# The Canadian Network for Modelling Infectious Diseases: Progress and Next Steps

## BIRS Workshop 23w5151

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# 1 Background & Motivation

Infectious disease modelling that aims to contribute to public health decision-making has a long history, going back to Daniel Bernoulli's work on smallpox control in the 18th century [1]. In the early 20th century, Ronald Ross developed a mathematical model to help identify effective malaria control strategies [2], and Kermack and McKendrick developed the foundations of modern mathematical epidemiology [3]. While theoretical work on disease modelling continued [4–6], attention from decision-makers and politicians was scarce until the 2001 Foot and Mouth Disease epidemic in the UK, and the SARS epidemic in 2003. Over the last 20 years, the perception of mathematical modelling as a valuable tool in the public health policy process has become more and more common, especially in the context of influenza pandemic preparedness, which set the stage for immediate, serious engagement with modellers when the SARS-CoV-2 pandemic exploded in early 2020.

From the start of the pandemic, many disease modellers around the world found themselves in constant demand from public health agencies and policy-makers. Recognizing the importance of this development, NSERC invested $10M with the aim of creating networks of disease modellers, public health professionals, and policy-makers. A quarter of the investment ($2.5M) was allocated to our CANMOD network (the remaining 75% was allocated to four other networks).

CANMOD aims to increase Canada's capacity for data-driven emerging infectious disease modelling (EIDM) to directly support short, medium, and long-term public health decisions. Our network comprises collaborative teams of modellers, statisticians, epidemiologists, public health decision-makers, and those implementing and delivering interventions. The questions we are tackling are grounded in public health needs and generated in partnership between research investigators and knowledge users – public health leaders, health administrators and policy-makers. This collaborative research supports data collection, curation and access, with the hope that it will increase the speed with which critical information is made available.

The COVID-19 pandemic in Canada has made clear the urgent and immediate need for modelling of local context to inform decisions that are often implemented in local jurisdictions, and across diverse epidemiologic and health system contexts. Effective public health benefits from the support of engaged modellers who understand the local data, local epidemiological, socio-cultural, and health-system contexts, and who are passionate about collaborating on public health research problems. Our 44 co-applicants and dozens of collaborators have been engaged in this kind of work since the beginning of the COVID-19 pandemic, and are ideally placed to ensure that the collaborations we continue to build are effective. Enthusiasm from public health institutions was clear from the immediate high level of engagement in early 2020, the regular use of our research results in decision-making, and from numerous and enthusiastic letters we have received from a wide range of public health institutions across Canada, spanning municipal, regional, provincial and national jurisdictions. Some of the high-priority scientific questions that have emerged through this collaborative research were discussed at the workshop are summarized by this report.

As researchers have moved from the daily challenges of decision-making during the COVID-19 pandemic to working on longer-term policy questions, CANMOD continues to build and coordinate national capacity in infectious disease modelling at the forefront of public health. This capacity will position public health across Canada for better control of any infectious disease, and will build better preparedness and resilience in case of future pandemics. We are providing extensive experiential training opportunities for postdoctoral fellows (PDFs), graduate and undergraduate students at the intersection of infectious disease modelling, public health policy and decision making, and we are committed to increasing equity, diversity, and inclusion in the next generation of infectious disease modellers. Our trainees are well-placed for quantitatively-oriented careers in academia, industry and the public sector, both in Canada and abroad.

CANMOD's multi-disciplinary and multi-sectoral network is addressing all infectious disease challenges with principles of equality, diversity and inclusion through its recruitment, training, and research, and through events like the November 2023 BIRS meeting that this report summarizes.

# 2 Structure of the Workshop

This five-day hybrid workshop featured several special sessions, 27 short (30 minute) talks from in-person participants, and one short talk from an online participant.

Special sessions included an introduction to the Historic Disease Data Portal (§3.1.1), a discussion about challenges in infectious disease surveillance across Canada (§3.1.2), and a workshop on the `macpan2` modelling software (§3.1.3).

Short talks were grouped thematically in the schedule and spanned many domains, including behavioural modelling, infectious disease surveillance, pathogen evolution and genetics, vaccination and within-host immunity, policy-making in response to infectious disease outbreaks, as well as more general mathematical and statistical methods to support epidemiological modelling. §3.2 features summaries for several talks presented at the workshop.

All talks were streamed live to online participants. Talk recordings and slides can be found online.

# 3 Presentation Highlights

## 3.1 Special Sessions

### 3.1.1 Historic Disease Data Portal

*Steven C Walker*

In addition to funding research, training, and networking opportunities for building applied infectious disease modelling capacity in Canada, CANMOD also funded a project to provide straightforward and convenient access to historical and publicly available incidence, mortality, and population data. This project led to three long-term Canadian datasets.

Although there is a great wealth of historical data on infectious diseases in Canada that is or could be technically available to the public, it tends to be locked up in inconvenient formats like handwritten documents and internal databases at Statistics Canada. With this project, we are building a Canadian data archive that will provide straightforward and convenient access to historical public Canadian infectious disease data.

