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.

Egger M et al. 2017 PMID: 29552335

model

- simple

  baseline risk x relative risk reduction = risk difference

- Sophisticated (decision analytical models)

  markov, S-I-R, discrete event simulation…

RESEARCH AND REPORTING METHODS | Annals of Internal Medicine

Models in the Development of Clinical Practice Guidelines

J. Dik F. 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. Feuer, PhD

Clinical practice guidelines should be based on the best scientific evidence derived from systematic reviews of primary research. However, these studies often do not provide 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 disease risk, 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 for 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.

Ann Intern Med. 2014;161:812-818. doi:10.7326/M14-0845 www.annals.org
For author affiliations, see end of text.

OPINION ARTICLE

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

Matthias Egger[1,2], Leigh Johnson[2], Christian Althaus[1], Anna Schöni[1], Georgia Salanti[1], Nicola Low[1], Susan L. Norris[3]

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

v1 **First published:** 29 Aug 2017, **6**:1584 (doi: 10.12688/f1000research.12367.1)
Latest published: 29 Aug 2017, **6**:1584 (doi: 10.12688/f1000research.12367.1)

Abstract

Open Peer Review

Referee Status: *AWAITING PEER*

Cochrane Library
Trusted evidence.
Informed decisions.
Better health.

Cochrane Database of Systematic Reviews

[Rapid Review]

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

Jacob Burns[1,2a], Ani Movsisyan[1,2b], Jan M Stratil[1,2], Michaela Coenen[1,2], Karl MF Emmert-Fees[3], Karin Geffert[1,2], Sabine Hoffmann[1,2], Olaf Horstick[4], Michael Laxy[3], Lisa M Pfadenhauer[1,2], Peter von Philipsborn[1,2], Kerstin Sell[1,2], Stephan Voss[1,2], Eva Rehfuess[1,2]

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

[a]These authors contributed equally to this work. [b]These 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 effectivenes 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 specfically tailored to model studies (i.e. Philips checklist)
- Most SRs did not asesses 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 asseessment)
  - 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 ítems might cover different aspects of the certainty of evidence
  - Relevance= indirecteness
  - Might include questions about reporting or input data (assesses separately with GRADE)

