

BACKGROUND

FACE VALIDITY

- Clinical validation, also referred to as face validation, is a critical requirement for any health economic (HE) analysis, including models, assumptions, and interpretation which is considered as the first order validation [1].
- Face validity is defined as the act of evaluating whether HE analysis can clinically and medically represent the health problem it intended to address [2]. It is subjective and mostly qualitative, so clinical experts in the problem area are eligible to be consulted for the face validation in HE studies [2–4].
- There are different validation approaches for HE analysis: general reporting, trial-based evaluation, and model-based evaluation. The wrong choice of validity method can affect the quality of validation [5].

GUIDELINES

- All available guidelines for the economic evaluation of health technologies consider the face validity of the model design, problem formulation, data sources, assumptions, and final results as an essential part of validation [3, 4].
- Although guidelines suggest clinical validity should be considered in all economic evaluations,, no specific timing for such a costly and time-consuming consultation is provided. The Canadian Agency for Drugs and Technologies in Health (CADTH) advises that the consultation should be done early and “iteratively” within the analysis process [4]. Moreover, no specific suggestion is available about how to ask HE questions to clinical experts who predominantly are not familiar with HE concepts.

OBJECTIVE

This paper aims to define a criterion-based approach to clinical validation in HE models in order to provide a timing schedule as well as a framework for the questions to ask clinical experts during model validation.

LITERATURE REVIEW

Table 1: The face validity of HE models in published guidelines or articles

ARTICLE	DEFINITION OF EXPERTS	FIELD(S) THAT NEED TO BE FACE VALIDATED	TIMING PROVIDED	QUESTIONS GUIDE PROVIDED (DIRECTLY OR INDIRECTLY)
CADTH guideline (2017) [4]	Content experts	1) Model structure and conceptualization 2) Assumptions 3) Data 4) Results	Yes, early and iteratively throughout the analysis	No
Vermer (2016) [6]	Experts (not any mention of clinical knowledge)	1) Model conceptualization* 2) Input data 3) Model outcome	No	Yes, general questions for the assessment of the face validation status are available in three out of four sections of the questionnaire: validation of the conceptual model (A), input data validation (B), operational or model outcome validation (D).
Caro-ISPOR (2014) [7]	Experts (not any mention of clinical knowledge)	1) Model structure 2) Assumptions 3) Data sources 4) Results	No	Yes, six questions were designed to address face validity.
Eddy-ISPOR (2012) [3]	People who have clinical expertise in the problem.	1) Model structure** 2) Model inputs (evidence) including assumptions and data sources 3) Problem formulation 4) Results	No	Yes, but general suggestions for each field of model structure, evidence, problem formulation and results.
Phillips (2004) [1]	Person knowledgeable about the problem.	1) Model structure and type with enough treatment complexity including model's health states 2) Model inputs including assumptions 3) Model outputs (results)	No	Not directly; a general checklist for quality assessment in decision analytic models was provided. This checklist included three sections: structure (S), data (D), and consistency (C). Questions for face validity exist in all three sections.

- To determine whether any specific suggestion is available in timing and the process of consultation with clinical experts, a literature review was conducted. A framework for clinical validation was then established, based on the results of the targeted literature review and the experience of authors.
- The literature review emphasized the importance of clinical validation by clinical experts during three main phases of building an HE model: model structure, inputs and assumptions, and results.
- Face validity should be started early and iteratively within the analysis timeframe; however, no specific schedule or timing has yet been published.