We systematically contacted data stewards across Canada to access the disparate source documents that contain Canada's public historical infectious disease data, in an effort to be comprehensive. We entered the information provided by the source documents into spreadsheets such that they can be compared with the original sources, and have produced automated pipelines for converting the digitized spreadsheets into convenient csv files with metadata. We worked with Statistics Canada to obtain mortality data that they have not made public before, collaborating with their analysts to balance strict anonymity requirements with our intention to make these data publicly-accessible. We systematically digitized official documents on Canadian populations for normalizing disease incidence and mortality data. All-in-all, we now have a systematic and comprehensive data archive ($\sim 2$ million records) of the following communicable disease incidence, mortality, and population data:

- Notifiable Communicable Disease Incidence (CDI) (1924-2000)
  - 1924-1980 (weekly), 1980-1990 (monthly), 1990-2000 (quarterly)
  - Broken down by province/territory
  - Broken down by disease
  - Some diseases broken down by age and sex (before 1956)
- Mortality (1950-2010)
  - Weekly
  - Broken down by province/territory
  - Broken down by 12 cause groups selected by Statistics Canada
  - Extends the public data portal back from 2010 to 1950
- Population (1881-present)
  - Population estimates every ten years (1881-1921), every year (1921-present)
  - Broken down by sex
  - Broken down by age
  - Broken down by province/territory

To enhance accessibility of this archive we developed the following tools, which will be made public once we have a pre-print describing this work:

- All data available on GitHub with open data pipelines
- Web-based and R-based APIs for programmatically accessing and searching the data on GitHub
- Dashboard for searching, downloading, and combining data

We provided meeting participants with sample API commands for accessing the archive.

We identified and adopted best practices for archiving research data. We developed a controlled data dictionary and CSV format used by all datasets in the archive, making it easier to combine data from different historical sources. We used the widely-adopted DataCite standard for metadata on research datasets, which allows our archive to be integrated in any number of pre-existing data portals. Ultimately, we plan to contribute our archive to a long-term storage and data access service for researchers (likely the Federated Research Data Repository).

This project has the potential to contribute to Canadian pandemic preparedness by providing long-term data on a diversity of infectious diseases that have significantly impacted the health of Canadians. The convenient access to these data provided by this project will help epidemiologists to learn from past public health challenges.

### 3.1.2 Surveillance Discussion

The effective collection, analysis, and application of diverse infectious disease surveillance data streams are paramount to understanding and managing infectious disease threats. Recently, the WHO released guidelines for ethical public health surveillance, arguing that societies have an obligation to design and deliver effective public health surveillance. We explore infectious disease surveillance from the point of view of researchers, primarily infectious disease modellers, working at the interface between research and policy during the COVID-19 pandemic.

We held a roundtable discussion on surveillance. Our discussion moved through infectious disease surveillance (and related) data types, their collection, and the ways in which they inform surveillance questions.

There is a wide range of data types that play important roles in understanding and managing infectious diseases; here we focus primarily on respiratory infectious disease and issues that arose during the COVID-19 pandemic. Many of these apply to influenza, RSV and other respiratory illnesses, and some (like the “First 100”) are relevant mainly to a potential new emerging infectious disease.

Data streams include:

- **Lab-Based Data**: These data comprise the results of testing, which indicate whether an individual is infected, for a specific virus or infectious agent. There is typically some stratification by age, perhaps sex, location.
- **Case-Level Data**: This refers to detailed information on each case, such as line lists and contact tracing records.

- **First 100 cases**: especially in the early stages of a new emerging infectious disease, this can provide essential characterization of the course of infection, exposure, pace of transmission, severity, clinical needs
- **Genomics**: Genomic analysis (viral sequencing) helps track the mutation and spread of pathogens. Interpretation can be challenging, due to lack of linkage with epidemiological, clinical, demographic or immunity data, and due to sampling that is a mixture of travel-related cases, random sampling (but only within the schema of the testing system), and priority sequencing (for example of outbreaks)
- **Outcomes**: hospitalization, acute care needs, by age (aggregate; individual outcomes would be in individual-level data)
- Tools like the **WHO Ordinal Scale**, which measure the severity of cases: however, there are challenges in standardizing these scales across different regions, hospitals, or countries, particularly when data is incomplete or inconsistent. If hospitals are overwhelmed, data on these scales will be impacted
- **Mortality Data**: this can lack timeliness, consistency across jurisdictions and completeness
- **Immunity**: serology, vaccination levels
- **Denominator/population-level data**

Additional non-health data that are relevant for interpretation and modelling of infectious disease surveillance data:

- **Policy data**:
- **Behavioural data**: this is a large area, not typically considered part of routine respiratory surveillance data. It comprises mobile phone (mobility) data, contact data derived from surveys, and other information about behaviour relevant to infectious disease transmission (use of NPIs, response to illness). This could also include information about test-seeking and health-care-seeking behaviour.
- **Travel and Movement Data**: Data on travel, both international and interprovincial
- **Demographic changes over time**

Our discussion continued, to explore the epidemiological pyramid, which connects some of these layers of data together, conditional on others. For example, the relationship between detected cases and infections depends on test seeking, testing policy, immunity including vaccination, and the intrinsic severity of the virus variant, to name a few.

Several participants emphasized the importance of data linkage, and of context. The integration of genomic data with epidemiological, clinical, vaccination, and demographic data is especially important. Without these connections, the full potential of genomic insights remains largely untapped. For instance, determining whether a new variant is transmitting among vaccinated individuals requires a synthesis of genomic, epidemiological and vaccination data. Determining severity requires information about clinical outcomes, in individuals with and without the new variant.

One of the main focal points for our discussion was to solicit modellers' input on how infectious disease surveillance data could be made more useful to modellers, as throughout

the pandemic, modellers were asked to support policy-makers in questions about COVID-19 scenarios, forecasts and healthcare impacts.

