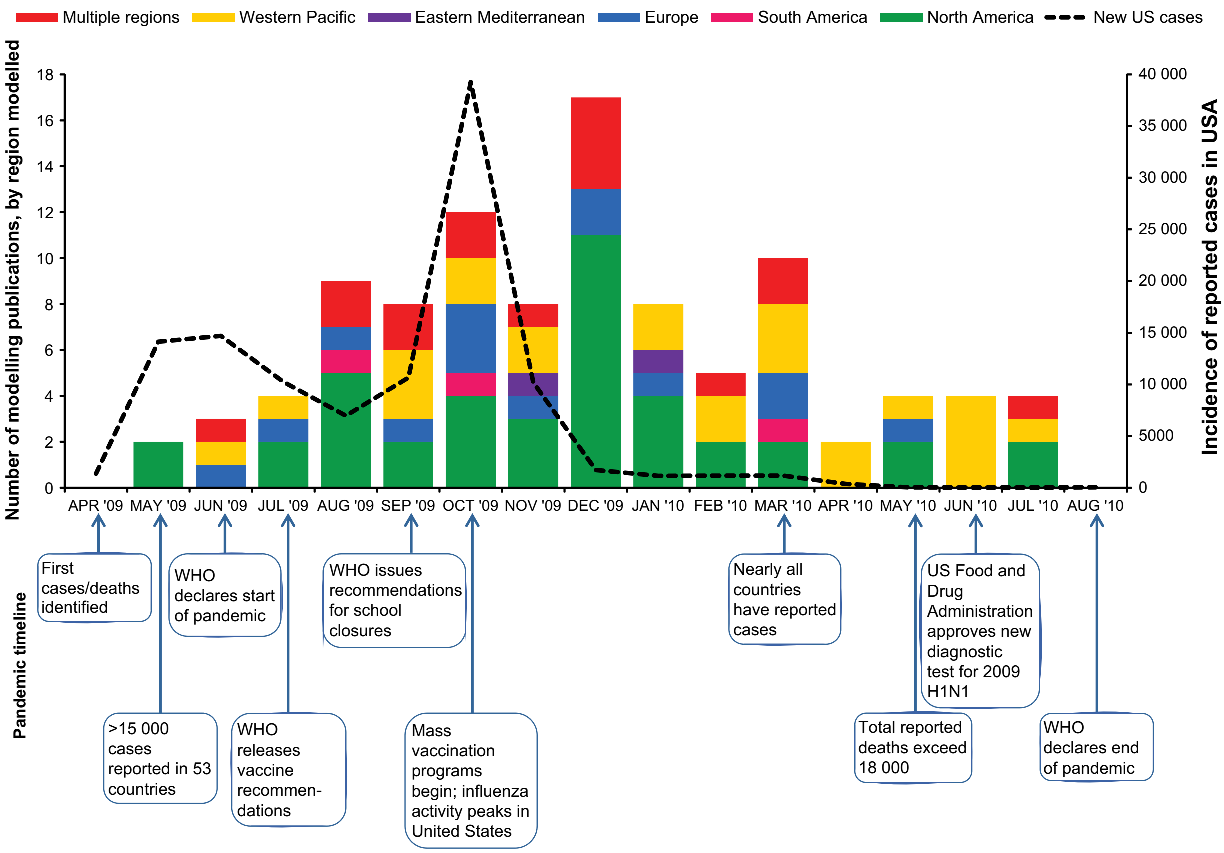

FIG. 1. Timeline of H1N1 pandemic and modelling publications. Sources: pandemic timeline [21–25], and US case incidence [26].

Although part of the delay in results dissemination reflected the later start in modelling activities, journal review and publication time also played a role. Even though some journals tried to fast-track pandemic-relevant studies, time-lags still occurred, especially as many potential reviewers may have been quite occupied by the pandemic. The existence and formation of modelling networks did facilitate some communication among modellers and between modellers and decision-makers. The Models of Infectious Disease Agent Study network formed working groups to share modelling data sources and results, and coordinate interactions with decision-makers. The WHO's informal mathematical modelling network convened in July 2009 [20]. However, it is unclear how much competition among modellers may have hindered cooperation, and whether data and results sharing occurred to the fullest possible extent.

