# Understanding and Assessing Quantitative Modelling Research

### A Guide for Infectious Disease Public Health Professionals

Wendy Xie, PhD Seyed Moghadas, PhD Margaret Haworth-Brockman, MSc

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National Collaborating Centre for Infectious Diseases

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#### Understanding and Assessing Modelling Research Studies A Guide for Infectious Disease Public Health Professionals

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Contact us at:

#### **National Collaborating Centre for Infectious Diseases**

Rady Faculty of Health Sciences University of Manitoba Tel: (204) 318-2591 Email: <u>nccid@umanitoba.ca</u> <u>www.nccid.ca</u>

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## Understanding and Assessing Quantitative Modelling Research

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## Preface

During the early stages of the COVID-19 pandemic, at a time when there was limited knowledge and evidence, many modelling studies were published over a short period of time that presented very different results (1-15). This raised concerns about the quality of the models and results of these studies given the limited knowledge and evidence available at the time (16–18). This guide was written to help public health professionals critically assess infectious disease modelling research for application in public health. It includes considerations and guiding questions about how a disease is modelled and interpreted for real-world settings. An appropriately structured mathematical model can simulate real-world population health scenarios. For public health planning, this creates possibilities to better understand the factors that can affect interventions and their outcomes. providing information for policy decisions and resource allocation. In the context of infectious disease spread, such factors include the diversity (heterogeneity) and contact patterns in populations; the type, intensity, and effect of interventions; and strategies for prevention, treatment, and elimination. However, mathematical models are limited by how well the causes (etiological), health burden (epidemiological), and clinical aspects of the disease are understood, what is known about interactions within the population of interest, and how these vary over time depending on demogrphic, geographic, and socioeconomic characteristics.

This guide provides a way to assess the rigour and utility of modelling studies without being mired in calculations. It is designed to help readers think critically about the conclusions made by the authors of a modelling study and how the research can be applied to public health action.

#### **About this document**

This document provides an overview of how to critically assess a research article which uses quantitative, data-driven mathematical modelling to examine infectious disease transmission. Included is a Quick Reference Guide which aligns with the process of quantitative model development and the format of research articles and is meant to assist in a critical review of the research. Additional resources on mathematical modelling for public health, including the <u>Comprehensive Glossary for Infectious Disease</u> <u>Modelling</u>, can be found in Appendix: Supporting Resources.

This document does not describe qualitative modelling methods or how to interpret the results of qualitative modelling studies. It also does not attempt to rank mathematical models or research articles. It supports a critical review of modelling research studies by providing an overview of how model analyses and outcomes can be useful for public health.

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### Mathematical Modelling: what public health wants to know

Mathematical modelling research involves the development and analyses of models representing real-world phenomena to project and examine the outcomes for plausible scenarios or conditions. In public health, mathematical modelling can help to answer difficult questions and understand complex relationships among biological, epidemiological, demographic, and environmental factors in the context of infectious diseases.

Both qualitative (theoretical) and quantitative (numerical or data-driven) mathematical models can be useful for public health to examine how various interventions might perform under different conditions (19–22). Qualitative models are useful when empirical data is very limited, and a more generalizable analysis is useful. While quantitative models require much more data to inform parameters, the results tend to have more precision. Not all modelling studies are applicable to every setting or context, and all models come with limitations and are subject to uncertainty.

The assumptions and uncertainties in models resulting from insufficient data or lack of evidence should be examined in a sensitivity analysis and addressed in the discussion section to prevent misleading conclusions for public health. Despite limitations, modelling is an invaluable tool to understand the underlying mechanisms of disease spread and control and can inform evidence-based decision-making with transparency. The predictive ability of infectious disease models can be used to evaluate public health strategies and identify the most efficient and cost-effective interventions to control disease spread. For public health professionals, evaluating a model to determine whether it describes the real world accurately involves assessing the data sources and model assumptions to understand the model limitations and the constraints on the interpretations and conclusions.

## In this guide: the modelling process

This Guide describes the quantitative modelling process to help answer common questions about:

QUALITY	RELEVANCE	SIGNIFICANCE
How do I assess the	How do I determine if the	How do I efficiently
scientific foundation of a	results of a modelling study are	identify and interpret key
mathematical modelling	relevant to ongoing, past, or	findings of the modelling
study?	future public health concerns?	study?

When assessing a modelling study, it is helpful to reflect on the steps used in model development and how these translate into a scientific article. **Figure 1** shows the relationship between public health research and mathematical modelling. **Table 1** provides an overview of what to look for at each stage depicted in **Figure 1** and where to find it in a research article.



