

I Jornada UNED-Empresa  
*Inteligencia Artificial en Medicina*

Madrid, 20 February 2019

**Probabilistic graphical models:  
from diagnosis to cost-effectiveness analysis**

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[www.cisiad.uned.es](http://www.cisiad.uned.es)

# OVERVIEW

- ◆ Bayesian networks
- ◆ Influence diagrams
- ◆ Cost-effectiveness analysis
- ◆ Temporal models
- ◆ Impact: bilateral cochlear implantation in Spain
- ◆ Conclusion

# 1. Bayesian networks for medical diagnosis

# A very simple Bayesian network

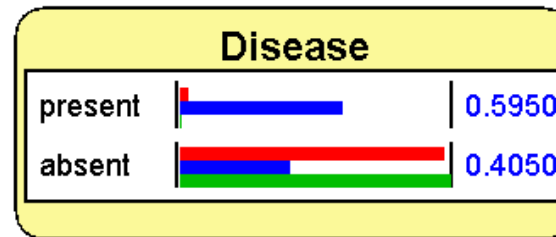
Node Potential: Disease

Relation Type: Table

present	0.03
absent	0.97

Disease

Symptom



Symptom

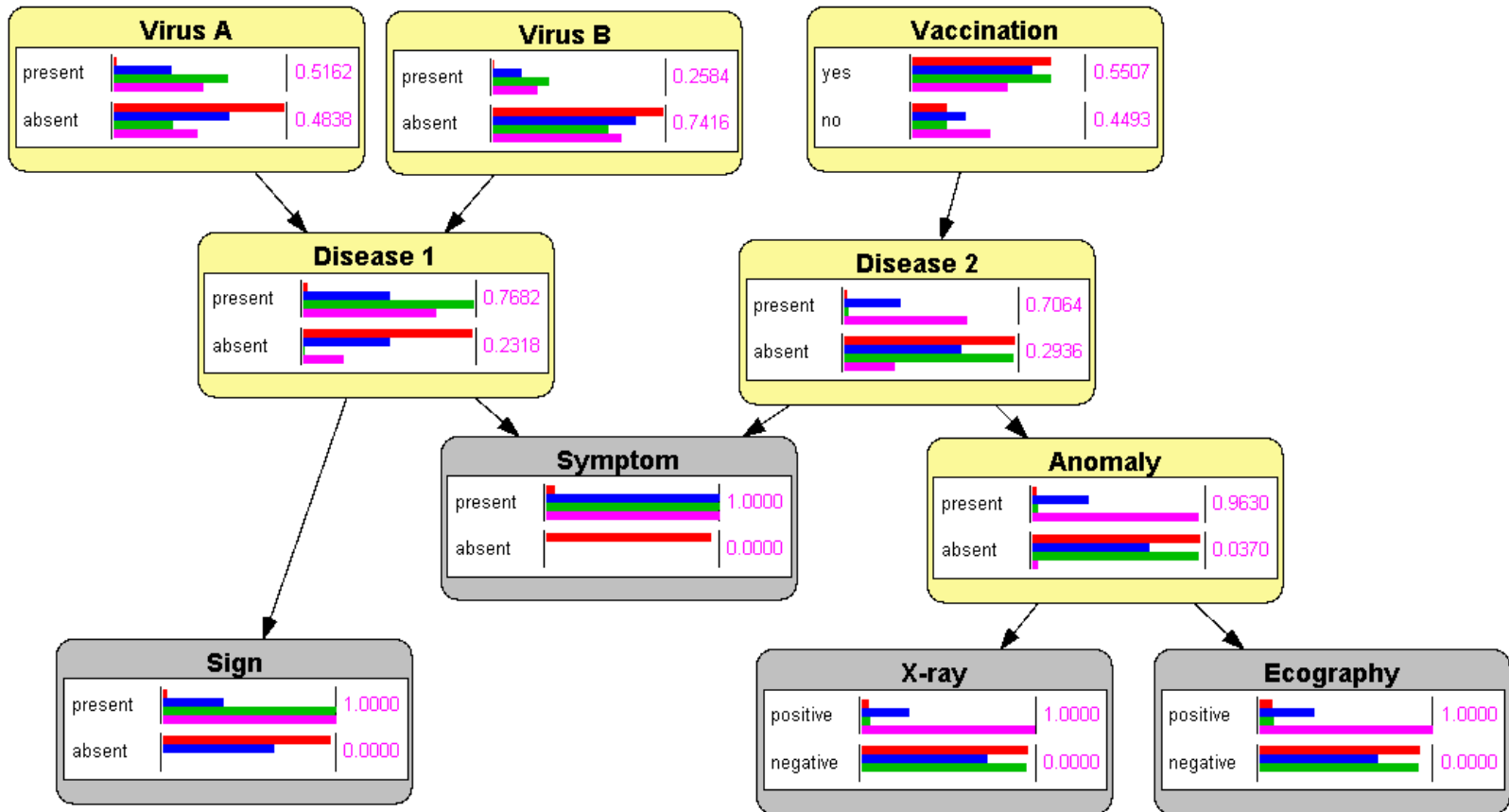


Node Potential: Symptom

Relation Type: Table

Disease	absent	present
present	0.02	0.95
absent	0.98	0.05

# A more complex Bayesian network



# Bayesian networks we have built

- ◆ 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

# DIIVAL

**INTRODUCIR ECO** [ \_ ] [ □ ] [ × ]

Archivo Datos previos Hallazgos eco Diagnóstico Especial Ayuda

**DATOS ADMINISTRATIVOS** [ \_ ] [ □ ] [ × ]

Eco número:  Fecha:    Transtorácico: SI  
Cinta:  Hora grabación:  Transesofágico: NO

Nombre:   
Apellidos:

Sexo: MUJER DNI:  Edad:  años  
Peso:  Kg Estatura:  cm Sup. corporal: 1.58 m<sup>2</sup>

\* Solicitante:   
Situación: INGRESADO Sector:  Cama:

Introducir los datos del paciente.

**INTRODUCIR ECO** Archivo Datos previos Hallazgos eco Diagnóstico Especial Ayuda

**PARAMETROS DEL ECO DOPPLER (M y T)**

? E	<input type="text" value="164"/>	cm/s	" <b>+105%</b> "	"mod. aumentada"
? A	<input type="text"/>	cm/s		
? Cociente E/A				
? T.R.IV.	<input type="text"/>	ms		
? T. desaceleración	<input type="text"/>	ms		
? Grad. máx. mitral	<input type="text" value="10.8"/>	mmHg		"est. moderada"
? Grad. med. mitral	<input type="text" value="7.0"/>	mmHg		"lev. aumentado"
? T.H.P. mitral	<input type="text" value="255"/>	ms	" <b>+183%</b> "	"sev. aumentado"
? Area mitral (THP)	<input type="text" value="0.9"/>	cm <sup>2</sup>	" <b>-76%</b> "	"esten. crítica"
? Vel. máx. tric.	<input type="text"/>	cm/s		
? Grad. máx. tric.	<input type="text"/>	mmHg		
? Grad. med. tric.	<input type="text"/>	mmHg		

Pulsar "?" para obtener más información sobre un parámetro.



**INTRODUCIR ECO** Archivo Datos previos Hallazgos eco Diagnóstico Especial Ayuda

**ECO BIDIMENSIONAL: VALVULA MITRAL**

<b>Ausente</b> Leve Moderada Severa <b>CALC. VALVAS</b>	Ausente Leve <b>Moderado</b> Severo <b>ENGR. VALVAS</b>	Normal <b>Reduc. leve</b> Reduc. mod. Reduc. sev. <b>MOVILIDAD</b>	<b>SCORE MITRAL: 9</b> <input type="text" value="Prolapso"/> <input type="text" value="Válvula mixoide"/> <input type="text" value="Engr. anillo"/>
<b>Ausente</b> Leve Moderada Severa <b>CALC. COMIS.</b>	Abiertas Fus. leve <b>Fus. mod.</b> Fus. severa <b>FUS. COMIS.</b>	<b>Simétrica</b> Pred. ant. Pred. post. <input type="text" value="SAM"/>	<input type="text" value="Ausente"/> <input type="text" value="Leve"/> <input type="text" value="Moderada"/> <input type="text" value="Severa"/> <b>CALC. ANILLO</b>
<input type="text" value="Sin afectación"/> <input type="text" value="Afect. leve"/> <b>Afect. moderada</b> <input type="text" value="Afect. severa"/> <b>APARATO SUBVALV.</b>	<input type="text" value="Elongación cuerdas tendíneas"/> <input type="text" value="Rotura cuerdas tendíneas"/> <input type="text" value="Rotura músculo papilar"/>	<input type="text" value="No vegetaciones"/>	<input type="text" value="Ausente"/> <input type="text" value="Leve"/> <input type="text" value="Moderada"/> <input type="text" value="Severa"/> <b>DILAT. ANILLO</b>

