Introduction

By 2006, many countries had responded to WHO initiatives to update contingency plans to mitigate the consequences of an influenza pandemic. However, some general concerns arose in connection with these national plans, as it became clear that there would be a shortage of antiviral drugs and vaccine and that a pandemic would place new demands on public health information systems. At the global level, WHO's Global Influenza Surveillance Network (FluNet) collects and processes influenza data from 83 countries, but at the national level few public health surveillance systems can either detect pandemic outbreaks or warn relevant agencies and the public. This inadequacy persists despite a 2005 report to the Government of the United States of America (USA) that identified public health information systems as a priority area for restructuring and investment to secure preparedness for pandemics and bioterrorist attacks. The development of a National Health Information Infrastructure in the USA had, at the time of the 2005 report, been proposed to detect atypical patterns of health-care use and to provide essential health information to citizens. This recommendation, however, has not translated into widespread practice, and many health information infrastructure projects remain in the planning stages.

Given that surveillance systems for collecting and analysing pandemic data are not sufficiently robust as a resource for policy planning and decision-making, attention has shifted towards computer-based simulation models. Using artificially generated community models as a basis, workers have forecast the effectiveness of different intervention strategies for containing or delaying the influenza pandemic at its expected source (e.g. rural south-east Asia). Longini et al. found that if the basic reproductive number (R0) is below 1.60, a prepared response with targeted antiviral drugs would have a high probability of containing the disease. When prevaccination was introduced into the model, targeted antiviral prophylaxis was found to contain an outbreak with an R0 as high as 2.1. Addressing the same research question, but using an individual-based stochastic simulation model, Ferguson et al. reported that a combination of geographically targeted prophylaxis and social distancing measures is feasible only if the R0 is below 1.8. Simulation studies have also included international air transportation patterns in the analyses of the early phases of a pandemic. Colizza et al. reported that the large-scale therapeutic use of antiviral drugs in all affected countries would
mitigate a pandemic effect with an $R_0$ as high as 1.9 during the first year, if one assumes the antiviral drug supply is sufficient to treat approximately 2–6% of the population and that case detection and drug distribution are efficient. More recently, methods for representing specific social-contact networks in analyses of local influenza transmission have been developed. Using artificially generated social networks grounded in typical American community structures in their analyses, Glass & Glass\(^6\) have suggested that high-school students may form the local transmission backbone of the next pandemic. Therefore, closing schools and keeping students at home during a pandemic would remove the transmission potential in these age groups and could effectively thwart subsequent spread of the disease within a community.

In the absence of reliable pandemic detection systems, computer-based simulations have become an important information tool for both policy-makers and the general public. In this study we examine the validity and usefulness of population-based pandemic simulations from a national-level public health perspective. Specifically, we assess a simulated pandemic influenza outbreak in a Scandinavian community using a non-statistical nominal group technique.

**Methods**

**Case-study simulation**

The purpose of the case-study simulation was to investigate two intervention strategies – antiviral drugs and public policy interventions – on influenza transmission in a Swedish municipality. Specifically, we aimed to examine the effects on simulated intervention outcomes of variations in local sociodemographic data, such as alternative population distributions and household structures.

We simulated two different supply situations for each drug and quantified their respective effects as coefficients that modify the basic transmission probabilities assigned to mixing groups. Public policy interventions aimed at reducing the number of contacts were represented as the probabilities that individuals would withdraw from particular mixing groups. In our simulation experiment, we closed schools in an attempt to eliminate interaction within such groups. The resultant information was used to plan a public health response based on the Haddon matrix\(^7\) (Table 1). Details of the simulator design, the case study and the results are provided in Appendix A and Appendix B (available at: http://www.crisim.org/documents).

**Assessor panel**

We formed a multidisciplinary group of experts with skills in the realistic and practical application of simulations in public health policy-making to assess the plausibility, formal validity and predictive validity of the case-study simulation.\(^8\) The panel of nine assessors was made up of an experienced public health manager, a professor of social medicine, a professor of computer science, a professor of social and economic geography, a professor of medical anthropology, a former head of the simulations section at a national department of defence, a software developer with extensive commercial experience, a social forecasting researcher and a cognitive scientist. Two assessors (HE, MM) designed and implemented the case-study simulation environment, and two (TT, JJ) contributed to its design.

