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Medical decision analysis with probabilistic graphical models

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OVERVIEW

- The naïve-Bayes method
- Bayesian networks
- Influence diagrams
- Decision analysis networks
- Cost-effectiveness analysis
- Markov models
- Conclusion

Naïve-Bayes method for probabilistic diagnosis

- *n* diagnoses, *m* possible findings
- 1st hypothesis: diagnoses are mutually exclusive
  (i.e., the patient has at most one disease)
- 2nd hypothesis: findings are conditionally independent

$$P(f_1, \ldots, f_m \mid d_i) = P(f_1|d_i) \cdot \ldots \cdot P(f_m|d_i)$$

- Bayes' theorem (naïve method)

$$P(d_i|f_1, \ldots, f_m) = \alpha \cdot P(f_1|d_i) \cdot \ldots \cdot P(f_m|d_i) \cdot P(d_i)$$

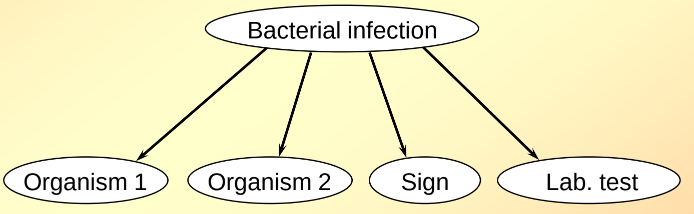
Successful applications of the naïve-Bayes

- Lodwick GS, Haun CL, Smith WE, et al. , "Computer diagnosis of primary bone tumors: A preliminary report," *Radiology* **80** (1963) 273-275.
- Overall JE, Williams CM, "Conditional probability program for diagnosis or thyroid function," *JAMA* **183** (1963) 307-313.
- Toronto AF, Veasy LG, Warner HR, "Evaluation of a computer program for diagnosis of congenital heart disease," *Progress in Cardiovascular Diseases* **5** (1963) 362-377.
- Warner HR, Toronto AF, Veasy LG, "Experience with Bayes' theorem for computer diagnosis of congenital heart disease," *Annals New York Acad. Sciences* **115** (1964) 558-567.
- de Dombal FT, Leaper JR Staniland JR, et al., "Computer-aided diagnosis of acute abdominal pain," *BMJ* **2** (1972) 9—13.
- Gorry GA, Kassirer JP, Essig A, Schwartz WB, "Decision analysis as the basis for computer-aided management of acute renal failure," *Amer. J Med* **55** (1973) 473-484.
- Gorry GA, Silverman H, Pauker SG, "Capturing clinical expertise: A computer program that considers clinical responses to digitalis," *Amer. J. Med* **64** (1978) 452-460.

Some approximations were necessary for the sequential selection of tests [Gorry and Barnet, 1968].

Limitations of the naïve-Bayes method

- In general the diagnoses are not mutually exclusive: how to diagnose multiple disorders.
- In general findings are not conditionally independent.



Bayesian networks

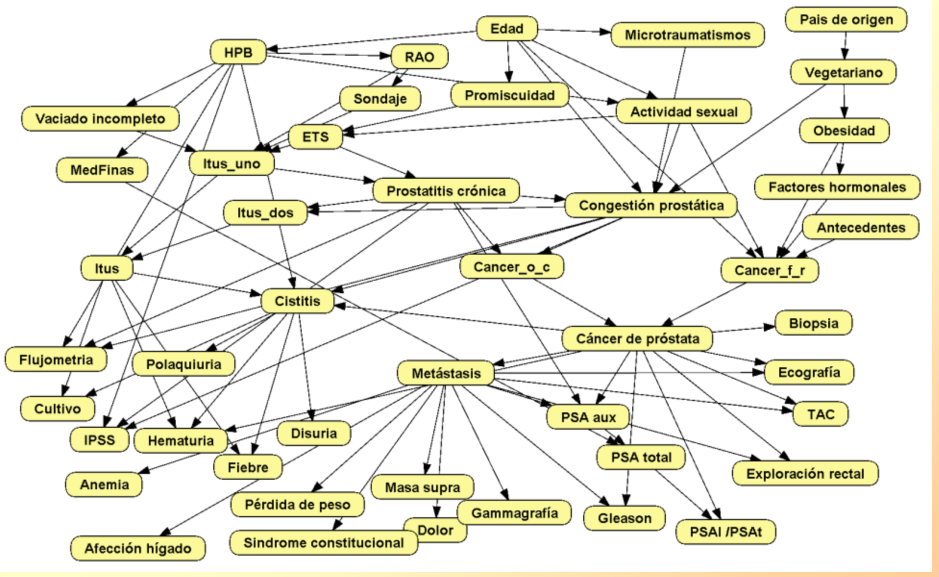
Advantages of BNs w.r.t. naïve-Bayes

- BNs can diagnose several diseases simultaneously
- BNs do not assume conditional independence
- BNs are usually causal models
  - closer to doctors' reasoning: explanation of reasoning
  - probabilities are in general easier to obtain
- Three types of reasoning:
  - abductive
  - deductive
  - inter-causal
- Canonical models simplify the construction of the model.

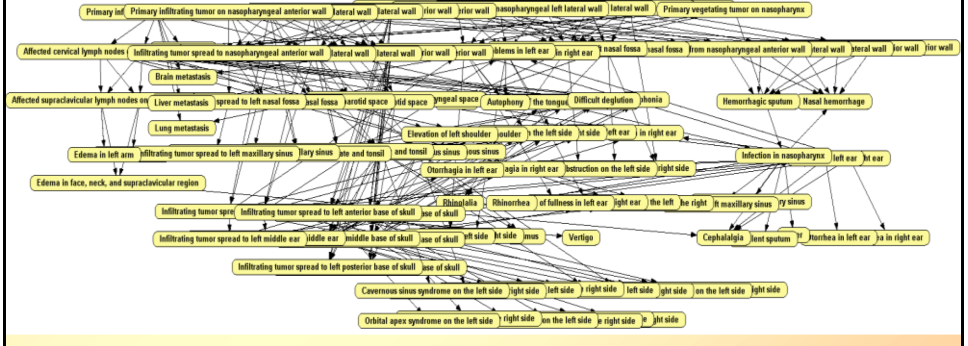
Examples of BNs

- Medical Bayesian networks we have built
  - DIAVAL: echocardiography (valvulopathies)
    F. J. Díez' thesis, 1994
  - Prostanet: urology (prostate cancer)
    Carmen Lacave's thesis, 2003
  - Nasonet: nasopharyngeal cancer spread
    Severino Galán's thesis, 2003
  - HEPAR II: liver diseases
    Agnieszka Onisko's thesis, 2003
  - Catarnet: Cataract surgery
    Nuria Alonso's thesis, 2009

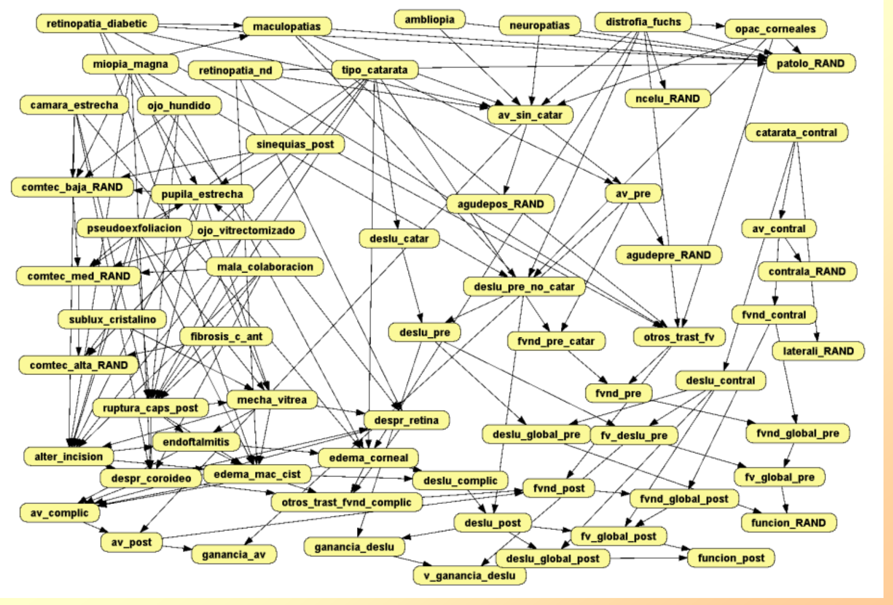
Prostanet (for prostate diseases)



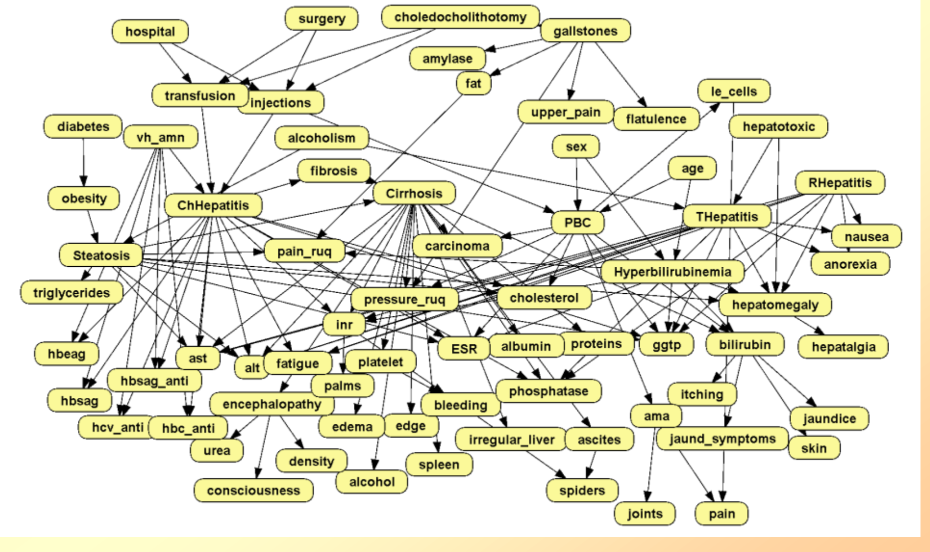
Nasonet (nasopharyngeal cancer spread)



Catarnet (cataract surgery)

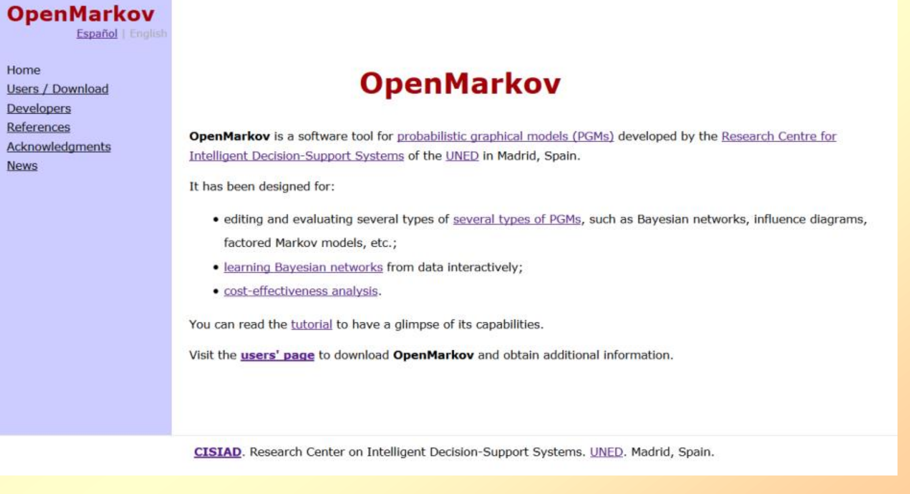


Hepar II (liver diseases)



OpenMarkov. Main features

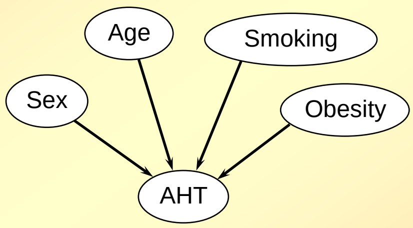
- Strengths
  - Written in Java: portability (Windows, linux, MacOS…)
  - Open source
  - Software engineering tools: JUnit, maven, mercurial (bitbucket), nexus, bugtracker, etc.
  - Easily extensible: users can adapt it to their needs
  - Many types of models, potentials, etc.
  - Very active: new features are continuously added
  - Support for users and developers: wiki, lists, mail…
  - Well-documented format for encoding networks: ProbModelXML.
- Weaknesses
  - Written in Java: relatively slow (in some cases)
  - No on-line help, documentation still poor
  - Still a prototype; needs debugging
  - Support is limited, due to scarcity of human resources.