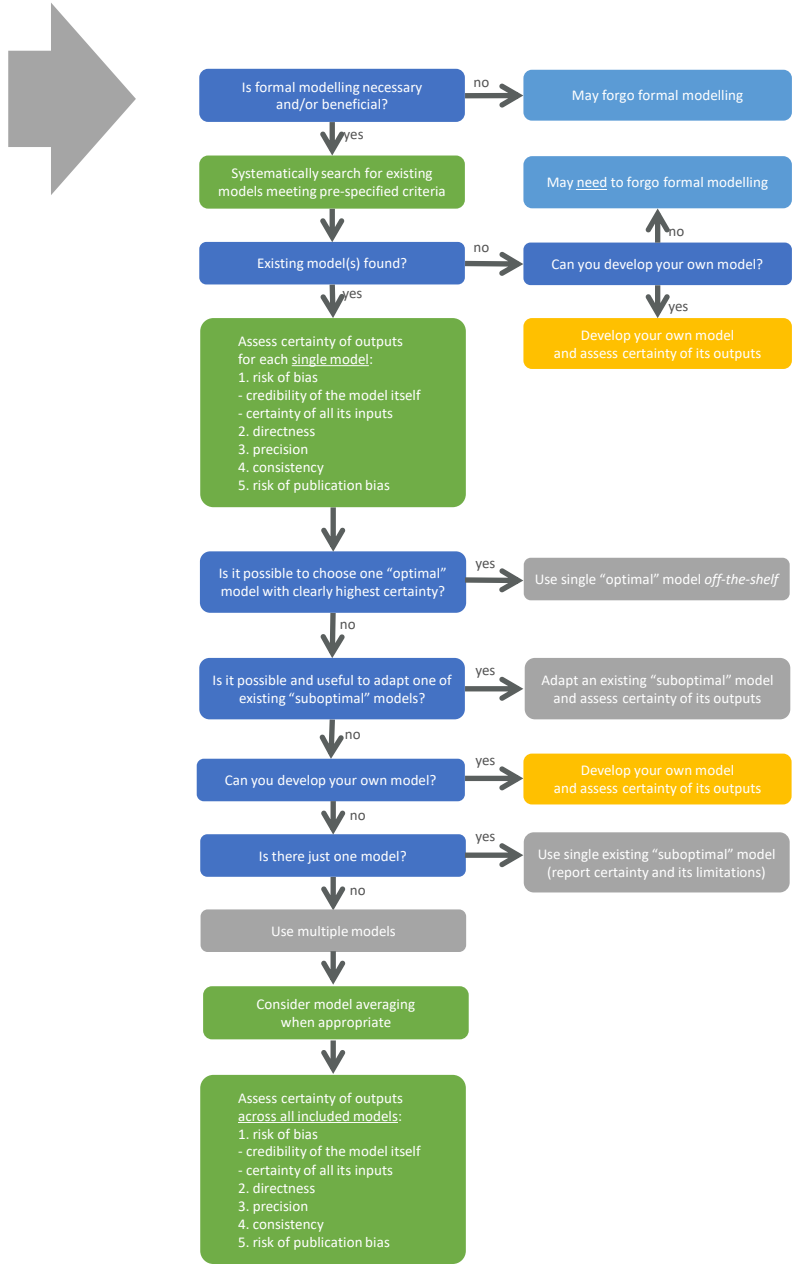
GRADE approach for modeling studies

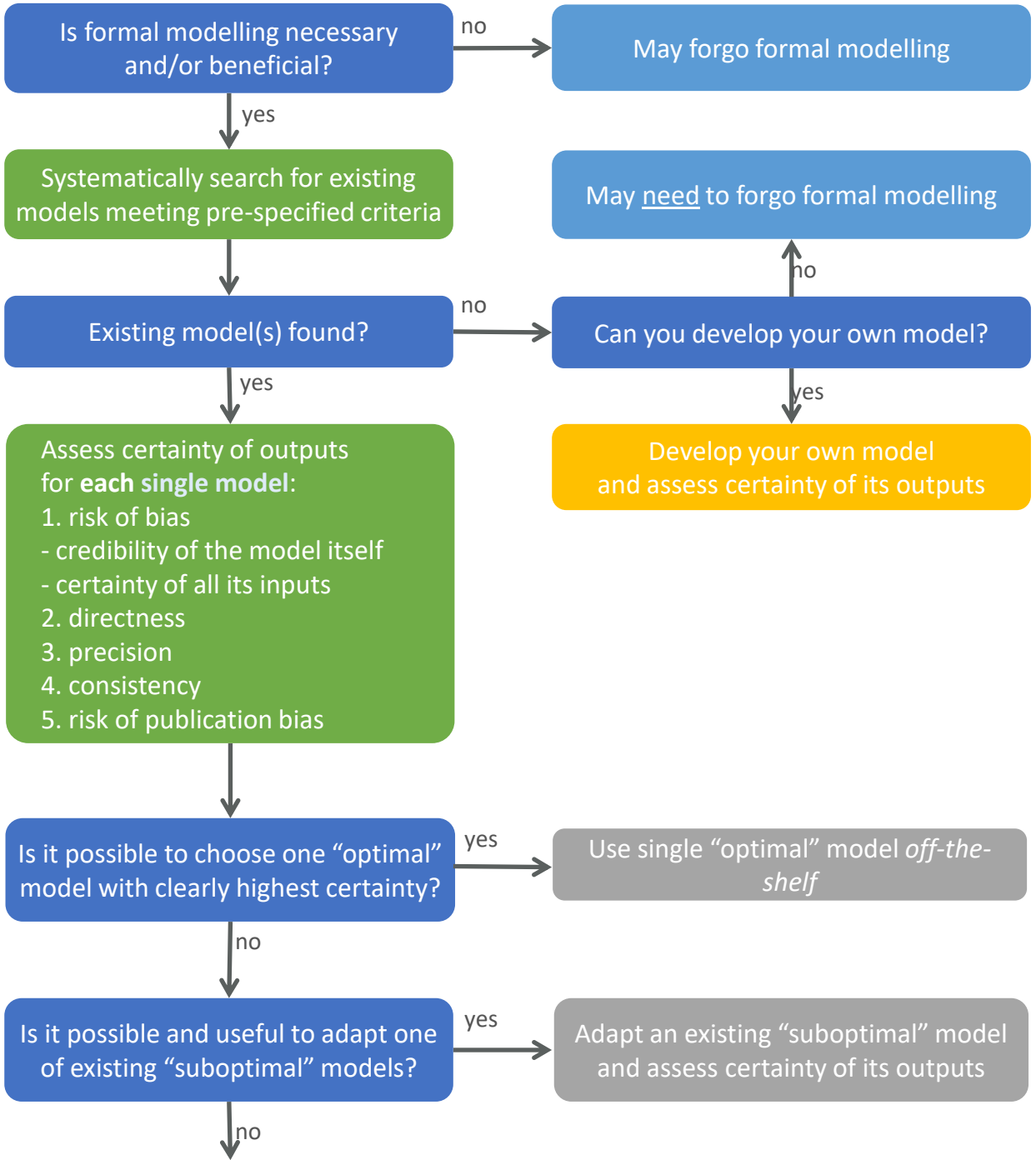
GRADE conceptual papers discuss concepts that may not have been piloted on examples and that may not result in GRADE guidance.