**INTRODUCIR ECO**

Archivo Datos previos Hallazgos eco Diagnóstico Especial Ayuda

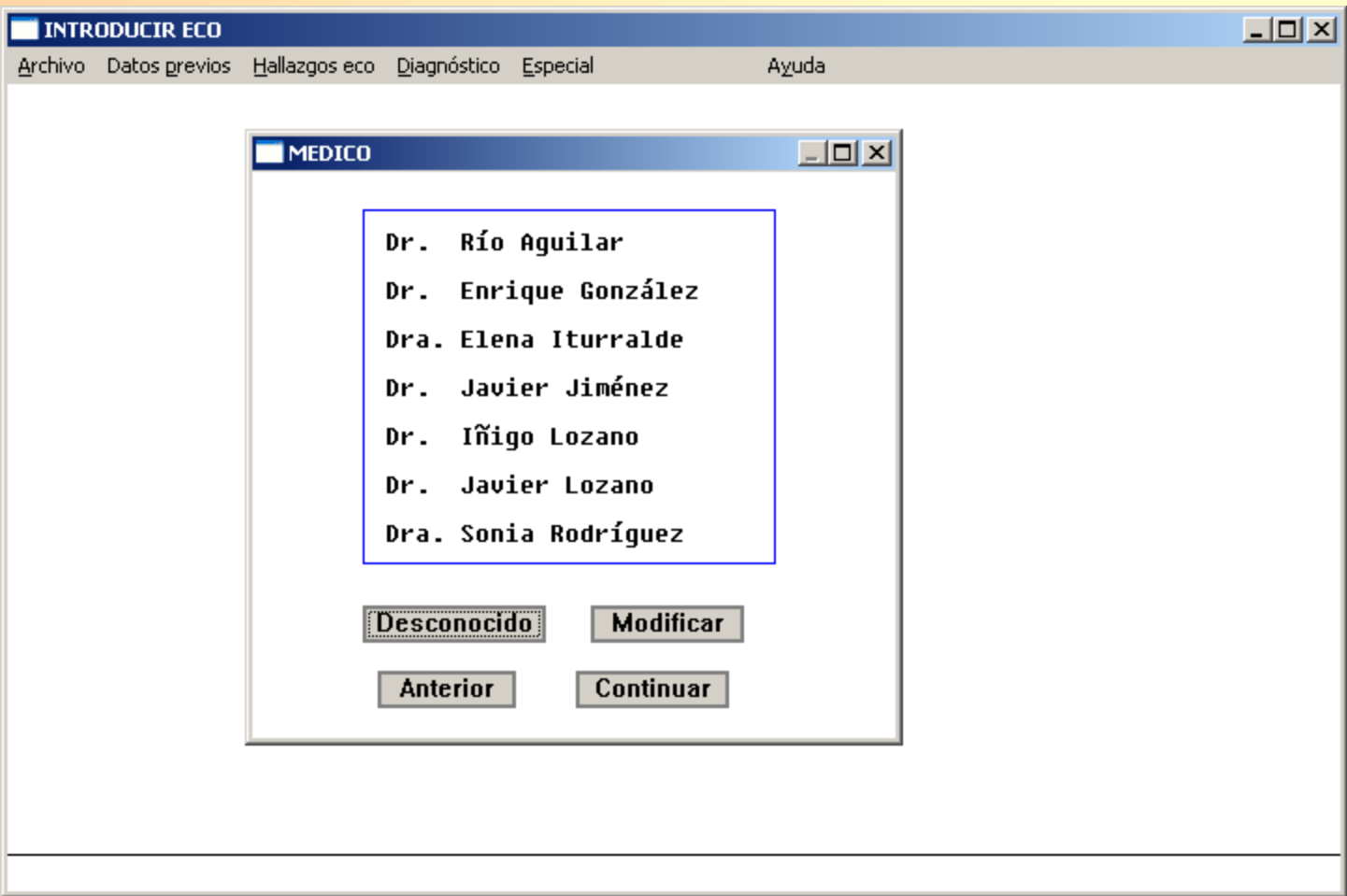
**DIAGNOSTICO**

Estenosis mitral reumática moderada. (100%)  
Insuficiencia mitral leve. (96%)  
Estenosis reumática severa de la válvula aórtica. (100%)  
Insuficiencia tricuspídea funcional leve. (72%)  
Retraso de la relajación diastólica. (65%)  
Hipertensión pulmonar moderada. (100%)

Anterior

Resto normal

Continuar



## Datos administrativos

=====

Nº eco: 104382. Fecha: 29/10/3. Cinta: 512.  
MARIA GARCIA PEREZ. DNI: 1234567.  
Edad: 51 años. Mujer.  
Peso: 58 Kg. Estatura: 158 cm. Sup. corporal: 1.58 m².  
Solicitante: CARDIOLOGIA.  
Ingresada, sector 3, cama 512A.

## Síntomas

=====

Disnea de grado II.

## Válvula mitral

=====

Area (eco 2D): 1.2 cm².  
Velocidad onda E: 164 cm/s.  
Gradiente máximo: 10.8 mmHg.  
Gradiente medio: 7.0 mmHg.  
Tiempo de hemipresión: 255 ms.  
Area (THP): 0.9 cm².  
Engrosamiento moderado de las valvas.  
No calcificación de las valvas mitrales.  
Reducción leve de la movilidad.

[...]

Contractilidad segmentaria normal.

Pericardio normal.

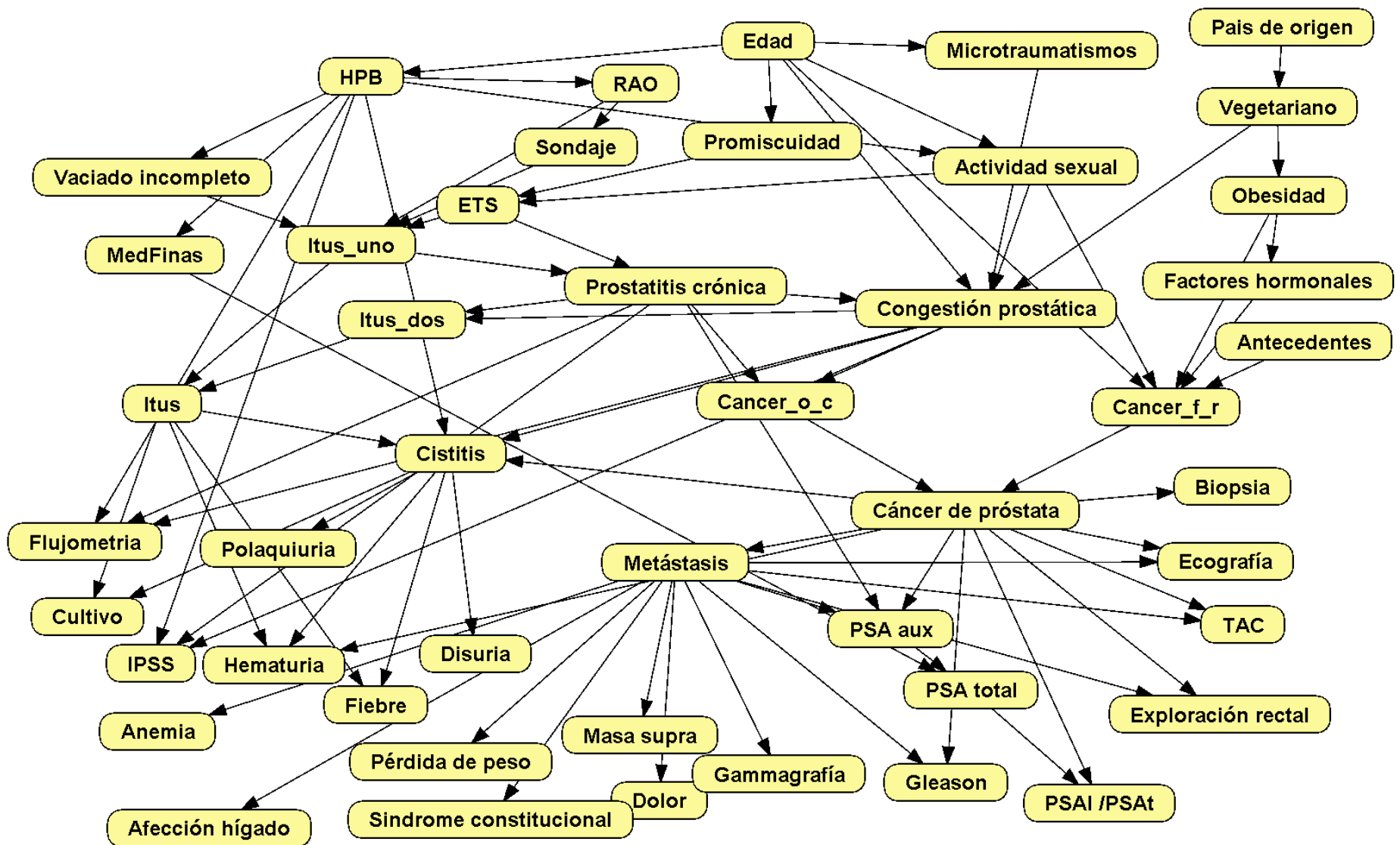
## DIAGNOSTICO

=====

Estenosis mitral reumática moderada.  
Insuficiencia mitral leve.  
Estenosis reumática severa de la válvula aórtica.  
Insuficiencia tricuspídea funcional leve.  
Retraso de la relajación diastólica.  
Hipertensión pulmonar moderada.

Dra. Elena Iturralde |

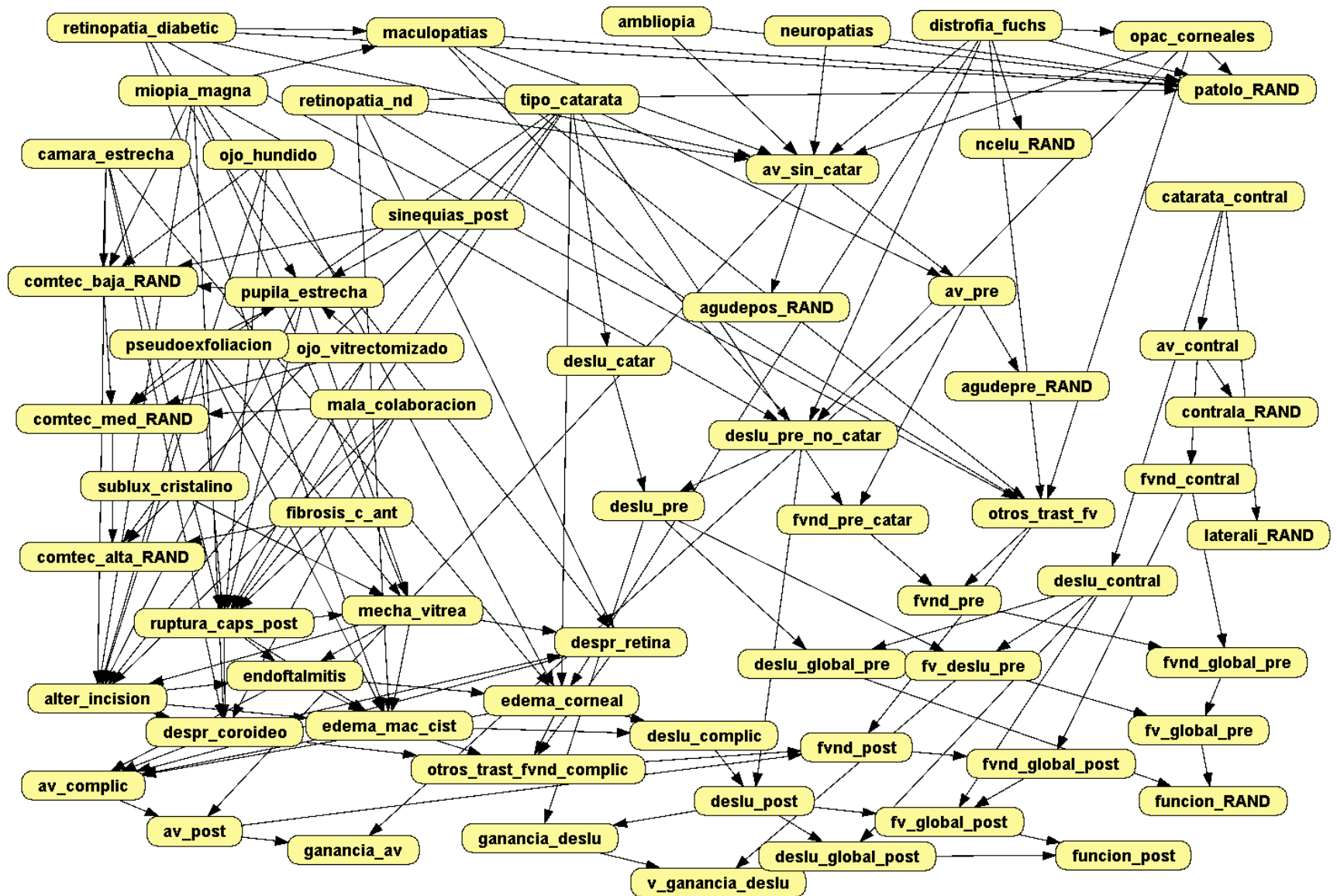
# Prostanet (for prostate diseases)