Canonical models

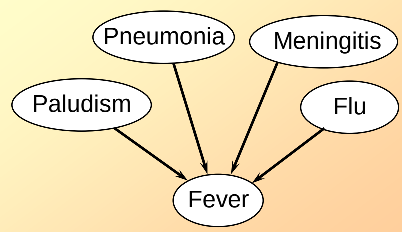
General model

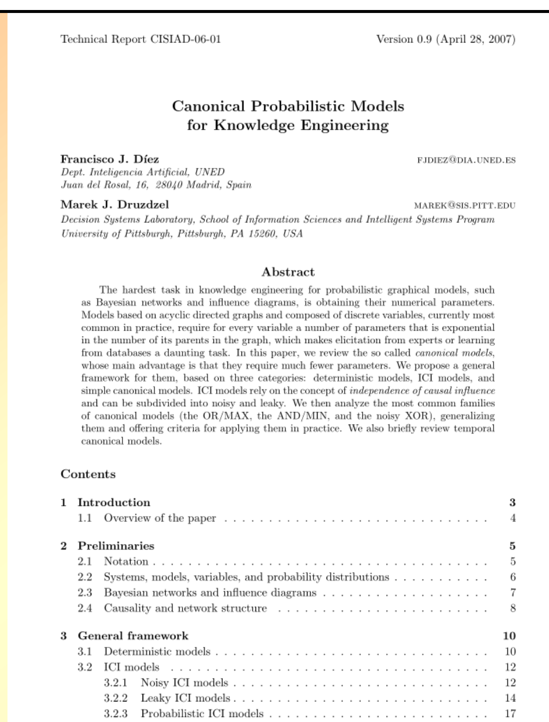
- Probability table:
  $P(y \mid x_1, \ldots, x_n)$
- Factors that influence the prob. of X



Noisy OR

- Efficiency of each link:
  c_i
- Causes that may produce X





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Canonical Probabilistic Models for Knowledge Engineering

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Abstract

The hardest task in knowledge engineering for probabilistic graphical models, such as Bayesian networks and influence diagrams, is obtaining their numerical parameters. Models based on acyclic directed graphs and composed of discrete variables, currently most common in practice, require for every variable a number of parameters that is exponential in the number of its parents in the graph, which makes elicitation from experts or learning from databases a daunting task. In this paper, we review the so called *canonical models*, whose main advantage is that they require much fewer parameters. We propose a general framework for them, based on three categories: deterministic models, ICI models, and simple canonical models. ICI models rely on the concept of *independence of causal influence* and can be subdivided into noisy and leaky. We then analyze the most common families of canonical models (the OR/MAX, the AND/MIN, and the noisy XOR), generalizing them and offering criteria for applying them in practice. We also briefly review temporal canonical models.

Contents

How to build a Bayesian network

- From a database

Data base $\xrightarrow{\text{algorithm}}$ Bayesian network

  - There are many algorithms, several new algorithms every year
  - Similar to statistical methods (logistic regression, neural nets...)

- With a human expert's help

Causal knowledge $\xrightarrow{\text{modeling}}$ Causal graph $\xrightarrow{\text{probabilities}}$ Bayesian network

- Hybrid methods:
  - experts $\rightarrow$ structure; database $\rightarrow$ probabilities
  - experts $\rightarrow$ initial model; new cases $\rightarrow$ refine the probabilities

Learning BNs with OpenMarkov

- Two possibilities of learning
  - automatic, interactive
- Two main algorithms:
  - Search-and-score
    - search
      - depart from a network with no links
      - add/remove/invert a link in each iteration
    - score
      - use a metric (there are several metric available)
  - PC
    - departs from a fully-connected undirected graph
    - remove a links when the two variables are independent
      - more precisely,when the correlation is not statistically significant (α)
    - remove a link when the two variables are conditionally indep.
    - orient the remaining links to obtain a directed graph

Advantages of interactive learning

- The system proposes, the user decides
  - Very useful for tuition
  - Useful for combining data with expert knowledge
  - Useful for debugging new algorithms (workbench)
  - See www.openmarkov.org/docs/tutorial.

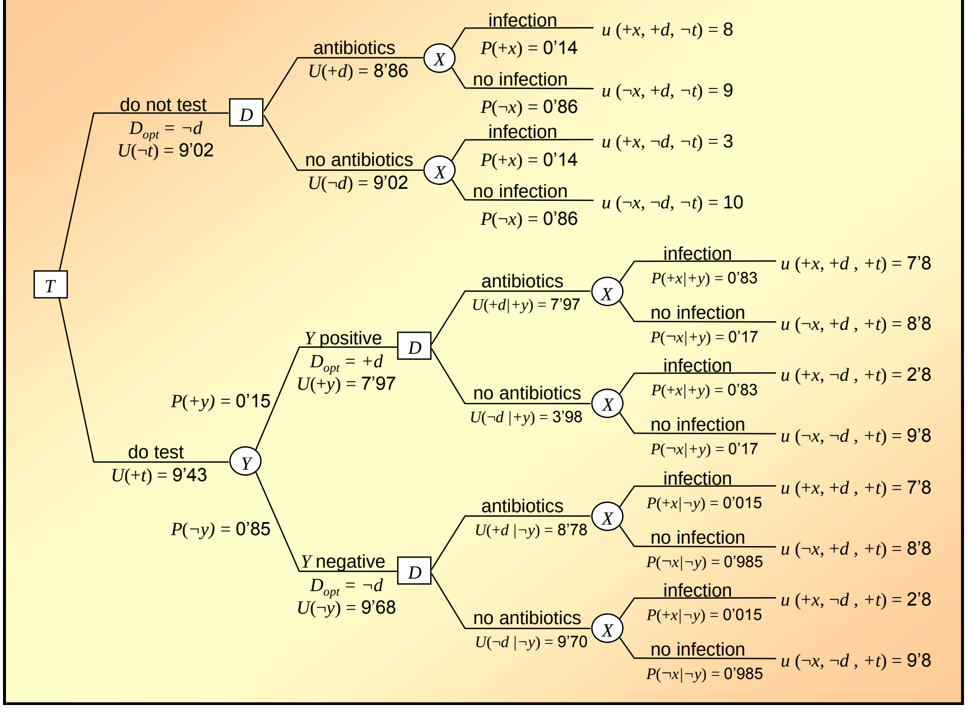
Influence diagrams

A medical problem

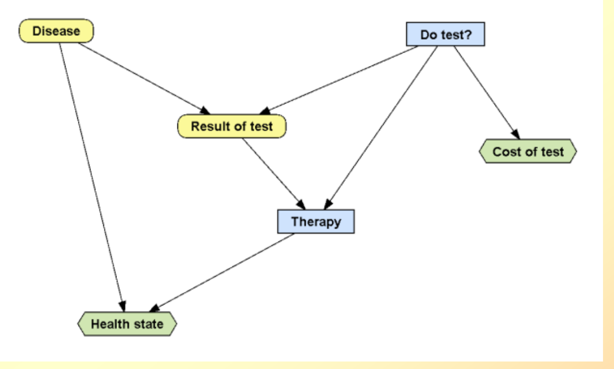
- **Disease X**
  - Prevalence: $P(+x) = 0'14$
- **Therapy D**
  - Utility:

$u(x, d)$	$+x$	$\neg x$
$+d$	8	9
$\neg d$	3	10

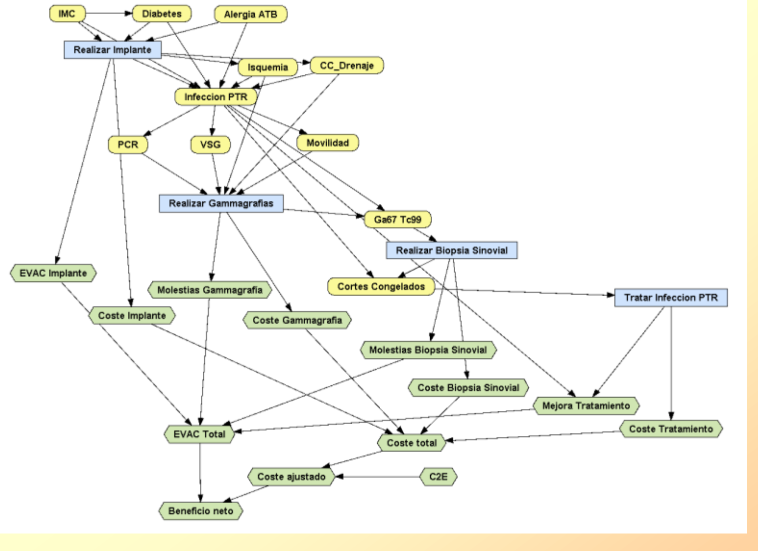
- **Test Y**
  - Sensitivity: $P(+y|+x) = 0'91$
  - Specificity: $P(\neg y|\neg x) = 0'97$
  - Cost: $u_{\text{test}}(x, d) = u_{\text{not-test}}(x, d) - 0'2$
- **Decisions:**
  - Is it worth doing the test?
  - In what cases should we apply the therapy?



