

Standardization of Model Validation in Reimbursement Dossiers and Research Dissemination

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Despite its acknowledged importance, validation practice and reporting are not standardized for reimbursement dossiers and research dissemination.

INTRODUCTION

In many countries, health economic (HE) decision models have become an important part of the healthcare policy decision process.¹ Since the outcomes of these models can have significant consequences for reimbursement, payment, or resource allocation decisions, it is important that these models are valid — that is, these models are in accordance with the current knowledge about the medical intervention and economic effects, and suitable to serve as a solid basis for decision making.² Although there is widespread support for the idea of model validation, the validity of HE models remains elusive. For example, a study towards the quality of models used in Australian policy making reported important flaws in 203 of the 247 reviewed models.³ A lack of validation presents a potential loss of invested resources and a risk to the decision-making process.

Several widely accepted tools discuss validation in some form or another, such as the CHEERS guidelines on reporting,⁴ the guidelines by Philips et al,⁵ the questionnaire by Caro et al,⁶ and the model validation assessment tool, AdViSHE, which is designed solely for model validation.⁷ However, despite the availability of these tools, validation practice and reporting are not standardized in the HE processes. Some standardized validation seems desirable, as it is likely that it will improve the transparency for other model builders and users, increase the possibilities for comparing models, and reduce the loss of invested resources and the risk to the decision-making process. The objective of this article is to discuss factors that will hinder or incentivize the standardization of model validation efforts and its reporting, identified by modelling experts. We look at two important application areas which involve HE models, namely dossiers sent to the

(national) decision maker when applying for drug reimbursement, and research dissemination. The factors discussed were identified using expert interviews.

INTERVIEWS

This article was based on 6 interviews,⁸⁻¹³ which addressed the following questions. First, how can model validation tools in general — and the model validation assessment tool AdViSHE (Assessment of the Validation Status of Health-Economic decision models) in particular — be useful in daily practice? And secondly, are there any barriers and facilitators to implementation of a standardized model validation tool? Three interviews were conducted with 4 people with many years of experience in building reimbursement dossiers. They either had a history of working in consultancy or worked directly for pharmaceutical companies.⁸⁻¹⁰ The other 3 interviews were held with editors of academic journals that publish HE modelling studies.¹¹⁻¹³

MODEL VALIDATION IN DAILY PRACTICE

Fortunately, the importance of model validation seems to be understood by many model builders. For example, the consultancy firm MAPI has an internal validation process, which includes sending a model to another office in another country, where the model is validated by going over their internal checklist. Validation efforts were mentioned in publications, although not in detail.⁸ At BMS, a pharmaceutical company, a chapter on model validation is included in reimbursement dossiers.⁹ At Roche, a base model was developed for oncological models, which is considered well-known, well-validated and therefore accepted.⁹ Finally, AstraZeneca always validates their models, in detail.¹⁰ Private companies have developed their own tools⁸, and there are some tools without any official status (eg., published in gray literature, educational textbooks).¹¹ >

With the importance of model validation so widely accepted, it is surprising that it is not always reported extensively (see for example, reference 14) or in a transparent and consistent way. Because of this, model validation — and model quality — are very different between reimbursement submissions.⁹ Model users such as decision makers, or journal readers, have 3 options to address model validation when presented with a model result. Since the cost of model validation can be significant,¹⁵ a user could assume that the model was already validated by the modelers and rely on its outcomes without further examination. However, this requires a lot of confidence in the model and its makers. For example, for some applications core models are used and translated to local settings, but these core models often have errors in them.⁸ A loss of confidence happens faster when the modelling team has an economic interest in the outcomes.⁶ The second and opposing option is for model users to validate the model themselves. This increases the confidence in the model but may also lead to spending scarce time and money on work that the modelling team has already performed.

A third, middle-ground option is for model users to request a standardized report of the model validation efforts that were performed, with the following questions in mind:

- 1) How have the validation techniques been applied?
- 2) Can and should we replicate (some of) the reported results?
- 3) What is missing?