Figure 1. A simplified representation of the relationship between mathematical modelling and public health research (23,24).

Steps (and where to Where to look in What to look for look in this Guide) the article 1. Real-world infectious Introduction • Rationale based on support from existing literature or other forms of evidence, including data disease problem • Justification of how research outcomes can support public (Sections 1-3) health to improve the health and lives of the population of interest • Consideration of how the research goals can address the needs of equity-deserving populations 2. Simplifying assumptions Introduction and • Discussion of relevance and quality of data (reliability and Methods completeness) and parameter uncertainty (Sections 1-3) • Description of biological and historical characteristics of the infection and disease transmission • Description of sources of data, method of collection, ethics of data collection and use 3. Model development Methods • Discussion of the model assumptions and variables with a +h

Table 1. The general framework for assessing a quantitative mathematical modelling research article.

(Sections 3-5)		<ul> <li>Conceptualization of the model structure</li> <li>Description of model and parameter uncertainty to be addressed in sensitivity analysis</li> </ul>
4. Model analysis (Sections 5-6)	Methods and Results	<ul> <li>Description of the model at a disease-free state and/or at disease equilibrium</li> <li>Description of statistical inference of model outcomes including interventions examined</li> <li>Discussion of sensitivity and uncertainty analyses of model structure, assumptions, and parameters</li> </ul>
5. Interpretation of results and model limitations (Sections 6-7)	Discussion and Conclusions	<ul> <li>Implications of the model outcomes for public health communication, policy, and program delivery</li> <li>Comparison of findings with existing modelling research with similar structure or questions</li> <li>Discussion of model assumptions and uncertainty (i.e., data quality, depth of literature review) and how these may affect the interpretations of the outcomes</li> <li>Examination of how the study methods and results can address relevant issues related to the social determinants of health, socioeconomic disparities, and the needs of equity-deserving populations</li> <li>Discussion of future applications</li> </ul>
6. Application to the real-world problem (All sections in the Guide)	Entire article, bibliography	<ul> <li>Appropriate use of existing data and/or relevant evidence published in previous studies</li> <li>Model applicability and usefulness for public health</li> <li>Incorporation and interpretation of factors that can be related to systemic inequities in infectious disease modelling</li> </ul>

### **SECTION ONE**

### **Research question**

The research question will be the first indication of how applicable a modelling article will be to public health. The question should be stated clearly in the introduction of the article, which should also provide context and the rationale for the study. Some examples of research questions are:

- What is the optimal rate of screening to decrease syphilis in an urban population?
- What are the potential effects of three different interventions on tuberculosis incidence in a province?
- Are new intervention strategies (such as vaccination) for protection against Respiratory Syncytial Virus (RSV) disease in older adults cost-effective?

When reviewing the introduction of a research article, look for clear answers to the following questions:

- Who is the population of interest and what are the population characteristics?
- What is the infectious disease of interest and which interventions are being studied?

- Where might the population of interest become infected with the disease (e.g., within communities, households, congregate settings, or place of employment)?
- When was/is the period of possible disease transmission (i.e., time period to be studied in the model)?
- Why is the study significant for public health? What is the added value of the study? What are the gaps in knowledge being addressed?

The research question may refer to the existing evidence related to the population and disease of interest, the relevant literature and/or type of data to be used, and the type of mathematical model to be developed or adapted. It should be precise enough to be thoroughly investigated in the study (feasibility of the study) with the potential for future application. In short, assessing the relevance and clarity of the research question allows the reader to quickly determine if the study can help to address a public health problem.

## Sources of data and evidence

Quantitative models for public health should be based on high-quality data or existing evidence from the literature relevant to the research guestions. Mathematical modelling studies of infectious diseases often source data from epidemiologic investigations, health records, experimental and clinical studies, and population statistics. To ensure that the model outcomes are consistent with observed, real-life scenarios, the model parameters can be derived in a process known as fitting to the data. This is often referred to as model calibration, where parameters are estimated through a mathematical process so that the model output reflects the observed data. The data selected and the methods used to calibrate the model directly affect the model outcomes and the strength of the conclusions that can be drawn from it.

Data sources should be:

- Applicable to the study research questions (considering the population and disease of interest).
- Sufficient for model calibration (i.e., consider if there is enough quality data, or if the data are too sparse, and if the data sufficiently represent the biological progression of the disease).
- Publicly accessible or sufficiently described to allow the study design to be replicated (25).

Calibration of a model with data that are not relevant to the research question (e.g., data from a different population which may not reflect the study population) (Section 8) or with poor-quality data could result in misleading conclusions.