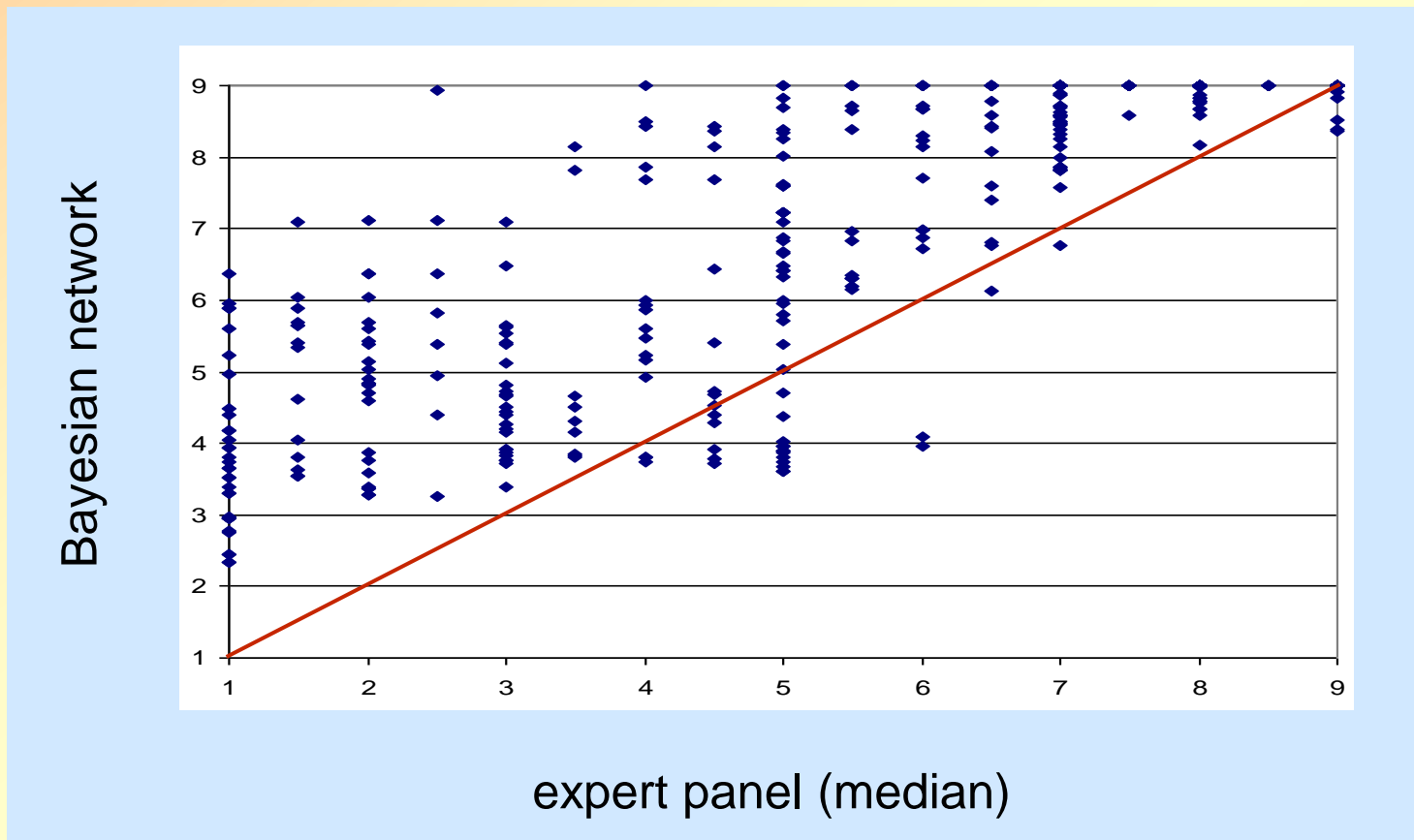
# Catarnet (cataract surgery)





# BN vs. a panel of experts (Delphi)

- ◆ Comparison in 429 clinical scenarios



- ◆ Result: ICC=0.83 [IC95%: 0.80 – 0.86] ( $p < 0.001$ )

# Input: 1. General data

(1ml)

Historias clínicas

05 May 2010

+ Nueva Historia

- Eliminar Historia

🔍 Buscar Paciente

+ Nuevo Paciente

- Eliminar Paciente

✕ Cerrar la sesión del Paciente

Prequirúrgico

Recomendaciones

Postquirúrgico

Revisión mensual

## Formulario prequirúrgico

Datos generales

Comorbilidad ocular

Complejidad técnica

Ojo que se recomienda operar

izquierdo ▼

Intervención quirúrgica previa

Tipo de catarata ojo operar

blanca ▼

Agudeza visual (corregida) ojo operar

0.3

Tipo de catarata contralateral

blanca ▼

Agudeza visual contralateral (corregida)

0.3

Deslumbramiento ("glare")

no puede precisar en qué ojo ▼

Efectos del deslumbramiento

no puede precisarlo ▼

Función global

limitación para la vida diaria ▼

Agudeza visual esperada post-intervención (ojo operar)

> 0,70 ▼

Comentarios

Siguiente

Ver recomendaciones

## Input: 2. Ocular comorbidity

Prequirúrgico

Recomendaciones

Postquirúrgico

Revisión mensual

### Formulario prequirúrgico

Datos generales

Comorbilidad ocular

Complejidad técnica

Ambliopía

Distrofia de Fuchs

Maculopatías

Neuropatías

Opacidades corneales

Retinopatía diabética

Retinopatía no diabética

Laser argon previo

Otras

Siguiente

Ver recomendaciones

# Input: 3. Surgical complexity

Prequirúrgico    Recomendaciones    Postquirúrgico    Revisión mensual

## Formulario prequirúrgico

Datos generales    Comorbilidad ocular    **Complejidad técnica**

Cámara estrecha	<input type="checkbox"/>
Fibrosis de la cápsula anterior	<input type="checkbox"/>
Mala colaboración del paciente (prevista)	<input type="checkbox"/>
Miopía magna	<input checked="" type="checkbox"/>
Ojo hundido	<input type="checkbox"/>
Ojo vitrectomizado	<input type="checkbox"/>
Pseudoexfoliación	<input type="checkbox"/>
Pupila estrecha	<input type="checkbox"/>
Sinequias posteriores	<input type="checkbox"/>
Subluxación de cristalino	<input type="checkbox"/>
Otras	<input type="text"/>

Ver recomendaciones

# Output: 1. Expert panel's recommendations

Prequirúrgico **Recomendaciones** Postquirúrgico Revisión mensual

## Recomendaciones de SAD-Catar

### Panel de expertos

**Recomendación:** **Facoemulsificación apropiada**

Mediana de las puntuaciones (1 a 9): 8,5

Grado de acuerdo: Acuerdo

▼ Escenario

Variable	Valor
A.V. contralateral	$\geq 0,2$ y $\leq 0,4$
A.V. previa en el ojo a operar	$\geq 0,2$ y $\leq 0,4$
Patología asociada a la catarata	Catarata simple
Lateralidad de la catarata	Bilateral
Complejidad técnica	Moderada por presencia de: <ul style="list-style-type: none"><li>▪ miopía magna (leve)</li><li>▪ catarata blanca (moderada)</li></ul>
Función visual	Dificultades en las actividades de la vida diaria

[Explicación](#)

# Output: 2. BN recommendation

## Red bayesiana CatarNet

<b>Recomendación:</b>	<b>9 (Totalmente recomendada)</b>
Mejoría en A.V. (máx. 6):	5,2
Mejoría en deslumbramiento (máx. 5):	1,7

### ▼ Probabilidades

<b>Función visual post-intervención</b>	<b>Probabilidad</b>
Sin problemas	0,057
Dificultades para el ocio	0,830
Dificultades para la vida diaria	0,113
<b>AV post-intervención</b>	<b>Probabilidad</b>
$\leq 0,15$	0,029
$> 0,15$ y $\leq 0,4$	0,088
$> 0,4$ y $\leq 0,7$	0,047
$> 0,7$	0,836
<b>Deslumbramiento post-intervención</b>	<b>Probabilidad</b>
Deslumbramiento	0,544
<b>Complicaciones</b>	<b>Probabilidad</b>
Desprendimiento de coroides	0,001
Desprendimiento de retina	0,080
Edema corneal	0,042
Edema macular cistoide	0,020
Endoftalmitis	0,002

# A review of explanation methods for Bayesian networks\*

CARMEN LACAVE<sup>1</sup> and FRANCISCO J DÍEZ<sup>2</sup>

<sup>1</sup> *Dept. Computer Science, University of Castilla-La Mancha, Paseo de la Universidad, s/n 13071 Ciudad Real, Spain; e-mail: clacave@inf-cr.uclm.es*

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## Abstract

One of the key factors for the acceptance of expert systems in real-world domains is the ability to explain their reasoning (Buchanan & Shortliffe, 1984; Henrion & Druzdzel, 1990). This paper describes the basic properties that characterise explanation methods and reviews the methods developed to date for explanation in Bayesian networks.

