Cost-effectiveness analysis
with probabilistic graphical models

Francisco Javier Díez[1,2]   Manuel Luque[1,2]   Manuel Arias[1,2]   Jorge Pérez-Martín[1,2]

[1]Dept. Artificial Intelligence, Universidad Nacional de Educación a Distancia (UNED), Madrid, Spain
[2]DeciSupport AI, Madrid, Spain

Abstract

The two formalisms most widely used for the representation and analysis of decision problems in medicine are decision trees and Markov flat models, which seriously limit the complexity of the problems that can be addressed. In contrast, probabilistic graphical models (PGMs) can represent the state and the evolution of the system (the patient) using much richer structures, but they are rarely used for economic evaluations in medicine given that, until recently, they could not perform cost-effectiveness analysis (CEA). In this paper we summarize the research done by our group, developing new types of PGMs and new algorithms for CEA and implementing them in OpenMarkov, an open-source tool especially designed for medicine.

1 INTRODUCTION

Due to the rapid increase of medical expenditures in all countries, rich and poor, every health system must determine whether the benefit of each intervention outweighs its economic cost. The main tools that health economists use for cost-effectiveness analysis (CEA) are decision trees (DTs) [Drummond et al., 2015] and flat Markov models, usually implemented in Excel or in the commercial software TreeAge. By "flat" we mean that the system—the patient, in this case—is modeled with a set of mutually exclusive states. This imposes a serious limitation in the complexity of the problems that can be addressed. In particular, the size of a DT grows exponentially with the number of variables, even in the unicriterion case, and much faster for CEA because the standard algorithm [Raiffa and Schlaifer, 1961] cannot evaluate DTs with embedded decision nodes, which are those other than the root of the tree [Kuntz and Weinstein, 2001, Arias and Díez, 2014]. Flat Markov models, in turn, cannot represent multiple properties of the system, because

having mutually exclusive states amounts to representing the system with a single variable, and they often require "tunnel states" [Drummond et al., 2015] and other modeling tricks to represent the complexity of real-world systems.

In contrast, probabilistic graphical models (PGMs) [Koller and Friedman, 2009] can represent the state of the system (the patient) using much richer structures. For example, Bayesian networks can represent the dependencies and independencies among the variables that model a system, while DTs cannot. Similarly, a dynamic Bayesian network can explicitly represent different features of the system and their evolution by having several variables for each time slice, linked by causal intra- and inter-temporal edges, while flat Markov models (basically equivalent to Markov chains) cannot.

Even though many real-world PGMs have been developed for medical problems, probably more than for any other field, the uncertainty in artificial intelligence (UAI) community has in general overlooked the relevance of CEA in medicine, and they have only addressed unicriterion problems.

2 PGMS AND ALGORITHMS FOR CEA

Models for CEA involve three types of entities: decisions, chance variables (for representing uncertain outcomes), and values (for representing the decision maker's payoffs, with two criteria: cost and effectiveness). For this reason, DTs have these three types of nodes , the same as IDs [Howard and Matheson, 1984]. Given that the standard algorithm for IDs could only evaluate unicriterion models, we developed an algorithm for CEA, with two versions, based on variable elimination and arc reversal, respectively [Arias and Díez, 2015]. This way we could perform a CEA for Mediastinet [Luque et al., 2016], an ID for lung cancer whose equivalent DT contains more than 10,000 branches.

The main limitation of IDs is that they can only represent symmetric decision problems [Díez et al., 2018]. In particular, they require a total ordering of the decisions. This was

a problem when building Mediastinet because the pulmonologist collaborating in the project was uncertain about the optimal order of the tests. For this reason, we introduced introduced *decision analysis networks* (DANs), which, in addition to representing all symmetric problems as easily as with IDs, can also model and solve asymmetric problems [Díez et al., 2018]. We have recently published an algorithm for CEA with DANs [Díez et al., 2021], with which we could find the optimal order of the tests for the mediastinal staging of lung cancer, with cost-effectiveness criteria, using a DAN version of Mediastinet.

