Planning for and using modelling studies in public health evidence synthesis

Carlos Canelo-Aybar
Iberoamerican Cochrane Centre
Conflict of interest

• I am a member of the GRADE working group.

• I am a full-time employee at the Iberoamerican Cochrane Centre

• No other relevant conflict of interest
Agenda

• Introduction

• Planning of SRs of modeling studies

• GRADE approach for modeling studies
Why models?

• “A framework representing variables and their interrelationships to describe observed phenomena or predict future events”

• Modelling studies are particularly relevant when there is limited evidence, no RCTs (i.e. it is not feasible or is unethical) or observational studies, or when there is a need to extrapolate results to different target groups or to a long horizon time
Mathematical modelling studies typically address complex situations and tend to rely more heavily on assumptions about underlying mathematical structure than on individual-level data.

Statistical modelling is typically concerned with characterizing sources of variation and associations between variables in observed individual-level data drawn from a target population of interest and tends to address questions of a narrower scope than mathematical models.

The results from statistical analyses of empirical data often inform mathematical models.
model

- **simple**
  baseline risk $\times$ relative risk reduction = risk difference

- **Sophisticated (decision analytical models)**
  markov, S-I-R, discrete event simulation...
Models in the Development of Clinical Practice Guidelines

J. Dil T Habbema, PhD; Timothy J. Wilt, MD, MPH; Ruth Etzioni, PhD; Heidi D. Nelson, MD, MPH; Clyde B. Schechter, MD, MA; William F. Lawrence, MD, MS; Joy Melnikow, MD, MPH; Karen M. Kuntz, ScD; Douglas K. Owens, MD, MS; and Eric J. Feiner, PhD

Clinical practice guidelines should be based on the best scientific evidence derived from systematic reviews of primary research. However, these studies are often not available evidence needed by guideline development groups to evaluate the tradeoffs between benefits and harms. In this article, the authors identify 4 areas where models can bridge the gaps between published evidence and the information needed for guideline development, applying new or updated information on risks, diagnostic test properties, and treatment efficacy; exploring a more complete array of alternative intervention strategies; assessing benefits and harms over a lifetime horizon; and projecting outcomes on the conditions for which the guideline is intended. The use of modeling as an approach to bridge these gaps (provided that the models are high-quality and adequately validated) is considered. Colorectal and breast cancer screening are used as examples to show the utility of models for these purposes. The authors propose that a modeling study is most useful when strong primary evidence is available to inform the model but critical gaps remain between the evidence and the questions that the guideline group must address. In these cases, model results have a place alongside the findings of systematic reviews to inform health care practice and policy.

For author affiliations, see end of text.

OPINION ARTICLE

Developing WHO guidelines: Time to formally include evidence from mathematical modeling studies [version 1; referees: awaiting peer review]

Matthias Egger1,2, Leigh Johnson2, Christian Althaus1, Anna Schöni1, Georgia Salanti1, Nicola Low1, Susan L. Norris3

1Institute of Social and Preventive Medicine (ISPM), University of Bern, Bern, 3012, Switzerland
2Centre for Infectious Disease Epidemiology and Research (CIDER), University of Cape Town, Cape Town, 7925, South Africa
3World Health Organization, Geneva, Switzerland


Abstract

Open Peer Review
Referee Status: AWAITING PEER
[Rapid Review]

Travel-related control measures to contain the COVID-19 pandemic: a rapid review

Jacob Burns1,2a, Ani Movsisyan1,2b, Jan M Stratil1,2, Michaela Coenen1,2, Karl MF Emmert-Fees3, Karin Geffert1,2, Sabine Hoffmann1,2, Olaf Horstic4, Michael Laxy1, Lisa M Pfadenhauer1,2, Peter von Philipsborn1,2, Kerstin Sell1,2, Stephan Voss1,2, Eva Rehfuess1,2

1Institute for Medical Information Processing, Biometry and Epidemiology, IBE, LMU Munich, Munich, Germany. 2Pettenkofer School of Public Health, Munich, Germany. 3Institute of Health Economics and Health Care Management, Helmholtz Zentrum München, Munich, Germany. 4Heidelberg Institute of Global Health, Heidelberg University, Heidelberg, Germany

aThese authors contributed equally to this work. bThese authors contributed equally to this work

Selection criteria

We considered experimental, quasi-experimental, observational and modelling studies assessing the effects of travel-related control measures affecting human travel across national borders during the COVID-19 pandemic. We also included studies concerned with severe
Overview of systematic reviews (preliminary results)

• January 2018 to June 2021 (Medline, EMBASE, Cochrane Library)

• Systematic reviews including only modeling studies to inform effectiveness or cost-effectiveness

• 27 SRs already preliminary included in the overview
Overview of systematic reviews (preliminary results)

• 3 SRs applied the GRADE approach concepts to assess the certainty of evidence (all related to COVID19).