It can be difficult to procure high-quality data that can be used to calibrate all the model parameters (Section 4), and if the necessary data do not exist, a range of parameter values identified through an exhaustive literature review may be used in the model. Often, a combination of literature-informed and data-calibrated parameters are used in models. The amount and variation in the available data may contribute to parameter uncertainty and should be clearly described in the methods of the study (e.g., the study authors may comment on how noisy and complete the data are). Similarly, there may be uncertainty in parameters informed by the literature, and both literature-informed and datacalibrated parameters require thorough review in a sensitivity analysis (Section 5)(26).

### **SECTION THREE**

### **Model variables and structure**

The study introduction and methods should include a clear description of the biological processes which are relevant to the assumptions used to inform the model structure and variables. These may include the natural history and characteristics of the pathogen (e.g., different stages of illness, mode of transmission, infectious period, disease severity) (19), population demographics, and public health interventions. (e.g., vaccination, school closure, masking). The clarity and the precision of how the relationships between model parameters, variables, and the proposed interventions are described help determine the applicability and confidence of the results to the real-world problem.

As previously mentioned, a model uses mathematical concepts to describe a simplified version of a real-world scenario (Section 2). These concepts (also called the structural framework) represent the relationship between the assumptions made about disease progression and transmission and the model variables (27). The authors should describe how the selection of model variables and structure allows for the research question(s) to be examined. The model variables may represent aspects of the disease biology or population characteristics that can influence the transmission of a pathogen. Interventions to be examined (e.g., vaccination, quarantine, social distancing) may also be incorporated into the model structure or parameters.

**Figure 2** is an example of a simple model structure where the clinical progression of disease – susceptible, exposed (i.e., latently infected, non-infectious), infectious, and recovered health states – are represented by a series of compartments (a compartmental model) (19). The purple arrows between model compartments correspond to the rates at which individuals move from one health state to another; different rates can be represented by different parameters in the model. A more complex model might use separate compartments to include other clinical states of a disease (e.g., incubation period, presymptomatic, symptomatic, asymptomatic) (19).

In the model development process, compartments may be added or removed based on the research question and the biology of the disease being represented. The addition of compartments in the model typically increases the number of parameters, which adds complexity and uncertainty to the model. However, if data are available or if parameter values already exist in the literature, the model can be expanded without significant changes to uncertainty.

#### **Model Compartments**



**Figure 2.** A simple compartmental model of susceptible, exposed (latent), infectious, and recovered health states and the corresponding progression of clinical disease (19).

In some cases, a specific model structure may not be able to accurately represent the observed patterns of a disease outbreak or epidemic. This may be due to a lack of model parameters or variables (e.g., important disease stages or population characteristics are missing), or because the assumptions used to create the model framework are inaccurate. Before conducting numerical analysis of the hypothetical scenarios, the authors may undergo a model selection process to determine which model framework is best able to represent the known biology of the disease and the real-world scenario (i.e., best-fit model). If a model selection process is used, the authors should describe the qualities of each model and the methods used to determine the best-fit model (usually provided in a table in the article). The selected model can then be used to analyze different scenarios (e.g., public health interventions).

To ensure the study design is reproducible, the mathematical concept of the model should be included in the Methods section, supplementary materials, or other publicly accessible forums (e.g., GitHub). A schematic or simplified representation of the model structure is usually presented as a figure.

### **SECTION FOUR**

## **Model parameters**

A mathematical model establishes a relationship between variables and parameters intended to portray a real-life public health concern (28). The parameters in infectious disease modelling represent rates or probabilities of disease progression, disease spread, and/or the effect of interventions in the model. In **Figure 2**, the arrows between compartments depict the transition between disease states and are associated with different rates of disease progression.

Model parameters values can be informed through literature reviews or calibrated using empirical data that are relevant to the disease biology and epidemiology. The model parameters used in a research article may be found in:

- A series of equations used to describe the disease in the model, represented by some mathematical symbols.
- A table with representative symbols, definitions/descriptions, values or ranges, and references/sources for their quantification.

Authors may compare models with different numbers of well-supported parameters to weigh model accuracy in representation of an infectious disease (i.e., through comparison of qualitative or quantitative models to the observed biology or available datasets) against model uncertainty (29). This comparison helps to identify the model structure and parameters The number of parameters used in a model depends on many factors. First it is necessary to consider parameters that are directly related to the research question. It is also necessary to consider uncertainty in parameter values. This can be informed through literature reviews and the availability of representative data. There are times when a more complex model may fit the data better than a model with fewer parameters. However, this does not mean that a model with more parameters is more accurate; a model with parameters that have been "overfit" to data is an important example.

