Mathematical modelling for pandemic preparedness in Canada: Learning from COVID-19

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Abstract

Background: The COVID-19 pandemic underlined the need for pandemic planning but also brought into focus the use of mathematical modelling to support public health decisions. The types of models needed (compartment, agent-based, importation) are described. Best practices regarding biological realism (including the need for multidisciplinary expert advisors to modellers), model complexity, consideration of uncertainty and communications to decision-makers and the public are outlined.

Methods: A narrative review was developed from the experiences of COVID-19 by members of the Public Health Agency of Canada External Modelling Network for Infectious Diseases (PHAC EMN-ID), a national community of practice on mathematical modelling of infectious diseases for public health.

Results: Modelling can best support pandemic preparedness in two ways: 1) by modelling to support decisions on resource needs for likely future pandemics by estimating numbers of infections, hospitalized cases and cases needing intensive care, associated with epidemics of "hypothetical-yet-plausible" pandemic pathogens in Canada; and 2) by having ready-to-go modelling methods that can be readily adapted to the features of an emerging pandemic pathogen and used for long-range forecasting of the epidemic in Canada, as well as to explore scenarios to support public health decisions on the use of interventions.

Conclusion: There is a need for modelling expertise within public health organizations in Canada, linked to modellers in academia in a community of practice, within which relationships built outside of times of crisis can be applied to enhance modelling during public health emergencies. Key challenges to modelling for pandemic preparedness include the availability of linked public health, hospital and genomic data in Canada.

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See Appendix

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Introduction

The COVID-19 pandemic, caused by SARS-CoV-2, underlined the need for planning for future pandemics. There have been multiple pandemic preparedness initiatives at national and international levels (1,2). Modelling has supported previous pandemic plans, and the World Health Organization (WHO) has included modelling as a source of evidence to support planning (3). In Canada, modelling supported decisions during the pH1N1 pandemic (4–6) and subsequent pandemic influenza planning (7). During the COVID-19 pandemic, the role of modelling to support decisions was brought into focus. Mathematical models synthesize information on disease transmission in the population, disease severity in different age or population groups, population immunity, effectiveness of non-pharmaceutical interventions (NPIs) and vaccine effectiveness, among other aspects. In so doing, models produce a narrative that is interpretable by decision-makers and the public, and supports evidence-based decision-making, transparency and public trust.

The objective of this article is to describe how modelling efforts can support pandemic preparedness, including a description of the model types, their roles, best practices for their use and the expertise that is required, as informed by past pandemics and our recent experiences with COVID-19. For this article, modelling is considered to include mathematical and simulation approaches to understanding and predicting the introduction, invasion, spread, evolution and control of pandemic-causing pathogens, as well as impacts on healthcare capacity. The focus is on preparedness for pathogens that spread in the human population via human-to-human transmission, with the capability of dispersing through the global travel network. It is likely that such pathogens would emerge from animal reservoirs by zoonotic transmission. While spill back to animal reservoirs, as has occurred with SARS-CoV-2, may be a feature of the transmission and ecology of such pathogens, the significance for pandemic preparedness depends on its impact on human-to-human transmission (i.e., whether ongoing animal-human contact causes the basic reproduction number R_0 to be greater than one). WHO has produced a list of priority pathogens based on their importance to public health, but their criteria are broad and go beyond the capacity to cause a pandemic (8), so this list is too long to consider in its entirety for pandemic planning. For example, zoonoses including MERS-CoV, Nipah, Crimean-Congo haemorrhagic fever and Rift Valley fever are listed, though they often have limited human-to-human transmission, complex transmission cycles and routes of spillover into human populations involving arthropod vectors and wild and domesticated animal reservoirs. Outbreaks of these diseases may be defined by WHO as pandemics because they affect multiple countries. However, the absence of sustained human-to-human transmission, or conditions for zoonotic transmission in Canada, means that, without further evolution, they are unlikely to cause outbreaks in Canada at the scale of COVID-19 or the 1918 and 2009 influenza pandemic, for which pandemic planning aims to prepare us. Modelling supports our understanding of the potential risk from these diseases, particularly in the context of climate change (9), but that is out of scope for this article.