An ID for this example

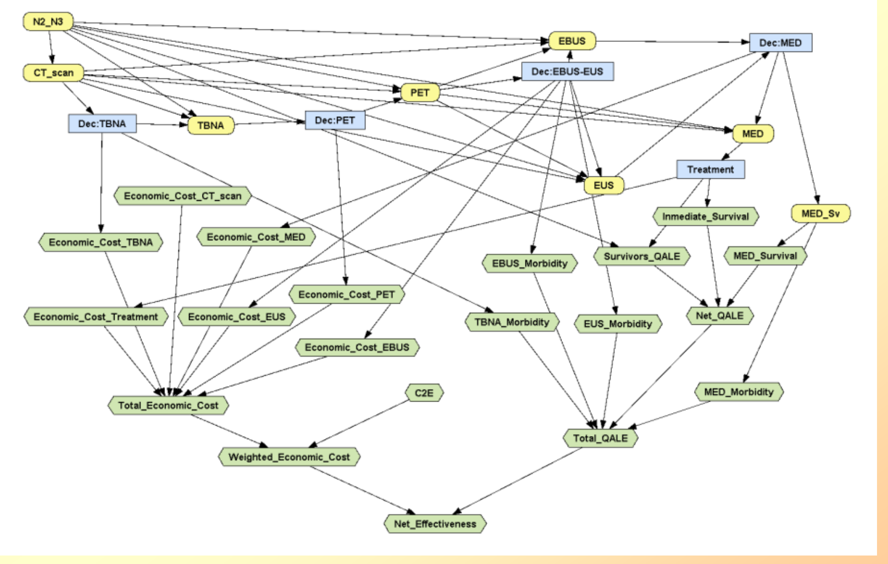


Arthronet (total knee arthroplasty)



Equivalent to a decision tree containing ~10^4 branches.

Mediastinet (lung cancer)



Equivalent to a decision tree containing ~10^4 branches.

Advantages of influence diagrams (1/3)

- IDs are more <u>compact</u> than decision trees
  - An ID having *n* binary nodes ~ a DT having 2^n branches
- IDs transform automatically into decision trees
  - ... but the reverse is not true (no general algorithm)
  - If you build a decision tree, you only have a decision tree.
  - If you build an ID, you have both.
- IDs are <u>much easier to build</u> than decision trees
  - IDs use direct probabilities (prevalence, sensitivity, specificity...) and costs (mortality, morbidity, economic cost...)
  - ID can use canonical models (noisy OR, noisy AND, etc.)
  - Each parameter appears only once in the ID
    - in many cases it is not necessary to have parametric variables
  - IDs can use super-value nodes: explicit combination of utilities

Advantages of influence diagrams (2/3)

- No external pre-calculation of probabilities is required
- Having all the information, no debugging is usually needed
  - On the contrary, "all trees have bugs" (*Primer on MDA*)
- IDs are much easier to modify than decision trees
  - Refine the model with new decisions and chance variables
  - Structural sensitivity analysis
  - Can adapt to different regional settings
  - Can adapt to patient's medical characteristics and preferences
- Explicit representation of causality
  - a link indicates causal influence
  - the absence of a link means "no causal influence" (hypothesis)

Advantages of influence diagrams (3/3)

- Two possibilities of evaluation:
  1. expansion of an equivalent decision tree
     - exponential complexity (time and space)
     - equivalent to the brute-force method for Bayesian networks
     - many problems can not be solved by this method
  2. operations on the ID (recursive reduction of the ID)
     - direct manipulation of the graph and/or potentials of the ID
     - similar to the best algoritms for Bayesian networks
     - canonical models and SV nodes can lead to more efficient evaluations
- More possibilities of explanation of reasoning
  - computation of posterior probabilities on the ID (as if it were a BN)
  - value of information (EVPI and other measures) can be computed easily
  - other methods from Bayesian networks and qualitative prob. networks.
  - These methods can be used for debugging/refining IDs.

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The Influence of Influence Diagrams on Artificial Intelligence

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Howard and Matheson's article "Influence Diagrams" has had a substantial impact on research in artificial intelligence (AI). In this perspective, I briefly discuss the importance of influence diagrams as a model for decision making under uncertainty in the AI research community; but I also identify some of the less direct, but no less important, influences this work has had on the field.

Key words: influence diagrams; decision theory; artificial intelligence; value of information; graphical models; perspective, the focus on graphical modeling research
History: Received on November 14, 2005. Accepted by Eric Horvitz on November 23, 2005, without revision.

Howard and Matheson's (1984/2005) "Influence Diagrams" has had a profound impact on developments in artificial intelligence. Some of these influences have been quite direct; others are more indirect, but in many ways, more substantial. The paper

vision (Binford and Levitt 2003), dialog management, user interface design, multiagent systems, and game theory (Koller and Milch 2003), to name but a few.

Another reasonably direct impact of "Influence Diagrams" derives from its role in the development

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The Influence of Influence Diagrams in Medicine

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Although influence diagrams have used medical examples almost from their inception, that graphical representation of decision problems has disseminated surprisingly slowly in the medical literature and among clinicians performing decision analyses. Clinicians appear to prefer decision trees as their primary modeling metaphor. This perspective examines the use of influence diagrams in medicine and offers explanations and suggestions for accelerating their dissemination.

Key words: decision analysis; influence diagrams; clinical decision making; medicine
History: Received December 12, 2005. Accepted by Eric Horvitz on January 5, 2006, after 1 revision.

Introduction

Two decades after Howard's landmark paper (Howard and Matheson 1984/2005) that introduced the concept of the influence diagram and three decades since Miller's initial report (Miller et al. 1976), *Decision Analysis* reproduced that paper in

modeling paradigm slowly spread from Stanford, both with courses offered at meetings of the Society for Medical Decision Making (Society for Medical Decision Making 2005) and with the development of software that could conveniently capture and evaluate such models.

IDs in the literature on MDM (1/3)

- Books that mention decision trees but do <u>not</u> mention IDs
  - Weinstein, Fineberg. *Clinical Decision Making*. 1980.
  - Sloan (ed.). *Valuing Health Care*. 1995.
  - Gold et al. *Cost-Effectiveness in Health and Medicine*. 1996.
  - Sackett et al. *Evidence-Based Medicine*. 1997 (and three other books on EBM).
  - Petiti. *Meta-Analysis, Decision Analysis and CEA*. 2nd ed., 2000.
  - Drummond, McGuire (eds.). *Economic Eval. in Health Care Programs*. 2001.
  - Levin and McEwan. *Cost-Effectiveness Analysis*. 2nd ed., 2001.
  - Parmigiani. *Modelling in Medical Decision* Making. 2002.
  - Haddix et al. *Prevention Effectiveness*. 2nd ed., 2003.
  - Fox-Rushby and Cairns. *Economic Evaluation.* 2005.
  - Briggs et al. *Decision Modelling for Health Economic Evaluation*, 2006.
  - Arnold. *Pharmacoeconomics: From Theory to Practice*. 2009.
  - Kassirer et al. *Learning Clinical Reasoning*. 2nd ed., 2010.
  - Mushlin and Greene. *Decision Making in Medicine*. 3rd ed., 2010.

(cont'd)

IDs in the literature on MDM (2/3)

- Books that mention decision trees but do <u>not</u> mention IDs (cont.)
  - Gray et al. *Applied Methods of CEA in Health Care*, 2011. Alfaro-LeFevre. *Critical Thinking, Clinical Reasoning, and Clinical Judgment*. 5th ed., 2013.
  - Morris et al. *Economic Analysis in Healthcare*. 2nd ed., 2012.
  - Rascati. *Essentials of Pharmacoeconomics*. 2nd ed., 2013.
  - Sox et al. *Medical Decision Making*. Latest ed., 2013.
  - Hunink et al. *Decision Making in Health and Medicine*. 2nd ed., 2014.
  - Drummond et al. *Methods for the Economic Evaluation of Health Care Programmes*. 4th ed. 2015.
  - Edlin et al. *Cost Effectiveness Modelling for HTA…* 2015.
- One book that mentioned IDs
  - Muenning. *Designing and Conducting Cost-Effectiveness Analyses in Medicine and Health Care*. 2002.

    "An influence diagram (also known as a tornado diagram) ..." [p. 242]

    The mistake is (partially) corrected in the second edition of the book, 2007.

IDs in the literature on MDM (3/3)

- Three books that describe IDs
  - Chapman and Sonnenberg (eds.). *Decision Making in Health Care*. 2000 (5 pages out of 421, in a chapter authored by Mark Roberts).
  - Schwartz and Bergus. *Medical Decision Making. A Physician's Guide*. 2008.
  - Kattan. *Encyclopedia of Medical Decision Making*. 2009 (4 pages out of 1200+)
- Summary of the informal survey of books on MDM and EBM
  - 26 books published after 1984
  - All of them explain DTs but only 3 describe IDs, very briefly.
- Some books on medical informatics mention IDs:
  - Shortliffe and Cimino. *Biomedical Informatics*. 4th ed., 2013 (2.5 pages out of 991).
  - Kalet. *Principles of Biomedical Informatics*. 2nd ed., 2013 (3 pages out of 708).
- Why are IDs so little known in health sciences after 30+ years?

Limitations of IDs

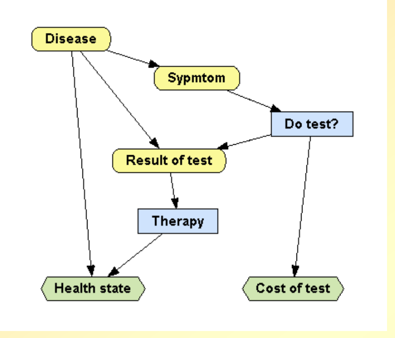
1. The “reasoning” of an ID is not easy to understand
2. The evaluation returns large policy tables
3. Algorithms could only evaluate unicriterion IDs
   - They cannot perform cost-effectiveness analysis
4. Temporal reasoning was not possible with IDs
   - Dynamic IDs are computationally unfeasible.
5. IDs can only model symmetric problems
   - IDs require a total ordering of the decisions
   - IDs cannot represent incompatibilities between values
     - Non-standard versions of IDs partially solve this problem, but none of the alternatives is completely satisfactory.

Solutions we have proposed

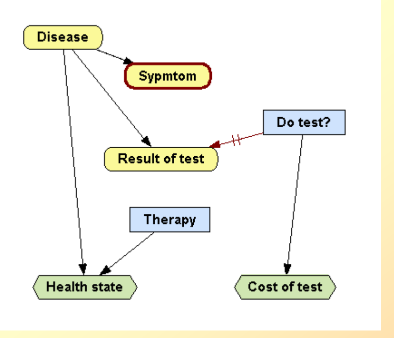
1. Explanation in influence diagrams
   - showing the posterior probabilities and expected values
   - introduction of evidence
   - hypothetical reasoning (what if) by means of imposed policies
2. Synthesizing the optimal intervention
   - in the form of a compact tree
3. Cost-effectiveness analysis with IDs
4. Markov influence diagrams
   - including cost-effectiveness analysis
5. Decision analysis networks
   - an alternative to IDs for asymmetric decision problems.