A model can be overfit to data in various ways, which can include (28):

- An overly complex model framework/ structure.
- Alternative parameter values used to fit the data which may not be biologically relevant or have much uncertainty.

An overfit model is not useful for the analysis of public health interventions since there is little confidence in the model results given the large uncertainties lying within its framework and parameters.

that are needed to represent the disease biology accurately while reducing uncertainty. Bayesian information criterion (BIC) and the Akaike information criterion (AIC) are examples of commonly used methods to compare models with different parameter sets (30). Models with fewer parameters that capture the key aspects of the disease and address the research question are more suitable, especially when the authors can satisfactorily explain their rationale for the assumptions (a more parsimonious model). Authors justify their assumptions based on the biology of the disease, the research question, and the availability of empirical data (31,32). Parameter uncertainty in the model should be addressed in the sensitivity analysis (see below)(33).



### **SECTION FIVE**

## **Model uncertainty**

The usefulness of a mathematical model in public health decision-making depends on the model's predictive value and the strength of the conclusions drawn from the model outcomes. Every model relies on simplifying assumptions due to the limited availability of empirical data, making uncertainty inevitable.

Identifying the major sources of uncertainty in the model involves reviewing existing literature and logic and through assessing any available empirical data that can be used to calibrate unknown parameters. Researchers can try to examine the degree to which uncertainty in the parameters leads to variation in the outcomes of interest using a sensitivity analysis. Without addressing parameter uncertainty, it would be difficult for a reader to determine how applicable the simulated scenarios are for public health planning. Sensitivity analysis is an essential step in understanding how the reported outcomes should be interpreted and applied to real-world scenarios (28,34).

# Understanding sensitivity analyses

A sensitivity analysis measures how the model outcome changes when the literature- or data-informed parameter values are varied across plausible ranges of biologically relevant values. Univariate sensitivity analysis identifies the type of relationship between individual parameters and the model outcomes. Once these relationships have been determined, a multivariate sensitivity analysis can assess how the model outcomes change when multiple parameters are varied across their respective ranges simultaneously. Such analysis identifies parameters that have significant influence on the results when the uncertainty of all parameters is considered (35). Small changes to parameters may result in large variations in the model outcomes, which are important to consider in the interpretation of the model outcomes when:

- The parameter is related to the biological process of the disease which influences transmission dynamics. The parameter should be well-informed using either high-quality data or drawn from existing literature, which can help to limit parameter uncertainty and strengthen the conclusions drawn.
- The parameter is related to interventions in the simulated scenarios, and therefore determines how effective a particular intervention may be.

Sensitivity analysis can play an important role in parameter estimation studies. It helps to identify parameters that have a high level of uncertainty, which may also have significant influence on model outcomes. This would imply that further collection of empirical data may be needed to better inform future models of the biological processes and interventions. A range of model outcomes as a result of parameter uncertainty may be presented with statistically calculated means and confidence intervals.

#### Interpretation and implications

The results section of the article will often describe the most influential parameters identified using sensitivity analysis. Depending on what a parameter represents in the model, an influential parameter can have different implications for the real-world scenarios. For example, if a vaccination rate is found to be the most influential intervention-related parameter in a model used to estimate epidemic size, increasing vaccination can further reduce the epidemic size compared to the other simulated interventions. The Discussion and Conclusions sections of the article should further elaborate on the implications of the range of outcomes resulting from parameter variation and how this may affect public health policy decisions.



### **SECTION SIX**

## **Model results**

The results of a mathematical modelling study may present the estimated parameters and/or outcomes related to the disease processes, population dynamics, or the effect of intervention measures. The following is a general framework for the results section of modelling research, which may vary between studies:

#### Initial conditions and model equilibria:

- Description of how the model captures key aspects of the disease-free state and/or an endemic equilibrium (when the number of infections neither dies out nor increases rapidly, or a steady state). In quantitative models, these conditions are related to the model parameters, which are calibrated using empirical data or derived from the literature.
- Presentation of parameter estimates which were fit to data (usually in a table).
- Description of areas (if any) in which the model output deviates from the empirical data.

## Key findings related to the simulated scenarios of potential interventions and how they affect the model outcome of interest:

- Presentation of the range of potential outcomes depending on the scenarios explored using the model, usually with confidence/credible intervals, or some range of uncertainty (7).
- Description of how various degrees of intervention (in addition to other factors explored in the model) affect the outcome of interest. For example, the results can show how varying degrees of vaccine uptake can lead to a range of epidemic outcomes.