Methods

A narrative review of how modelling can best support pandemic preparedness was developed by members of the Public Health Agency of Canada External Modelling Network for Infectious Diseases (PHAC EMN-ID), a national community of practice on mathematical modelling of infectious diseases for public health. Authors sought and reviewed scientific papers and grey literature published in the last 20 years on pandemic preparedness in Canada, and the use of modelling during the COVID-19 pandemic. As most authors were involved in modelling to support decisions at federal, provincial and/or territorial levels, their expert opinion and lived experiences on how modelling supported public health decision-makers during the pandemic were captured.

Results

There are two components to modelling support for pandemic preparedness:

1. Modelling the transmission of ”hypothetical-yet-plausible” pandemic pathogens to support decisions on preparatory activities, such as emergency stockpiles

2. Developing validated modelling methods and tools that are maintained, capable of rapid adaptation to the biology of emerging pathogens and are thus ”ready-to-go” to support decisions in the event of the emergence of a pathogen with pandemic potential

In either case, there are considerations of good practices for modelling methods, communication of the results of modelling and data needs for modelling. People trained to recognize and fill modelling needs, embedded with, or having strong relationships with, public health organizations and decision-makers are also essential (10). While not explicitly a part of pandemic planning, modelling can also support resilience to pandemics, which is discussed at the end of this article.

Good practices

Mathematical models currently used to support public health and health policy decisions need to balance biological realism with tractability (11,12). While models should be simple enough to understand and implement efficiently (13), useful realism involves incorporating the biological processes of infection and recovery, outcomes of infection, human behaviour that underpins pathogen transmission and effectiveness of NPIs and pharmaceutical interventions (see below). However, the more complex a model, the more prone it is to undetected errors and inaccurate parameterization (13–15). Overcomplexity may also limit standard model-evaluation methods, such as sensitivity analyses (16) and the ability for models to be calibrated to data (17). However, developments in computing power, data availability and synthesis increasingly allow tractable modelling based on transmission with a digital twin of society to model social contacts in detail (18). Outputs of very simple models can also have value as an adjunct to communicating aspects of an emerging epidemic to a lay audience, which may be the public or non-expert managers, as was the case during the COVID-19 pandemic (19). Development of criteria that can be universally used to distinguish "good models" from "bad models," discussed as verification and validation of modelling in the broader simulation literature (20,21), remains a work in progress (11,12,22).

Types of models

The main model types relevant to pandemic preparedness are 1) dynamic transmission models of spread of an infectious pathogen within a population, both for prediction, assessment of alternative response strategies and impact of evolutionary changes; 2) importation models that explore the estimated risk of disease importation into and within Canada based on the global network of air and land travellers and knowledge of transmission in source countries (23); and 3) geographic spread models that are capable of identifying spatial pathways of pathogen spread within Canada (24).

Dynamic transmission models typically divide human (or animal) populations into "compartments," such as susceptible-exposed-infectious-recovered (SEIR) models. Flows (or transitions) among these compartments reflect the fundamental processes of the biology of transmission, infection and recovery. They are described by event rates, which can be used to define deterministic, continuous flows between compartments or stochastic transitions.

The simplest SEIR models assume that the population mixes homogeneously. As a result, these models usually overestimate the spread of infections, including the peak size of epidemics. Age-based contact matrices can improve these models by using the results of population surveys (25) or demographic data (26) to estimate the frequency of daily contacts between individuals. Furthermore, SEIR models can be constructed with more complexity to model different sections of the population (27,28) or to model variants and evolutionary changes (29,30).

