Lies, Damned Lies, and Cost-Effectiveness: Open-Source Models Are Essential if Cost-Effectiveness Analyses Are to Be Widely Accepted

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Cost-effectiveness models synthesize a wide range of evidence and require assumptions that are not directly testable. Open-source models encourage greater transparency in pharmacoeconomic modeling and allow faster access to critical knowledge.

Health economic models go beyond what we can directly measure within randomized controlled trials and help determine the full value of a technology by synthesizing a wide range of evidence to facilitate extrapolation over time and from intermediate to final decision endpoints.[1] They help us to make trade-offs between risks, benefits, and costs. These models are often statistically sophisticated and make assumptions that are not directly testable. This can lead to decision makers "discounting" their results, particularly if the developer is seen as partial, the modeling assumptions and "guts" are not transparent, or if it is unclear how the results were derived.[2] Indeed, the *New England Journal of Medicine* in 1994 derived their policy on publishing cost-effectiveness models by stating that "some cost-effectiveness analyses are funded by companies that hope these analyses will put their products in a favorable light. Companies might even use this favorable analysis to justify the price of their drug."[3] By the same token, patient groups may be skeptical of health technology assessment (HTA) body rulings. How, then, to allay these concerns and develop models that are believable and allow for credible decision making?

Making these models "open-source," in the sense that all code is openly viewable and available, has the potential to address some of the concerns of decision makers and to improve the quality of economic evaluations by both allowing investigators to access a range of candidate models and facilitating the internal validation of these models.[4,5] The analogy here is that of "shining a light" on the model to illuminate its inner workings. Indeed, the United Kingdom Court of Appeals ruled that the UK's National Institute for Health and Care Excellence (NICE) should release a fully executable copy of a model used in an appraisal of a treatment for Alzheimer's disease in order to comply with the principle of procedural fairness.[6] A survey of a small segment of the UK public ranked the characteristics of procedural justice—accuracy, consistency, impartiality, reversibility, and transparency—in terms of their importance to public healthcare resource allocation.[7] If public decisions are to be seen as socially just, the people affected by those decisions need to be able to question them, to ascertain that these models are fair and that consistent decisions are being made. Mistakes can easily be made and only by making these models "checkable" can one illuminate these potential errors. The formation of the Open Source Initiative (OSI), the main accrediting body for open-source software, was largely driven by concerns with finding and correcting bugs. OSI accreditation requires meeting 10 criteria, among which are (1) free distribution, (2) provision of source code, and (3) allowance of modification and derivative forms. Although OSI does allow for protecting the integrity of software by keeping the derivative forms separate from the original model, this third criterion may be of concern in our field.

Some organizations require parties other than the original developer to vet models, they hope to use. For example, the US Department of Defense has many models, and vendors are required to have their models verified, validated, and accredited.[9] Among the recommendations of the ISPOR-SMDM task force on good modeling practice,[10] several tenets held that:

- trust and confidence are critical to the success of models
- technical documentation must be made available in sufficient detail to be evaluated and reproduced
- source code of the model must be made available either openly or by anyone under a nondisclosure agreement

And yet, distrust of models persists. Six years later, a member of one of the evidence review groups for NICE stated that he felt all of the submitted models were highly biased.[11] >

Nevertheless, models in our field are rarely openly available. This may reflect concerns (real or perceived) with the potential impact on intellectual property rights, trust issues, and the effort involved in developing and maintaining them.[8]

The remainder of this article details some of the issues and barriers to broad implementation of open-source models in healthcare.

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Issues

Why are other models (eg, NASA path to Mars, trajectories for hurricanes, quantitative Wall Street predictions) not pressured to be open-source? The reason is that life provides validation of these models: their inaccuracies are soon evident. Unlike these models, those used in health economics are not easily subject to refutation as the outcomes are typically not directly observable and we do not see the counterfactual (eg, what would have happened had the patient received an alternative treatment?). Thus, they need to be explicitly validated. This can be quite difficult to achieve convincingly because data tend to be sparse and the effort involved is substantial.[12] Without diminishing the importance of validation, we propose that all models that are being used to support healthcare decisions be made available for anyone to see, including the source code, a detailed technical report, verification report, and results of any validation exercises. Whether redistribution, modification, or creation of derivative works should be allowed without restriction is at issue. This last point brings up a number of barriers to adopting open-source models.