The utility of data is intrinsically linked to the specific question it aims to answer. For prediction purposes, it's useful to clarify what is being predicted. For example, predicting the dynamics of infections requires different data compared to predicting the impact on healthcare resources. The following aspects were identified as important ways that surveillance systems could take these needs into account.

**Timeliness**: The value of surveillance data is heavily dependent on its currency. Real-time or near-real-time data acquisition enables public health officials to respond swiftly to emerging threats, adjust strategies based on current trends, and predict future outbreaks with greater accuracy. Delayed data can lead to missed opportunities in containing and mitigating outbreaks.

**Testing policy**: Knowing who is being tested and recognizing any shifts in this demographic is important. Changes in testing patterns can significantly impact the interpretation of surveillance data. For instance, if testing becomes more widespread or targeted at specific groups, this shift needs to be factored into the analysis to avoid misinterpretation of disease trends.

**Stratification (lab data)**: Stratifying lab data by variables such as age, sex, and immune status can help unpack nuance and changes in testing, and help build a more nuanced understanding of a disease's impact and spread. Stratification may be helpful in understanding changes in testing policy or test-seeking behaviour. Including vaccination status (including the recency of vaccination and time since the last dose) adds another layer of depth, enabling improved understanding of immunity in the population and the effectiveness of vaccines against current strains.

**Linkage**: Linking across datasets enhances the richness and depth of analysis and adds value. For instance, connecting laboratory data with clinical outcomes, vaccination records, and demographic information provides a comprehensive picture of the disease's impact, spread, and evolution (and see above for the benefits of genomic data with linkage).

**Consistency**: In addition to the above, it is important for data to be consistently reported across local jurisdictions, hospitals, and laboratories, and as such, the creation of standards can help move the needle forward when thinking about surveillance data for infectious disease modeling.

### 3.1.3 `macpan2` Modelling Software

*Steven C Walker, Irena Papst*

`McMasterPandemic` is an `R` package for compartmental modelling that was developed to provide forecasts and insights to public health agencies throughout the COVID-19 pandemic. Forecasts created with `McMasterPandemic` were prepared for the Public Health Agency of Canada, the Ontario COVID-19 Science Table, the World Health Organization, and Public Health Ontario. Much was learned about developing general

purpose compartmental modelling software during these experiences, but the pressure to deliver regular forecasts to these organizations made it difficult to focus on the software itself. With the support of CANMOD, the `macpan2` project was launched to re-imagine `McMasterPandemic`, building it from the ground up to address lessons learned while responding to a global public health emergency.

The special session on `macpan2` started with a presentation by Steve Walker introducing the project. Steve traced the history of `McMasterPandemic` and `macpan2`, using it to argue that impactful modelling requires many interdisciplinary steps along the path from epidemiological research teams to operational decision-makers. Researchers must quickly tailor a model to an emerging public-health concern, validate and calibrate it to data, work with decision-makers to define model outputs useful for stakeholders, configure models to generate those outputs, and package up those insights in an appropriate format for stakeholders. `macpan2` targets bottlenecks along this path that can be solved with thoughtful software engineering. The goal is to ease the software development burden on modellers, especially when they are working on an urgent public health response, so that they can devote their time and energy to the modelling itself.

After discussing the project's history and motivation, the presentation transitioned to exploring `macpan2`'s modular model building, a key feature meant to address a commonly-encountered bottleneck in modelling. New public health concerns often demand new modules to be added to existing models. For example, as vaccines against COVID-19 were deployed, models needed to be modified to include vaccination. Even beyond responding to a public health emergency, a common paradigm in modelling (and in writing code) is to start simply and add complexity incrementally, testing outputs at every step of the way. Experience shows that it can be surprisingly difficult to add new modules to a modelling pipeline if your existing toolkit is not designed for modular model building. Steve briefly reviewed existing approaches to modular compartmental modelling based on mathematical tools from graph theory and category theory. Steve described how modules in `macpan2` can be represented by tables (like tables in a database), and that widely-understood table manipulation tools (like join and group-by) can be used to combine modules without the need for advanced mathematical concepts.

After the presentation, participants were invited to a hands-on session to explore `macpan2`, led by Steve Walker, Irena Papst, and Ben Bolker. There were roughly 20 participants in the session, representing a wide range of career phases, from graduate students to tenured faculty. We started the session by helping participants download and install the software on their computers. There were several installation hiccups that we were able to troubleshoot on the fly. These issues gave us valuable insight into potential difficulties deploying this tool more widely, and have inspired further work on the software.

We then invited participants to work through a getting started vignette to enable them to further familiarise themselves with the software's model specification grammar, which enables modular model building. The vignette walks users through specifying a very simple epidemiological model, and then introduces software features that make it easy to add additional structure to models, such as modules for multiple infection types (*e.g.*, asymptomatic, symptomatic), multiple locations (often referred to as "metapopulation" models),

stratification by vaccination status, and more. The vignette specifically works through the example of specifying a two-strain model while demonstrating `macpan2` functions key to easily specifying "structured" models.

After participants worked through the vignette, some worked on specifying other models in `macpan2`, as a way to test their understanding of the model specification grammar and to experiment with other features of the package. Two participants worked together to try to specify a Lotka-Volterra predator-prey model, and their attempts revealed interesting points of friction in the software that have directly inspired further development. These attempts also spurred the addition of Lotka-Volterra models to `macpan2`'s model library. Three participants independently provided the same feedback about how calibrating models to data is a bigger bottleneck than modular model building, which has inspired us to make existing calibration tools more accessible via the `macpan2` interface.