Agent-based models (ABMs, also called individual-based models) can incorporate even more heterogeneity. Simpler ABMs are conceptually similar to SEIR models but explicitly model individuals in a population (i.e., "agents") who exist in susceptible, exposed, infected or recovered states. Agent-based models allow the integration of contact matrices, the construction of quasi-realistic environments (e.g., home, workplace, schools, leisure venues, public transit) within and between which the agents move according to their demographics, and potentially drawing on more extensive use of socioeconomic data. This structure allows for more realistic exploration of targeted NPIs, such as limited closures (31), and combinations of NPIs with vaccination (32). Both compartmental and agent-based models can be used to study the geographic spread of an infectious disease, in which case transmission can be modelled relatively simply in each grid cell of a landscape with plausible cell-to-cell spread of infection that depends on geographic or other physical constraints (24,33), or more elaborately based on more detailed data synthesis including small area estimation.

At the beginning of a pandemic that has emerged in another country, importation models can be used to estimate the probability of importation and the number of cases that may have recently been introduced into Canada by points of entry (23). Importation models typically consider travel volumes from different countries and/or provinces, and infection prevalence and immunity within those countries and/or provinces. Importation models can also inform travel measures within a country. Once within-country transmission has begun, importation models can provide imported case input to models of community transmission (34,35). As seen during COVID-19, for smaller provinces and territories, importation, rather than community transmission, can be the focus. There may be relatively few travel routes into small jurisdictions, which can be monitored and managed to prevent community outbreaks, at the outset of, and during a pandemic.

Coupling the analysis of geographic spread with genomic analyses is increasingly being used to model transmission and detect sources of new cases for a variety of pathogens, most notably COVID-19 (36–38). A real-time practical use of these methods is Nextstrain (39), an open-source platform and dashboard that allows decision-makers, scientists and the general public to watch, in real time, how the virus is evolving and spreading globally. Underlying phylogeographical and phylodynamic methods are mathematical and statistical models that rely on population genetics models, Bayesian modelling and linked SEIR-type models.

There is an array of modelling and estimation tools to provide intelligence during outbreaks. These include estimation of the instantaneous reproduction number, R_t (40), forecasting based on wastewater signals (41,42), branching process models to explore control methods early in outbreaks (43–45) and analysis of phylogenetic trees of whole genome sequence data to obtain estimates of the basic reproduction number, R_0, of the pathogen and/or emerging variants to compare with estimates from surveillance data (46).

Biological realism

During the COVID-19 pandemic, the importance of models for public health decision-making strengthened, not least because it was recognized that their outputs were biologically realistic (47). To achieve this, the structure of models (i.e., compartments/states and flows/transitions between compartments and states) needs to be realistic in terms of 1) the biology of infection, age and sex-related likelihood of clinical outcomes and recovery (infections being asymptomatic, mild, requiring hospital, or intensive care [i.e., in ICU]), accounting for heterogeneity in different population groups where these are important in transmission, and data that are available; 2) age and sex-related patterns of contacts between infected and uninfected people, vectors or animal reservoir hosts (48) and how these are likely to change; 3) public health interventions (NPIs and vaccinations); and 4) where possible, realistic direct impacts on healthcare resources and indirect impacts, such as cancelled surgery and avoidance of emergency department visits (**Figure 1**). Parameter values (e.g., the duration of latent and infectious periods, the basic reproduction number, R0, contact patterns within the population) need to be realistic and obtained from prospective studies or inferred from digital twin-style data synthesis and the scientific literature using established knowledge synthesis methods (49). They can also be obtained by fitting models to surveillance or hospital data, particularly for parameters that are difficult to measure in studies, such as the probability of transmission when infected people contact susceptible people. The capacity to fit models to surveillance data (e.g., human cases, hospitalizations and wastewater data) depends on the availability of reliable data, which has been a problematic and largely unresolved issue during and after the COVID-19 pandemic in Canada (50). To achieve biological realism (and ideally socioeconomic realism) useful for public health objectives, modelling must be a multidisciplinary endeavour, synthesizing knowledge and data from a spectrum of scientists and clinicians involved in public health. With these principles in place, evidence provided by models will be more reliable.