Barriers

Concerns with opening up the "guts" of health economic models to scrutiny by people other than the creators and/or sponsors have been expressed. The issues fall into the following buckets:

- intellectual property rights/payment
- whom to trust
- model access (terms, means, versioning)
- model storage/maintenance/updating

Not included here are issues of data confidentiality and legal and regulatory concerns, which are beyond the scope of this review. Each of these above points is explored separately below.

Intellectual property rights

To understand intellectual property barriers, it is necessary to explore the distinction between proprietary and open access software. Proprietary software is developed and owned by an individual or entity. The "source code" is kept secret and is protected by copyright. If someone wants to use the software, they have to enter into a license agreement with terms that restrict any modification of the software or distribution to others. Think of any Microsoft license or any other license you have "clicked to accept." In contrast, open-source software makes the source code openly available to others who can use it without restriction, troubleshoot, build on it for their own analyses, etc (Figure 1). There are several forms of open-source licenses (eg, the MIT license), but in general, they grant users permission to view and use the software for any purpose they wish.

Some open-source licenses are what people call "copyleft" licenses, which stipulate that anyone who releases a modified open-source program must also release the source code for that program alongside. Some open-source licenses stipulate that anyone who alters and shares a program with others must also share that revised code without charging a licensing fee. These are the aspects of open-source that may concern those who do not want to expend effort on developing a model yet allow others to derive works from which they can profit.

Figure 1. Crowdsourcing

Trust

Open-source software encourages others to access, view, and modify it. With this open exchange, someone might spot and correct errors or omissions that a model's developers might have missed, and this may be done more expediently than otherwise. How does one determine whom to trust with the code: whether the potential user is sufficiently knowledgeable about the disease state, the type of model, and the rationale behind model development? Will they use it or modify it "correctly?" Who determines what is the "correct" way to use or modify it?

Figure 2. Model access

Model access (terms, means, versioning) (Figure 2)

Model developers might share published models that may, in turn, require permission from any number of stakeholders—data holders, publishers, sponsors, grantors, and codevelopers. These stakeholders may have different reasons and incentives for not allowing model access "freely," that is, without encumbrances. Some concerns about model access are as follows:

1. Terms of access: On what terms will users gain access? Free, by fee, time limitations, restrictions on use, recovery of expenses? Can an institution access it, or will only individual licenses be acceptable? Can a license fee be charged

so that the developer(s) feel fairly compensated, but is not so onerous that use by others becomes cost-prohibitive? Even more crucial, what is the incentive for the developer to maintain the model they have made available and to keep it current? Who will adjudicate copyright and other use issues? Will it be by panel or by individuals? If by panel, who will comprise the panel? Will this process be partially or fully automated to make it less onerous to developers and users?

2. Means of Access: Perhaps most important are the logistics for making open-source models available. Where will the model be stored—on the developer's or other secure server and accessed remotely only, or downloadable to the user's computer?

3. Version control: Who will maintain the model and control versions? If an apparent error is found in the model, who verifies it, corrects it, and with what incentive? If there are multiple modifications, will these be integrated into one version and by whom? Or, who will determine which modifications to make?

Although the topic of open-source models in health economics is garnering attention, a cultural shift in model development is necessary to ensure these see the light of day. Questions remain as to who will lead this shift from proprietary to open-source models and how this can be encouraged in a culture where secrecy, competition, and one-upsmanship have been the norm. ISPOR is making strides in this regard, including the initiation of the Open Source Model Special Interest Group that will attempt to tackle these issues.

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Additional information

The preceding article was based on an Issue Panel presented at ISPOR 2019. For more information on the ISPOR Open-source Model Special Interest Group, go to www.ispor.org/specialinterestgroups.