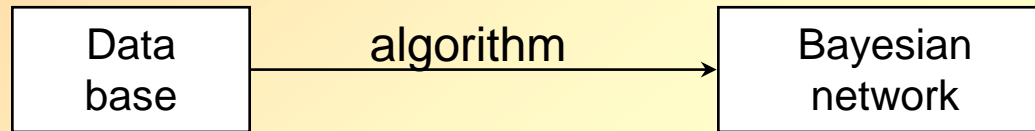
## 1 Introduction

Expert systems originated in the 1970s as computer programs capable of imitating human experts and even substituting them when necessary. One of the essential qualities of real experts is their ability to communicate their knowledge and explain their reasoning. This ability is especially important in the case of expert systems, not only for tracing performance during the construction and evaluation of the system, but also for justifying their results when the system is deployed in an operating environment. In fact, an experiment performed at the MYCIN project showed that physicians are very reluctant to accept the advice of a machine if they do not understand how it was obtained (Teach & Shortliffe, 1984).

In the decades that followed, i.e. the 1980s and 1990s, the main goal of artificial intelligence shifted from *imitating* natural intelligence to *supporting* human beings in a synergistic way. In fact, Clancey (1993) points to the notes to authors' in the *Knowledge Acquisition* journal: "The key issue is not *artificial intelligence*, but how to extend *natural intelligence* through knowledge based systems." In

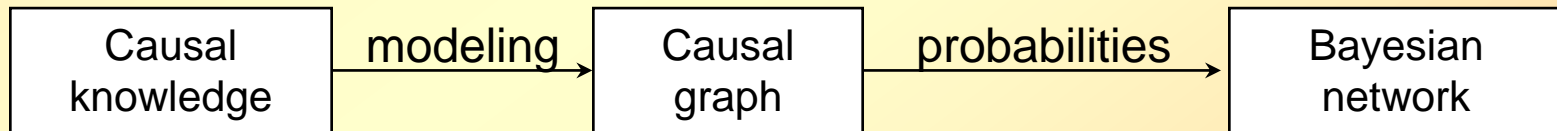
# How to build a Bayesian network

## ◆ From a database



- There are many algorithms, several new algorithms every year
- Similar to other machine learning methods but the model is easily interpretable: “white box”

## ◆ With a human expert’s help



## ◆ Hybrid methods:

- experts → structure; database → probabilities
- experts → initial model; new cases → refine the probabilities



# OpenMarkov

[Español](#) | [English](#)

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[Developers](#)

[References](#)

[Acknowledgments](#)

[News](#)

# OpenMarkov

**OpenMarkov** is a software tool for [probabilistic graphical models \(PGMs\)](#) developed by the [Research Centre for Intelligent Decision-Support Systems](#) of the [UNED](#) in Madrid, Spain.

It has been designed for:

- editing and evaluating several types of [several types of PGMs](#), such as Bayesian networks, influence diagrams, factored Markov models, etc.;
- [learning Bayesian networks](#) from data interactively;
- [cost-effectiveness analysis](#).

You can read the [tutorial](#) to have a glimpse of its capabilities.

Visit the [users' page](#) to download **OpenMarkov** and obtain additional information.

[CISIAD](#). Research Center on Intelligent Decision-Support Systems. [UNED](#). Madrid, Spain.

# OpenMarkov. Main features

## ◆ Main advantage: open source

- Free
- Users can adapt it to their needs
- Software engineering tools:  
JUnit, maven, mercurial (bitbucket), nexus, bugtracker, etc.

## ◆ Strengths

- Written in Java: portability (Windows, linux, MacOS...)
- Many types of models, potentials, etc.
- Algorithms not available in any other package
  - interactive learning
  - cost-effectiveness analysis with IDs, Markov IDs and DANs
- Very active: new features are continuously added
- Support for users and developers: wiki, lists, mail...
- Well-documented format for encoding networks: ProbModelXML.

# OpenMarkov's users

## ◆ Used in:

- universities, research centers
  - Los Alamos National Laboratory,  
National Oceanic and Atmospheric Administration...
- large companies

## ◆ In more than 30 countries:

- Europe: Spain, Portugal, France, Italy, UK, Belgium, The Netherlands, Germany, Slovenia, Norway, Sweden, Finland, Poland, Ukraine
- Asia: Turkey, Saudi Arabia, Iran, China, India, South Korea, Malaysia, Singapore, Japan
- America: United States, Mexico, Cuba, Colombia, Ecuador, Venezuela, Brazil
- Africa: Algeria, Ghana, Nigeria

# Neural networks vs. Bayesian networks

## ◆ Advantages of Bayesian networks:

- can be built from data, statistical reports (medical literature), expert knowledge, or any combination of them
- can learn causal models from data
- can be built interactively
- easy to interpret → explanation of the model and the results

All these advantages are very important for health applications

## ◆ Advantages of neural networks:

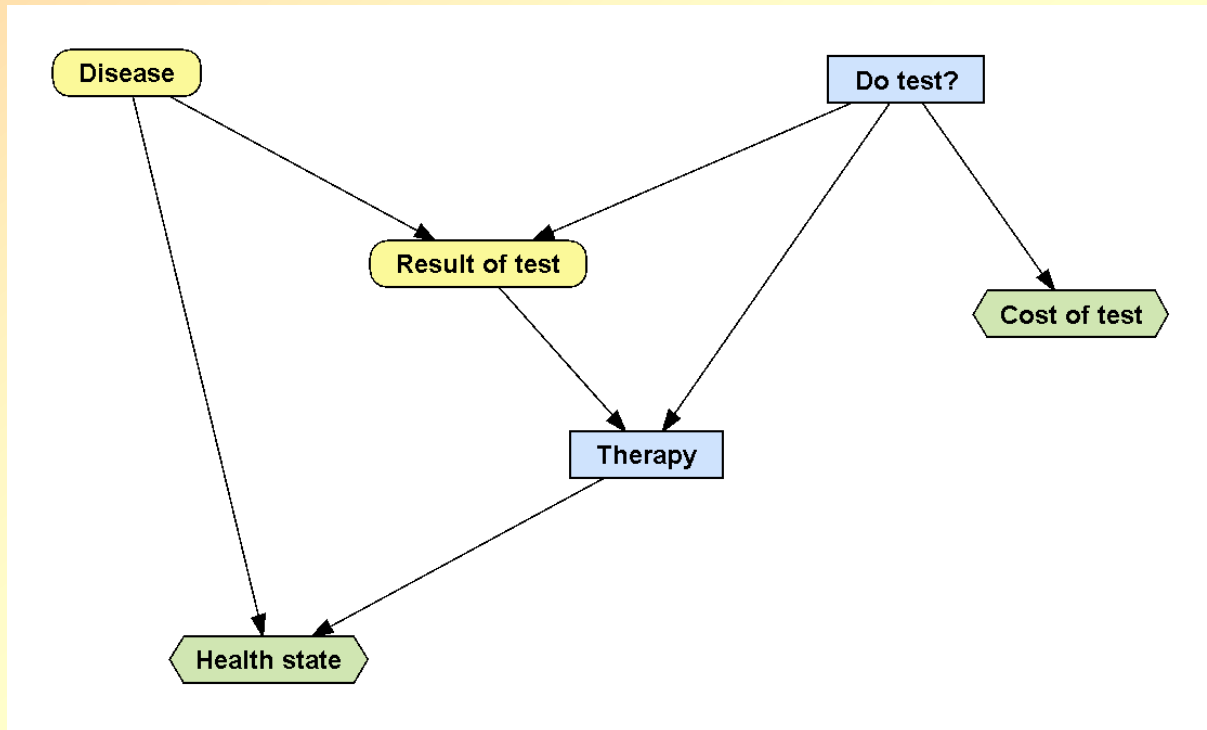
- can build networks with thousands of variables
- suitable for computer vision, natural language processing...

## ◆ A promising novel method: sum-product networks (SPNs)

- may have the advantages of neural nets and Bayesian nets
- but they are still in their infancy: “born” in 2011.

## **2. Influence diagrams for medical decision making**

# An influence diagram



# The Influence of Influence Diagrams on Artificial Intelligence

Craig Boutilier

Department of Computer Science, University of Toronto, Toronto, Ontario, M5S 3G5 Canada, cebly@cs.toronto.edu

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.

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**H**oward 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 itself is representative of developments that had been

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 of graphical models for probabilistic modeling and

# The Influence of Influence Diagrams in Medicine

Stephen G. Pauker, John B. Wong

Division of Clinical Decision Making, Informatics and Telemedicine, Department of Medicine,  
Tufts–New England Medical Center, Tufts University School of Medicine, 750 Washington St., NEMC 302,  
Boston, Massachusetts 02111 {spauker@tufts-nemc.org, jwong@tufts-nemc.org}

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.

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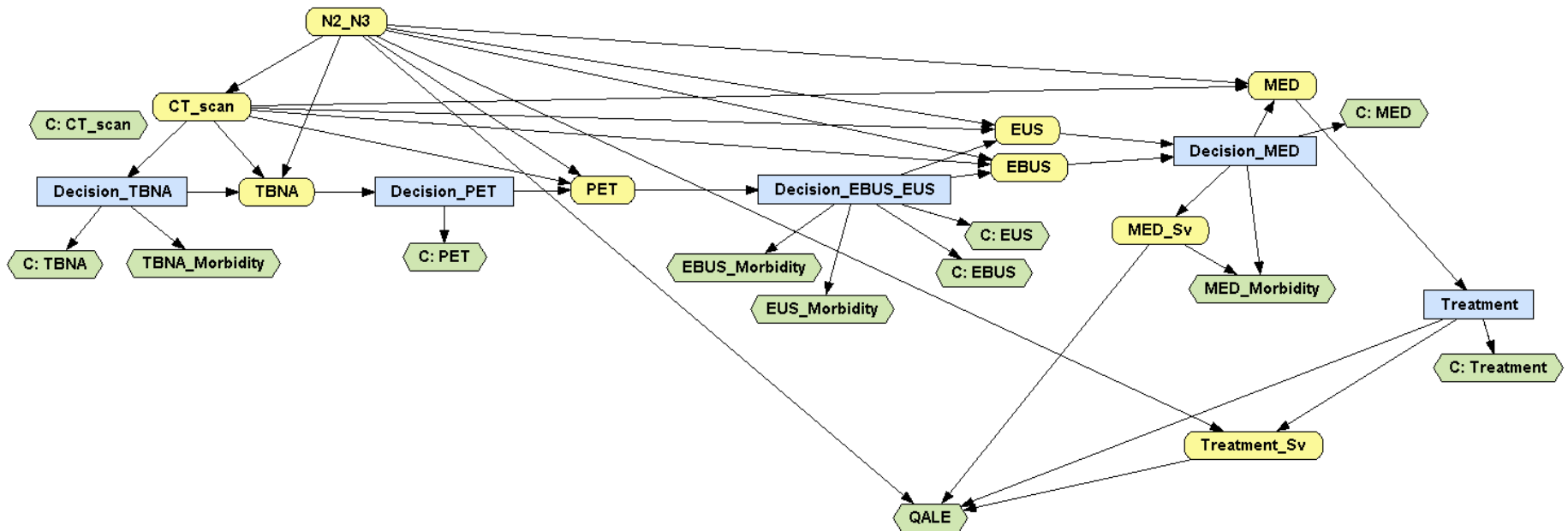
## Introduction

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 2005 and solicited a set of commentaries. This paper

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.

