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ISPOR Reports–Editorial

Are We Ready to Use Constrained Optimization in Health Outcomes Research?

Decision-analytic modeling is an accepted approach used by many health technology assessment agencies to assess the cost-effectiveness (i.e., value) of new and existing health care technologies [1,2]. These agencies (along with payers, physicians, and other stakeholders) recognize that decision analysis can be used to forecast health outcomes and to understand the value of medical technologies based on clinical trial data before they are used in clinical practice. In fact, decision modeling as an analysis tool has expanded and helps us to understand a variety of additional outcomes issues associated with health care, including the budget impact, cost of care, and risk versus benefit.

Mathematical programming, *mathematical optimization*, and *constrained optimization* are terms used to describe a mathematical technique to find the best or "optimal" solution to a problem for a given set of decision variables and a series of constraints. It is a decision-analytic modeling approach that, in its simplest form, is made up of an objective function (i.e., equation) that is to be maximized or minimized subject to a set of constraint equations (i.e., limits). Finding the maximum or minimum solution for the objective function requires finding the best set of values for the decision variables.

Constrained optimization is typically used to find an optimal allocation of resources. It has been used to solve problems in many fields, such as allocating available funds among different investments in financial planning, blending materials in manufacturing (e.g., blending different types of crude oils to produce different types of gasoline), or logistics planning in the military. Even in health care, these methods have been used to optimize things such as radiation administration, operating room scheduling, and staff scheduling. Nevertheless, their use is typically not seen in outcomes research.

ISPOR's task force on Constrained Optimization Methods in Health Services Research was set up to introduce the value of these methods in health systems and outcomes research. The aim is to describe problems for which these methods may be appropriate and to identify good practices for these methods (https://www.ispor.org/TaskForces/Optimization-Methods-in-Healthcare-Delivery.asp). The first task force report introduces the concepts of constrained optimization and presents the methodology through a simple two-dimensional example [3]. Steps to assist researchers in constructing, solving, and reporting these methods are reviewed. The approach is then compared with other decision-modeling contexts traditionally seen in health outcomes research.

The second task force report, which is published in this issue of *Value in Health*, takes the next step and reviews various applications of constrained optimization methods in health decision-making [4]. The steps of the optimization process are reintroduced and applied in in-depth reviews of actual published applications of these methods. From this second report, the reader gets a real sense of what these methods can do and the value they can bring to health care decision-making.

The application of constrained optimization methods has both commonalities with and unique features to other decision analysis methods; for example, Markov models are great for modeling disease progression, whereas constrained optimization is typically used for resource allocation. In addition, although decision trees, Markov models, and constrained optimization models can be set up in a stochastic form, simulation is stochastic in its natural form. The list of differences goes on. Nevertheless, as with any decision-modeling exercise, applying these methods is a process, and the process of constructing and solving the problem enables us to identify gaps in the availability of data and understand and identify relationships and processes.

In some manner, constrained optimization methods provide us with a more efficient approach for assessing value across health technologies, and they force us to look at problems differently. In a typical cost-effectiveness analysis used for assessing value, we compare the outcomes from one treatment to another treatment using simple calculations (or decision tree), Markov, or simulation approaches. We use these same methods for assessing affordability or the budget impact, in which we compare a budget scenario made up of one mix of treatments (e.g., the current mix) compared with a budget scenario made up of another mix of treatments (e.g., the new intervention). As a result, we are conditioned to think about comparing treatments with treatments or keeping the type and number of health technologies to a minimum because problem complexity increases tremendously with the number of technologies considered. We can see this in the first case study reviewed in the second task force report, in which an allocation of the prevention strategies (screening, vaccination, screening at different time intervals plus vaccination, and no prevention) is considered. Rather than a comparison of one vaccine versus another vaccine or one screening approach versus another screening approach, the problem approach expands across various prevention modalities, which deviates from the typical comparison considered in cost-effectiveness or budget-impact analyses. In addition, although still difficult to solve (i.e., requiring a large number of

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decision variables), the problem structure is contained to a reasonable set of equations. In fact, there are 52 decisions or combinations of prevention approaches that are considered. Nevertheless, even with 52 choices to consider, the problem structure is still straightforward. The second case study also presents an application that could not readily be included in a typical cost-effectiveness or budget-impact analysis. Specifically, rather than allocating treatments, Denton et al. identify the best time (i.e., age) to initiate statin treatment in patients with type 2 diabetes, based on patient age and clinical history [5]. The objective is to produce better health outcomes when considering the timing of treatment in patients with different clinical histories.

In each of these case studies, the objective requires decisions different from those typically made using the results of cost-effectiveness or budget-impact analysis. Constrained optimization methods are used to solve different types of problems. Thus, these methods motivate us to consider broader applications of decision analysis relating to health outcomes and budgets that are value based and that may be of interest to a broader set of stakeholders. As a result, a more active use of these methods to drive health interventions could help improve health outcomes.

Despite the potential value of constrained optimization, application of these methods in our field has been slow. One reason may be that these methods may be viewed as more complex. We have seen the widespread use of decision-analysis methods, such as decision trees and Markov processes. These methods are relatively straightforward in their calculations and are thus relatively easy to perform and, for decision makers not trained in these methods, easier to understand. In contrast, the uptake of simulation modeling has been slower. Both the complexity of the model structure and calculations and the data needed to populate these models have been challenging for the researcher and for transparency to the nontechnical decision maker. Nevertheless, over time, we have found and continue to find ways to deal with these challenges, allowing more widespread use of simulation modeling. With constrained optimization formulations being very heavily mathematical, it may be that more technical expertise is required to formulate the model structure. In addition, these complexities make it difficult for many decision makers to comprehend.

Optimization is seen as a tool for deciding a very specific problem rather than generating information to assist in the decision making. With this approach, we not only are proclaiming that a solution exists, but we are also proclaiming that the solution we give is the best or "optimal" solution. It is easy to tell people what the optimal or best solution is when dealing with inanimate objects. But this approach can be very scary and can result in pushback when the solution involves humans; for example, when allocating prevention strategies for patients at risk for cervical cancer, a patient may accept being allocated to vaccination, but she may be less accepting if she is allocated to receive no prevention because of her lower risk of disease or her ready access to screening facilities.

The benefit of constrained optimization is that an "optimal" solution is found considering a variety of constraints. As a result, constraints can include not only budgets but also measures of equity in allocating treatments to patients in a population. The latter can help alleviate potential criticisms around fairness when using the results of cost-effectiveness or budget-impact analyses [6–8]. Nevertheless, even though these additional constraints are considered, the recommended solution still might not be feasible in practice. More important, the "optimal" solution represents the "most efficient" solution to the decision problem. Because the constrained optimization approach gives us the "most efficient" solution, other feasible solutions, should we choose to use them, can be measured against it. As a result, we now have a benchmark to compare how efficient we are. By having this benchmark, we may be able to improve processes without using the actual optimal solution.

This second task force helps us see real-life applications of constrained optimization. Hopefully, the presentation of these examples will promote consideration of different types of problems we can solve and foster a better understanding of how to approach constructing them. Even if the work produced by these task forces is insufficient to convince folks to think about broader applications in the field of health outcomes and the potential importance of these methods, a third task force—the Economic Analysis of Vaccination Programs: ISPOR Good Practices Task Force (https://www.ispor.org/TaskForces/Vaccines-Economic-Evaluation.asp)—has acknowledged that these methods have value and application for economic assessments of prevention programs. We hope to see more use of these methods in the future.

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