The establishment of certain *ad hoc* communication channels was aimed at facilitating data and results sharing. Two prominent examples were the Program for Monitoring Emerging Diseases (ProMED)-mail, a programme of the International Society for Infectious Diseases serving electronic, Internet-based, emerging disease and outbreak detection and reporting, and *PLOS Currents: Influenza*, an online publication channel that aimed to minimize the publication delay and published peer-reviewed content that was citable and publicly archived in PubMed and indexed by Scopus. The WHO formed a mathematical modelling network, through which some modellers confidentially disclosed unpublished results across countries, but this work remained largely within the group during much of the pandemic [28]. Although modelling results were eventually published, many recommendations and actions stemming from these results were not [28].

Although these channels were helpful, they did not go far enough. As Table 1 shows, mechanisms and incentives to facilitate information-sharing will be important for future emergencies. Otherwise, the world will not fully benefit from the potential insights that modellers can offer.

Challenge 4: decision-makers could not always decipher the structure and assumptions of the models

The types of model utilized ranged from decision-analytical to compartment to large-scale agent-based models. The complexity of the models, even within each model category, varied substantially. A review of the methods sections of many publications revealed descriptions such as 'spatially structured

meta-population approach' [29], 'geographical backcalculation model' [30], 'stochastic, spatially structured, individual-based discrete time simulation' [31], 'age and risk group structured deterministic transmission dynamic model' [32], 'agent-based, social contact network model' [33], 'network-based statistical approach' [34], 'transmission model for which parameters are estimated from the data via Markov chain Monte Carlo sampling and data augmentation techniques' [35], 'discrete time epidemic model' [36], 'individual-based stochastic simulation model' [37], 'age-structured transmission model is embedded within a Bayesian framework' [38], 'deterministic compartmental model' [39], and 'logistic models involving generalized estimating equations' [40]. Such terminology may be familiar among modellers, but may not resonate with decision-makers. Decision-makers may have concerns about models being 'black boxes,' opaque constructs understood only by the persons who built the model. The use of language that is more accessible to the lay audience could facilitate decision-makers' understanding of and consequently trust in a model.

Although communication may be part of the problem, some models may, in fact, be too complex for the questions of interest. Excessively complex models violate the principle of parsimony, i.e. utilization of the simplest model that can adequately answer the question of interest. In fact, the goal of modelling is often to simplify a system or problem to make it more readily addressable. This is in contrast to constructing a single 'uber-model' that includes excessive detail and aims to address every possible question. Very complex models may prevent decision-makers from discerning why different models are yielding different results.

Challenge 5: modelling studies varied in intervention representations and reported results

Various modelling studies represented interventions in vastly different manners, causing substantial variation in results. This was especially true with vaccination, for which efficacy, number of doses, timing of availability and administration, and coverage are key parameters. Earlier vaccination, higher coverage and greater efficacy can all significantly improve the value of a vaccine. As the timing of vaccine availability was known only to a limited number of people involved in vaccine procurement, manufacturing, and distribution, many modellers had to make simplifying (and incorrect) assumptions: for example, the vaccines are administered at once to the population on a particular day, or at a steady rate throughout the beginning of the pandemic. As vaccine development, procurement and manufacturing mobilization were emergent and complex, predictions of when the vaccines would be available continued to change throughout the pandemic. Additionally, questions remained concerning the population's acceptance of and access to a novel strain vaccine, complicating representations of vaccination coverage. Moreover, time constraints prevented extensive testing and the establishment of vaccine efficacy. Some, but not all, studies tried to overcome the uncertainty about vaccine efficacy and vaccination timing and coverage by sensitivity analyses ranging these parameter values. However, even when sensitivity analyses were conducted, discrepancies existed among the ranges explored. For example, a study by Lugner *et al.* [41] ranged vaccination coverage from 45% to 90% vs. 20–100% for a study by Lee *et al.* [42]. Brouwers *et al.* [43] ranged vaccine efficacy after one dose between 10% and 100%, whereas Conway *et al.* [44] assumed vaccine efficacy to be at least 90%. Dang *et al.* [45] modelled vaccination programmes lasting for between 1 and 6 months, whereas Kenah *et al.* [46] modelled all vaccinations as occurring at once. Lee *et al.* [47] incorporated vaccine prioritization strategies into studies of vaccination impact, whereas Bajardi *et al.* [29] assumed uniform vaccine administration across the population. Differing ranges and assumptions could lead to different results, which could confuse decision-makers who did not have the time to carefully read through the methods sections of studies. Therefore, the modelling community may want to identify clearer ways of communicating key differences in the manner of representing interventions.