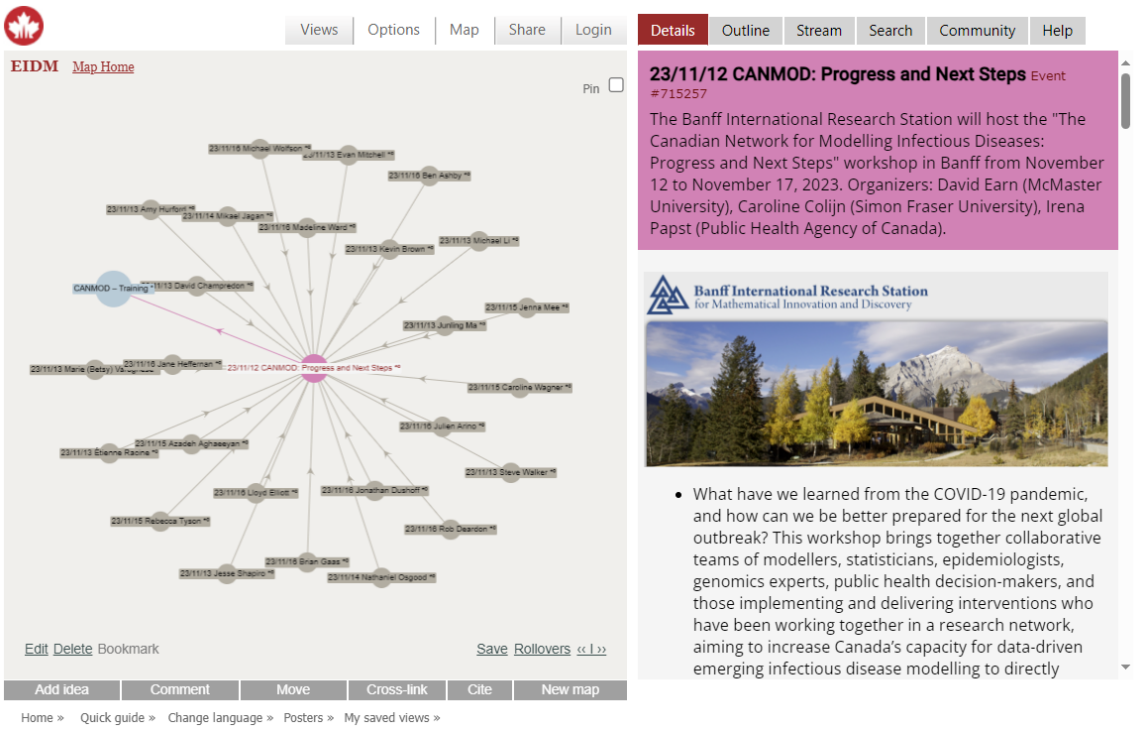
This session was the first `macpan2` training ever run, and overall, we received a lot of valuable feedback from participants on it. We continue to use this feedback to both improve guides for the software, as well as the software itself.

## 3.2 Short Talks

### The CANMOD/EIDM Knowledge Graph

*David Price, DebateGraph*

This opening talk of the workshop explored the content, structure, and rationale of the EIDM dynamic knowledge graph (`https://eidm-mmie.net`), which is being developed by CANMOD to support, document, and interconnect the work conducted across the five EIDM networks. Workshop participants were guided through the exploration and use of the graph as a repository of knowledge and as a resource for search-based discovery. As illustrated in the figure below, the graph identifies and interweaves multiple aspects of the EIDM initiative, including: the participants, their organizational affiliations and collaborations, research interests, publications, goals, datasets, software, and training materials. Interactive visualisations make it simple to traverse the graph (which already contains thousands of nodes and edges), focusing on the immediate connections around the individual elements and zooming out to see the wider patterns and connections emerging as the network continues to grow.




## Association between Delayed Nursing Home Outbreak Identification and SARS-CoV-2 Infection and Mortality in Ontario, Canada

*Kevin Brown, Public Health Ontario*

Delayed outbreak identification is likely an important driver of respiratory infection transmission in nursing homes. Most studies examining outbreak identification have been descriptive and there are no measures of delayed outbreak identification in nursing homes. We conducted a longitudinal cohort study of SARS-CoV-2 outbreaks from 623 nursing homes in Ontario, Canada in the March 1, 2020 to November 14, 2020 period prior to the rollout of COVID-19 vaccination. Our exposure was the timeliness of outbreak identification, defined as late ($\geq$ 3 resident-days of infection pressure) versus early ($\leq$ 2 resident-days of infection pressure) on the date of outbreak identification. Residents were considered to contribute infection pressure from 2 days prior to onset to 8 days afterwards while non-residents (including staff and visitors) were not considered to contribute infection pressure. Our outcomes were 30-day secondary infections and mortality, defined as the proportion of at risk residents with a laboratory-confirmed SARS-CoV-2 infection with onset within 30-days of the outbreak identification date, and mortality among these residents.

We identified 632 SARS-CoV-2 outbreaks across 623 Ontario nursing homes during the study period. Of these, 230 (34.3%) outbreaks were identified late. Outbreaks identified late had higher secondary infections (10.3%, 4,437/43,078) and mortality (3.2%, 1374/43,078) compared to outbreaks identified early (infections: 2,015/61,061, $p < 0.001$,

mortality: 0.9%, 579/61,061, $p < 0.001$). After adjustment for 12 nursing home risk factors, the incidence of secondary infections in outbreaks identified late was 2.90-fold larger than that of outbreaks identified early (OR=2.90, 95%CI: 2.04, 4.13). Each 1-person-day increase in infection pressure at the time of outbreak identification was associated with an 1.10-fold increase in the secondary infections (OR=1.10, 95%CI: 1.08, 1.12) and a 1.07-fold increase in secondary mortality (adjusted OR=1.07, 95%CI: 1.06, 1.09). In the nursing home setting, SARS-CoV-2 outbreaks identified late evolved to be much larger than outbreaks identified early. The timeliness of outbreak identification can be used to predict the trajectory of an outbreak and plan for increased staffing demands, infection control measures, and antiviral administration, with the goal of mitigating harms to residents.