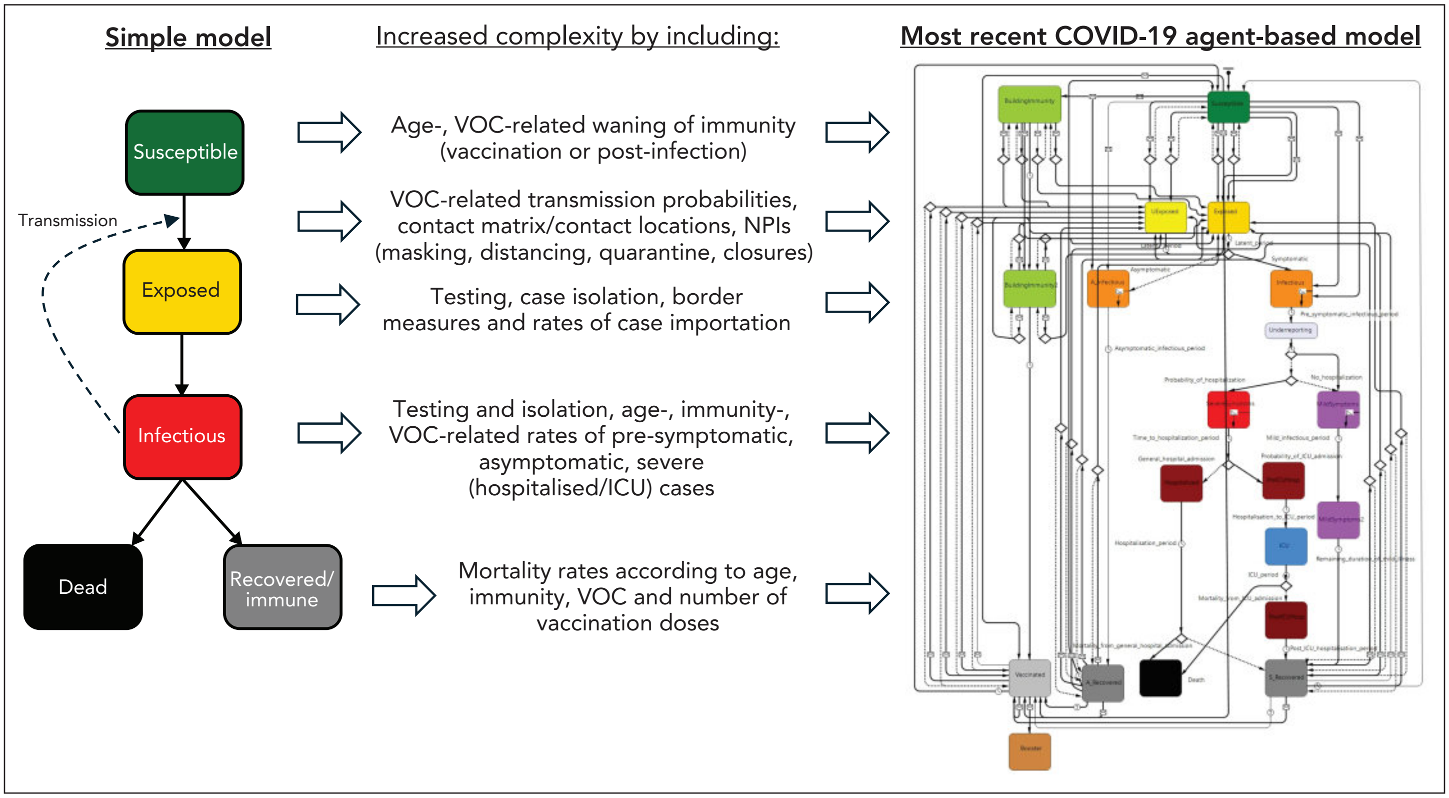
Uncertainty

In general, modelling approaches should account for plausible ranges and distributions of parameter values (e.g., the duration of infectivity) or probabilities of event occurrence (e.g., transmission probability estimates) to allow for exploration and quantification of uncertainty. There are at least three types of uncertainty to consider:

1. Data uncertainty due to measurement error
2. Uncertainty due to inherently variable parameters
3. Uncertainty as to whether the model structure fully represents the true system

