Economic Model Choice, Validation and Sharing

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Research Institute

Uncertainty for Decision Modeling Concepts and Terminology

Preferred Term	Concept	Other Terms Sometimes Employed	Analogous Concept in Regression
Stochastic uncertainty	Random variability in outcomes between identical patients	Variability; Monte Carlo error; first-order uncertainty	Error term
Parameter uncertainty	The uncertainty in estimation of the parameter of interest	Second-order uncertainty	Standard error of the estimate
Heterogeneity	The variability between patients that can be attributed to characteristics of those patients	Variability; observed or explained heterogeneity	Beta coefficients (or the extent to which the dependent variable varies by patient characteristics)
Structural uncertainty	The assumptions inherent in the decision model	Model uncertainty	The form of the regression model (e.g., linear, log-linear, etc.)

Ref: Briggs A H et al. Med Decis Making 2012;32:722-732

Approximations are unavoidable in modeling

- **“Remember that all models are wrong: the practical question is how wrong do they have to be to not to be useful*”**
- The search for ‘absolute accuracy’:
  - adds complexity
  - imposes costs (evidence gathering, computation time)
  - complicates communication
  - increases potential modeling errors
  - need to justify in terms of better decisions

**Schulpher M. ISPOR, Athens 2008 based upon Box and Draper (1987) Emprirical Model-Building and Response Surfaces p.424 Wiley*

Non-scientific factors influencing model choice

- Monopoly: complex models are more difficult to
  - develop or replicate
  - modify
  - adapt
  - submit
  - (validate)
- Preferable results for the sponsor
  - maximising the impact of product benefits
  - ignoring or minimising the impact comparative disadvantages of products

Economic model choice should be based on scientific rationale

Potential steps to justify model choice

1. Consensus on the research question
2. Review
   - Literature review of published models in related fields
   - Patient pathways
   - Economically meaningful outcomes
3. Draft conceptual modelling framework
4. Challenge meeting with relevant clinicians and health economists
5. Final conceptual modeling framework
6. Model building
7. Model validation
8. Publication and sharing models

Polling Software

- Please open the ISPOR application to participate in polling for this workshop
- Click MORE on bottom right and choose TAKE A POLL
- Find session W6: ECONOMIC MODEL CHOICE, VALIDATION, AND SHARING: PRAGMATIC ROADMAPS FOR PHARMACOECONOMIC PRACTICE (Advanced Workshop)
- Poll will unlock with each question presented

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Poll: What interested you most about attending this workshop?

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Poll: What is your level of modeling experience?

Model Choice: Patient versus Cohort

Jonathan D Campbell, PhD

Associate Professor

Center for Pharmaceutical Outcomes Research Director

ISPOR EU Workshop November 12, 2018

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Model's purpose

- Models are designed to estimate the mean costs and health outcomes (i.e. benefits and risks) of alternative interventions for the population likely to be affected by a particular decision
  - Coverage and payment decisions are made for populations (or sub-populations), not individual patients
  - Mean costs and health outcomes can be used to address efficiency goals such as achieving value for money in health.

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Definitions

- Cohort level model: outcomes are estimated for the cohort as a whole without considering individual patients within that cohort
  - Compromises exist around building in characteristics that have different estimates of either costs or outcomes (i.e. subgroups)
- Patient level model: outcomes are logged for individual patients and then the average is taken across a sufficiently large, representative sample of patients

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Is there a one-size fits all approach?

- The choice around whether to use cohort or patient-level modeling should be driven by the research question and often involves trade-offs. Therefore, this choice should be considered on a case-by-case basis.
  - » The precision or lack of bias within the model findings in practice, is often traded off against resources for evidence generation or evidence synthesis or modeling (including generating model findings and uncertainty).
  - » Precedence in modeling building is often used as rationale but can miss key differences across the purpose of prior models.

Modeler's right to choose

- Stick to a simple model unless it matters
  - » May lead to burden of proof being shown against conducting a cohort-level model and for conducting a patient-level model
  - » Caveats include personal biases and comfort with cohort-level models as well as conducting many models where patient-level models were not thought to produce different mean costs and outcomes

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Burden of proof that can tip the scales

- When non-linearity is present
- When history or time since prior event matters
- When discrete time intervals cause trouble
- When building a model for multiple and flexible purposes
- When people interactions matter

Davis, S., Stevenson, M., Tappenden, P., Wailoo, A.J. NICE DSU Technical Support Document 15: Cost-effectiveness modelling using patient-level simulation. 2014. Available from http://www.nicedsu.org.uk