### The need to evaluate existing data resources and knowledge gaps to support future needs for respiratory disease surveillance and modelling

*Michael Li, Public Health Agency of Canada*

Infectious disease surveillance and health data sharing have always been topics of discussion, even before the SARS-CoV-2 pandemic. The SARS-CoV-2 pandemic amplified the value of these discussions, providing researchers and government scientists with a small glimpse of the data possibilities—such as the high frequency of time series data reporting positive cases, testing, sequencing, hospitalization, and death. However, what we had for SARS-CoV-2 is still far from the ideal data structure (e.g., linkable data, health status, etc.) needed to learn more about the questions of interest. Before we can make further progress, the capacity diminishes due to low-frequency/quality reporting.

Lack of surveillance and data sharing are often viewed as the same problem; however, it is important to recognize that they are separate issues. Our focus should be on learning from data, not just on the data itself. The key is not sharing data per se, but fostering effective collaborations to obtain information from data—referred to as "data-info or data-knowledge sharing"

This talk proposes a pandemic and peacetime preparedness vision called the "PREP" vision, which stands for Profiling, Reflection, Exploring alternative options, and Proof of concept. Profiling identifies what different people want to know and the bottlenecks of knowledge gaps. Reflection evaluates existing resources used to seek answers to understand what needs improvement. Exploring alternative options goes beyond the current status quo to see what can be done to improve access and, eventually, enhance the resources. Lastly, a proof of concept aims to validate whether the ideas are worth implementing using the model world.

### The Decision Uncertainty Toolkit

*Megan Wiggens, Marie Betsy Varughese, Ellen Rafferty, Jeff Round, Sasha van Katwyk, Erin Kirwin*

*Presented by: Marie Betsy Varughese, Institute of Health Economics*

Infectious disease (ID) models played an important role in decision making during the COVID-19 pandemic. While ID modelling has methods to address structural and parameter uncertainty, communicating decision uncertainty is another important interface between ID modelers and decision-makers. This talk presented the Decision Uncertainty Toolkit aimed to address and develop methods for communicating uncertainty to decision makers where there are multiple policy options. The toolkit includes visualizations, risk measures, descriptions, and interpretations. As this work is on-going, we included an opportunity for further involvement through a planned workshop in 2024 to try out the tool and provide additional feedback on the codes, visualizations, and descriptions.

### Academic collaborations to improve wastewater-based modelling at the Pubic Health Agency of Canada

*David Champredon, Public Health Agency of Canada*

Since the COVID-19 pandemic, the surveillance of respiratory viruses in municipal wastewater has emerged as a valuable new data source for modellers. However, there are still many unknowns regarding the various causes that can impact the viral concentration in wastewater during the journey of viruses in the sewer system. Understanding the processes that can affect viral concentration in wastewater is critical for epidemiological surveillance at the Public Health Agency of Canada, and it involves many scientific fields, not all represented within the Agency. In this talk, I highlighted several projects done in collaboration with academic groups that brought their expertise to help better understand how various processes can impact viral concentration in wastewater. I also presented the different ways academic groups can collaborate with PHAC.

### Infections, hospitalizations, and deaths prevented by COVID-19 vaccines in Canada

*Evan Mitchell, McMaster University*

How many infections, hospitalizations, and deaths did COVID-19 vaccines prevent during the pandemic in Canada? This talk presented research aimed at answering this question. A compartmental model was fit to daily infection report and hospitalization occupancy data for Ontario from the start of the pandemic through the end of the Delta wave in December 2021. We use this model to simulate counterfactual scenarios where vaccines were not present, vaccine introduction was delayed 60 days, or vaccines were 25% less effective. Results from these simulations show that the predicted numbers of infections, hospitalizations, and deaths would be orders of magnitude larger than they actually were. To follow this up, we consider the effects of introducing a hypothetical stay-at-home order in an attempt to control these counterfactual scenarios. Our main finding from these explorations is that we would have a much easier time controlling the situation in the case of less effective vaccines than in the other two cases, suggesting that it is important to release a vaccine as early as possible during a pandemic even if that vaccine is less effective than it might be otherwise. We are currently in the process of extending these results to five other provinces: Alberta, British Columbia, Manitoba, Québec, and Saskatchewan.

### Within-host diversity of SARS-CoV-2 across animal host species

*Jesse Shapiro, McGill University*

Viral transmission across different host species makes eradication very challenging and also opens new evolutionary trajectories for the virus. Since the beginning of the ongoing COVID-19 pandemic, SARS-CoV-2 has been transmitted from humans to several different animal species, and novel variants of concern could plausibly evolve in a non-human animal. Previously, using available whole genome consensus sequences of SARS-CoV-2 from four commonly sampled animals (mink, deer, cat, and dog) we inferred similar numbers of transmission events from humans to each animal species but a relatively high number of transmission events from mink back to humans (Naderi et al., 2023). In a genome-wide association study (GWAS), we identified 26 single-nucleotide variants (SNVs) that tend to occur in deer, more than for any other animal, suggesting a high rate of viral adaptation to deer. Here we show that deer harbor more intra-host SNVs (iSNVs) than other animals, providing a larger pool of genetic diversity for natural selection to act upon. Deer contain more distinct viral lineages than other animals, indicating possible co-infections, but this effect is unlikely to explain the overall higher diversity within deer. Compared to other animals, iSNV frequencies in deer are skewed toward higher frequencies, which is unexpected after a recent population bottleneck or population expansion and therefore suggests that deer are sampled relatively late in the course of infection. Combined with extensive deer-to-deer transmission, the high levels of within-deer viral diversity help explain the apparent rapid adaptation of SARS-CoV-2 to deer.