Comparing initial model results to observed data may suggest that the model outcomes have very high uncertainty, and the models are insufficiently robust to support decisions without significant changes to model structure, parameters and/or calibration, in order to progress from a development stage. Validation may indicate that model results are robust enough to be useful for decision-making in two ways. If uncertainty is very small, models may have a high enough precision to say, "if public health effort is changed by X%, incidence will change by Y%." However, models may result in outcomes that have a high degree of uncertainty, yet still have enough precision to be useful

Figure 1: Adding complexity to a simple Susceptible-Exposed-Infectious-Recovered (SEIR) model to realistically model public health interventions[a]



Abbreviations: ICU, intensive care unit; NPIs, non-pharmaceutical interventions; VOC, variant of concern

[a] The left hand diagram shows the structure of a simple Susceptible-Exposed-Infectious-Recovered (SEIR) model, next to which are examples of the factors that had to be introduced to realistically model COVID-19 transmission with emerging VOCs, and the use of NPIs and vaccinations, resulting in a complex model structure (right-hand diagram). In this case, the complex model is the Public Health Agency of Canada agent-based model, as described, in an earlier form, in Ng *et al*., 2020 (30)

in answering less granular questions, such as, "will this be big or small?" or "is it better to do X, Y or nothing?"

Types of modelling projects

There are two main types of predictive modelling projects: 1) forecasting and 2) scenario exploration. Forecasting is the use of mathematical models to predict the trajectory of an epidemic or outbreak in the near or far future (e.g., Slide 7 in (51)). Scenario-based modelling is the use of models to answer "what if?" questions. Common "what if?" questions include the potential epidemiological impact (e.g., on incidence, hospitalizations, deaths) of various interventions (e.g., treatment or vaccination roll out, NPIs) (31,52). Scenario-based modelling often assesses outcomes over the course of multiple generations of infections. Sometimes, forecasts may also have simplified scenarios. For example, PHAC COVID-19 forecasts included a forecast of the current disease trajectory and scenarios of what might happen in a short time scale if NPIs were tightened or relaxed.

Communicating modelling results to decision-makers and the public

Effective communication of modelling results to public health managers and decision-makers is essential. Beyond simply the general need for good oral and visual communication methods that use accessible, accurate and jargon-free language, there are some modelling-specific requirements. First, objectives of modelling need to be clear and placed in the context of decision-maker needs and, ideally, modellers, managers and decision-makers discuss and agree upon what is needed and possible at the outset (12). Assumptions and limitations of models, results of validation, as well as sources and degrees of uncertainty need to be communicated to clarify the degree to which model outputs are actionable by decision-makers (11,53). Communicating the results of models in an early stage of development and models that perform poorly in validation, as well as poorly communicated results, will likely be unproductive or even counterproductive, resulting in managers, decision-makers and stakeholders losing confidence in modelling. A further layer of care needs to be added when communicating model outcomes to the public. For example, scenario-based modelling conducted early in the COVID-19 pandemic was misinterpreted by some members of the public, press and politicians as being a forecast. When the worst-case scenario did not happen (because public health measures were implemented), there was a perception that modelling was simply wrong and that COVID-19 was overblown (47).

Modelling "hypothetical-yet-plausible" pandemic pathogens before pandemics occur

Objective

Pre-pandemic modelling aims to provide a foundation for decisions on pandemic planning, including the healthcare resources that need to be maintained in national stockpiles. Scenario-based modelling is needed to explore the full potential impacts on Canadian health systems of "hypothetical-yet-plausible" pandemic pathogens in Canada. Outcomes of interest are the numbers of cases, hospitalizations, ICU treatments and deaths and the rate at which they occur. With these values, healthcare needs (hospital capacity, ICU capacity, ventilators, personal protective equipment, antivirals) can be estimated (54) and the quantities of healthcare stockpiles (such as the National Emergency Strategic Stockpile (55)) and NPI measures needed, accounting for their negative health impacts, can be evaluated.

Models

Both compartmental models and ABMs can be used for this purpose. Agent-based models may be particularly useful to explore impacts in smaller and/or more heterogeneous communities.