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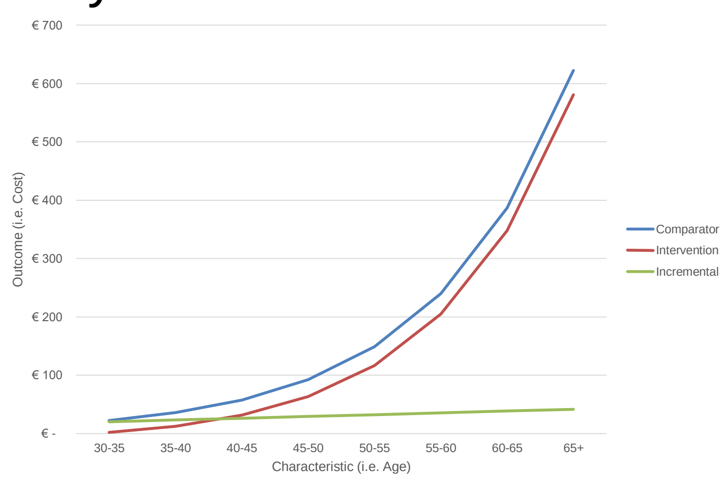
Non-linearity?



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History or time since prior event matters

- Problematic to model using cohort
  - » Possible solutions exist
    - tunnel states
    - Multi-dimensional arrays (include more than just starting state and ending state, such as time in state or prior events or characteristics)
  - » When such solutions are problematic for model users and corresponding software, then a patient-level model may be preferred.

Davis, S., Stevenson, M., Tappenden, P., Wailoo, A.J. NICE DSU Technical Support Document 15: Cost-effectiveness modelling using patient-level simulation. 2014. Available from http://www.nicedsu.org.uk

When discrete time intervals cause trouble

- Problems exist when more than one transition can occur within one cycle for Markov cohort models.
- This problem is less challenging to overcome as cycle lengths can generally be shortened without much issue.
  - » However rapid events followed by limited events over longer periods causes inefficiencies in discrete time short cycles

Davis, S., Stevenson, M., Tappenden, P., Wailoo, A.J. NICE DSU Technical Support Document 15: Cost-effectiveness modelling using patient-level simulation. 2014. Available from http://www.nicedsu.org.uk

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When building for multiple purposes

- Adding health states or characteristics to a decision tree or cohort Markov model can be painstaking work after the model is built.
  - » A discrete event patient-level simulation is more easily changed or modified after the initial build
  - » A policy or disease-level model with multiple forecasted modifications may lend itself more toward a patient-level model choice

Davis, S., Stevenson, M., Tappenden, P., Wailoo, A.J. NICE DSU Technical Support
Document 15: Cost-effectiveness modelling using patient-level simulation. 2014. Available from http://www.nicedsu.org.uk

When people interactions matter

- Options exist for patient-level models such as discrete event simulation, or agent-based models whereas cohort-level models also exist including the systems dynamic approach.

Davis, S., Stevenson, M., Tappenden, P., Wailoo, A.J. NICE DSU Technical Support
Document 15: Cost-effectiveness modelling using patient-level simulation. 2014. Available from http://www.nicedsu.org.uk

Brennan, A., Chick, S.E., Davies, R. A taxonomy of model structures for economic
evaluation of health technologies. Health Economics 2006; 15(12):1295-1310.

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Summary

- Stick to the simplest model unless there is a good case for a more complex model
  - Patient level models add an additional loop for generating uncertainty in the findings; however cohort level models can also be complex in their attempts to resolve issues such as patient history
- Cohort-level model may be an easier starting point, especially for those looking to learn modeling
- Patient-level models should be considered especially when a cohort model becomes challenged to build due to reasons discussed

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Model validation

Quick checklist for modellers and users

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Validation

- To demonstrate and evaluate whether the model is a **proper and sufficient representation of the system** under assessment and whether the results of the **analysis can serve as a solid basis for decision making** (Vemer, Ramos et al. 2016)

- So far the focus has been on both the **hard numbers** and the **softer processes** of model development and problem structuring and **ranges from the theoretical to practical rules of thumb** (Brennan and Akehurst 2000, Vemer, Ramos et al. 2016).

What kind of validity?

Face validity

- Problem formulation, structure, source and results correspond with reality

Internal validity - internal consistency, or technical validity

- equations, codes or formulae, data against their sources

Cross-validity - external consistency, comparative modelling

- comparision with other models

External validity

- model outcomes compared with the real world outcomes

Predictive validity

- comparing the forecasted outcomes with the actual ones

What type of model?