**Data collection**

The nominal group technique was used to assess the case-study simulation. A nominal group analysis is the structured use of group processes for systematically soliciting a set of informed judgments on issues described by limited scenarios or case descriptions.

The health-effect assessment structure was used as a framework for data collection.\(^9\) Specifically, we used an adaptation of the scheme suggested by Veerman et al.\(^10\) and focused the assessment on plausibility, formal validity (verification) and predictive validity. Further details of the framework used for assessing the case-study simulation are in Appendix C (available at: http://www.crisim.org/documents). The experts were instructed to “assess the case-study methods and results with reference to the health impact scheme”.

**Data analysis**

The experts provided the first round of individual comments to the study coordinator, who included them in a case-study assessment document. The data analysis proceeded in cycles during which the experts first individually reviewed the assessment document and then participated in telephone group conversations.

### Table 1. Strategic pandemic response framework, based on the Haddon matrix,\(^7\) used for planning case-study simulations

<table>
<thead>
<tr>
<th>Pandemic timeline</th>
<th>Individual</th>
<th>Physical environment</th>
<th>Social environment</th>
<th>Agent/vector</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-event phase:</td>
<td>Immmunization status</td>
<td>Community structure:</td>
<td>Pandemic policies</td>
<td>Mapping</td>
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<tr>
<td>Underlying risk factors for viral spread</td>
<td>- day care</td>
<td>- schools</td>
<td></td>
<td></td>
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<tr>
<td>Event phase:</td>
<td>Nutritional state</td>
<td>Information infrastructure</td>
<td>Social networking patterns</td>
<td>Infecitivity</td>
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<tr>
<td>Determinants of viral spread</td>
<td>Quarantine possibilities</td>
<td>Availability of first-aid kits</td>
<td>Sustainability of social order</td>
<td></td>
</tr>
<tr>
<td>Post-event phase:</td>
<td>Self-care resources</td>
<td>Health-care facilities</td>
<td>Mobilization of civic resources</td>
<td>Vinulence</td>
</tr>
<tr>
<td>Determination of final severity and consequences of the epidemic</td>
<td>Antiviral medication</td>
<td>Equipment and supplies</td>
<td>Mobilization of industrial response (production of vaccine and antivirals)</td>
<td></td>
</tr>
</tbody>
</table>
conference discussions (12 sessions lasting 90 minutes each). When new analysis cycles did not yield significant changes to the document, the assessment findings were considered to be established. In the second step of the analysis, the experts were asked to formulate the implications of the assessment results for simulation strategies on the basis of their own expertise and of the published literature. Specifically, the instructions for the second task were to “analyse the assessment results with respect to practical implications for the application of simulations in public health planning”. The experts first provided individual comments, which were composed by the case-study coordinator. Thereafter implications continued to be formulated in a process in which the experts independently reviewed a preliminary case-study document describing the case-study implications. The comments thus gathered were subsequently circulated to the entire expert group, and a consensus document was iteratively drawn up.

Results

Verification of social assumptions
The assessment came to focus on the intersection between the simulations of biological events and of societal processes in the case-study, particularly on the model of social order. When assessing the formal validity of the simulation, the assessors noted that central aspects of the baseline situation in the case-study community had not been included in the models. The implementation of pandemic response plans assumes a close collaboration between many groups, including public health organizations, commercial companies, and law enforcement agencies, and the successful operation of these plans is critically dependent on the protection of these coordinated processes. Although important lessons were learned during previous influenza pandemics16 and the 2003 epidemic of severe acute respiratory syndrome (SARS),17 the interdependence among the broad range of processes occurring in a society under true stress (such as a pandemic) is not fully understood. In other words, even relatively minor breaches of the social order may significantly affect key infrastructural elements underpinning current pandemic response strategies. This frailty in the response strategies was not reflected in the description of the baseline situation in the case-study community.