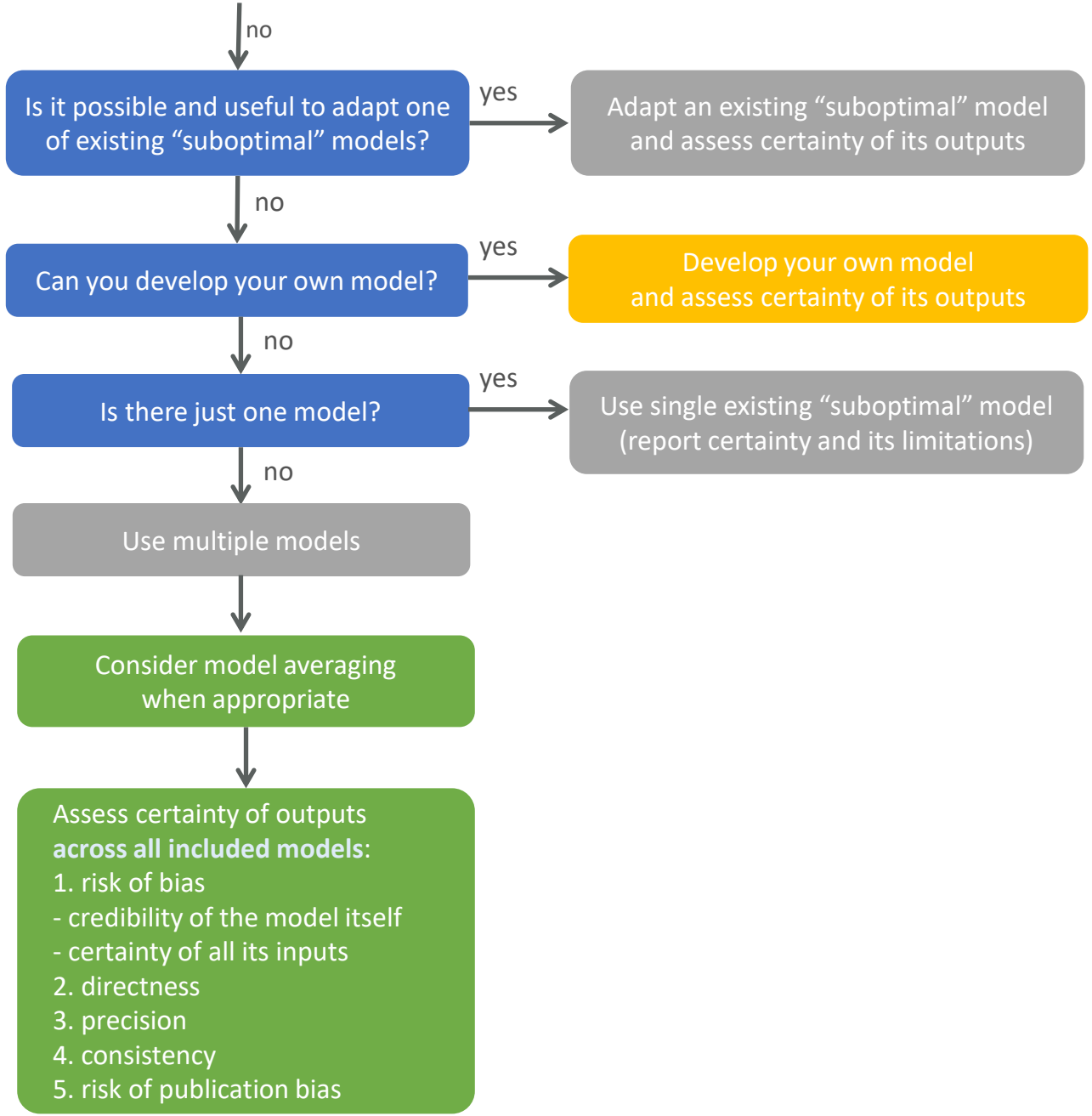
GRADE guidance papers provide specific guidance on how to make judgments in line with the GRADE methodology. GRADE guidance papers will typically include examples how to apply the guidance.