Budget impact

Simple cohort model

Complex cohort model

Simple individual simulation model

Complex individual simulation model

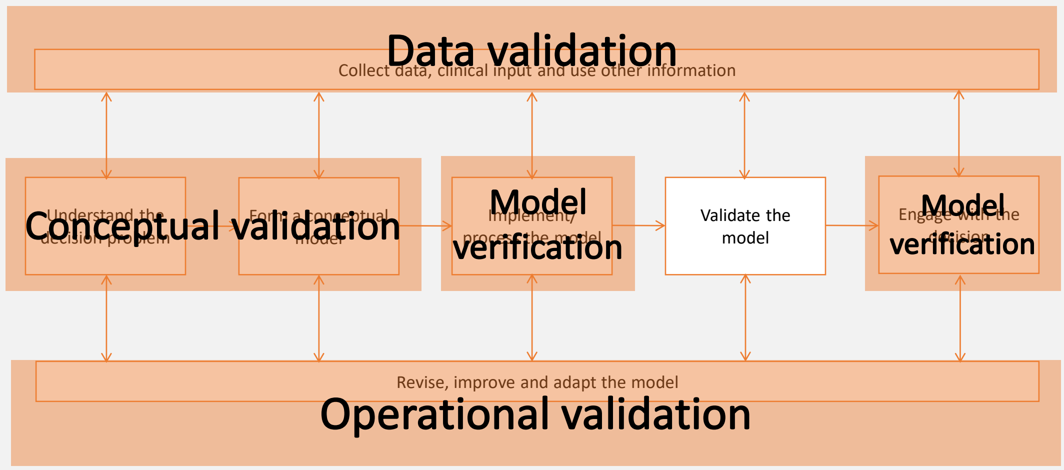
How much time do you have?

To build the model

- 1-3 months
- 4-6 months
- 7-12 months
- more than 1 year

To check validity

- 1-5 days
- 1-3 weeks
- 1-2 months
- beyond 2 months



In which phase what types of action?

Development phase
Model conceptualization
form model concept

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Development phase
Model conceptualization
form model concept
Technical model development
build modelling tool including formulas, codes
incorporate value drivers
populate the model with parameters
build draft model
develop user interface
run deterministic sensitivity analysis
run probabilistic sensitivity analysis

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draft report + model 1
draft report + model 2
final report with final model interface

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Optional tasks
rebuild model with alternative technique
reprogram model with alternative software
externally validate model

In which phase what types of action?

Development phase	Validation task	Action of validation
Model conceptualization		
form model concept	examine the model concept in the light of available data	review the model structure and evidence
Technical model development		
build modelling tool including formulas, codes		
incorporate value drivers		
populate the model with parameters		
build draft model		
develop user interface		
run deterministic sensitivity analysis		
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In which phase what types of action?

Development phase	Validation task	Action of validation
Model conceptualization		
form model concept	examine the model concept in the light of available data	review the model structure and evidence
Technical model development		
build modelling tool including formulas, codes	compare programed model structure with model concept	review excel spreadsheet
incorporate value drivers	check and validate the critical inputs/assumptions	critical input/assumption review and supporting analysis when needed
populate the model with parameters	compare parameters with sources	review model parameters and sources
build draft model	check formulas and results	run technical checklist pewview results
develop user interface	check functionality of formulas	review formulas and functionality
run deterministic sensitivity analysis	check functionality and face validity of results	review formulas, programming and results
run probabilistic sensitivity analysis	check functionality and face validity of results	review formulas, programming and results
Reporting		
draft report + final model 1		
draft report + final model 2		
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Optional tasks		
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run probabilistic sensitivity analysis	check functionality and face validity of results	review formulas, programming and results
Reporting		
draft report + final model 1	write up the report and check all details in the model	check as you write up the report
draft report + final model 2	compare report with the model	check document with model + run technical checklist
final report with final model interface	review report and model from a user perspective	check usability and readiness of model and document
Optional tasks		
rebuild model with alternative technique		
reprogram model with alternative software		
externally validate model		

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draft report + final model 2	compare report with the model	check document with model + run technical checklist
final report with final model interface	review report and model from a user perspective	check usability and readiness of model and document
Optional tasks		
rebuild model with alternative technique	rebuild the model using an alternative modelling technique	build new model
reprogram model with alternative software	reprogram the model using another software	build same model with other program
externally validate model	check validity of results based on empirical evidence and external clinician input	use the existing model to make comparisons with empirical evidence

Who should validate?

- Model developer
- Internal quality assurance modeller
- External quality assurance modeller
- Project/Modelling supervisor
- Clinician

What should the outcome be?

- Internal comments for the modeller
- Technical checklist
- Paragraph in the model report
- Separate validation report
- Alternative (re-programmed) model

Development phase to validate	Type of model to check	Type of validity to check	Estimated time in weeks	Contributor	Validation task	Action of validation	Outcome of validation
Model conceptualization							
form model concept							
Technical model development							
build modelling tool including formulas, codes							
incorporate value drivers							
populate the model with parameters							
draft model							
user interface							
deterministic sensitivity analysis							
probabilistic sensitivity analysis							
Reporting							
draft report + final model 1							
draft report + final model 2							
final report with final model interface							
Optional phases							
rebuilt model with alternative technique							
reprogrammed model with alternative software							
final report with externally valid model							

You'll need to make a number of choices

Presumably cannot do everything!