Decision analysis networks

Influence diagram

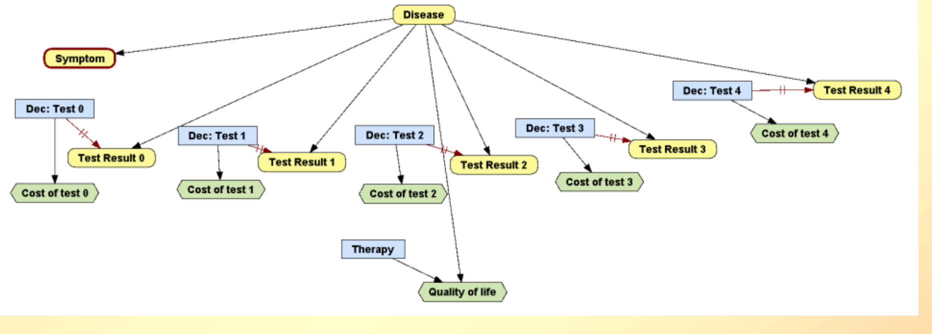


Decision analysis network



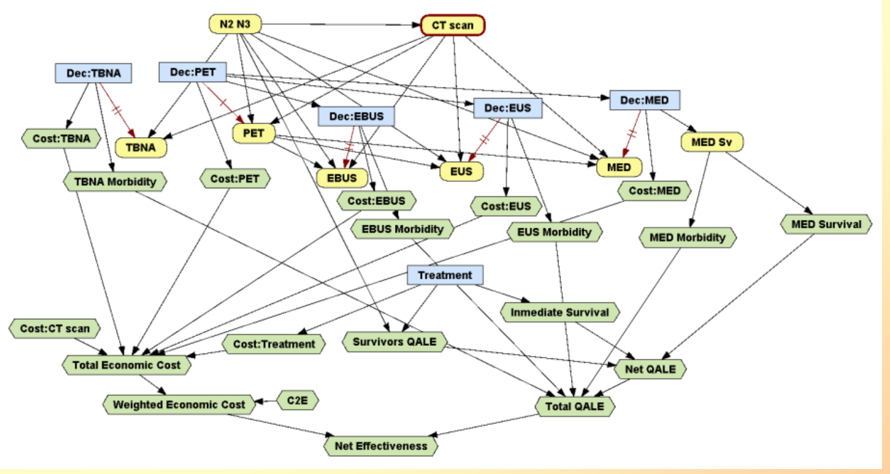
- The ID contains two information arcs:
  - because the symptom is always observed (spontaneously)
  - because the result of the test is known just after doing the test
- The variable “Result of test” does not make sense when the test is not performed

The *n*-test problem



- Computationally complex: n! possible orderings of the tests.
- We have developed an any-space algorithm for this problem
- and a fast algorithm (9 minutes for the 7-test problem).
- We are developing more efficient algorithms.

Mediastinet (DAN version)



Decisions are partially ordered.

DANs vs. IDs

- DANs can replace IDs as the standard decision analysis tool (in AI, MDM, operations research…) because:
  - For every ID there is an equivalent symmetric DAN
  - Virtually all real-world problems are asymmetric.
  - There many problems that cannot be modeled with IDs.
  - Even if a problem can be modeled with an ID, a DAN is usually better because it does not need dummy states.

Cost-effectiveness analysis with influence diagrams

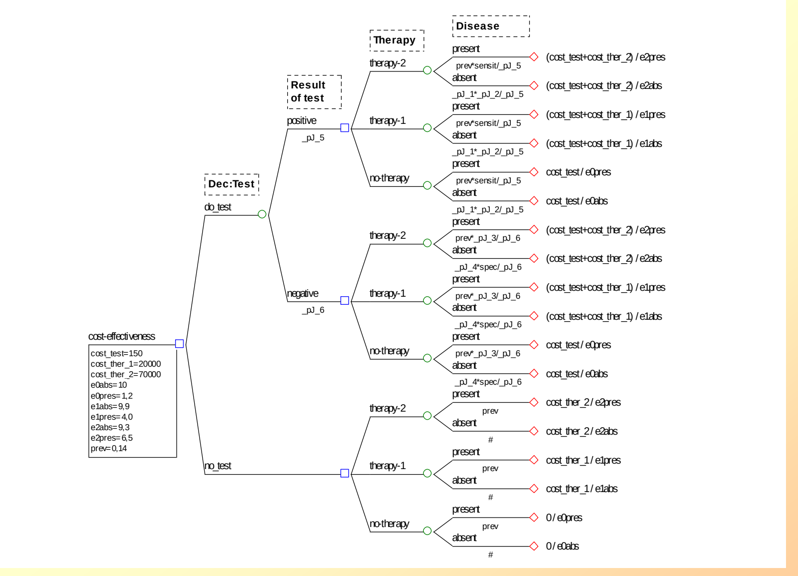
Example: Cost-effectiveness of a test

- Disease prevalence = 0.14
- Test sensitivity = 0.90, specificity = 0.93, cost = 150 €
- Therapy 1 cost = 20,000 €
- Therapy 2 cost = 70,000 €
- Effectiveness (QALYs)

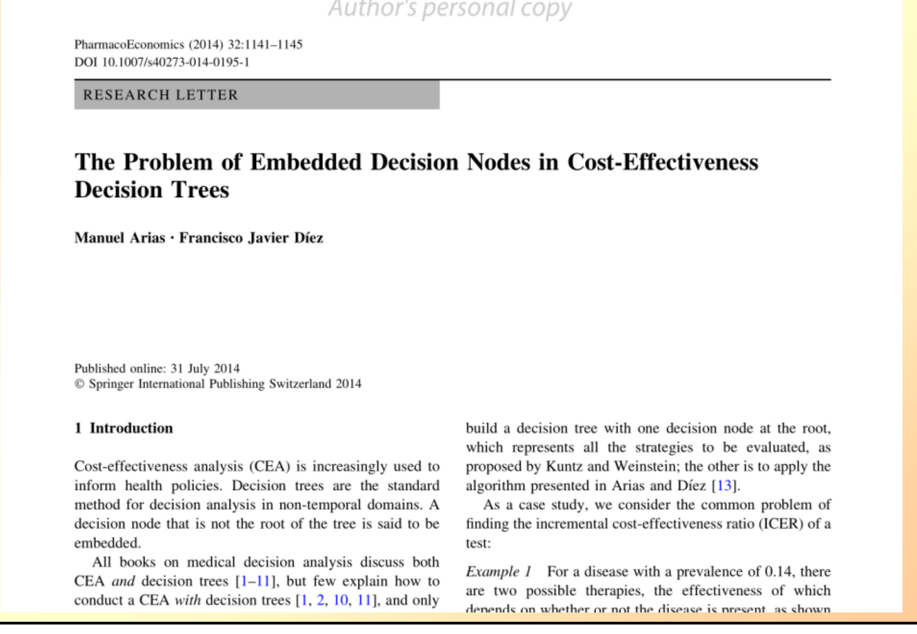
	No therapy	Therapy 1	Therapy 2
Disease present	1.2	4.0	6.5
Disease absent	10	9.9	9.3

- Is the test cost-effective?
- What is the most cost-effective therapy?

A decision tree for cost-effectiveness analysis



TreeAge usually returns wrong results for this tree.



PharmacoEconomics (2014) 32:1141–1145
DOI 10.1007/s40273-014-0195-1

RESEARCH LETTER

The Problem of Embedded Decision Nodes in Cost-Effectiveness Decision Trees

Manuel Arias · Francisco Javier Díez

Published online: 31 July 2014

1 Introduction

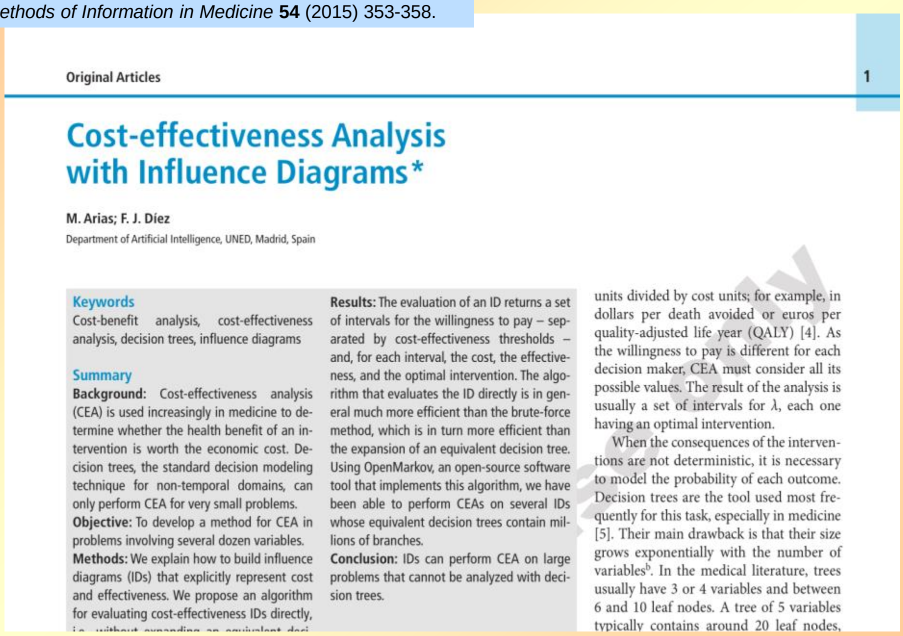
Cost-effectiveness analysis (CEA) is increasingly used to inform health policies. Decision trees are the standard method for decision analysis in non-temporal domains. A decision node that is not the root of the tree is said to be embedded.

All books on medical decision analysis discuss both CEA *and* decision trees [1–11], but few explain how to conduct a CEA *with* decision trees [1, 2, 10, 11], and only build a decision tree with one decision node at the root, which represents all the strategies to be evaluated, as proposed by Kuntz and Weinstein; the other is to apply the algorithm presented in Arias and Díez [13].

As a case study, we consider the common problem of finding the incremental cost-effectiveness ratio (ICER) of a test:

Example 1 For a disease with a prevalence of 0.14, there are two possible therapies, the effectiveness of which depends on whether or not the disease is present, as shown

Methods of Information in Medicine **54** (2015) 353-358.



Original Articles 1

Cost-effectiveness Analysis with Influence Diagrams*

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Department of Artificial Intelligence, UNED, Madrid, Spain

Keywords
Cost-benefit analysis, cost-effectiveness analysis, decision trees, influence diagrams

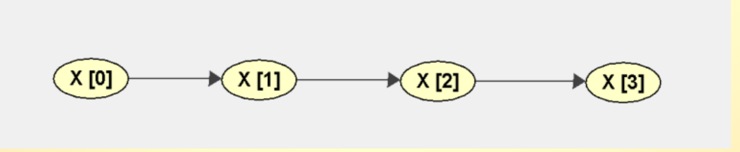
Summary
Background: Cost-effectiveness analysis (CEA) is used increasingly in medicine to determine whether the health benefit of an intervention is worth the economic cost. Decision trees, the standard decision modeling technique for non-temporal domains, can only perform CEA for very small problems.
Objective: To develop a method for CEA in problems involving several dozen variables.
Methods: We explain how to build influence diagrams (IDs) that explicitly represent cost and effectiveness. We propose an algorithm for evaluating cost-effectiveness IDs directly,
Results: The evaluation of an ID returns a set of intervals for the willingness to pay – separated by cost-effectiveness thresholds – and, for each interval, the cost, the effectiveness, and the optimal intervention. The algorithm that evaluates the ID directly is in general much more efficient than the brute-force method, which is in turn more efficient than the expansion of an equivalent decision tree. Using OpenMarkov, an open-source software tool that implements this algorithm, we have been able to perform CEAs on several IDs whose equivalent decision trees contain millions of branches.
Conclusion: IDs can perform CEA on large problems that cannot be analyzed with decision trees.

units divided by cost units; for example, in dollars per death avoided or euros per quality-adjusted life year (QALY) [4]. As the willingness to pay is different for each decision maker, CEA must consider all its possible values. The result of the analysis is usually a set of intervals for λ, each one having an optimal intervention.