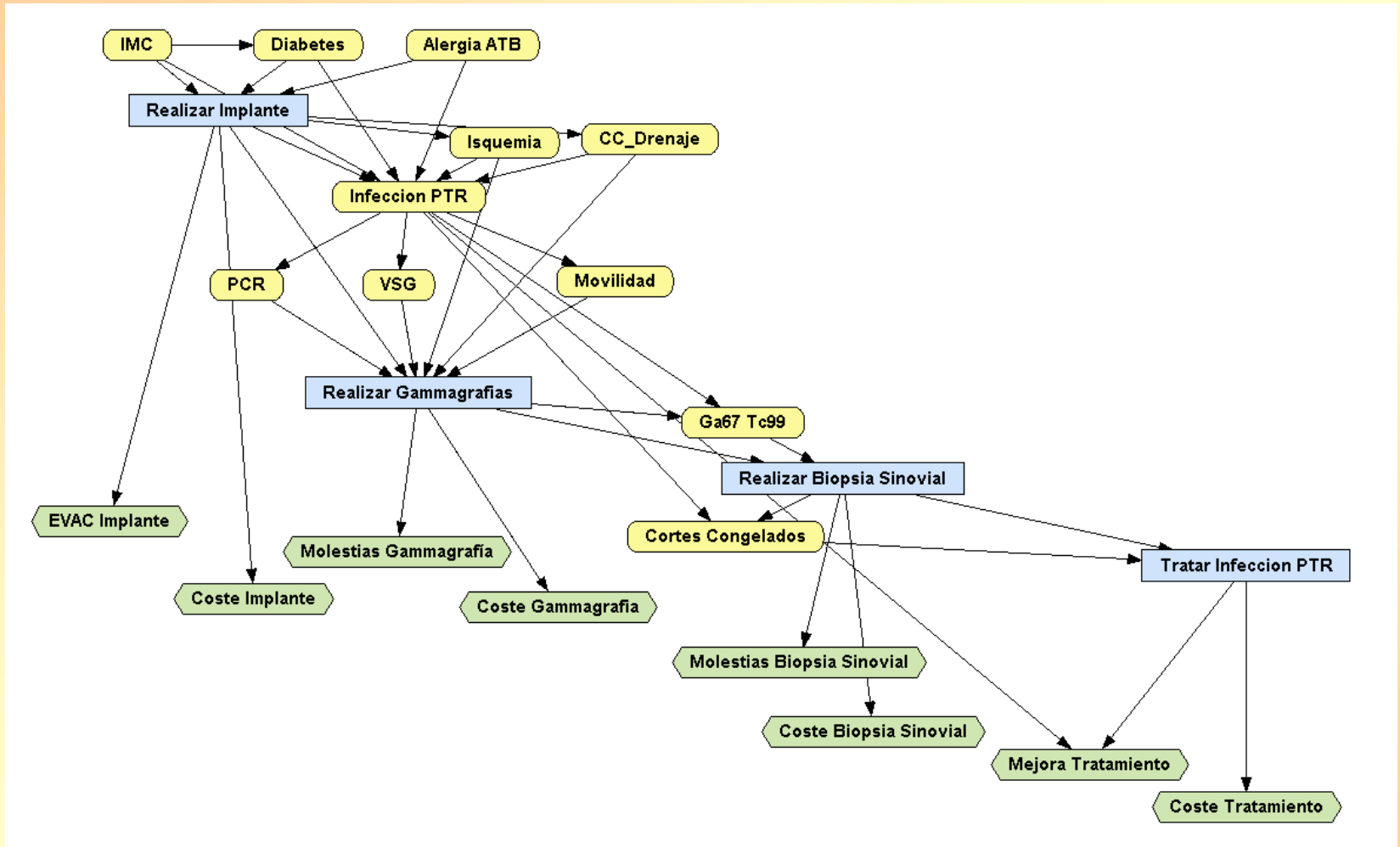


# Mediastinet (lung cancer)



Equivalent to a decision tree containing  $\sim 10^4$  branches.

# Arthronet (total knee arthroplasty)



Equivalent to a decision tree containing  $\sim 10^4$  branches.

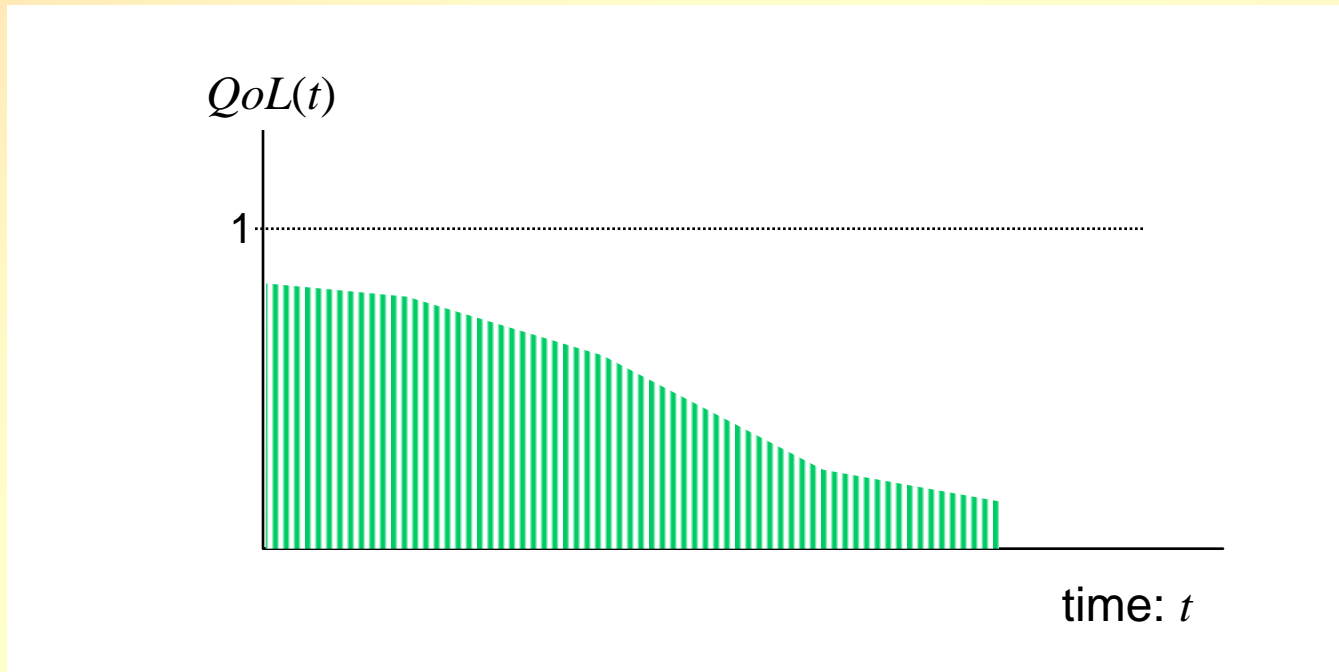


## **3. Cost-effectiveness analysis**

# Quantity and quality of life

- ◆ Effectiveness (in cost-utility studies):

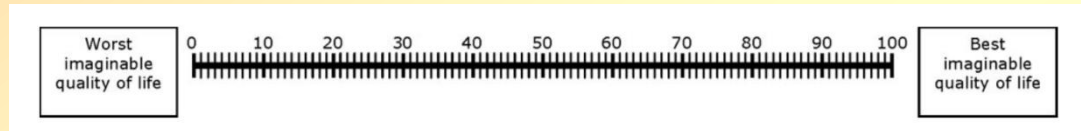
$$eff = \int QoL(t) \cdot dt$$



- 1 QALY = effectiveness accrued in one year of perfect health

# QoL is subjective: how can we measure it?

## ➤ Visual analog scale (VAS)



- does not measure quantitative preferences
- cannot be directly used in cost-utility analyses

## ➤ Standard gamble

- “Do you prefer to live in state  $s$  or to enter a lottery with probability  $p$  of recovering perfect health and  $(1-p)$  of dying?”

## ➤ Time trade-off (TTO)

- “Do you prefer to live in state  $s$  for 50 years or do you prefer to live with perfect health for 45 years?”
- “Imagine you are in state  $s$  and your life expectancy is 50 years. How many years of your life expectancy would you give up to recover perfect health?”