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IN THE END…NO MATTER HOW GET A GOOD MODEL!!!

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Model Transparency and Considerations for Model Sharing

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Definition of model transparency

- Documentation on a model's structure, equations, parameter values, and assumptions*
  - » Non-technical description of the model for non-modelers interested in the topic
  - » Technical information for modelers who may want to replicate the model and findings
    - Documentation should be made available openly or under agreements that protect intellectual property

*Eddy et al. Model Transparency and Validation: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force – 7. Medical Decision Making/Sep-OCT 2012

Recent transparency efforts

- Technical report accompanying model results
  - » No disclosure of model but detailed technical report so modelers can replicate findings
- Confidential model access only for trained stakeholders*
  - » For review and validation purposes only
- Fully open source models/model repositories
  - » Public may alter model under specific licensing

*Institute for Clinical and Economic Review Announces New Program to Make Available Draft Executable Economic Models During Drug Assessment Review Process. Accessed at: https://icer-review.org/announcements/model-transparency-program/

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PharmacoEconomics (2017) 35:125–128
DOI 10.1007/s40273-016-0479-8

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RESEARCH LETTER

Benefits, Challenges and Potential Strategies of Open Source Health Economic Models

William C. N. Dunlop[1] · Nicola Mason[2] · James Kenworthy[1] · Ron L. Akehurst[2]

IDEAS AND OPINIONS

Annals of Internal Medicine

A Call for Open-Source Cost-Effectiveness Analysis

Joshua T. Cohen, PhD; Peter J. Neumann, ScD; and John B. Wong, MD

Can Economic Model Transparency Improve Provider Interpretation of Cost-effectiveness Analysis? Evaluating Tradeoffs Presented by the Second Panel on Cost-effectiveness in Health and Medicine

William V. Padula, PhD, MS, MSc, Robert Brett McQueen, PhD, MA,† and Peter J. Pronovost, MD, PhD‡*

Benefits of improving transparency

- Increase reproducibility of modeling studies
- Reduce errors and bias
- Increased uptake of cost-effectiveness findings for clinical and policy decision making

Sources: Cohen JT, Neumann PJ, Wong JB. A Call for Open-Source Cost-Effectiveness Analysis. Annals of Internal Medicine. 2018 Apr.; Padula WV, McQueen RB, Pronovost PJ. Can Economic Model Transparency Improve Provider Interpretation of Cost-effectiveness Analysis? Evaluating Tradeoffs Presented by the Second Panel on Cost-effectiveness in Health and Medicine. Medical Care 2017 Nov.

What level of transparency?

- Open source modeling is not realistic for all stakeholders
- Depends on incentives and implications of model findings
  - Universities and commercial entities may not allow sharing of models due to intellectual property concerns/risk of releasing models to competitors
  - Health technology assessment models may require more transparency such as sharing of model with trained reviewers or open source given the impact of findings on resource allocation decisions

Key considerations for decisions on level of transparency

- Consider risk/benefit trade-off of shared information
  - Legal ownership of model vs. scholarly credit of model findings
  - What level of transparency is legally feasible at your organization?
  - Will the model impact resource allocation decisions? And if so, will level of transparency impact uptake of findings?
  - Can the model be replicated using a detailed technical report?

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Key Considerations for open source models

- Set-up infrastructure for model registration
- Create a model license that is flexible*:
  - Allow or deny commercial use of the model
  - Allow or deny outside users to update the model for new applications
- Copyright definitions differ between countries
  - In U.S. raw facts not copyrightable, only “selection and arrangement”
  - In Europe raw facts are copyrightable
- Develop detailed “user guide” to reduce question and answer

*https://creativecommons.org/licenses/

Links for more information on open source licensing and software initiatives

- Open Source Initiative: https://opensource.org/licenses
- Creative Commons Licensing: https://creativecommons.org/licenses/
- Example discussions outside of HEOR:
  - Morin et al. Shining Light into Black Boxes. Science 13 Apr 2012.
  - Stodden et al. Towards Reproducible Computational Research: An Empirical Analysis of Data and Code Policy Adoption by Journals. PLoS One June 2013.

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Poll: Do you have a preference for one type of model?

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Poll: What is typically your pivotal factor for choosing a patient vs. cohort model?

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Poll: How much time do you think is needed to validate a model?

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When playing as a slideshow, this slide will display live content

Poll: When are you sure a model is valid?

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Poll: When do you think model validation is important?

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Poll: Have you had challenges reproducing model findings using the status quo in health economics (i.e., technical appendix)?

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Poll: What is the value of improving model transparency such as increased access to modeling experts or releasing open source models?