For instance, assumptions were made about an efficient and sustained distribution of available antiviral drugs. However, in the USA pharmaceuticals are often distributed through retail and food stores, whose employees are at particular risk of becoming infected because of the large number of customers. Moreover, many professionals involved in the pandemic response may fail to report to work during a pandemic for reasons other than actually falling ill, e.g. because of breakdown of transportation systems, deficient law enforcement or having to take care of children due to school closures.18

We do not know how an influenza pandemic might affect logistics and staff in the distribution chains for pharmaceuticals, hygienic supplies and sanitary equipment during a catastrophic event.19 Unforeseen changes in behavioural patterns may also occur among acute care and hospital workers,20 who in particular may be prone to abandoning their tasks if they have shorter tenure, high work stress and already strained social relationships.21

Cumulative increase of predictive validity
The global spread of an influenza pandemic has been estimated to accelerate at an exponential rate from around day 50.22 Thus, national governments have a short window of time to plan and implement appropriate response measures. The expert panel concluded that before the detection of an outbreak threatening to become a pandemic, effects on social order may not be predictable and the nature of the infectious agent, the efficacy of vaccines, and the availability of antiviral drugs can only be estimated. Thus, the predictive validity of simulations at early stages of a pandemic will inevitably be poor. To increase the validity of the predictions, the submodels used in simulations need to be modified as more information becomes available about factors such as the virulence of the strain and the efficacy of intervention strategies. In the case study, the simulation submodels were rendered flexible by separating them from each other and from the execution algorithms in the software. This separation saved both considerable programming and programme testing time. However, a major drawback of the flexible software identified in the assessment was the length of time each estimation took. For instance, a single estimation of R0 in the case-study community (140 000 population) lasted approximately 5 hours on a standard personal computer. This direct relation between flexibility and calculation time is a disincentive to using simulations with high predictive value for national-level policy-making during a pandemic, when time is critical.

Towards socially contingent pandemic simulations
In the case-study simulation, questions were formulated in a standard public health framework under the assumption of a sustained social order during the pandemic. A more valid strategy, however, would have been to alter key social structures and processes as a function of disease effect on the community. Unfortunately, little is known about the theoretical and practical means for integrating the simulation of biological events, such as virus transmission between human hosts, with dynamic models of changes in population behaviour. Multi-level simulations based on “synergetics” and game theory,23 simulations of policy strategies24 and simulations based on geographically explicit data25 are established fields of population research. Similarly, the simulation of virus dissemination in stable societies is also an established field of research on its own.26 Nevertheless, few frameworks are available to support integrated modelling in these conceptually discrete but practically interrelated areas. Moreover, before biological and societal factors can be integrated, a valid common theoretical basis must be established.

Time geography27,28 captures concurrent social processes as they unfold in time and space, based on the interaction between individuals and groups within the constraints of the physical and biological environment. This theory can be applied to integrate biological and societal tiers in pandemic simulations. In this way, questions analysed in standard public health planning...
frameworks can be made dependent on changes in the social order (Fig. 1). However, execution of such two-tier simulations requires even more complex and time-consuming computations. To save scarce planning time during a pandemic, generic (XML-based) software specifications can be used to distribute data and algorithms for parallel computing. Such computing arrangements can technically be administered in routine public health settings in the form of arrays of standard computers.

Discussion

Population-based simulations are important sources of knowledge when planning national-level public health responses to pandemic influenza. The results of the case-study simulation assessment primarily apply to the “mixing group” approach to population-based simulations but can be extended to all models in which societies are represented as “compartments” of identical individuals mixing randomly. However, we noted that the formal validity of these simulations is challenged by the failure to take into account the behaviour of people during a pandemic and its effect on the social order. Additionally, the assessment led to questions about how simulation models are adjusted to reflect dynamic changes in preconditions, e.g., disruptions to drug distribution routines.

Formal methods for macro-level societal forecasting were introduced early in the twentieth century. In this research area, disruptions of the normal social organization have been expected, mainly when material resources are scarce or misallocated. When societal forecasting methods are applied to pandemic simulations, the lack of empirical grounding for using formal methods representing social processes in societies under severe strain comes to constitute a dangerous source of error. For example, the estimated effects from quarantine measures in Toronto during the SARS outbreak were diminished because disruptions of the social order led to compliance rates of only 57%.