#### Sensitivity analysis (more in Section 5):

- Identification of the major sources of uncertainty in relationships between the parameters and the outcome of interest.
- Quantification of the degree of influence the model parameters have on the outcome of interest (e.g., changes in a certain parameter may result in large fluctuations in the model outcome of interest).

The major findings of the study are generally presented in the text, tables, and figures, with a focus on how the model outcomes have addressed the research question(s). Generated results should be interpreted for application in public health in the Discussion and Conclusions sections of the article.

### **SECTION SEVEN**

### **Discussion and conclusions**

The Discussion section interprets study results with an emphasis on the implications for public health decision-making and how the results of the current study compare to existing research. It should be clear how the authors arrived at the interpretations of the model results and include support and comparisons from other modelling studies.

Depending on the research questions, the Discussion section of a modelling study should include the following:

- A brief review of the research questions that the authors aimed to answer, how this was achieved, and a summary of the key findings.
- Interpretation of the study's results and how the model outcomes can be applied to inform public health interventions, resource allocation, and policy decisions for realworld scenarios.
- Comparison of the current study methods, results, and interpretation with existing studies in the field and a discussion of the similarities and differences. Most importantly, any differences between the presented results and previous work should be further interpreted and justified. For example, the discussion should explain if the differences in the outcomes were due to different model assumptions, the parameter values used, different datasets used to calibrate the model and/or if different methods were used for this calibration.

It should also elaborate on the implications for public health programming as a result of differing results.

A discussion of how the model assumptions and the availability of high-quality data for model calibration may affect the model outcomes.

This includes justification for important model assumptions, interpretation of the sensitivity analysis and how these factors may affect the implications of the study.

Description and justification of model limitations and how they were accounted for in the model assumptions and the interpretations of the model results.

Finally, the authors should address the gaps in knowledge which remain unaddressed, and how this study can be used directly or indirectly in subsequent work. This may include suggestions for further data collection that can be used to improve model calibration and development, expanding the current model framework to examine more components of the disease transmission system, and/or incorporating different intervention strategies.

The Discussion section is an opportunity for the authors to aid the reader in a critical assessment of the research conducted, but it is important to review relevant literature outside of what may be referenced in the study to inform the reader's opinion of the validity of the model, its assumptions, results, and interpretations.

### **SECTION EIGHT**

### **Other considerations**

#### Mathematical modelling with an equity lens

#### The determinants of health

Biological, social, economic, environmental, and structural determinants of health can influence the dynamics of disease transmission and the efficacy of public health interventions in different communities (36,37). When assessing the study research question(s), it is important to consider how the model outcomes may vary depending on the population being studied. The implications of the model outcomes for public health may also be different for equitydeserving groups compared to those for the general population. Studies that focus on equitydeserving communities should clarify how the research aims to address distinct priorities in these communities without drawing from or highlighting existing stereotypes and stigma. Click here for more information on the language of health equity (38).

The determinants of health (e.g., income levels, urban or rural residence, sex, and gender) should be considered in the model development and the proposed interventions whenever possible to best represent disease transmission, prevention, and control in the study population. Language and framing should recognize the context and nuances of the public health issues from the perspective of the individuals within the community for which the research is being conducted. Not all modelling studies are able to examine the disproportionate effects of an infectious disease on different populations, often due to a lack of data or privacy concerns. If not directly addressed in the research question, the model outcomes may have different implications for public health programming depending on the population of interest. The authors may provide alternate interpretations of the results for different populations in the Discussion section. Input from individuals in the population of interest and existing evidence from the literature may be provided to support the validity of these alternate interpretations.

#### **Disaggregated data**

Aggregated data are commonly used to inform model parameter values. Using aggregated data means that different sub-populations or communities may not be precisely represented in the model, and differences which may affect disease biology and epidemiology between subpopulations may not be accurately accounted for. If the aggregated data come with some knowledge of the distribution of the study population (not just the mean, or average, of the population), this knowledge can be used to examine outcomes outside of the average. A lack of disaggregated data, or data which contains information from sub-populations or communities of interest, can also be accounted for in the sensitivity analysis.

When there are sufficient data to use disaggregated data in modelling, the effects of different outbreak scenarios and the implications of interventions within sub-populations that were previously hidden may become visible, thus providing an equity lens. Modelling with an equity lens should highlight existing health inequities respectfully and responsibly through collaboration with the sub-population for which the research is being conducted, starting from the conceptualization of the research questions. The goal of modelling with an equity lens is to provide evidence for more targeted public health policies and intervention strategies to support equity-deserving communities.