# Cost-effectiveness Analysis with Influence Diagrams\*

M. Arias; F. J. Díez

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, i.e. without expanding an equivalent deci-

**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  $\lambda$ , 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<sup>b</sup>. 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,

## 4. Temporal PGMs

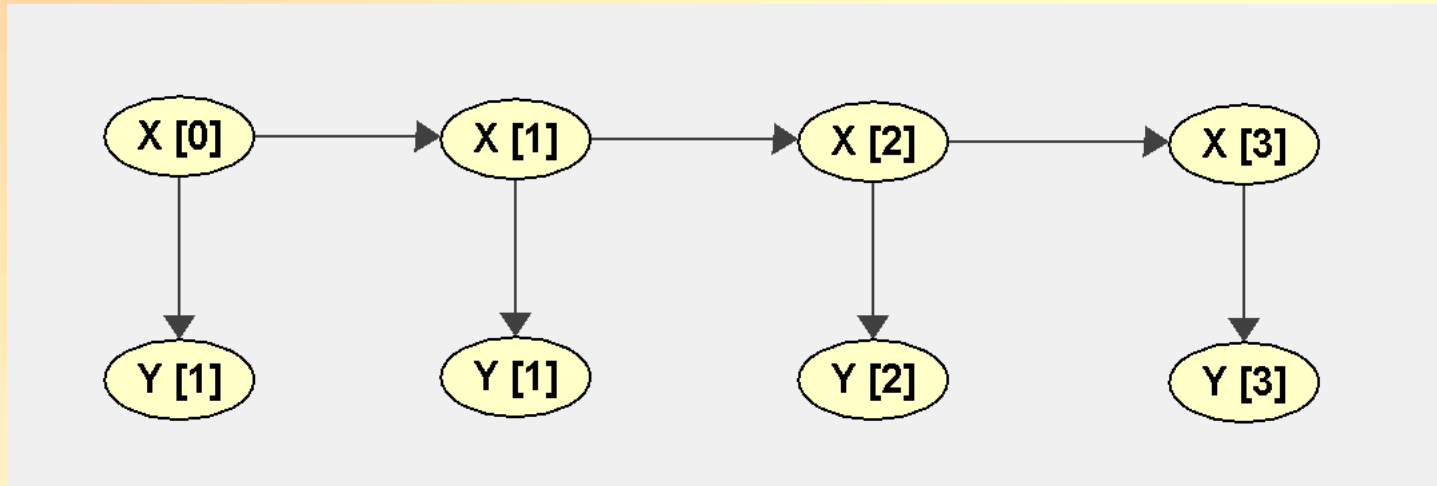


# Markov chain



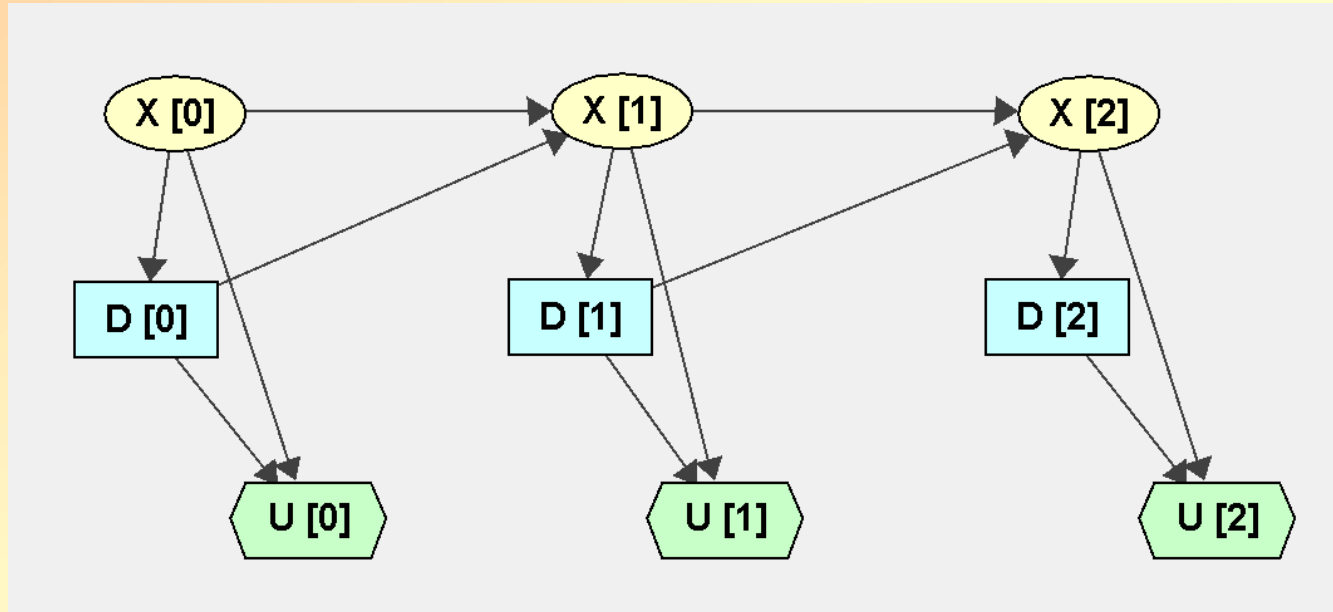
- ◆ One variable that evolves over time
- ◆ Transition probabilities:  $P(x_{i+1}|x_i)$

# Hidden Markov model (HMM)



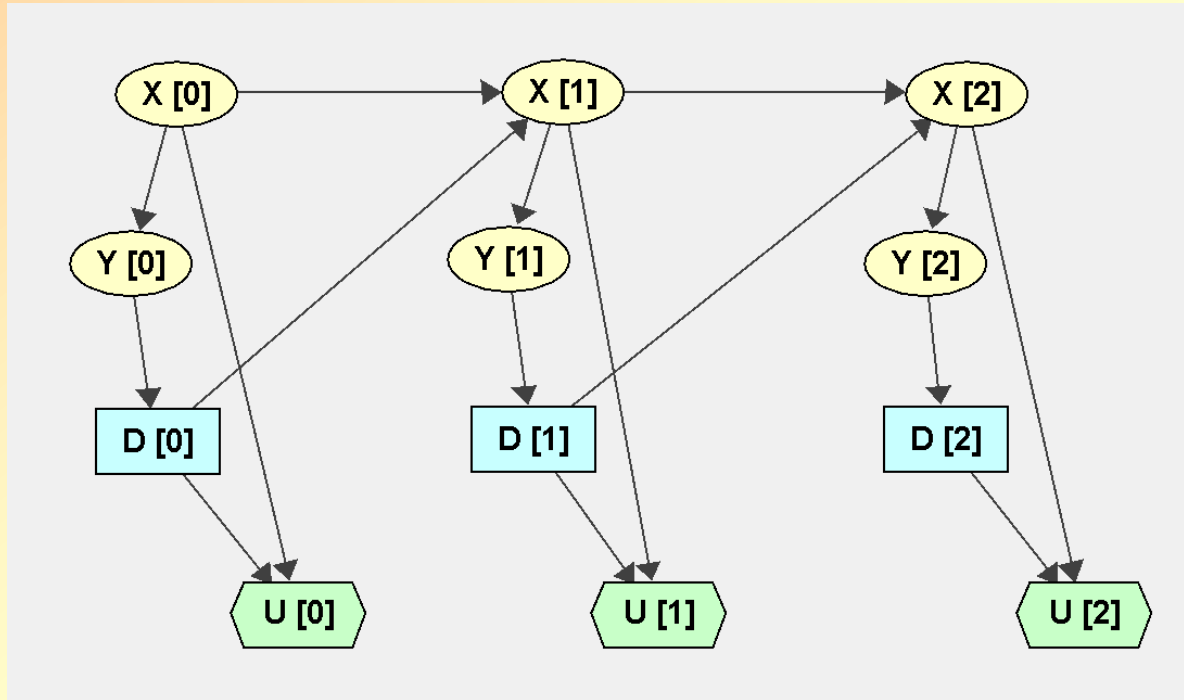
- ◆ Observed variable:  $Y$
- ◆ Non-observed (hidden) variable:  $X$
- ◆ Probability of each observation:  $P(y_i|x_i)$
- ◆ Transition probability:  $P(x_{i+1}|x_i)$

# 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)

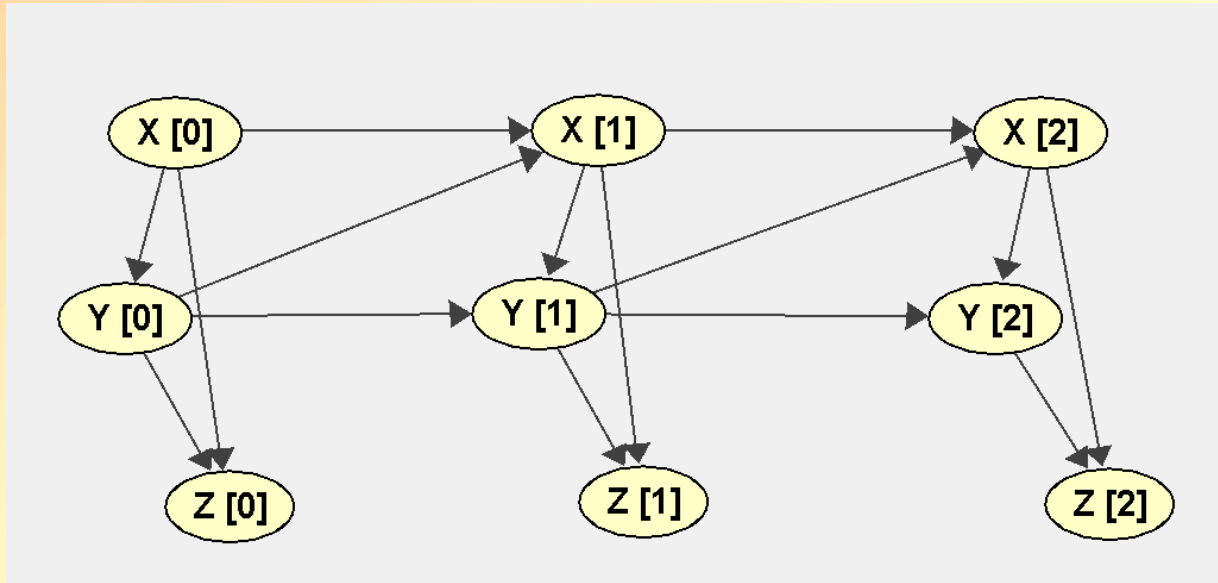


- ◆ Hidden variable:  $X$
- ◆ Observed variable :  $Y$
- ◆ Decision:  $D$
- ◆ Observation prob.:  $P(y_i|x_i)$
- ◆ Transition prob.:  $P(x_{i+1}|x_i)$
- ◆ Reward:  $U(x_i, d_i)$

# 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:  $P(y_i|x_i), P(z_i|x_i, y_i), P(x_{i+1}|x_i, y_i) \dots$

## 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, Open-Markov, 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 20th 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).

**5. Markov influence diagrams:  
cost-effectiveness analysis  
in temporal domains**



# Markov Influence Diagrams: A Graphical Tool for Cost-effectiveness Analysis

Francisco J. Díez, PhD, Mar Yebra, MEng, Iñigo Bermejo, PhD,  
Miguel A. Palacios-Alonso, MSc, Manuel Arias Calleja, PhD,  
Manuel Luque, PhD, Jorge Pérez-Martín, MEng

*Markov influence diagrams (MIDs) are a new type of probabilistic graphical model that extends influence diagrams in the same way that Markov decision trees extend decision trees. They have been designed to build state-transition models, mainly in medicine, and perform cost-effectiveness analyses. Using a causal graph that may contain several variables per cycle, MIDs can model various patient characteristics 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. **Key words:** Markov models; influence diagrams; cost-effectiveness analysis; outcomes research. (Med Decis Making 2017;37:183–195)*

Received 3 September 2015 from Department Artificial Intelligence, UNED, Madrid, Spain (FJD, MA, ML, JP); Centre for Biomedical Technology, Technical University of Madrid, Spain (MY); School of Health and Related Research, University of Sheffield, UK (IB); and Computer Science Department, National Institute for Astrophysics, Optics and Electronics, Tonantzintla, Puebla, Mexico (MAP). Financial support for this study was provided in part by the Spanish Ministry of Education and Science (grant TIN2006-11152), the Ministry of Science and Technology (TIN2009-09158), FONCICYT (no. 95185), the 7<sup>th</sup> Frame Programme (no. 262266 and FP7-PEOPLE-2012-IAPP-324401), the Health Institute Carlos III of the Spanish Government (PI13/02446) and the European Regional Development Fund. This work was also funded by a predoctoral grant from UNED (IB), MED-EL GmbH (JP), a predoctoral FPU grant of the Ministry of Education, Science and Sport (JP), a Santander Bank–UNED mobility grant (FJD), the Ministry of Science and Technology (MY) and UNED (IB). Revision accepted for publication 4 September 2016.