main points

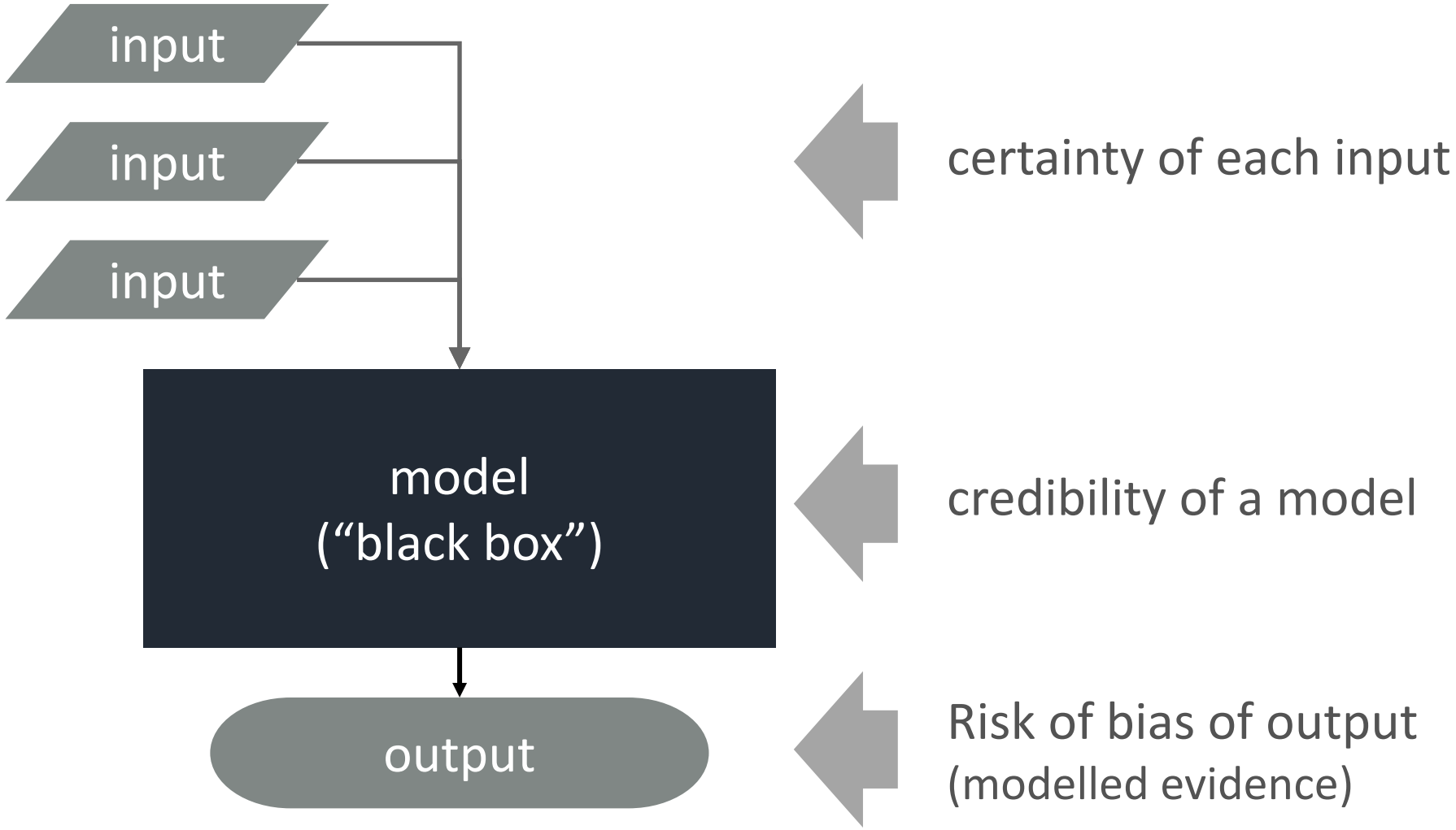
- 3 scenarios:
  1. develop a new model
  2. use off-the-shelf or adapt an existing model
  3. use results from multiple existing models
  4. forgo modelling


Is formal modelling necessary and/or beneficial?
no
May forgo formal modelling
yes
Systematically search for existing models meeting pre-specified criteria
May need to forgo formal modelling
Existing model(s) found?
no
Can you develop your own model?
no
yes
yes
Develop your own model and assess certainty of its outputs
Assess certainty of outputs for each single model:
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
Is it possible to choose one "optimal" model with clearly highest certainty?
yes
Use single "optimal" model off-the-shelf
no
Is it possible and useful to adapt one of existing "suboptimal" models?
yes
Adapt an existing "suboptimal" model and assess certainty of its outputs
no
Can you develop your own model?
yes
Develop your own model and assess certainty of its outputs
no
Is there just one model?
yes
Use single existing "suboptimal" model (report certainty and its limitations)
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


Is formal modelling necessary and/or beneficial?
no
May forgo formal modelling
yes
Systematically search for existing models meeting pre-specified criteria
May need to forgo formal modelling
no
Existing model(s) found?
no
Can you develop your own model?
yes
yes
Assess certainty of outputs for each single model:
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
Develop your own model and assess certainty of its outputs
Is it possible to choose one "optimal" model with clearly highest certainty?
yes
Use single "optimal" model off-the-shelf
no
Is it possible and useful to adapt one of existing "suboptimal" models?
yes
Adapt an existing "suboptimal" model and assess certainty of its outputs
no


no
Is it possible and useful to adapt one of existing “suboptimal” models?
yes
Adapt an existing “suboptimal” model and assess certainty of its outputs
no
Can you develop your own model?
yes
Develop your own model and assess certainty of its outputs
no
Is there just one model?
yes
Use single existing “suboptimal” model (report certainty and its limitations)
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

Risk of bias domain (GRADE)



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