• 7 SRs (26%) used instruments to assess the quality/credibility of studies specifically tailored to model studies (i.e. Philips checklist).

• Most SRs did not assess the quality/RoB of studies.
Planning a SRs of modelling studies

• Some common components
  • Population
  • Intervention (might be more complex or include combinations)
  • Comparator
  • Outcomes (patient important outcomes)

• Search strategy:
  • Consult a medical librarian
  • Might include specific terms for modeling studies (i.e. "Decision Support Techniques"[MeSH Terms])
Planning a SRs of modelling studies

• Other aspects might differ
  • Conceptualization
  • Risk of bias (quality assessment)
  • GRADE approach
Conceptualization

Researches should start by designing a conceptualizing the problem and the ideal target model that would best represent the actual phenomenon they are considering.
Risk of bias (credibility/quality)

• Search for tools tailored to modeling studies (i.e. Philips, ISPOR)

• Credibility of model: model development and analysis

• Be aware that some items might cover different aspects of the certainty of evidence
  • Relevance = indirectness
  • Might include questions about reporting or input data (assesses separately with GRADE)
GRADE approach for modeling studies

GRADE conceptual papers discuss concepts that may not have been piloted on examples and that may not result in GRADE guidance.

GRADE guidance papers provide specific guidance on how to make judgments in line with the GRADE methodology. GRADE guidance papers will typically include examples how to apply the guidance.
main points

- 3 scenarios:
  1. develop a new model
  2. use off-the-shelf or adapt an existing model
  3. use results from multiple existing models
  4. forgo modelling
Systematically search for existing models meeting pre-specified criteria.

Existing model(s) found?

Is it possible to choose one “optimal” model with clearly highest certainty?

Are there just one model?

Assess certainty of outputs for each single model:
1. Risk of bias
2. Credibility of the model itself
3. Certainty of all its inputs
4. Precision
5. Consistency
6. Risk of publication bias

Is it possible and useful to adapt one of existing “suboptimal” models?

Consider model averaging when appropriate

Assess certainty of outputs across all included models:
1. Risk of bias
2. Credibility of the model itself
3. Certainty of all its inputs
4. Precision
5. Consistency
6. Risk of publication bias

Use single existing “suboptimal” model (report certainty and its limitations)

Use single “optimal” model (off-the-shelf)

May need to forgo formal modelling

Is formal modelling necessary and/or beneficial?

May forgo formal modelling

Can you develop your own model?

Develop your own model and assess certainty of its outputs

Can you develop your own model?

Develop your own model and assess certainty of its outputs

Assess certainty of outputs for each single model:
1. Risk of bias
2. Credibility of the model itself
3. Certainty of all its inputs
4. Precision
5. Consistency
6. Risk of publication bias

Use single existing “suboptimal” model (report certainty and its limitations)

Is there just one model?
Systematically search for existing models meeting pre-specified criteria

Is formal modelling necessary and/or beneficial?

Is it possible to choose one “optimal” model with clearly highest certainty?

Is it possible and useful to adapt one of existing “suboptimal” models?

Develop your own model and assess certainty of its outputs

Use single “optimal” model off-the-shelf

Adapt an existing “suboptimal” model and assess certainty of its outputs
Is there just one model?

no

Is it possible and useful to adapt one of existing “suboptimal” models?

no

Can you develop your own model?

no

Use multiple models

Consider model averaging when appropriate

Assess certainty of outputs across all included models:
1. risk of bias:
   - credibility of the model itself
   - certainty of all its inputs
2. directness
3. precision
4. consistency
5. risk of publication bias

yes

Adapt an existing “suboptimal” model and assess certainty of its outputs

yes

Develop your own model and assess certainty of its outputs

Use single existing “suboptimal” model (report certainty and its limitations)
Risk of bias domain (GRADE)

Input

Model ("black box")

Output

Certainty of each input

Credibility of a model

Risk of bias of output (modelled evidence)
Risk of bias (input data)

Certainty of evidence in each of model inputs (II)

• Certainty of evidence across all model inputs should be limited by the lowest certainty rating for any body of evidence (input data) to which the model output(s) have been found sensitive

• Examination of the results of back-end sensitivity analyses
Risk of bias (model credibility)

- **Credibility of the model**: its conceptualization, structure, calibration, validation, and other factors.

- Determinants of model credibility are likely to be specific to a modelling discipline.
Conclusions

• Modeling studies are an important source of evidence

• There is room for improvement in the methodology to conduct SRs of modeling evidence

• The GRADE conceptual paper presents a framework to assess modeling evidence
THANKS