Likely pathogens/disease types

A prioritization of likely emerging pandemic pathogens remains to be done, but zoonotic pathogens that become human-to-human transmissible by contact or the respiratory route (e.g., influenzas, coronaviruses, haemorrhagic fevers) (56,57) are considered likely candidates. At the time of writing, WHO is undertaking a process that is more specifically aiming for a list of priority pathogens of pandemic potential (58).

Data needs

"Most likely" epidemiological parameter values can be sourced from the literature using established knowledge synthesis methods (49).

Development of modelling methods, tools and personnel "ready-to-go" in the face of a pandemic

Objectives

Modelling development in the face of an epidemic should ensure that modelling methods and the necessary highly qualified personnel (HQP) are present and ready to respond to an emerging epidemic in Canada.

Models

Generic, adaptable and preferably validated compartmental models and ABMs need to be developed in advance so that they can be adapted to an emerging pandemic in Canada for the purpose of forecasting and conducting scenario-based modelling to guide public health interventions. Models based on a design for modelling respiratory diseases would likely be readily adaptable to other forms of direct human-to-human transmission, but it would also be valuable to have models that are more explicitly designed for a variety of transmission routes (e.g., sexual transmission (59)). Importation models need to be ready to estimate rates and routes of importation of infectious people into Canada. Ideally, models of geographic spread within Canada, allowing exploration of interventions that limit spatial spread, would also be ready for adaptation to an emerging pathogen. There is also a need for modelling and estimation methods that enhance analysis of surveillance data, including estimation of the instantaneous reproduction number, R_t, forecasting from clinical surveillance and wastewater data and assessing genomic data to provide estimates of key epidemiological parameters, including R_0 and selection advantage of emerging variants.

Data needs

In the face of an emerging pandemic that begins outside Canada, as experienced during the COVID-19 pandemic, key parameter values for modelling emerge in the evolving scientific literature and knowledge synthesis skills are needed to be ready to source them (49). Ideally, estimates of key parameter values for a range of pathogens from the current literature would allow models to be populated with "best estimates" at the start of a pandemic prior to quantification of parameters specific to the emerging pandemic. Canada needs to be prepared in terms of data collection, sharing and linkage of case data with hospitalization and genomic data by learning from the difficulties encountered during the COVID-19 pandemic, along with the success in obtaining and linking case, hospitalization, vaccination and genomic data in countries such as the United Kingdom (50). In particular, Canada would benefit from building a framework of access to linked data for skilled experts, under appropriate conditions of access, well before it is next needed.

The need for highly qualified personnel

A key lesson learned from the COVID-19 pandemic is that public health organizations need in-house HQP to be able to create models, bring together the multidisciplinary skills needed and conduct modelling of utility for public health purposes. Knowledge synthesis teams are crucial for incorporating rapidly evolving evidence into models; geographers and mathematicians are needed for importation, network and spread modelling; epidemiologists and medical, microbiology and immunology experts are required for ensuring biological reality; communication experts are necessary for explaining technical modelling results to the public; methods are needed for bringing these skills together (10). Explicit linkage of these HQP with modellers in academia provides opportunities for modelling within public health organizations to benefit from ongoing innovations, peer review, enhancement of modelling capacity, development of modelling ensemble approaches and transparency that enhances public confidence in the modelling being conducted (60). Without in-house modelling expertise, public health is unprepared to adequately respond to outbreaks and pandemics and must turn to external modellers to undertake the work. The availability and capability of external modellers would not be guaranteed, and without internal experts, public health would not be able to review or adapt the resulting models nor ensure that results are accurately communicated with decision-makers associated with loss of corporate memory of modelling.