#### Interpretation

As discussed in Section 1 (Research question) and Section 2 (Data collection sources and selection), other determinants of health may be considered in modelling studies in other ways than modelling to the average population. If determinants of health were not addressed in the current study, the reader may ask the following questions:

- Why was this study not able to apply an equity lens? Was it due to a lack of data or access to data?
- Could the interpretations outlined in the study be reasonably applied to equitydeserving communities considering the determinants of health?

How would the interpretations of the model outcomes for a specific equity-deserving population differ from the interpretations reported in the study? If the study explicitly examines how determinants of health affects disease outcomes, transmission dynamics, and the effects of interventions, the reader may consider the following questions:

- Is the representation of the public health issue affecting the population of interest appropriate? Do the research questions and model assumptions account for the determinants of health?
- Are there any other factors (e.g., societal, historical, cultural) that the model or interpretation has not accounted for that may have different implications for public health?

How might the interpretations of the model outcomes change if these other factors are accounted for?

How do the interpretations of this study compare to other studies that did not include an equity lens, and what are the public health implications?

In a good modelling study, questions like those above will have already been addressed in the Discussion section, even if the study did not directly examine specific determinants of health.

### All models have uncertainty

All models have uncertainty, but uncertain models can still be insightful and useful for public health. The original aphorism "all models are wrong, but some are useful" is generally attributed to statistician George Box from his article, Science and Statistics published in 1976, but the concept predates Box's article

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(32). The phrase 'all models are wrong' can now be updated to "all models have uncertainty, but uncertain models can still be insightful". This updated phrase reflects our improved knowledge of mathematical modelling and the availability of new methods but retains the original meaning that a model cannot perfectly capture the complexity and uncertainties of realworld situations.

The usefulness of a quantitative model depends on the strength of the research question, the quality of the data used, the thoroughness of the analysis (including the sensitivity analysis), and a discussion of how the model assumptions could affect the results and interpretations of the model outcomes (more on uncertainty in Section 5) (25,26). Often, both reasonable and simplifying assumptions are used in models (find descriptions below). Wrong assumptions are those which do not align with the biology of the disease or the transmission dynamics and should therefore not be included in a model.

**Reasonable assumptions** are usually those supported by expert opinion/ observation and/or existing research and data in the field. Although reasonable assumptions should still be considered in the interpretation of the model outcomes, they may not cause the interpretation of the model outcome to differ significantly from the real-world scenario.

**Simplifying assumptions** may be made during the modelling process, often due to a lack of existing data and knowledge, or a need to reduce the complexity of the model. With proper consideration and interpretation, it is not necessarily detrimental to have simplifying assumptions in a model. However, the study must acknowledge and discuss the influence of these assumptions on the model outcomes (32).

When assessing model uncertainties and limitations, it is important to note that the goal of infectious disease modelling is to support the development of public health policies and not to generate exact predictions. Often, the reader's and a review of the relevant literature are required to determine how adequate and useful a modelling study may be.



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## References

- 1. Wells CR, Townsend JP, Pandey A, et al. Optimal COVID-19 quarantine and testing strategies. *Nat Commun*. 2021;12(1). doi:10.1038/S41467-020-20742-8
- 2. Chin V, Ioannidis JPA, Tanner MA, Cripps S. Effect estimates of COVID-19 non-pharmaceutical interventions are non-robust and highly modeldependent. *J Clin Epidemiol*. 2021;136:96. doi:10.1016/J.JCLINEPI.2021.03.014
- 3. Xue L, Jing S, Wang H. Evaluating the impacts of non-pharmaceutical interventions on the transmission dynamics of COVID-19 in Canada based on mobile network. *PLoS One*. 2021;16(12). doi:10.1371/JOURNAL.PONE.0261424
- Chowdhury R, Heng K, Shawon MSR, et al. Dynamic interventions to control COVID-19 pandemic: a multivariate prediction modelling study comparing 16 worldwide countries. *Eur J Epidemiol.* 2020;35(5):389. doi:10.1007/S10654-020-00649-W
- Ferretti L, Wymant C, Kendall M, et al. Quantifying SARS-CoV-2 transmission suggests epidemic control with digital contact tracing. *Science (1979)*. 2020;368(6491). doi:10.1126/SCIENCE.ABB6936
- Wang S, Ramkrishna D. A model to rate strategies for managing disease due to COVID-19 infection. *Sci Rep.* 2020;10(1). doi:10.1038/S41598-020-79817-7
- Kwon O, Son WS, Kim JY, Kim JH. Intervention effects in the transmission of COVID-19 depending on the detection rate and extent of isolation. *Epidemiol Health*. 2020;42. doi:10.4178/EPIH. E2020045
- Son WS, Team Risewid. Individual-based simulation model for COVID-19 transmission in Daegu, Korea. *Epidemiol Health*. 2020;42. doi:10.4178/EPIH. E2020042
- Pei S, Kandula S, Shaman J. Differential effects of intervention timing on COVID-19 spread in the United States. *Sci Adv*. 2020;6(49). doi:10.1126/ SCIADV.ABD6370
- 10. Jackson ML. Low-impact social distancing interventions to mitigate local epidemics of SARS-CoV-2. *Microbes Infect.* 2020;22(10):611. doi:10.1016/J.MICINF.2020.09.006