### Estimating phenomenological epidemic models with mixed effects

*Mikael Jagan, McMaster University*

When dealing with emerging or historical epidemics, modelers must contend with uncertainty about the disease of interest. Sparse knowledge about the pathogen, the natural history, and primary modes of transmission impedes selection of appropriate mechanistic models and complicates interpretation of estimated model parameters. In this situation, much can still be learned from simple, phenomenological models that capture salient features of available disease incidence data without making strong assumptions about disease characteristics or mechanisms of spread.

In this talk, I motivated the use of generalized logistic models to estimate the initial rate of exponential growth of an epidemic, a quantity that, in an outbreak context, informs how fast public health interventions must be deployed in order to meaningfully curtail spread and reduce burden on health systems. I introduced statistical software (R package **epigrowthfit**) that implements our methods for both estimating growth rates and investigating variation in growth rates between waves and across jurisdictions. Discussion with workshop participants after the talk centered on the theoretical distinction between mechanistic and phenomenological epidemic models.

**Opinion dynamics and disease: One wave or many?**

*Rebecca Tyson, UBC Okanagan*

Opinion dynamics, that is, changes of opinions/behaviours in a population arising from interactions between individuals in the population, can have a strong effect on disease dynamics. In most modelling efforts however, such behaviours are considered to be fixed within a given subpopulation (divided by, e.g., age or socioeconomic class), or altered by top-down public policies. In this talk we present a suite of models coupling disease and opinion dynamics, and show how the interaction between these two processes can have a profound effect on the disease dynamics, creating, e.g., multiple epidemic waves, changes in peak size, and changes in final size. While there is a long history of modelling disease dynamics, the field of opinion dynamics modelling is still fairly new. We call for more research on how best to model opinion dynamics, particularly within the context of new diseases.

**Revealing the unseen: What portion of the Americans relied on others' satisfaction when deciding to take the COVID-19 vaccination**

*Azadeh Aghaeeyan, Brock University*

Efficient coverage for newly-developed vaccines requires knowing which groups of individuals will accept the vaccine immediately and which will take longer to accept or never accept. In this study, we assumed that, within the context of COVID-19 vaccination, non-vaccine refuser Americans behaved as either success-based learners, making decisions based on others' satisfaction, or as myopic rationalists, attending to their own immediate perceived benefit. We used COVID-19 vaccination data to fit a mechanistic model capturing the distinct effects of the two types on the vaccination progress. We estimated that about half of Americans behaved as myopic rationalists with a high variation across the states. The proportion was correlated with the vaccination coverage, proportion of votes in favor of Democrats in 2020 presidential election, and education score. The findings reveal the impact of the proportions of the decision-makers on the vaccination speed and, consequently, overall vaccination coverage.

**Multi-Pathogen Agent-Based Models for Disease Surveillance and Mitigation**

*Caroline Wagner, McGill University*

Understanding the dynamics of emerging infections and the efficacy of detection technologies in the context of the endemic circulation of other pathogens is a critical aspect of effective public health responses against infectious diseases. The use of compartmental models to simulate the effectiveness of different detection technologies is complicated by the importance of heterogeneity in numerous aspects of these systems, including underlying patterns of technology distribution within a population and variable in-host immune responses. Compartmental models also present challenges when modeling large numbers

of co-circulating pathogens with specific disease characteristics and immunological rules for pathogen-pathogen interactions.

In light of this, we presented Pathosim, a multi-pathogen agent-based model (ABM) that builds on the open-source COVID-19 model Covasim. Like Covasim, Pathosim allows for flexible population and transmission network structures, and can simulate individual in-host viral kinetics, the implementation of pharmaceutical interventions, and testing and quarantine procedures. In addition, Pathosim allows for the flexible characterization of any pathogen of interest along with the specification of immunological rules for pathogen-pathogen interactions (*i.e.*, cross-immunity and altered disease course during co-infection). We demonstrated the utility of Pathosim in terms of simulating and modeling various detection and surveillance systems including protocols for serosurveillance and early-detection systems based on sequencing data.

### Assessing the Impact of Non-Pharmaceutical Interventions on COVID Prevalence Using A Predator-Prey Lotka-Volterra Model Approach

*Lisa Kanary, Public Health Agency of Canada*

Understanding the dynamics of disease transmission and effective interventions is crucial due to a virus' rapid spread. Non-Pharmaceutical Interventions (NPIs) play a vital role in mitigating the spread of a virus through a population, especially when pharmaceutical interventions are limited or ineffective. Implementing NPIs (such as social distancing, face masks, hand hygiene, travel restrictions, and quarantine measures) has been essential in controlling the pandemic and reducing the burden on healthcare systems.

This study aims to investigate the relationship between NPIs and COVID prevalence. By incorporating NPIs into a modeling framework, this assessment will help determine the effectiveness of NPIs in reducing the transmission and overall prevalence of COVID-19, and effectively, disease in general.