DISCUSSION & RECOMMENDATIONS

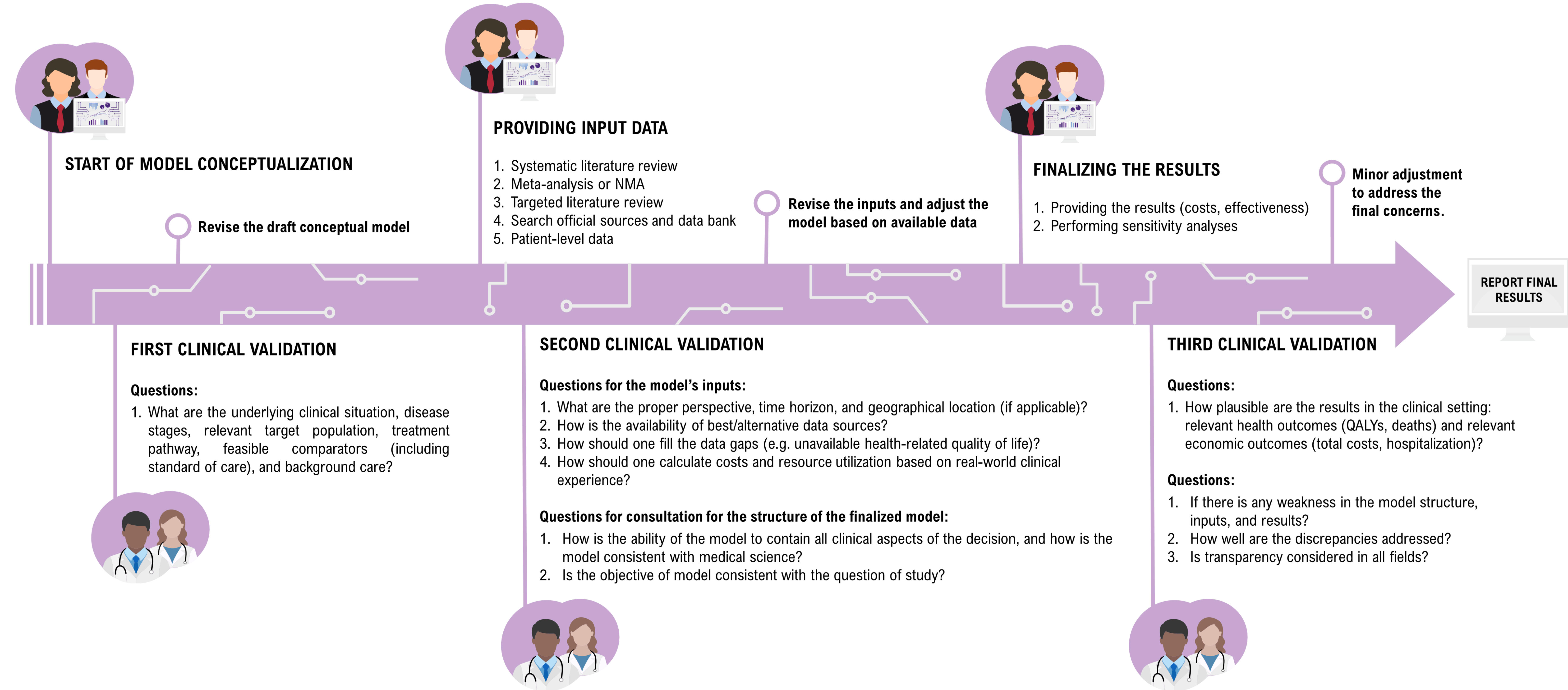
We suggest clinical validation in the process of HE model design should take place in three different phases:

- At the initial model design stage to provide clinical expertise about the underlying disease, patients, and treatment pathway.
- A clinical consultation following initial efforts at providing model inputs and assumptions should also be considered.
- A clinical validation should be scheduled when results from the model are available.

We recommend three or five clinical experts to be consulted via a modified Delphi panel with three rounds of emails — corresponding to the three phases described — including specific questions, but also utilizing targeted interviews when time and resources permit.

Table 2: A new time-oriented HE model validation framework for the questions that should be proposed to clinical experts

ARTICLE	DEFINITION OF EXPERTS	FIELD(S) THAT NEED TO BE FACE VALIDATED	TIMING PROVIDED
First clinical validation	Early, at the start of the model conceptualization	Three or five clinical experts in the field of problem and from different practice settings (should be blind to any possible results)	Modified Delphi panels or interview
Second clinical validation	During model development, consultation for the model's inputs	Three or five clinical experts in the field of problem and from different practice settings (should be blind to any possible results)	Modified Delphi panels
	During model development, consultation for the structure of the finalized model.		
Third clinical validation	Late, evaluation of the model's output consistency with clinical expectation.	Three or five clinical experts in the field of problem and from different practice settings	Modified Delphi panels or interview



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CONCLUSIONS

- Payers and economists commonly accept that clinical validation should be integral to the process of HE model-building.
- Timing of clinical validation is key to deriving full value to assist in conceptual framework design and filling data gaps.
- Clinical validation is considered as the first order validation that needs to be performed from the first development step of any HE model. Health economists require support from experts with clinical knowledge of the problem.
- To the extent of our knowledge, this is the first time-oriented HE model validation framework for the questions that should be proposed to clinical experts.