- 11. Id HC, He J, Song W, Wang L, Wang J, Chen Id Y. Modeling and interpreting the COVID-19 intervention strategy of China: A human mobility view. Published online 2020. doi:10.1371/journal. pone.0242761
- 12. Shinde GR, Kalamkar AB, Mahalle PN, Dey N, Chaki J, Hassanien AE. Forecasting Models for Coronavirus Disease (COVID-19): A Survey of the State-of-the-Art. *SN Comput Sci.* 2020;1(4). doi:10.1007/S42979-020-00209-9
- Zebrowski A, Rundle A, Pei S, et al. A Spatiotemporal Tool to Project Hospital Critical Care Capacity and Mortality From COVID-19 in US Counties. *Am J Public Health*. 2021;111(6):1113-1122. doi:10.2105/AJPH.2021.306220
- Santosh KC. COVID-19 Prediction Models and Unexploited Data. *J Med Syst.* 2020;44(9). doi:10.1007/S10916-020-01645-Z
- 15. Shah K, Abdeljawad T, Mahariq I, Jarad F, Deniz S. Qualitative Analysis of a Mathematical Model in the Time of COVID-19. *Biomed Res Int.* 2020;2020. doi:10.1155/2020/5098598
- Bagdasarian N, Cross GB, Fisher D. Rapid publications risk the integrity of science in the era of COVID-19. *BMC Med.* 2020;18(1):1-5. doi:10.1186/ s12916-020-01650-6
- 17. Jalali MS, DiGennaro C, Sridhar D. Transparency assessment of COVID-19 models. *Lancet Glob Health.* 2020;8(12):e1459-e1460. doi:10.1016/ S2214-109X(20)30447-2
- 18. Eker S. Validity and usefulness of COVID-19 models. *Humanit Soc Sci Commun.* 2020;7(1). doi:10.1057/ s41599-020-00553-4
- 19. Milwid R, Steriu A, Arino J, et al. Toward standardizing a lexicon of infectious disease modeling terms. *Front Public Health.* 2016;4(SEP). doi:10.3389/FPUBH.2016.00213
- 20. van Harmelen F, Lifschitz V, Porter B. *Handbook of Knowledge Representation*. Elsevier Science; 2008. doi:10.1016/S1574-6526(07)03009-X
- 21. Justus J. Loop analysis and qualitative modeling: Limitations and merits. *Biol Philos.* 2006;21(5):647-666. doi:10.1007/s10539-006-9050-x

### **References** continued

- 22. Justus J. Qualitative Scientific Modeling and Loop Analysis. *Philos Sci*. 2005;72(5):1272-1286. doi:10.1086/508099
- 23. Kretzschmar M. Disease modeling for public health: added value, challenges, and institutional constraints. *J Public Health Policy*. 2020;41(1):39-51. doi:10.1057/s41271-019-00206-0
- 24. NCCID. Promising Practices in Public Health: Behind the Curtain of Mathematical Modelling.; 2018.
- Eddy DM, Hollingworth W, Caro JJ, Tsevat J, McDonald KM, Wong JB. Model transparency and validation: A report of the ISPOR-SMDM modeling good research practices task force-7. *Value in Health*. 2012;15(6):843-850. doi:10.1016/j. jval.2012.04.012
- Briggs AH, Weinstein MC, Fenwick EAL, Karnon J, Sculpher MJ, Paltiel AD. Model parameter estimation and uncertainty: A report of the ISPOR-SMDM modeling good research practices task force-6. *Value in Health*. 2012;15(6):835-842. doi:10.1016/j.jval.2012.04.014
- 27. Moghadas S, Laskowski M. *A Logical Modelling Framework for Influenza Infection*.; 2014. www. ccnmi.ca.
- 28. Basu S, Andrews J. Complexity in Mathematical Models of Public Health Policies: A Guide for Consumers of Models. *PLoS Med*. 2013;10(10). doi:10.1371/journal.pmed.1001540
- 29. Moghadas SM, Haworth-Brockman M, Isfeld-Kiely H, Kettner J. Improving public health policy through infection transmission modelling: Guidelines for creating a community of practice. *Canadian Journal of Infectious Diseases and Medical Microbiology.* 2015;26(4):191-195. doi:10.1155/2015/274569
- Burnham KP, Anderson DR. Multimodel inference: Understanding AIC and BIC in model selection. *Sociol Methods Res.* 2004;33(2):261-304. doi:10.1177/0049124104268644
- Vandekerckhove J, Matzke D, Wagenmakers EJ. Model Comparison and the Principle of Parsimony. Oxford University Press; 2015.
- 32. Box GEP. Science and Statistics. *J Am Stat Assoc.* 1976;71(356):791-799.