To investigate the relationship between COVID prevalence and NPIs, we employ a predator-prey Lotka-Volterra model. The predator-prey model offers a theoretical framework that allows for the examination of the impact of NPIs on COVID transmission dynamics and provides insights into the effectiveness of these interventions in controlling disease prevalence. The insights provided by these mathematical models can inform decision-making processes for policy-makers, public health officials, and researchers, and can guide the development of targeted interventions, helping to control the spread of the virus and mitigate its impact on public health and society. Several methods for fitting model coefficients will be explored in this exercise.

### Better modeling through chemistry: quantifying COVID vaccine hesitancy

*Brian Gaas, Government of Yukon*

Much of the literature on vaccine hesitancy focuses on whether an individual receives a vaccine. However, the rate of vaccination—the number of people getting vaccinated in a given amount of time—is equally important. This work presents a conceptual framework for understanding and predicting vaccine adoption rates, following the transition state theory of chemistry.

The vaccine uptake framework hypothesizes people will only get vaccinated if their personal Vaccine Motivation exceeds a population-averaged Vaccine Hesitancy. Within the framework, Vaccine Motivation and Vaccine Hesitancy are functionally equivalent to temperature and activation energy, respectively, within the Arrhenius equation. The proportion of unvaccinated individuals getting vaccinated per unit time is related to the negative exponential of the Vaccine Hesitancy Ratio, defined as Vaccine Motivation divided by Vaccine Hesitancy. Neither Vaccine Motivation nor Vaccine Hesitancy are observable, but the Vaccine Hesitancy Ratio for a given time period can be estimated as the negative log-odds of vaccination status (individuals who changed vaccination status versus individuals who did not change status within that period). Logistic regression can be used to test whether the Vaccine Hesitancy Ratio varies over time, since it has the same log-odds form.

Dose 1 uptake rates from the Yukon (Canada) for COVID-19 were analyzed using the vaccine uptake framework. The population could be clustered into four groups of people based on how the Vaccine Hesitancy Ratio changed over time: low, medium, and high Vaccine Hesitancy Ratios, and one group who never got vaccinated. Further work could include applying clustering algorithms to better differentiate groups, identifying predictors that classify individuals into each of the four groups, and applying the vaccine uptake framework to forecast future dose uptake or uptake rates of different vaccines.

### Antigenic evolution of SARS-CoV-2 in immunocompromised hosts

*Ben Ashby, Simon Fraser University*

Prolonged infections of immunocompromised individuals have been proposed as a crucial source of new variants of SARS-CoV-2 during the COVID-19 pandemic. Longitudinal sampling of SARS-CoV-2 from immunocompromised hosts reveals evidence of accelerated adaptation relative to the wider population. In principle, sustained within-host antigenic evolution in immunocompromised hosts could allow novel immune escape variants to emerge more rapidly, but little is known about how and when immunocompromised hosts play a critical role in pathogen evolution. This talk discussed how a relatively simple mathematical model can provide powerful insights into the effects of immunocompromised hosts on the emergence of immune escape variants. Specifically, when the pathogen does not have to cross a fitness valley for immune escape to occur, a small number of immunocompromised hosts have no qualitative effect on antigenic evolution at the population-level. But if a fitness valley exists, then persistent infections of immunocompromised individuals allow mutations to accumulate so that the fitness valley can be traversed, thereby facilitating large jumps in antigenic space at the population-level. Our results suggest that better genomic surveillance of infected immunocompromised individuals and better global health equality, including improving access to vaccines and treatments for individuals who

are immunocompromised (especially in lower- and middle-income countries), may help to prevent the emergence of future immune escape variants of SARS-CoV-2.

## Toward Support for Epidemic Preparedness via Digital Twin Data + "Think Big" Proposal

*Michael Wolfson, University of Ottawa*

An essential component for pandemic preparedness is adequate data supporting ongoing analytical capacity. Since support for specialized pandemic-oriented data collection (+ analytical capacity) tends to wane between acute events, data for pandemic preparedness should, as much as possible, be designed to be useful during quiescent periods. One such kind of data is a realistic but synthetic "digital twin" that closely resembles detailed census data but is non-identifiable, hence non-confidential. Such digital twin data would provide individual-level details of Canada's population by small area geography and a range of socio-economic and infectious disease-relevant characteristics, substantially reflecting real-world heterogeneities. In turn, these data could provide a richly textured basis for more sophisticated infectious disease modeling, especially with regard to contact patterns more readily incorporated into agent-based modeling as compared to the more usual compartment models.

Such a digital twin database could be constructed by starting first with published census cross-tabs at the census tract level using simulated annealing, and then synthetically matching (with replacement) individual and household level records from census public use files, thereby substantially preserving important kinds of correlations. In addition, data from other key microdata files like the Canadian Community Health Survey (CCHS), the Labour Force Survey (LFS), and the time use results from the General Social Survey could also be synthetically matched. As these data sources are either already in the public domain, or versions could be so constructed, the resulting digital twin would also be non-confidential, hence completely open data.

Constructing this digital twin database and regularly updating it would incur considerable costs. However, it would also have a much broader range of uses than only to support epidemic modeling. With a broad range of users, it would be more easily sustained over time as a new and important addition to Canada's statistical system.

In order to keep the digital twin data current, "nowcasting" using a public domain version of Statistics Canada's DEMOSIM model could be used, along with other regular monthly data sets including the LFS and CCHS.