A standardized tool would be very helpful in standardizing validation, but also in saving time for agencies,⁹ while leading to improved confidence in models.¹²

STANDARDIZED REPORTING OF MODEL VALIDATION AS PART OF THE REIMBURSEMENT PROCESS

Reimbursement decisions based on models with incorrect outcomes may incorrectly limit access to new drugs or allocate budget to interventions that are not cost-effective. Because of these far-reaching consequences of a wrong decision, not only is academic credibility important in validating HE models (“Is the model logically and scientifically sound?”), but also salience (“Is the model applicable within this context?”) and legitimacy (“Are stakeholder concerns, values, and views included in a proper way?”).¹⁵

One facilitating factor for standardizing model validation is a growing perception of this being needed or useful. A validation report would give a standard, making it possible to compare between models: how good models are, how much effort was undertaken.⁸ For example, in both the Dutch and Australian pharmacoeconomic guidelines, reporting validation efforts systematically is obligatory, with AdViSHE being named as an example tool.^{16,17} In addition, as discussed earlier, recent publications stress the problems with the current situation and the need for more and better structured model validation reporting.

A second facilitating factor would be whether a standardized tool for validation is embraced by local trade organizations, such as the Dutch VIG (*Vereniging Innovatieve Geneesmiddelen*, Association

Innovative Medicines) or the French LEEM (*Les Entreprises du Médicament*, Pharmaceutical Companies Association). This will be beneficial for the support for such a tool from pharmaceutical companies.⁹

Another facilitating factor is the perceived level of HE expertise of model users, in this case, the employees at the local reimbursement bodies. Although this expertise has improved remarkably in the last few years,⁹ the experience with HE of regional payers is limited,¹⁰ with big variation between assessors.⁹ This leads to a discussion of (the interpretation of) results.^{9,10} If tools are structured for uniform validation, this may improve the quality of dossiers.⁹ Especially for smaller jurisdictions with less market power and possibly less resources for extensive validation, standardized validation may help to increase the quality of dossiers and hence, the quality of reimbursement decisions.

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The main limiting factor seems to be that models are often provided by — and validated at — a global office while implementation of standardized validation often starts locally, through local guidelines.^{9,10} Because of this, there is a risk that each jurisdiction will have its own way of standardizing validation. From the point of view of the local authorities, validation may be standardized over all submissions but may lead to different methodologies from the modeller’s point of view. If this is the case, standardized validation may be just another hurdle.⁹ It was therefore preferred if standardized validation is implemented in several countries, at the same time, and in the same manner.^{9,10} If a certain validation method is accepted more broadly, it can then be standardized on a global level. Since local changes are likely only for data, not for the model structure,¹⁰ only a short report might then be needed at a local level. If it’s a set of extra rules, for one or a few jurisdictions, it will only add work, which will make it difficult to get implemented by model developers at international firms.^{9,10}

Countries look at each other and learn from each other.⁹ Five EU countries (the United Kingdom, Germany, France, Spain, and Italy) are considered leading in this respect.^{9,12} Because the Nordic countries are considered to have strict guidelines, they are good countries on which to focus.⁹ In addition, decision makers look at the scientific community. For national bodies to accept it, it is expected that the scientific field should accept it first.¹⁰ It first must be a matter of course, integrated in the good modelling practice.¹³ Previous guidelines on model reporting in general have been widely adopted,⁴⁻⁶ suggesting that there is likely support for standardized validation.

STANDARDIZED REPORTING OF MODEL VALIDATION IN RESEARCH DISSEMINATION

In clinical publications, data sharing is something everybody wants, but it still seems to be a long way off in health

economics.¹² On the one hand, readers, editors, and reviewers of academic papers require transparency. On the other hand, model developers have concerns about sharing their model. Even though *Value in Health* has a system in place where a reviewer signs for confidentiality, generally there is a lot of hesitancy on this from authors. The same is true for pharmacoeconomics. Agencies want to protect their intellectual content against cloning, or confidential pricing information.^{12,13}

Standardization of model validation seems to be an acceptable middle ground, which is a major facilitating factor. As stated before, most current HE studies report only limited or no information about validation.¹² Reviewers have reported in the past that they don't have enough information to make the assessment whether a model is valid.¹³ Word limits can make it hard to explain what a model is doing well enough that the reader has confidence, persuading the reader it is legitimate. Technical appendices help, but since most readers don't read the appendix, they need to be persuaded by the information in the main article.¹¹ A standardized validation report will provide an inside view of the model validation process, without having the model code exposed.¹²

Even if a tool is useful, the question remains whether it can be made obligatory for research dissemination purposes. For example, after the CHEERS checklist was published in 13 journals at the same time, *Pharmacoeconomics* decided to adopt CHEERS, considering it good practice that contains basic items.¹² In contrast, *Value in Health*, one of the other journals that published CHEERS, thought that requiring CHEERS would be an extra barrier to publication,¹³ especially since the submission process is already time-consuming. Other examples were the probabilistic sensitivity analysis or a conflict of interest statement. Before these were a requirement, they were part of the standard modelling process.¹³