Another limitation of IDs is that they cannot model the evolution of a system. In turn, PGMs that model time explicitly, such as Markov decision processes (MDPs) and partially observable MDPs (POMDPs), could not perform CEA. For this reason we developed Markov influence diagrams [Díez et al., 2017], which have three types of nodes, like IDs, and discretize the time by setting a "cycle lenght", like MDPs and POMDs, but differ from them in the assumption that decisions are atemporal. In addition to creating MID versions of some Markov models published in the literature, we have also developed new MIDs for several medical problems, such as malignant pleural effusion [Bermejo et al., 2015] and bilateral cochlear implantation [Pérez-Martín et al., 2017].

All these models have been built with OpenMarkov, an opensource software tool implemented in Java, and most of them are available in ProbModelXML, a format for encoding PGMs.

References

M. Arias and F. J. Díez. The problem of embedded decision nodes in cost-effectiveness decision trees. *Pharmacoeconomics*, 32:1141–1145, 2014. doi: 10.1007/s40273-014-0195-1.

M. Arias and F. J. Díez. Cost-effectiveness analysis with influence diagrams. *Methods of Information in Medicine*, 54:353–358, 2015. doi: 10.3414/ME13-01-0121.

I. Bermejo, María J. Roca, and F. J. Díez. Cost-effectiveness analysis of PleurX catheter vs. talc pleurodesis for the treatment of malignant pleural effusions: A Markov model. In *37th Annual Meeting of the Society for Medical Decision Making*, St. Louis, MO, 2015.

F. J. Díez, M. Yebra, I. Bermejo, M. A. Palacios-Alonso, M. Arias, M. Luque, and J. Pérez-Martín. Markov influence diagrams: A graphical tool for cost-effectiveness analysis. *Medical Decision Making*, 37:183–195, 2017. doi: 10.1177/0272989X16685088.

F. J. Díez, M. Luque, and I. Bermejo. Decision analysis networks. *International Journal of Approximate Reasoning*, 96:1–17, 2018. doi: 10.1016/j.ijar.2018.02.007.

F. J. Díez, M. Luque, M. Arias, and J. Pérez-Martín. Cost-effectiveness analysis with unordered decisions. *Artificial Intelligence in Medicine*, 117:102064, 2021. doi: 10.1016/j.artmed.2021.102064.

M. F. Drummond, M. J. Sculpher, K. Claxton, G. L. Stoddart, and G. W. Torrance. *Methods for the Economic Evaluation of Health Care Programmes*. Oxford University Press, Oxford, UK, 4th edition, 2015.

R. A. Howard and J. E. Matheson. Influence diagrams. In R. A. Howard and J. E. Matheson, editors, *Readings on the Principles and Applications of Decision Analysis*, page 719–762. Strategic Decisions Group, Menlo Park, CA, 1984.

D. Koller and N. Friedman. *Probabilistic Graphical Models: Principles and Techniques*. The MIT Press, Cambridge, MA, 2009.

K. M. Kuntz and M. C. Weinstein. Modelling in economic evaluation. In M. F. Drummond and A. McGuire, editors, *Economic Evaluation in Health Care*, chapter 7, page 141–171. Oxford University Press, New York, 2001.

M. Luque, F. J. Díez, and C. Disdier. Optimal sequence of tests for the mediastinal staging of non-small cell lung cancer. *BMC Medical Informatics and Decision Making*, 16:1–14, 2016. doi: 10.1186/s12911-016-0246-y.

J. Pérez-Martín, M. A. Artaso, and F. J. Díez. Cost-effectiveness of pediatric bilateral cochlear implantation in Spain. *The Laryngoscope*, 2017. doi: 10.1002/lary.26765.

H. Raiffa and R. Schlaifer. *Applied Statistical Decision Theory*. John Wiley & Sons, Cambridge, MA, 1961.