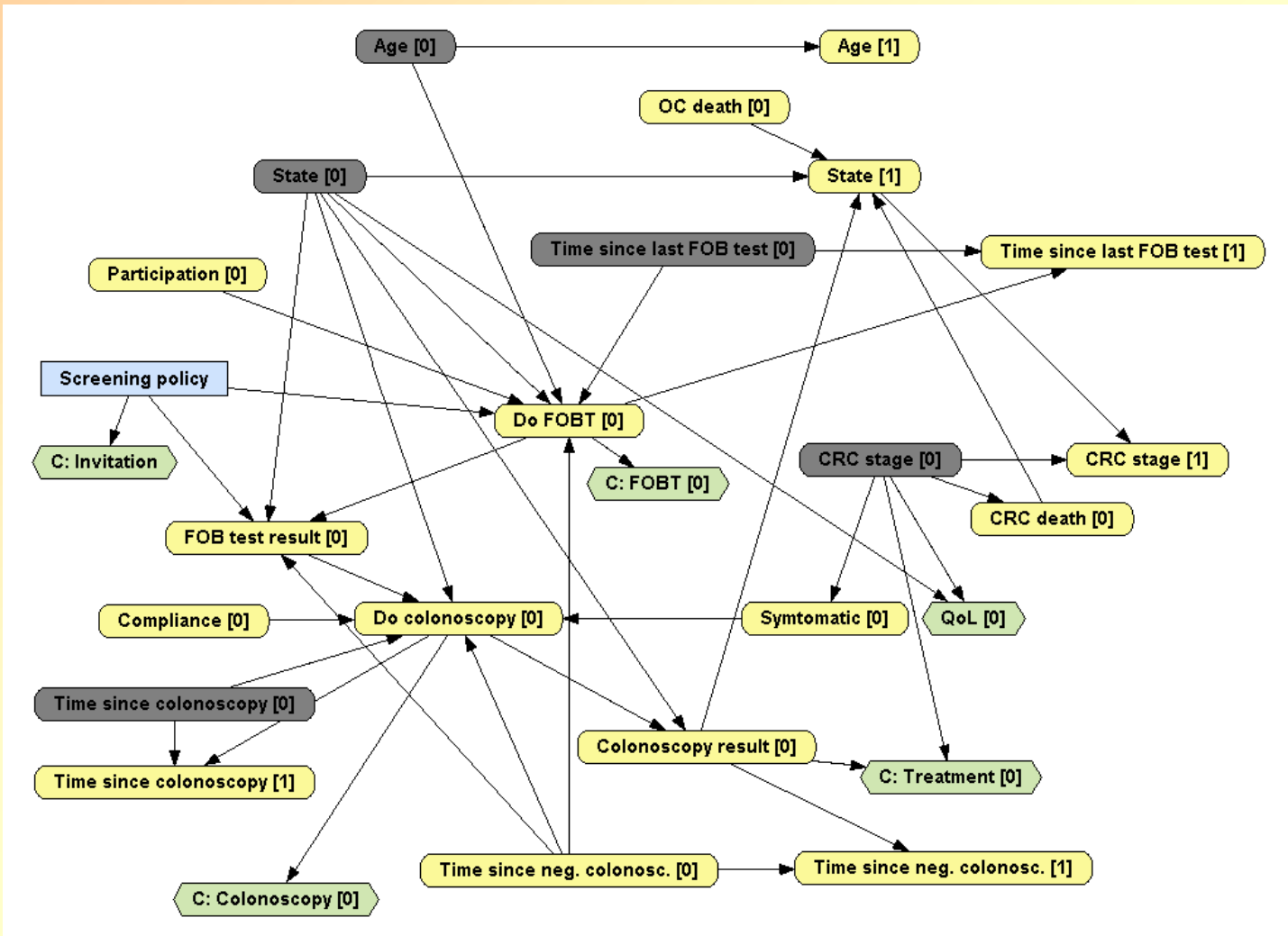
Several types of computational models are available for medical decision making. Decision trees<sup>1</sup> are the most popular, but they are suitable only for small problems because their size grows exponentially with the number of decisions and chance variables.

A probabilistic graphical model (PGM) consists of a set of variables, a graph in which every node represents a variable, a set of probability distributions and, in some cases, value functions. These probabilities represent a joint conditional probability distribution that satisfies some properties of independence—for example, the assumption that the results of 2 tests are conditionally independent both in the presence and in the absence of a disease—dictated by the graph.

Influence diagrams (IDs)<sup>2</sup> are a form of PGM that,

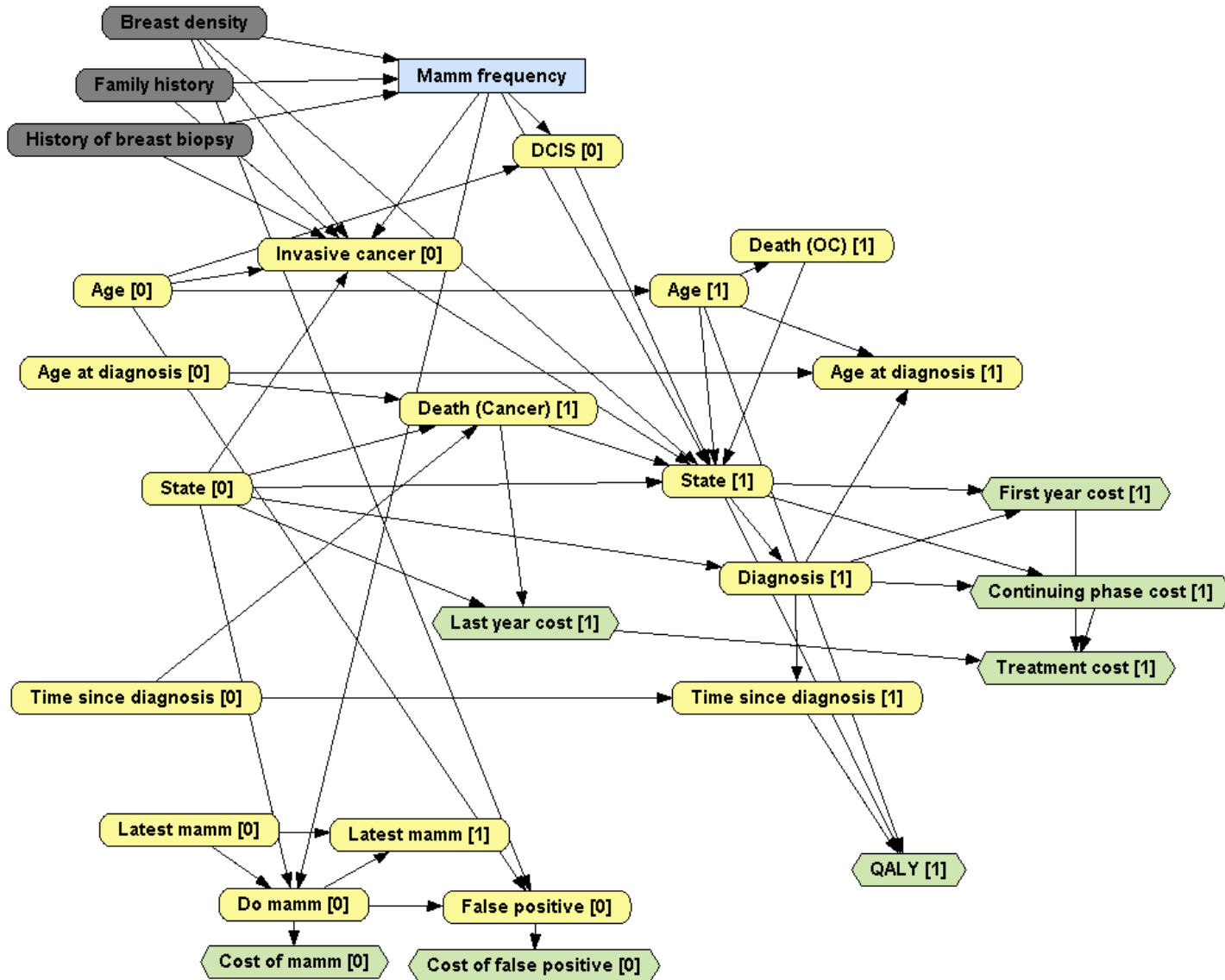


# A MID for colorectal cancer screening



- *European Conference of the Society for Medical Decision Making, London, UK, June 2015.*

# A MID for breast cancer screening



## **6. Estudio del coste-efectividad del I.C. bilateral en España**

## Mi motivación



## Objetivo

Que todos los niños que lo necesitan tengan dos implantes cocleares.

## ¿Cómo lograrlo?

Análisis de coste-efectividad del IC bilateral en España.

# Dos encuestas para medir calidad de vida y costes

## ◆ 1ª encuesta: población general

- Objetivo: medir el aumento de calidad de vida que aporta el 2º implante; detectar sesgos
- Demo: [www.cisiad.uned.es/implante-coclear/encuesta-demo](http://www.cisiad.uned.es/implante-coclear/encuesta-demo)
- Invitados: 3.465 estudiantes de informática de la UNED.
- Respondieron **583 personas**.
- Nuestra hipótesis se confirmó rotundamente: hay sesgos.

## ◆ 2ª encuesta: usuarios de uno/dos implantes, o sus padres

- Objetivo: medir el aumento de calidad de vida y costes
- Respondieron **273 personas**
- 69 personas respondieron por sí mismas
  - 92 con un implante (75%), 23 con dos (25%).
- 181 personas respondieron por su hijo/a
  - 66 con un implante (36'5%), 115 con dos (63'5%).