Challenge 6: modelling studies did not always present the results or outcomes that are useful to decision-makers

Emergencies may require special results or outcomes that are different from those normally reported in standard scientific settings. A review of the papers published reveals many standard epidemic parameters, such as reproductive number [16], epidemic doubling time [30], attack rates [48], relative susceptibility by age [40], incidence [49], prevalence [46], relative transmission rates [50], deaths [43], and hospitalizations [18], and some standard health economic outcomes, such as incremental cost-effectiveness ratio [32], quality-adjusted life-years [41], healthcare costs [33], and productivity losses [42]. Whereas some of these measures, such as costs by sector (e.g. productivity and healthcare costs), cost per case averted, incidence, prevalence, and attack rates, are of interest during an emergency, others that are more scientifically oriented may not resonate as well with decision-makers. For example, cost-effectiveness ratios and quality-adjusted life-years may be less relevant during emergency situations.

The Successes

Despite the aforementioned challenges, modelling seemed to make important contributions to the H1N1 pandemic

response. Although models may have been inexact in predicting the course of the pandemic, they may have been more effective in shaping whether and how various interventions/measures should be implemented. The published literature represents only a fraction of the contributions that modelling made to decision-making during the H1N1 pandemic, as a considerable proportion of the direct work with decision-makers may have been classified (e.g. working with data and decisions that could not be disseminated to the general public) and therefore not publishable. Moreover, much of the modelling performed in close collaboration with decision-makers was progressively iterative, continuously changing as new information emerged and the nature of the questions and decisions evolved, meaning that most of this intermediate-stage effort went unpublished. Additionally, much of the modelling occurred behind the scenes, helping those in various sectors to make decisions regarding production (e.g. manufacturers), procurement (e.g. purchasers and suppliers), distribution, capacity planning and resource allocation (e.g. hospitals and large employers), and investment (e.g. financial firms and other businesses). Therefore, the examples of successes outlined below capture only a portion of the impact that modelling had on decision-making:

Sample success 1: modelling characterized the role of social distancing measures such as school closure

Early in the pandemic, the question emerged of whether schools should be closed and other social distancing (i.e. limiting person-to-person interactions to curtail virus spread) measures should be implemented. Around this time, modelling suggested that short-term school closures may actually boost peak incidence somewhat by keeping susceptible students in 'reserve' during the school closure and then releasing them when schools re-open to mix again and re-fuel the epidemic. To be effective, school closure would have to be long term, from before the peak to well after the peak (over 8 weeks), which could be prohibitively expensive [51–53]. Another study showed how the cost-effectiveness of social distancing measures depends heavily on the infectivity and case-fatality rate, suggesting that school closure would only be cost-effective for a case-fatality rate of at least 1% and an R_0 of >1.6 [33]. Modelling also addressed other social distancing measures, such as limiting mass gatherings, and found that such a policy may not be helpful unless it is implemented near the epidemic peak [54]. Additionally, modelling studies (which showed that travel restrictions would probably not prevent local H1N1 epidemics, and could only delay such epidemics for a few weeks, at most) may have influenced the fact that no mass travel restrictions were enforced [55].

Sample success 2: modelling helped to guide data collection

Modellers were involved in investigating some prominent outbreaks during the 2009 pandemic [56]. Two such outbreaks occurred at a school in Queens, New York City [57] and a school in Berks County, Pennsylvania [58]. Running models and varying different input parameters helped to determine the relative importance of each parameter.