When the consequences of the interventions are not deterministic, it is necessary to model the probability of each outcome. Decision trees are the tool used most frequently for this task, especially in medicine [5]. Their main drawback is that their size grows exponentially with the number of variables[b]. In the medical literature, trees usually have 3 or 4 variables and between 6 and 10 leaf nodes. A tree of 5 variables typically contains around 20 leaf nodes,

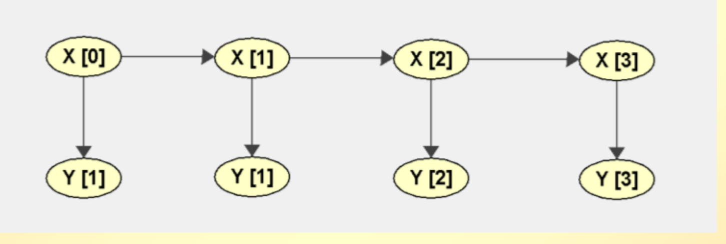
Temporal PGMs

Markov chain



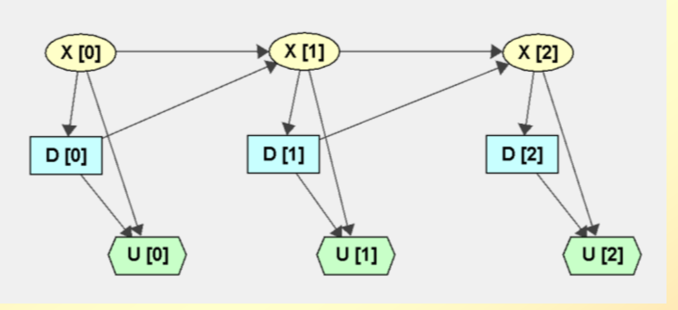
- One variable that evolves over time
- Transition probabilities: $P(x_{i+1}|x_i)$

Hidden Markov model (HMM)



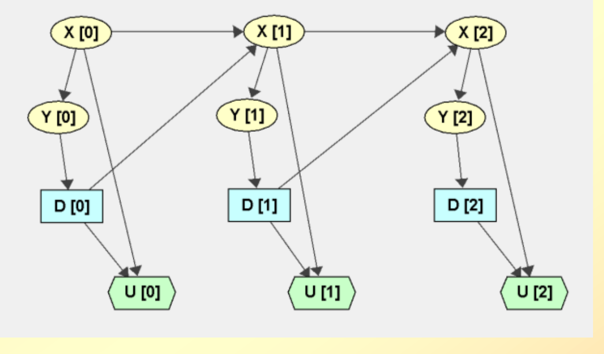
- Observed variable: Y
- Non-observed (hidden) variable: X
- Probability of each observation: $P(y_i|x_i)$
- Transition probability: $P(x_{i+1}|x_i)$

Markov decision process (MDP)



- Observed variable: X
- Decision: D
- Transition probability: $P(x_{i+1}|x_i)$
- Reward: $U(x_i, d_i)$

Partially observable MDP (POMDP)

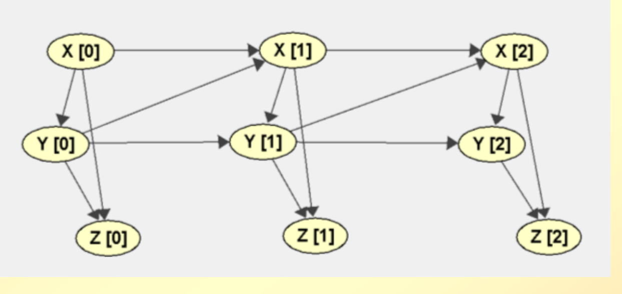


- Hidden variable: X
- Observed variable : Y
- Decision: D
- Observation prob.: $P(y_i|x_i)$
- Transition prob.: $P(x_{i+1}|x_i)$
- Reward: $U(x_i, d_i)$

Factored extensions of Markov models

Flat model	Factored model
Markov chain	Dynamic Bayesian network [Dean and Kanazawa, 1989]
Hidden Markov model	
Markov decision process (MDP)	Factored MDP [Boutilier et al., 1995, 2000]
Partially-observable MDP (POMDP)	Factored POMDP [Boutilier and Poole, 1996]

Dynamic Bayesian network (DBN)



- Markov chain or hidden Markov model:
  - one variable, X
  - one conditional probability: $P(x_{i+1}|x_i)$
- Dynamic Bayesian network:
  - several variables, $\{X, Y, Z\dots\}$
  - factored probability: $P(y_i|x_i)$, $P(z_i|x_i, y_i)$, $P(x_{i+1}|x_i, y_i)\dots$

IJCAI Workshop *Decision Making in Partially Observable, Uncertain Worlds: Exploring Insights from Multiple Communities*
Barcelona, July 2011

MDPs in Medicine: Opportunities and Challenges

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Abstract

In the last three decades hundreds of Markov models have been built for medical applications, but most of them fall under the paradigm of what we call *simple Markov models* (SMMs). Markov decision processes (MDPs) are much more powerful as a decision analysis tool, but they are ignored in medical decision analysis books and the number of medical applications based on them is still very small. In this paper we compare both types of models and discuss the challenges that MDPs must overcome before they can be widely accepted in medicine. We present a software tool, OpenMarkov, that addresses those challenges and has been used to build a Markov model for analyzing the cost-effectiveness of the HPV vaccine.

1 Introduction

Markov models were introduced in the beginning of the 20-th century by the Russian mathematician Andrei Andreyevich Markov [1906]. In the three decades passed since the pioneering work of Beck and Pauker [1983], hundreds of

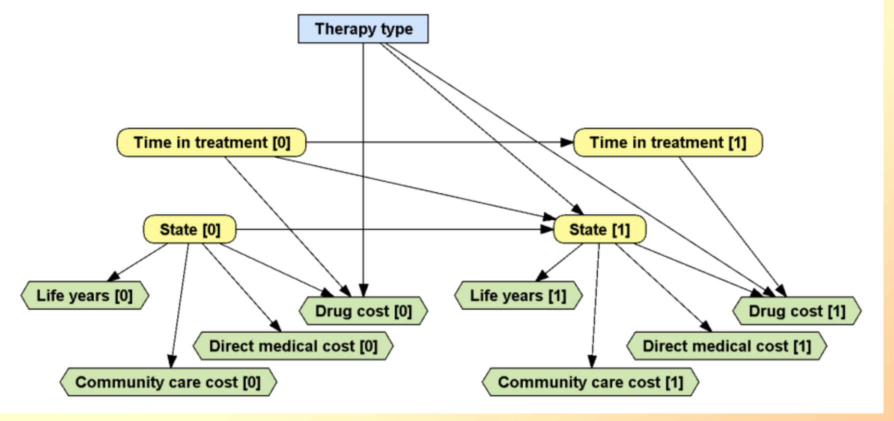
the emergence of partially observable Markov decision processes (POMDPs) [Åström, 1965], in which the state of the system is not directly observable, but there is a variable that correlates probabilistically with it. POMDPs were developed in the field of automatic control as an extension of MDPs, but currently most of the research about them is carried out in artificial intelligence (AI), again as a tool for planning, especially in robotics [Ghallab *et al.*, 2004]. The main contribution of AI to this field comes from the area of probabilistic graphical models: Bayesian networks [Pearl, 1988] led to the development of dynamic Bayesian networks [Dean and Kanazawa, 1989], which generalize Markov chains and hidden Markov models [Murphy, 2002]. The idea of using several variables to represent the state of the system, instead of only one, led to factored MDPs [Boutilier *et al.*, 1995; 2000] and factored POMDPs [Boutilier and Poole, 1996], which can model efficiently many problems that were unmanageable with flat (i.e., non-factored) representations; correspondingly, there are new algorithms that can solve problems several orders of magnitude bigger than in the recent past [Hoey *et al.*, 1999; Poupart, 2005; Spaan and Vlassis, 2005].

In the rest of the paper, we use the acronym MDPs to refer to both fully observable and partially observable models (FOMDPs and POMDPs, respectively).

Markov influence diagrams

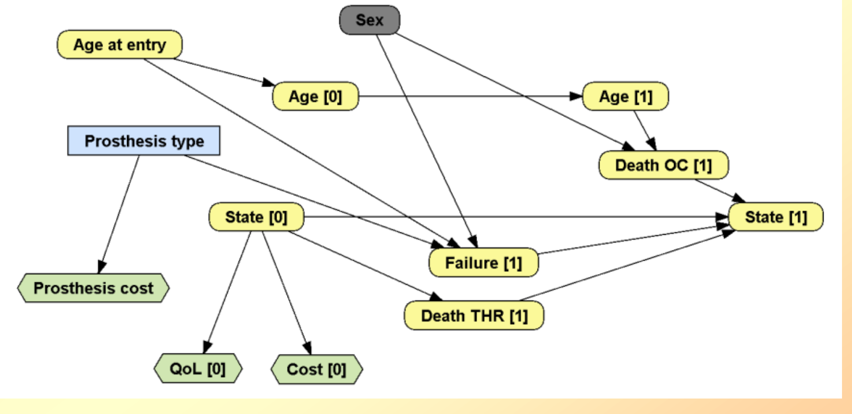
A MID version of the HIV model

[Chancellor et al., 1997]



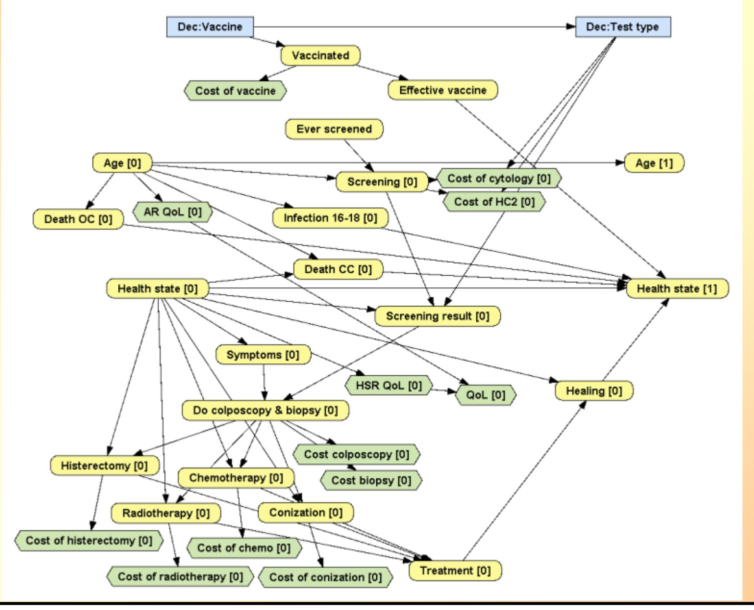
A MID version of the hip replacement model