The need for a national community of practice of modellers

Many countries have recognized the importance of academic modellers contributing to public health decision-making during the COVID-19 pandemic (47,61). In the aftermath of the SARS-CoV-1 pandemic in 2003, a community of practice of infectious disease modellers formed in Canada and eventually became known as Pandemic Influenza Outbreak Research Modelling, or Pan-InfORM, in 2008 (62). This community aimed to support the use of modelling to inform decisions during pandemics. Although not specifically targeting pandemic preparedness per se, this community of practice did support decisions during the pH1N1 pandemic in Canada (4,63) and had links to public health organizations (62). While this group continued "peacetime" activities of modelling infectious disease transmission in collaboration with public health organizations up to 2018, between that time and the onset of the COVID-19 epidemic in Canada in 2020, links with most public health organizations had been lost, and new communities of practice, such as the Ontario Science Table and PHAC's External Expert Modelling Group (64), had to be created in the face of the pandemic. The loss of Pan-InfORM as a recognized resource for public health in the face of COVID-19 underlines the need for public health organizations to have in-house HQP that can maintain collaborative modelling communities of practice outside of the times when we are responding to infectious disease emergencies.

Modelling to supporting pandemic resilience

Modelling studies can support resilience of public health organizations to pandemics. Such modelling has general application for outbreak management and design of interventions using NPIs. A summary of ways that modelling can support development of resiliency is presented in **Table 1**.

Discussion

Key challenges

Modelling requires computing infrastructure, software and mathematics, but it also requires the multidisciplinary teams of experts in all aspects of disease transmission and public health practice for the modelling to be grounded in the biological reality needed for decision-making in public health. Such teams were brought together in Canada during the COVID-19 pandemic, but they need to be maintained in some form to support future pandemic preparedness. An ongoing issue in Canada is the limitation of collection of granular data on disease cases, hospitalized cases, genomic characterization of causal agents and metadata that are crucial for analyses (75,76). Simultaneously, there is a current incapacity to link surveillance, hospital and genomic data across provinces and territories (50).

Table 1: Examples of modelling studies that may support design of policies to increase resilience to pandemics

Focus area	Example modelling objectives	References
Building design	Enhancing greater ventilation to reduce respiratory pathogen transmission, particularly in locations where large numbers of people congregate.	(65,66)
Estimations to support decisions on public health capacity	Estimation of the surveillance effort needed to detect cases of emerging pathogens.	(67,68)
	Estimation of the test-and-trace effort needed to control transmission, in the absence of restrictive measures, according to different characteristics of pathogens and the diseases they cause.	(31,69)
Tools for strategic decisions	Criteria for determining if elimination of a pathogen in a particular jurisdiction would be successful, or if public health measures should aim simply to "flatten the curve" to limit impacts on healthcare.	(70)
	Estimation of the likelihood of control by test-and-trace versus restrictive measures, according to characteristics of pathogens and the diseases they cause (R_0 and proportions of cases with asymptomatic, presymptomatic or severe manifestations).	(71)
	Criteria for targeting NPIs to specific demographic or geographic sections of the population.	(32,72)
Best practices for use of public health measures	Best practices for the use of restrictive measures if these are needed to control transmission.	(52,73)
	Recommendations for the use of NPIs that reduce the probability or impact of transmission, such as distancing, masking and cohorting at gatherings.	(73,74,78)

Abbreviation: NPIs, non-pharmaceutical interventions

These data issues are the subject of considerable efforts to remedy problems in collection, linkage and sharing within the Pan-Canadian Health Data Strategy (77) and, for health system data, in the Interoperability Roadmap of Canada Health Infoway (78), but they remain the most significant unresolved challenges to effective modelling of infectious diseases in Canada.

Conclusion

Mathematical modelling of infectious diseases is now recognized as a key support to decision-making in public health preparedness and responses to outbreaks, epidemics and pandemics. Judicious use of modelling can support pandemic preparedness in terms of the stockpiles and planning needed to be prepared for a pandemic, while ready-to-go models, methods and HQP will support decision-making early in a pandemic. Modelling resources, particularly HQP, need to be maintained in public health organizations and in academia, and in transdisciplinary collaborative networks with public health-relevant scientists in other disciplines. A key barrier to effective modelling for public health decisions in Canada remains the issue of health data collection and sharing.

Authors' statement

NHO instigated the article and provided a first draft framework into which all other authors contributed. This is a project of the PHAC External Modelling Network for Infectious Diseases (PHAC EMN-ID), a national community of practice on mathematical modelling of infectious disease for public health, of which all authors are members. The authors identify no competing interests.

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