Working the other way around, adding a tool as a requirement will not automatically mean that the scientific community will follow. The Netherlands are considered to have guidelines with items that are not always supported by the community.⁹ This runs the risk of losing support from submitters.^{9,10} If a technique is easy to work with and accepted by the scientific population, modellers will start to use it automatically — not because it's the guideline, but because they believe in it.^{9,10}

With the large number of tools already available, a legitimate question could be whether it is possible to do a meta-analysis of reporting tools.¹¹ Such a tool would do away with all overlap and synthesize everything into a single tool. It is an interesting suggestion for further research and a way to standardize over the different available journals.¹¹

CONCLUDING THOUGHTS

It was pointed out that a tension exists between reimbursement decision makers and pharmaceutical companies in model transparency. Decision makers, supported by the ISPOR/SMDM guidelines and ongoing discussions in the academic field,¹⁸ often ask for the software code of models — to make changes themselves and for validation, — but pharmaceutical companies cannot always provide that, either because they don't own the

code and the builders don't want to make sharing available,⁹ or the model contains sensitive information they are unwilling to share. This is currently solved by being as transparent as possible. Standardizing validation reporting may reduce this tension by further increasing transparency.

Any tool developed to standardize model validation reporting to aid model users will never fully replace the need of validation by model users or other methods like code sharing. Validation will still have to be performed, one way or another. In a reimbursement situation, for example, it may not be possible, or even desirable, to fully prevent the duplication of effort because you want somebody with the reimbursers' interest trying the model out, as well as someone from the point of view of the producer of the intervention.¹¹ These 2 different, and maybe even conflicting, points of view are both legitimate, as both model builders and users come from a different context. It is a matter of salience: is the model applicable in either or both contexts?

Although there are clear barriers, there are also clear facilitating factors in the implementation of tools to standardize model validation. Major facilitating factors are the growing perception of a need for systematic validation, and the discussion about HE model transparency. Standardization of the reporting of validation efforts in both an academic and applied context, may lead to a higher quality of models, better model-supported decisions in medical decision making, and a better acceptance of these decisions by various stakeholders. •

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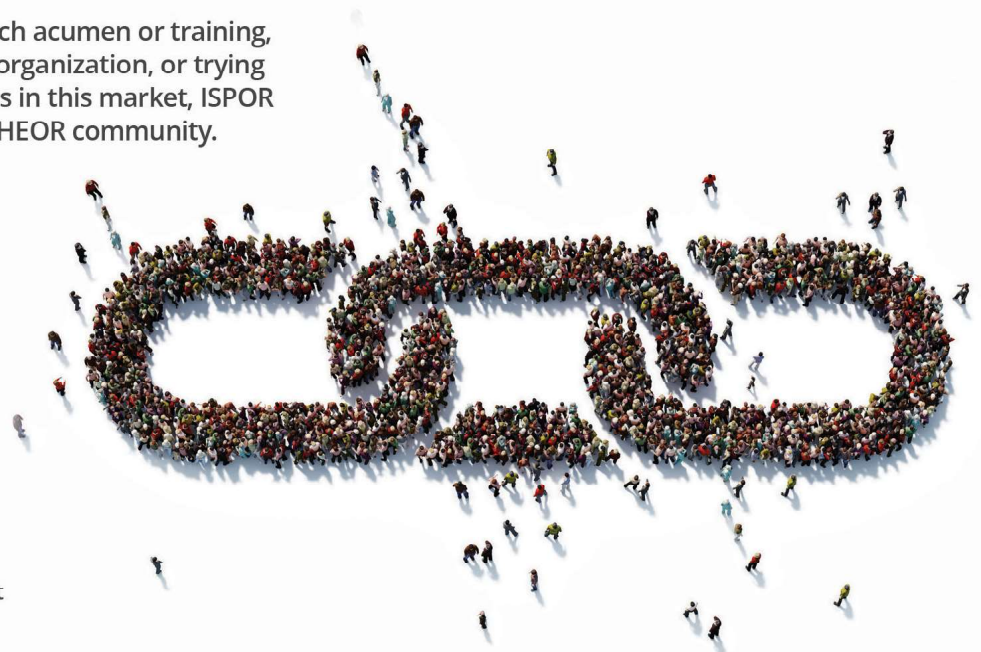
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