Sample success 3: modelling helped to justify the value of the vaccination programme

Modelling studies were fairly unanimous in showing vaccination to be the most efficacious (and cost-effective) available countermeasure when delivered to the population in a timely manner [44,48,59–64]. Even a vaccine with relatively low efficacy can help to mitigate the epidemic [32]. The most important variables seem to be the timing of administration and coverage, emphasizing the importance of establishing an effective vaccine distribution system, and suggesting that getting a vaccine out earlier is more important than developing a 'perfect' vaccine, as long as the vaccine is safe. When vaccines became available in October 2009 near the time of the second peak, questions emerged over whether vaccination would be too late to make a difference. However, a modelling study demonstrated how continuing the vaccination programme could prevent the emergence of a third pandemic wave, thereby justifying the value of continuing vaccination even during the descent of the second pandemic wave [65].

Sample success 4: modelling helped to prioritize target populations for vaccination

As vaccines became available in limited quantities during the autumn of 2009, decision-makers had to choose which populations should receive vaccines first [29]. Modelling runs evaluated the impact of prioritizing different population segments in different orders. Immunizing children first may best curtail transmission [44,66,67]. However, immunization based on CDC Advisory Committee on Immunization Practices prioritization instead may best reduce the combination of transmission, morbidity, mortality, and costs, by protecting high-risk individuals who are not children [47]. Modelling work also showed how society and even high-income populations would benefit from low-income populations being adequately immunized [68]. Low-income populations can extensively spread the pathogen, owing to their higher population density, heavy social mixing, and travel to other locations for work.

Sample success 5: modelling addressed the use of antiviral medications

Another question that arose was whether to use antiviral medications, both standard formulations and a new intrave-

nous formulation, peramivir, which received accelerated approval from the Food and Drug Administration. Antiviral medications are most effective when administered within 24–48 h of initial exposure to the virus, and, after this incubation period, their efficacy drops precipitously [69]. These qualities make antiviral medications poor candidates as sole countermeasures. However, modelling studies did support a role for antiviral medications in combination with other mitigation measures (e.g. to delay the epidemic peak if vaccination is delayed) and the use of intravenous peramavir for patients hospitalized with influenza-like illness [10,33,70,71].

Sample success 6: modelling helped with health system preparedness planning

Although models did not necessarily accurately predict the course or severity of the pandemic, they did help decision-makers to anticipate healthcare capacity needs under different scenarios, something that would be difficult to do without models. During an emergency, healthcare systems need to be ready for a variety of possible scenarios, as basing planning solely on the anticipated course of a pandemic may not leave room for unanticipated changes. For example, disease severity data from the USA and Mexico helped to estimate peak critical-care bed demand and peak ventilator usage in England, and identify thresholds at which demand would exceed capacity [18]. A similar study estimated antibiotic and critical-care demand for several northern hemisphere countries with varying vaccination campaigns, complication rates, and lengths of stay in intensive-care units [72].

Sample success 7: modellers and decision-makers gained a better understanding of how to work with each other

It would have been too much to expect all to go smoothly the first time that modellers worked with decision-makers during a global emergency. As mentioned before, expectations and infrastructure were not established before modellers rushed into the action. Decision-makers had to quickly learn what modellers could offer, and modellers what decision-makers needed. Fortunately, a milder than initially anticipated pandemic gave both sides a real-life educational opportunity with regard to future preparations.

Conclusions

Modelling is widely used in many other industries and professions to help decision-makers. The 2009 H1N1 pandemic marked the first time that mathematical and computational modelling and simulation were used to help respond to a worldwide infectious disease emergency. Although modelling provided benefits to decision-makers, several existing challenges kept it from reaching its full potential during the 2009 pandemic, which, in many ways, served as practice and a learning opportunity for both modellers and decision-makers. Modellers can continue working with decision-makers and other stakeholders to help overcome these challenges, to be better prepared when the next emergency inevitably arrives.

Transparency Declaration

The authors declare no conflict of interest.

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