- 33. Okaïs C, Roche S, Kürzinger ML, et al. Methodology of the sensitivity analysis used for modeling an infectious disease. *Vaccine*. 2010;28(51):8132-8140. doi:10.1016/j.vaccine.2010.09.099
- 34. Choisy M, Guégan JF, Rohani P. *Mathematical Modeling of Infectious Diseases Dynamics*.; 2007.
- 35. Okaïs C, Roche S, Kürzinger ML, et al. Methodology of the sensitivity analysis used for modeling an infectious disease. *Vaccine.* 2010;28(51):8132-8140. doi:10.1016/j.vaccine.2010.09.099
- Rozins C, Silk MJ, Croft DP, et al. Social structure contains epidemics and regulates individual roles in disease transmission in a group-living mammal. *Ecol Evol*. 2018;8(23):12044-12055. doi:10.1002/ece3.4664
- Reumers L, Bekker M, Hilderink H, Jansen M, Helderman JK, Ruwaard D. Qualitative modelling of social determinants of health using group model building: the case of debt, poverty, and health. *Int J Equity Health.* 2022;21(1). doi:10.1186/s12939-022-01676-7
- National Collaborating Centre for Determinants of Health. *Let's Talk: Language of Health Equity.*; 2023. 1.

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## **Appendix: Supporting Resources**

The following resources provide additional information about mathematical modelling of infectious diseases.

### **Infectious Disease Modelling Terminology**

 NCCID Comprehensive Glossary of Modelling Terms <u>https://nccid.ca/comprehensive-glossary-infectious-disease-modelling/</u>

### **Mathematical Modelling in Public Health**

- Mathematical Modelling in Public Health
   <u>https://nccid.ca/project-stream/mathematicalmodelling/</u>
- Mathematical Modelling in Public Health Planning: Flu Vaccine <u>https://nccid.ca/publications/mathematical-modelling-in-public-health-planning-flu-vaccine/</u>
- Mathematical Modelling in Public Health: Tuberculosis
   <u>https://nccid.ca/publications/mathematical-modelling-in-public-health-tuberculosis/</u>
- A Logical Modelling Framework for Influenza Infection <u>https://nccid.ca/publications/a-logical-modelling-framework-for-influenza-infection/</u>



22 Understanding and Assessing Quantitative Modelling Research

# QUICK REFERENCE GUIDE

Use the questions in this guide to help critically assess quantitative modelling studies for public health

#### **RESEARCH QUESTION**

How feasible and useful are the proposed interventions and model scenarios for public health programming?

#### DATA FOR CALIBRATION

Are the data appropriate for the study population and of sufficient quality to address the research question?

#### METHODOLOGY

What kind of model and methods are used for analysis, and does it make sense for the research question and the population of interest?

#### INTERPRETING MODEL OUTCOMES

What are the implications of the results for your work in public health policy, communication, and programming?

What influential factors were identified in uncertainty/sensitivity analysis that may have implications for your work?

How does the interpretation of these model outcomes compare to existing knowledge and other models?

#### **MODEL BUILDIING**

How well do the model structure and parameters reflect the biology of the disease and transmission dynamics?

What are the model assumptions in this study and and how are they justified?



#### **MODEL LIMITATIONS**

How do the model limitations affect interpretation of the outcomes?

What are the opportunities for future research and data collection based on the limitations of this model and study?



## MODELLING WITH AN EQUITY LENS

Does this modelling study consider any disproportionate effects the disease may have on different populations? If yes, how nuanced is this representation?

If not, how can this model be applied to better examine the needs of equitydeserving populations?

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