[Briggs et al., 2004]



A MID version of the HPV vaccination model

[Callejo et al., 2010]

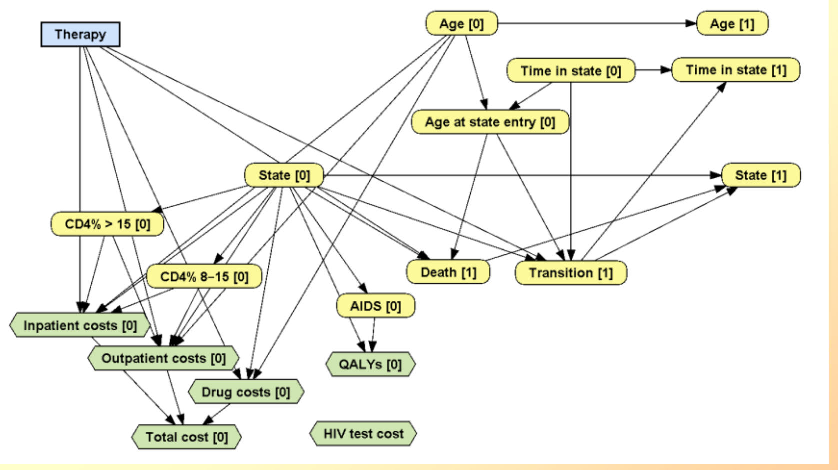


Content of one of the Excel cells for this model:

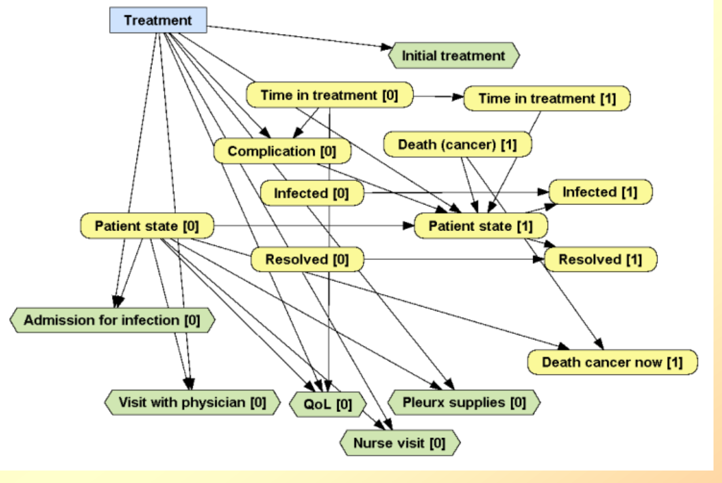
=VLOOKUP($C5;Variables!$A$4:$H$21;8;TRUE)*(((BI5+BJ5)+BK5*uCIN1+SUM(BL5:BP5)*uCIN2_3+(BQ5+BR5)*uLCC+(BS5+BT5)*uRCC+(BU5+BV5)*uDCC)+((BI4+BJ4)+BK4*uCIN1+SUM(BL4:BP4)*uCIN2_3+(BQ4+BR4)*uLCC+(BS4+BT4)*uRCC+(BU4+BV4)*uDCC)*VLOOKUP($C4;Variables!$A$4:$H$21;2;TRUE)+(BQ4+BR4)*uLCC*VLOOKUP($C4;Variables!$A$4:$H$21;4;TRUE)+(BS4+BT4)*uRCC*VLOOKUP($C4;Variables!$A$4:$H$21;5;TRUE)+(BU4+BV4)*uDCC*VLOOKUP($C4;Variables!$A$4:$H$21;2;TRUE))

A MID version of the CHAP model

[Ryan et al., 2008]

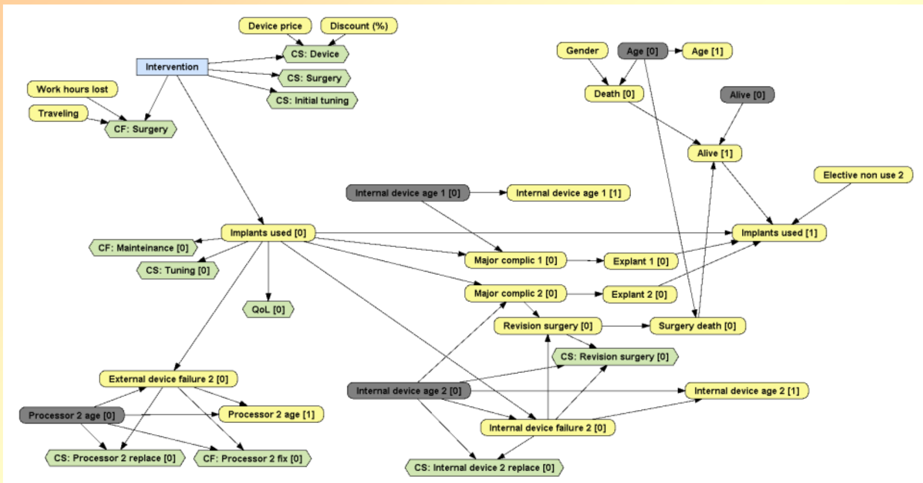


Our model for malignant pleural effusion



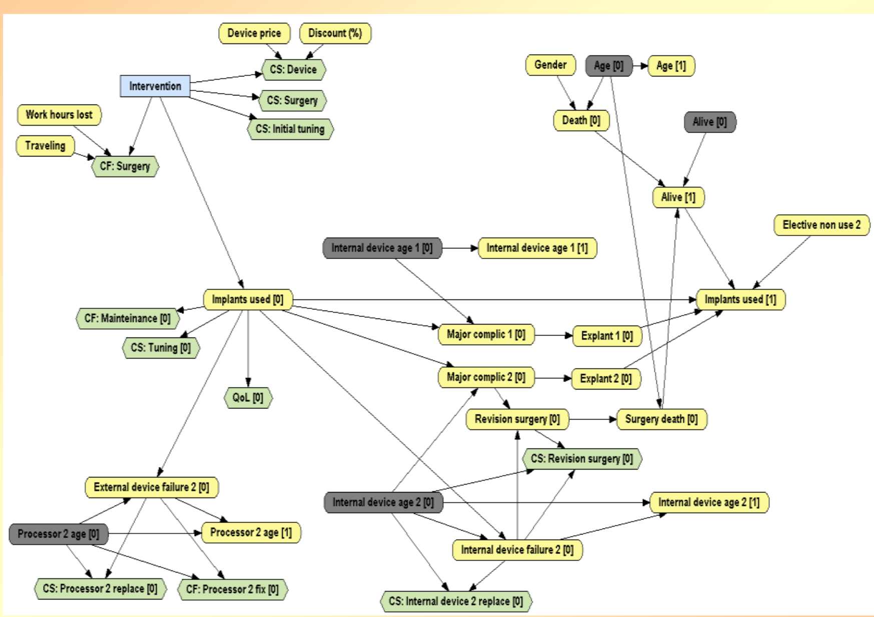
- *Meeting of the Society for Medical Decision Making*, St. Louis, October 19-21, 2015.

Our model for bilateral cochlear implantation

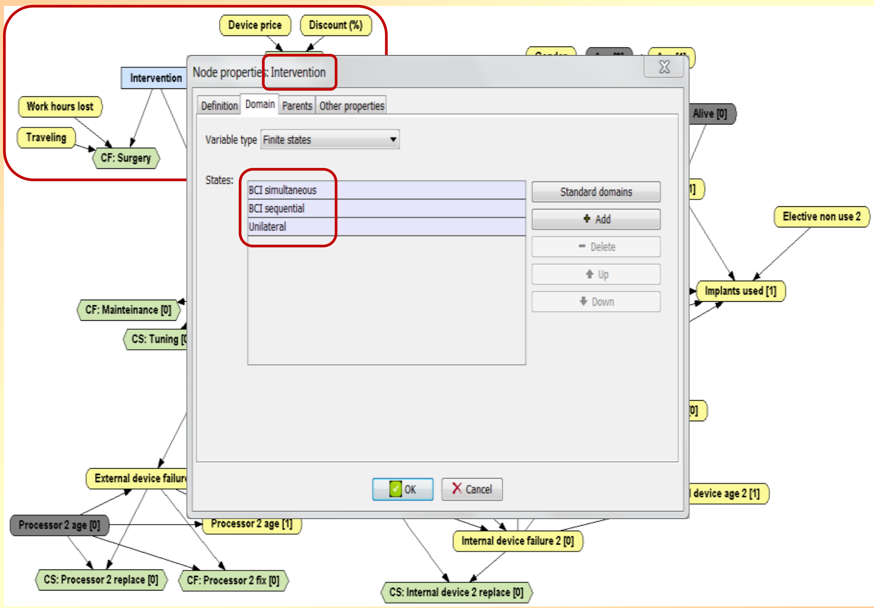


➢ *Cochlear Implant Symposium*, Washington DC, October 15-17, 2015.

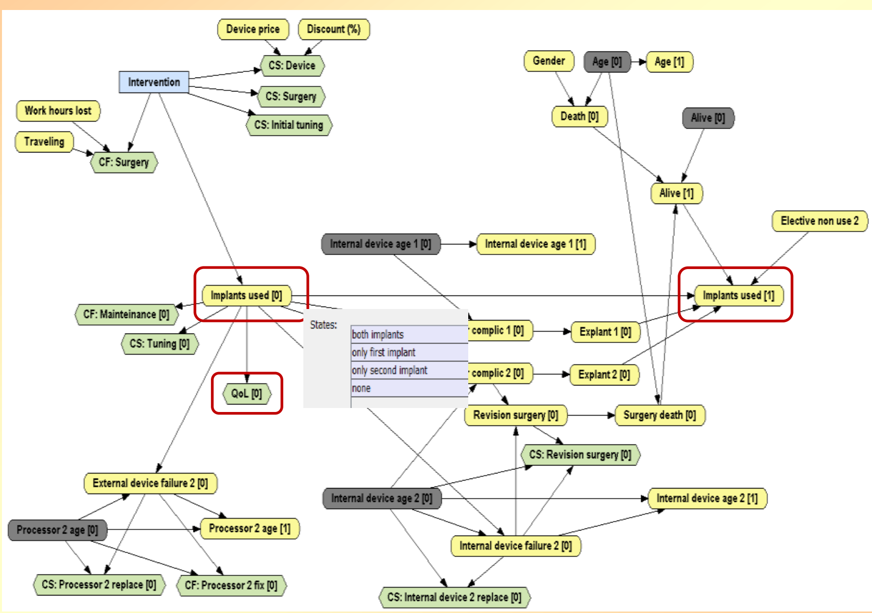
Our model for bilateral cochlear implantation