Furthermore, the application of formal methods to analyse societies under pressure has been strongly opposed by several prominent social scientists. Weber and more recently Giddens have argued that using poorly validated models of social order leads to misunderstandings about the social world and how it operates. Although a central belief during the Enlightenment was that the social order could be controlled if science were sufficiently strong, modern social science, despite being more exact, no longer claims that changes in the social order in societies under severe pressure can be predicted. Moreover, researchers have only just begun to understand how disease shapes behavioural norms, and through them, social structures. The limitation of societal forecasting to stable societies is valid for time geography as well. In the context of pandemic simulations, the use of models and concepts from time
Simulations en population d’une pandémie de grippe : validité et signification pour les politiques de santé publique

Objectif Examinier la validité et l’utilité de simulations d’une pandémie de grippe visant à informer les décisions pratiques en matière de santé publique.

Méthodes Nous avons recruté un groupe multidisciplinaire de neuf experts pour évaluer une simulation d’étude de cas sur la transmission de la grippe dans un comité suédois. Nous avons assemblé des experts de diverses disciplines, y compris médecins, épidémiologistes, experts en modélisation et statisticiens. Les experts ont été sélectionnés pour leurs compétences et leur expérience dans le domaine de la pandémie de grippe. Les simulations ont été exécutées en utilisant des modèles multi-agents, qui permettent de prendre en compte les interactions sociales et comportementales. Les experts ont fourni des commentaires sur la validité des assumpions, la pertinence des résultats et les implications pour les politiques de santé publique.

Résultats Les experts ont identifié plusieurs défis liés à la validité des simulations, notamment les problèmes de représentation des comportements sociaux et de l’incertitude des données. Ils ont souligné l’importance de la flexibilité des modèles dans la mise à jour des données et la prise en compte des changements de comportement. Les experts ont proposé des améliorations pour renforcer la validité des simulations, notamment en incorporant les données en temps réel, en prenant en compte les variations de comportement et en utilisant des modèles plus flexibles.

Conclusion Les simulations de la pandémie de grippe ont montré une certaine validité, mais les défis liés à la représentation des comportements et à l’incertitude des données nécessitent des améliorations. Les résultats soulignent l’importance de la flexibilité des modèles et la nécessité de prendre en compte les données en temps réel pour renforcer la validité des simulations. Ces résultats peuvent informer les décisions politiques et les plans de réponse à l’éventualité d’une pandémie de grippe.
Resumen

Simulaciones poblacionales de las pandemias de gripe: validez e importancia para las políticas de salud pública

Objetivo Analizar la validez y la utilidad de las simulaciones de pandemias orientadas a fundamentar la adopción de decisiones prácticas en materia de salud pública.

Métodos Organizamos un grupo multidisciplinario de nueve expertos para que evaluaran una simulación de estudios de casos de transmisión de la gripe en un distrito de Suecia. Mediante una técnica no estadística de grupos nominales se generaron evaluaciones de la plausibilidad, la validez formal (verificación) y la validez predictiva de la simulación. Como marco de recogida de datos se usó una estructura de evaluación de los efectos sanitarios.

Resultados La impredecibilidad de los cambios del orden social en las situaciones de desastre es un aspecto que los métodos de simulación no abordaron adecuadamente; incluso ligeras perturbaciones del orden social pueden restar toda validez a algunos supuestos básicos sobre las infraestructuras empleados en los actuales modelos de simulación de pandemias. Además, existe una relación directa entre la flexibilidad del modelo y el tiempo de simulación. El resultado es que, en la práctica, los métodos de simulación no admiten cambios integrados de los submodelos microbiológicos, epidemiológicos y espaciales, ni pueden tampoco manejar varios escenarios paralelos.

Conclusión La confluencia de unos datos de vigilancia incompletos y unos métodos de simulación que ignoran la dinámica social limita la capacidad de los organismos nacionales de salud pública para proporcionar a las instancias normativas y el público en general la información crucial y puntual que se necesita durante una pandemia.
Toomas Timpka et al.

Validity of influenza pandemic simulations


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