With the advent of an epidemic and the imposition of public health measures such as lockdowns, behaviors would change. These could be tracked via appropriately anonymized yet still geographically detailed real-time cell phone mobility data.

In sum, a well-conceived digital twin database could provide both a substantially improved real-time basis for infectious disease modeling and a substantial addition to Canada's statistical system that would have a broad range of other uses, thereby assuring its longer term sustainability.

Based on some of the preceding discussion in the conference, this presentation also offered the suggestion of "thinking big" – developing a brief for senior officials and governments outlining the idea of a digital twin along with other key improvements in linkable and coherent data flows such as infections, hospitalizations, vaccinations, and genotyping of infections. While this kind of initiative is not something fundable using the current Canadian and provincial granting council structures, there is a window of opportunity with recent reports on data from the Public Health Agency of Canada and Health Infoway, and the 2023 federal budget proposing over half a billion dollars for health data. There is also the recent Report of the Advisory Panel on the Federal Research Support System which could well open up the right kind of funding opportunities.

### Conceptual models of immunity

*Jonathan Dushoff, McMaster University*

A better understanding of patterns and processes underlying cross-immunity is needed to better understand future dynamics and burden of important diseases. Simple dynamical models of cross-immunity can often be classified as either history-based (classifying individuals by history of infections), or status-based (classifying individuals by what strains they are currently effectively immune to). There is a very strong analogy between these classifications and those of "leaky" and "polarized" vaccine models.

This talk discussed the importance of immune-boosting—that is, enhanced immune protection following an unsuccessful infection challenge—and demonstrated that a model with boosting provides a practical way to bridge between the dynamics of these two paradigms, while arguing that this mechanism is highly biologically relevant. Differences in such conceptual assumptions can lead both to different estimates of vaccine effectiveness, and different predictions about future dynamics.

### Modelling Immunity

*Jane Heffernan, York University*

'Immunity' is both a population- and an individual-level characteristic. We have developed individual- and population-level models of immunity using in-host modelling of vaccination, immune system and infection dynamics, and epidemiological models of disease spread and public health programming. In this talk, we discussed the multi-level models of immunity and their integration, which can be used to inform public health decision-makers. We focused on COVID-19 in Ontario.

## 4 Testimonials

*"The CANMOD BIRS workshop was a fabulous experience, both overall and in its specifics. Direct shuttles between Calgary and Banff, lodging and included*

*meals at the site of the conference, on-hand IT staff for presentations, giant mountains to look at... I'm not sure what else one might want for logistics. I imagine conference attendees everywhere were happy to see the people behind the Zoom and Teams screens for the first time in a few years, and this was no exception. It is perhaps the goal of every conference to provide a venue where people can learn what their colleagues are up to, and collaborate on future projects. The CANMOD workshop succeed admirably in this, and I am currently following up with a few different groups on work that was presented. My two complaints are me not bringing climbing shoes, and eating too much at the buffet dinners... both which are perfectly good problems to have."*

Brian Gaas, Government of Yukon

*"The CANMOD BIRS workshop was easily one of the best I have ever attended. All of the talks were excellent and the focus of the workshop on infectious disease modelling meant all of them were of interest to everyone. Communal meal times were also a great way to get to interact with other attendees and the small workshop size meant that, by the end of the four days, I was able to have a conversation with everyone at least once. I thoroughly enjoyed my time in Banff and left the workshop feeling reinvigorated about working on infectious disease research projects."*

Evan Mitchell, McMaster University

*"As a infectious disease epidemiologist working as a scientist at Public Health Ontario, I know the acute need for strong connections between the academic mathematical modeling community, public health, and government decision makers. At the BIRS-CANMOD meeting in November 2023, I made great connections that will support future public health responses to infectious disease threats, by supporting such connections. In addition to excellent applied presentations, we had beneficial discussions about how to strengthen public health surveillance data for respiratory infections, that could help support more robust forecasting of respiratory infections in the future."*

Kevin Brown, Public Health Ontario

*"Attending the conference was an invaluable experience that provided me with a unique platform for fostering meaningful research connections and collaboration. The opportunity to meet people in person was instrumental in developing new innovative ideas and projects geared towards enhancing future pandemic preparedness. The insights gained not only deepened my understanding of the research our CANMOD team is engaged in but also fueled a collective passion for addressing critical challenges.*

*This conference served as a catalyst for interdisciplinary discussions, sparking the exchange of ideas that have the potential to shape the future of pandemic*

*response strategies. The immersive environment facilitated networking, enabling me to connect with professionals who share a commitment to advancing our shared goals and learn from the diverse expertise of others. The experience has underscored the importance of such gatherings, emphasizing the need for more opportunities like this in the future."*

Lisa Kanary, Public Health Agency of Canada

# 5 Conclusion

A common experience since the start of the COVID-19 pandemic has been that we often meet people first virtually, and potentially never in-person. A large proportion of CANMOD's co-applicants had never met in-person before the BIRS workshop, and the opportunity to do so—for those of us who were able to attend in Banff—was greatly appreciated. For both in-person and virtual participants, the presentations and discussions were extremely valuable, and the connections made during the meeting will influence research and public health policy-making in the coming years. These types of events—which generate enthusiasm among participants for continued interactions between academics, government scientists, and policy-makers—are critical to the vision for EIDM modelling in Canada described in a white paper [7] drafted by several of the attendees together with members of other EIDM networks at an earlier BIRS meeting in January 2023. We are certain that all the attendees at the CANMOD BIRS workshop in November 2023 are looking forward to continuing to contribute to the realization of that vision!

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