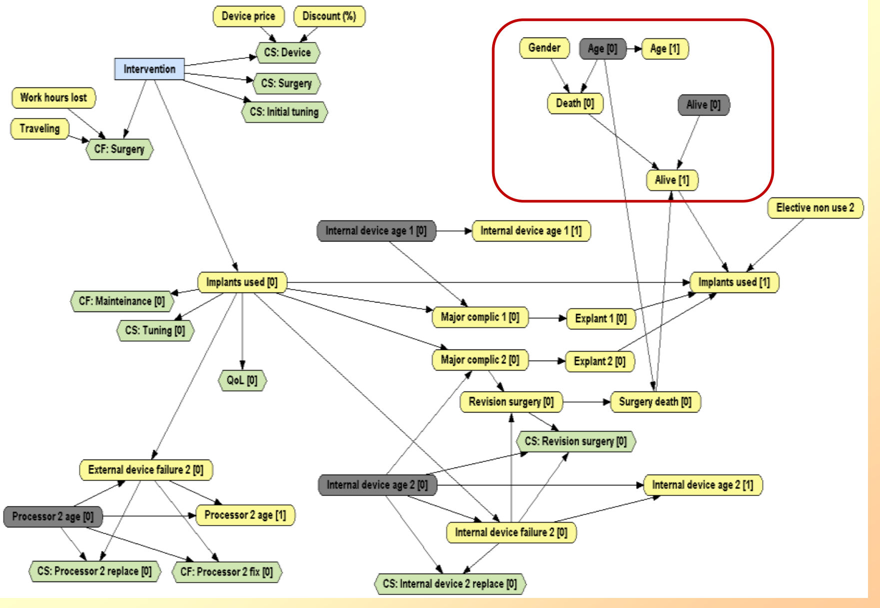
Our model for bilateral cochlear implantation



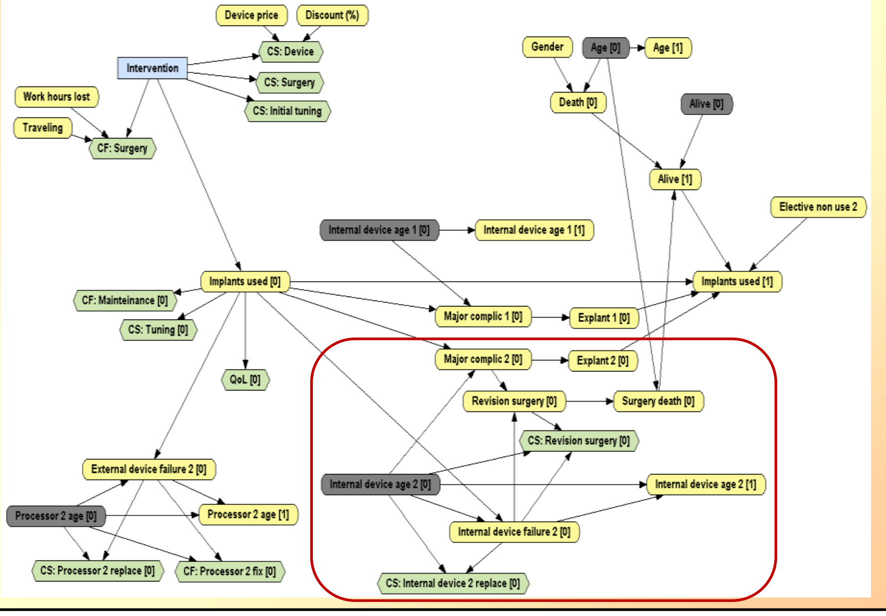
Our model for bilateral cochlear implantation



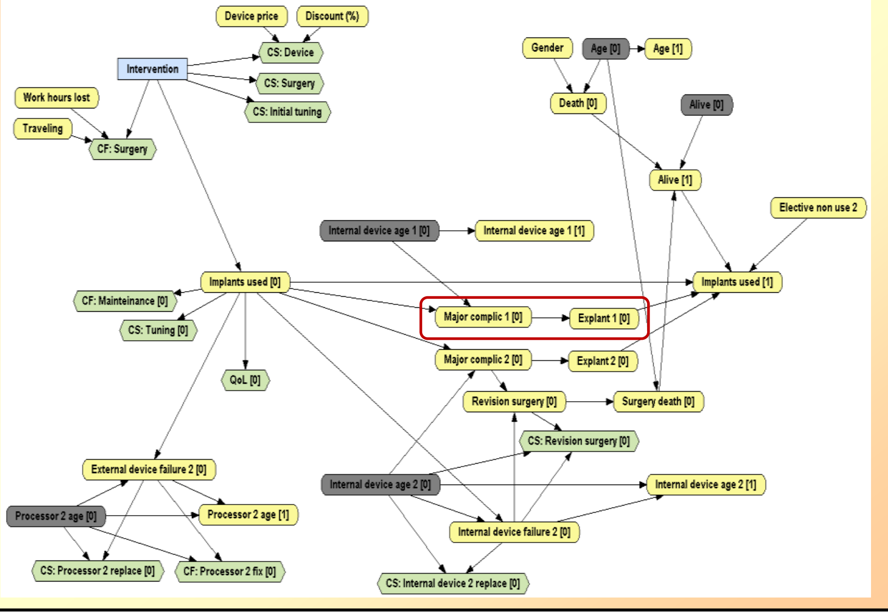
Our model for bilateral cochlear implantation



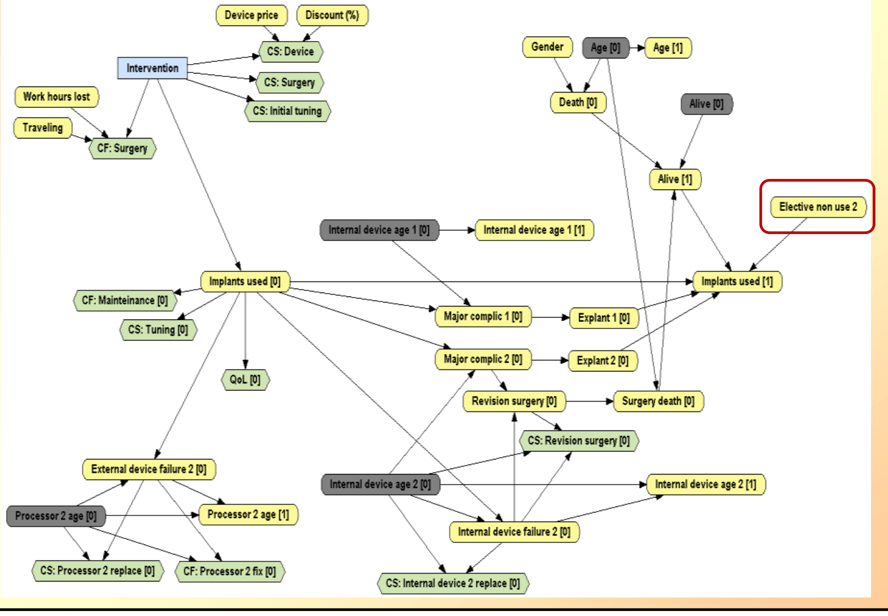
Our model for bilateral cochlear implantation



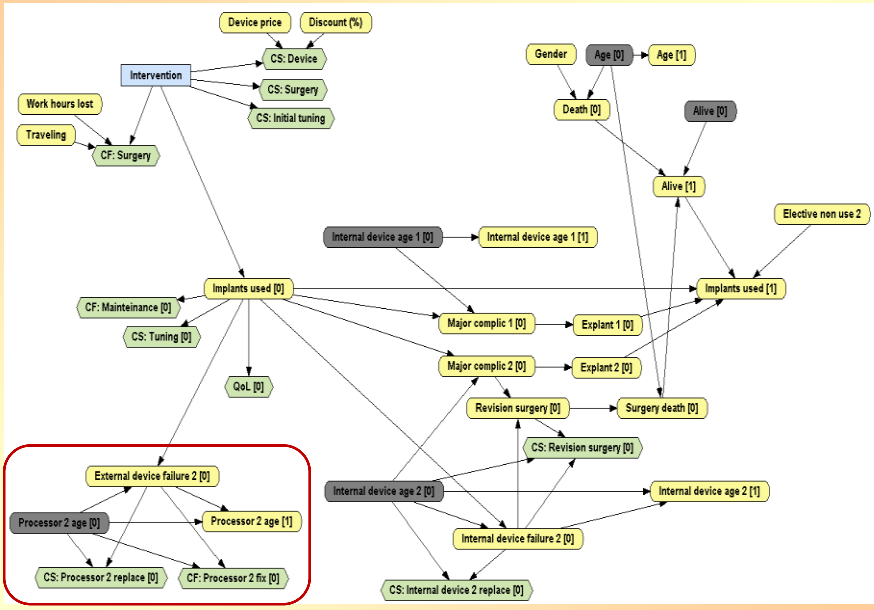
Our model for bilateral cochlear implantation



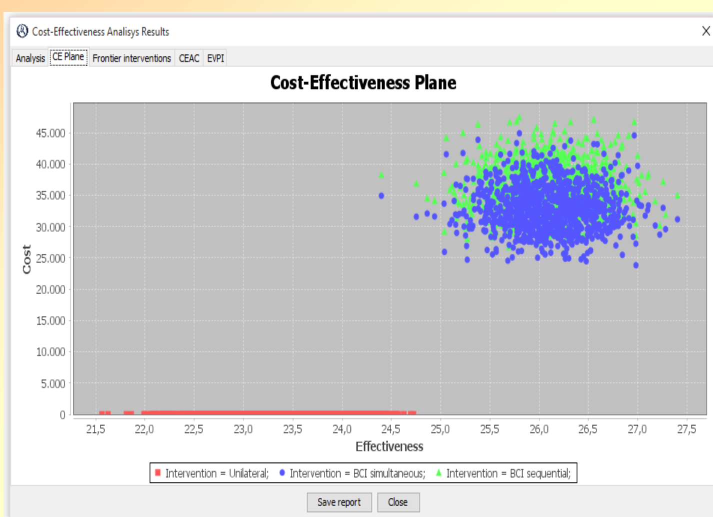
Our model for bilateral cochlear implantation



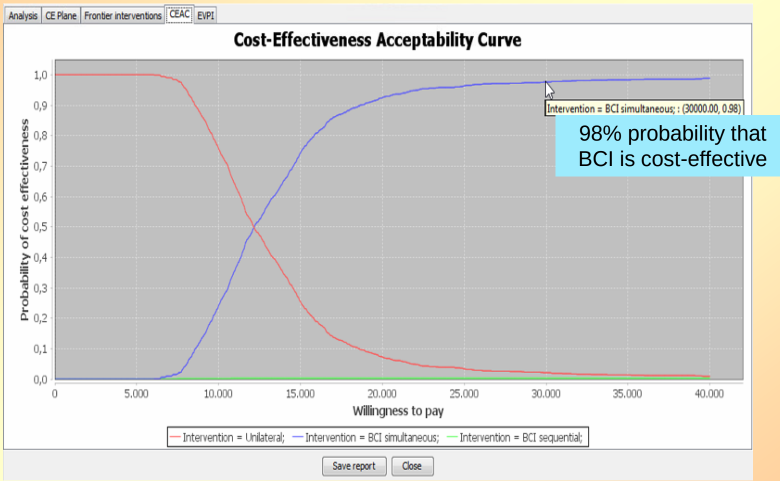
Our model for bilateral cochlear implantation



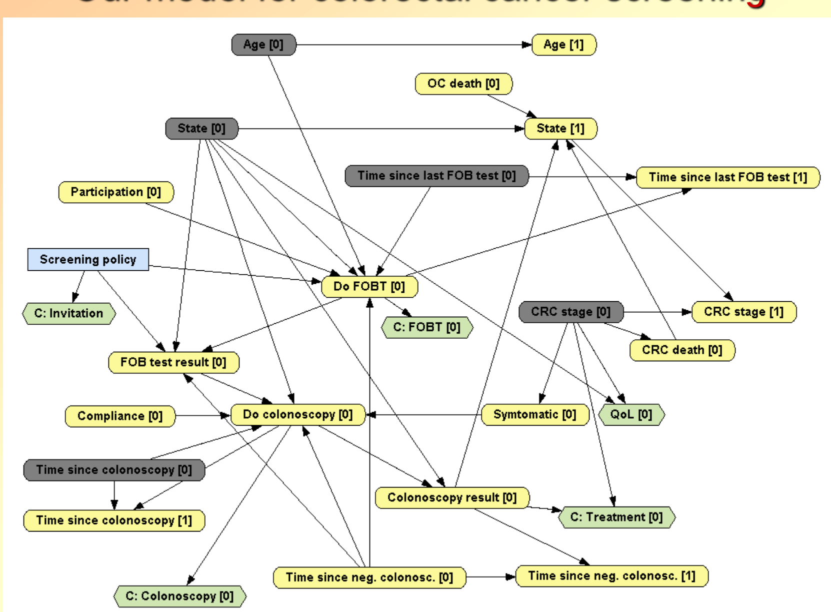
Probabilistic sensitivity analysis



Probabilistic sensitivity analysis

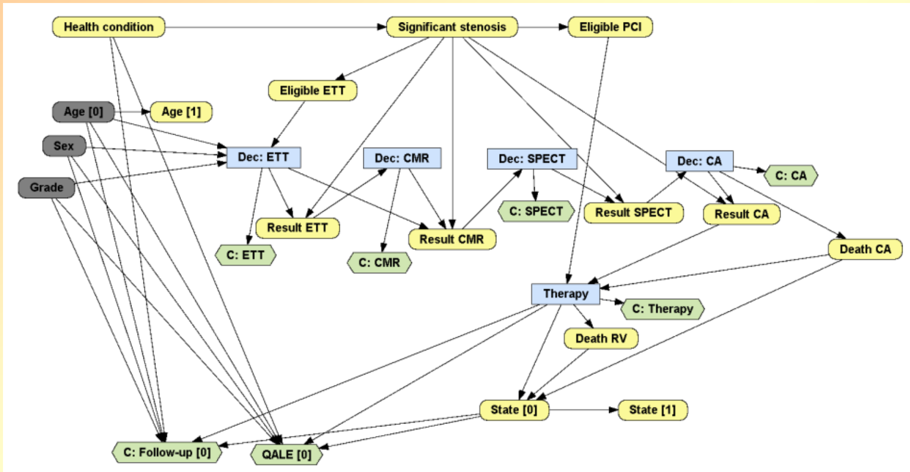


Our model for colorectal cancer screening

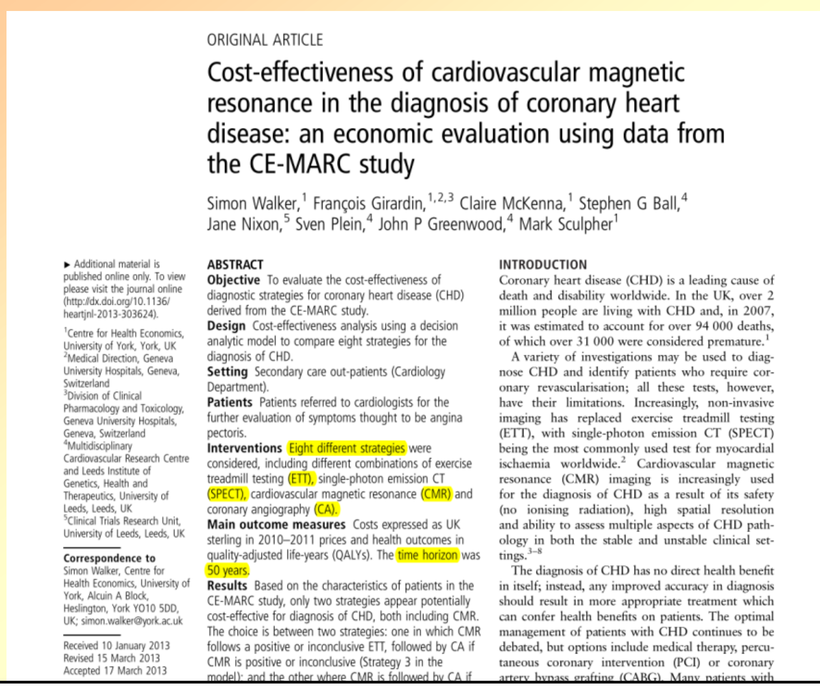


A MID with several decisions

Adapted from [Walker et al., 2013]



- This model evaluates all the possible interventions.
- It can cope with heterogeneity: sex, age, grade.



ORIGINAL ARTICLE

Cost-effectiveness of cardiovascular magnetic resonance in the diagnosis of coronary heart disease: an economic evaluation using data from the CE-MARC study

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ABSTRACT

Objective To evaluate the cost-effectiveness of diagnostic strategies for coronary heart disease (CHD) derived from the CE-MARC study.
Design Cost-effectiveness analysis using a decision analytic model to compare eight strategies for the diagnosis of CHD.
Setting Secondary care out-patients (Cardiology Department).
Patients Patients referred to cardiologists for the further evaluation of symptoms thought to be angina pectoris.
Interventions Eight different strategies were considered, including different combinations of exercise treadmill testing (ETT), single-photon emission CT (SPECT), cardiovascular magnetic resonance (CMR) and coronary angiography (CA).
Main outcome measures Costs expressed as UK sterling in 2010–2011 prices and health outcomes in quality-adjusted life-years (QALYs). The time horizon was 50 years.
Results Based on the characteristics of patients in the CE-MARC study, only two strategies appear potentially cost-effective for diagnosis of CHD, both including CMR. The choice is between two strategies: one in which CMR follows a positive or inconclusive ETT, followed by CA if CMR is positive or inconclusive (Strategy 3 in the model); and the other where CMR is followed by CA if

INTRODUCTION

Coronary heart disease (CHD) is a leading cause of death and disability worldwide. In the UK, over 2 million people are living with CHD and, in 2007, it was estimated to account for over 94 000 deaths, of which over 31 000 were considered premature.[1]

A variety of investigations may be used to diagnose CHD and identify patients who require coronary revascularisation; all these tests, however, have their limitations. Increasingly, non-invasive imaging has replaced exercise treadmill testing (ETT), with single-photon emission CT (SPECT) being the most commonly used test for myocardial ischaemia worldwide.[2] Cardiovascular magnetic resonance (CMR) imaging is increasingly used for the diagnosis of CHD as a result of its safety (no ionising radiation), high spatial resolution and ability to assess multiple aspects of CHD pathology in both the stable and unstable clinical settings.[3–8]

The diagnosis of CHD has no direct health benefit in itself; instead, any improved accuracy in diagnosis should result in more appropriate treatment which can confer health benefits on patients. The optimal management of patients with CHD continues to be debated, but options include medical therapy, percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). Many patients with

Model structure

To conduct the economic evaluation a decision analytic model was developed. For the initial diagnosis a decision tree allocates patients to the appropriate diagnostic group. The prognostic implications of being in one of these groups are then quantified using three distinct Markov models. An example of the decision tree for Strategy 2 (ETT, followed by CA if ETT is positive or inconclusive) is shown in figure 1.

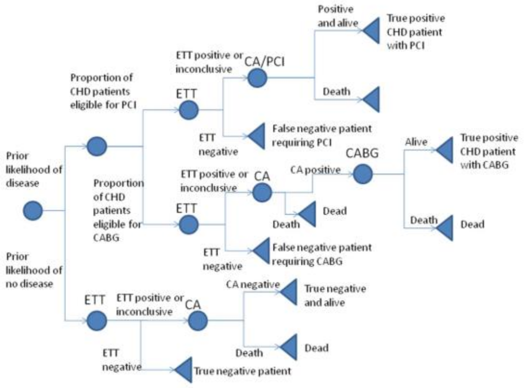

Figure 1 Structure of decision tree using Strategy 2 as an example. CA, coronary angiography; CABG, coronary artery bypass grafting; CHD, coronary heart disease; ETT, exercise treadmill testing; PCI, percutaneous coronary intervention.

Comparison of MIDs with other techniques

- MIDs vs. spreadsheets (Excel)
  - no need to write any formulas nor VisualBasic macros
  - no need to multiply the number of states
- MIDs vs. Markov decision trees
  - much more compact $\Rightarrow$ possible to build much larger models
  - no need to add tracking variables (microsimulation)
- MIDs vs. R
  - no need to write any code, not even for sensitivity analysis
  - but R is much more flexible
- MIDs vs. discrete event simulation
  - cohort propagation is often much faster
- MIDs vs. all the others: may contain several decisions.

Under evaluation at *Medical Decision Making.*

Markov influence diagrams: a graphical tool for cost-effectiveness analysis

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Abstract

Markov influence diagrams (MIDs) are a new type of probabilistic graphical model that extends influence diagrams, in the same way as Markov decision trees extend decision trees. They have been designed to build state-transition models, mainly in medicine, and perform cost-effectiveness analysis. Using a causal graph that may contain several variables per cycle, MIDs can model various features of the patient without multiplying the number of states; in particular, they can represent the history of the patient without using tunnel states. OpenMarkov, an open-source tool, allows the decision analyst to build and evaluate MIDs—including cost-effectiveness analysis and several types of deterministic and probabilistic sensitivity analysis—with a graphical user interface, without writing any code. This way, MIDs can be used to easily build and evaluate complex models whose implementation as spreadsheets or decision trees would be cumbersome or unfeasible in practice. Furthermore, many problems that previously required discrete event simulation can be solved with MIDs, i.e., within the paradigm of state-transition models, in which many health economists feel more comfortable.

Conclusions

- BNs overcame the limitations of the naïve Bayes method.
- IDs have several advantages over decision trees,
  but also have serious limitations for medical decision making.
- DANs are similar to IDs, but more suitable for asymmetric decision problems.
- It is possible to do cost-effectiveness analysis with IDs.
- and also with Markov IDs (MIDs) if all decisions are atemporal.
- There are other types of Markov PGMs having one or more decisions per cycle: MDPs, POMDPs, DLIMIDs…

Future work

- New models and algorithms
  - CEA with DANs and Markov DANs
  - CEA with models having one or several decisions per cycle
  - new methods of CEA, sensitivity analysis, explanation of "reasoning"…
- Integration of PGMs, cost-effectiveness analysis, and Bayesian inference
  - integration of OpenMarkov with OpenBUGS and/or STAN.
- Dissemination in the fields of MDM and health economics
  - seminars, short courses, MOOC…
  - tutorials, journal papers, book…

Thank you very much for your attention!