# Preference-based quality of life increment in children with bilateral cochlear implantation. A general population survey.

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## 1 Introduction

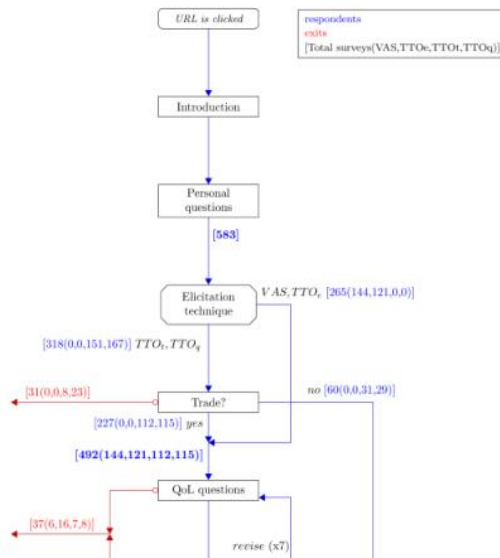
- ◆ Bilateral cochlear implantation (BCI):
  - No study has been able to prove beyond all doubt that it is cost-effective
  - Not universally covered even in developed countries.
  - The parameter that most affects the cost-effectiveness is the **increment in quality of life (QoL)** with respect to unilateral implantation (UCI).
- ◆ Objective: to measure the QoL increment of pediatric BCI, in order to use this result in cost-effectiveness analyses.

## 2 Methods

- ◆ Online self-administered survey
- ◆ Respondents: students of our university (UNED)
- ◆ Two vignettes describing children with BCI vs. UCI
- ◆ Four elicitation methods
  - Visual analog scale (VAS)
  - Time trade-off giving up time (TTOt)
  - Time trade-off giving up QoL (TTOq)
  - Time trade-off via equivalence (TTOe)
- ◆ Feedback: VAS ↔ TTO(e)
  - and warnings for absurd responses.

## 3

### Responses obtained for each elicitation technique

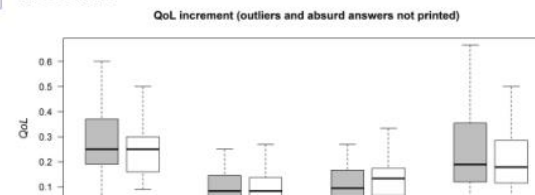


## 4 Results

Incentive	Students invited	Respondents	Response rate	% over total responses
No incentive	866	126	14,55%	21,61%
€100 (raffle)	867	149	17,19%	25,56%
€300 (raffle)	1732	308	17,78%	52,83%
<b>Total</b>	<b>3465</b>	<b>583</b>	<b>16,83%</b>	<b>100,00%</b>

Elicitation technique	Question proposed	Process completed	Agreed with result	Absurd answers	% absurd answers	ΔQoL (initial)	ΔQoL (confirmed)
VAS	144	138	77	23	16,67%	0.28	0.25
TTOt	121	105	90	65	61,90%	0.15	0.10
TTOe	112	105	87	33	31,43%	0.13	0.15
TTOq	115	107	98	55	51,40%	0.26	0.23
<b>Total</b>	<b>492</b>	<b>455</b>	<b>352</b>	<b>176</b>	<b>38,68%</b>		

## 5 Results









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iatrics

## Cost-effectiveness of pediatric bilateral cochlear implantation in Spain

Jorge Pérez-Martín MEng , Miguel A. Artaso MEng, Francisco J. Díez PhD

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[Funding Information](#)

Francisco Javier Díez is the father of a bilaterally implanted child.

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The authors have no other funding, financial relationships, or conflicts of interest to disclose.

### Abstract

#### Objectives/Hypothesis

To determine the incremental cost-effectiveness of bilateral versus unilateral cochlear implantation for 1-year-old children suffering from bilateral sensorineural severe to profound



[View issue TOC](#)  
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# La Orden SSI/1356/2015



OR 1 0 Implante de conducción ósea.

OR 1 0 0 Percutáneo.

OR 1 0 1 Transcutáneo, valorando en el caso de niños el adecuado espesor óseo.

OR 1 1 Implante activo de oído medio.

OR 1 2 Implante coclear, incluyendo la implantación bilateral tras valoración individualizada en niños y en adultos. Se considerarán especialmente las siguientes situaciones:

– pacientes con hipoacusia postinfecciosa (como posmeningitis o poscitomegalovirus) o asociada a otras discapacidades (ceguera, déficits multisensoriales o Síndrome de Usher)

– pacientes con resultados pobres tras el primer implante que puedan obtener ganancias con el segundo por presentar otras alteraciones (malformaciones del oído interno con poco resultado funcional unilateral, trastornos de conducta asociados a hipoacusia), o una patología que pueda interferir con los resultados del primer implante coclear (Síndrome de Pendred u otros síndromes hereditarios que se asocian a pérdida progresiva bilateral).

OR 1 3 Implante de trazo cerebral

- España es el primer país que cubre (en la ley) el ICB para niños y adultos.
- Hay cierta ambigüedad en la ley → dificultades en la práctica.

## Observatorio del Implante Coclear

Francisco Javier Díez Vegas (UNED)



Según la OMS, el 5% de la población mundial padece una deficiencia auditiva incapacitante. La pérdida auditiva leve y moderada puede tratarse con audífonos, pero la sordera severa y profunda requiere implante cocleares. El objetivo del Observatorio del Implante Coclear es prestar ayuda a las personas que padecen hipoacusia o sordera (niños, adolescentes, jóvenes, adultos y ancianos), a sus familiares, y a los profesionales de la salud.



Muchas gracias por tu donación y hacer posible que este proyecto avance.

- Campaña de microfinanciación (*crowdfunding*)
- Gran repercusión en los medios de comunicación.



## Inicio

El *Observatorio del Implante Coclear (IC)* es un proyecto de investigación y divulgación de la [Universidad Nacional de Educación a Distancia \(UNED\)](#). Su propósito principal es ofrecer información de interés a quienes padecen deficiencia auditiva, a sus familiares y a los profesionales relacionados con la audición. Los rasgos característicos, que en su conjunto lo diferencian de otros sitios web y de los blogs, son los siguientes:

- **Clasifica** la información por **temas**.
- Intenta cubrir en la medida de lo posible **todos los aspectos** del IC.
- **Selecciona** cuidadosamente los contenidos, pues "el exceso de información es desinformación".
- En la medida de lo posible, la información estará avalada por la **evidencia científica**, mediante citas bibliográficas y enlaces a instituciones de reconocido prestigio.
- Ofrecerá también enlaces a **todas las asociaciones** relacionadas con el IC, clasificados por países, regiones y ciudades, con un breve resumen de los servicios que presta cada una de ellas.
- El *Observatorio* contará con un equipo de **asesores** formado por profesionales y usuarios, que revisarán los contenidos.
- Los usuarios que decidan **registrarse** recibirán información por correo electrónico **ajustada al perfil** de cada uno (usuario, padre/madre, otorrino, audiólogo, logopeda, etc.), a su lugar de residencia, etc.

Además de esta labor de difusión de información, el *Observatorio* realiza **investigación propia** sobre el IC.

El *Observatorio* se rige por estrictos **criterios éticos** y garantiza que todas las aportaciones recibidas se emplean adecuadamente.

## **INFORME SOBRE LA COBERTURA DEL IMPLANTE COCLEAR EN ESPAÑA**

13 de abril de 2018  
(revisado el 30 de abril de 2018)

### **Resumen**

El implante coclear (IC) es un dispositivo electrónico que restaura la audición en casos de sordera severa o profunda. Se calcula que en España lo llevan aproximadamente 6.000 niños y 9.000 adultos. Este trabajo analiza la cobertura del implante coclear en el Sistema Nacional de Salud, especialmente en cuanto al IC bilateral y al mantenimiento de los componentes externos. El informe pone de manifiesto importantes deficiencias de las normas legales actuales así como graves variaciones interterritoriales, que perjudican especialmente a las familias de menor poder adquisitivo.

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SALUD / DISCAPACIDAD

## La conmovedora carta de la madre de una niña sorda a Susana Díaz que cambió la vida a estos niños

- "Ningún niño andaluz tendrá que volver a irse a otra Comunidad para que le reconozcan su derecho a escuchar por los dos oídos"- celebra Rosario, madre de Marta.
- Niños sordos con chararra dentro: cuando no puedes pagar que tu hijo siga oyendo



## La carta a la presidenta

La pareja tenía claro que no aceptaría un único implante. Por el camino, encontraron apoyo en dos investigadores. El primero es **Francisco Javier Díez**, director del **Centro de Investigación sobre Sistemas Inteligentes de Ayuda a la Decisión (CISIAD) de la UNED** e impulsor del [Observatorio del Implante Coclear](#). Especialista en la aplicación de la inteligencia artificial y la probabilística a la medicina, y padre de un niño con implantes cocleares, su trabajo motivó la inclusión del biimplante en la cartera de Servicios Básicos. Probaba, entre otros factores, que los beneficios de la biimplantación a la hora de lograr la **integración** de una persona sorda compensaban económicamente sus costes.

El segundo es **Serafín Sánchez**, jefe del **Servicio de Otorrinolaringología** del Virgen de la Macarena. Rosario logró contactar con él para exponerle su caso: él contestó pidiéndole paciencia. El especialista revelaba que estaban informando a la **Dirección de Gerencia del Servicio Andaluz de Salud** para introducir el biimplante desde hace tiempo, y estaban cerca de conseguirlo. Mientras trabajaba en documentar su caso, la madre recibió un chivatazo: Susana Díaz iba a venir a inaugurar la guardería de su pueblo, **Los Molares**. "Yo nunca había hecho nada parecido"- confiesa. "Pero vi ahí una oportunidad".



# Collaboration with other groups

## ◆ We offer:

- Expertise in probability and medical decision analysis
- Experience in national and international projects
- OpenMarkov, an open-source tool for:
  - building probabilistic models from expert knowledge
  - building probabilistic models from data: white-box models
  - building probabilistic models interactively
  - cost-effectiveness analysis

## ◆ We are looking for:

- Financial support (of course!)
- Collaboration in new national and international projects

***Thank you very much for your attention!***

◆ Links

- [www.cisiad.uned.es](http://www.cisiad.uned.es)
- [www.OpenMarkov.org](http://www.OpenMarkov.org)
- [www.ProbModelXML.org/networks](http://www.ProbModelXML.org/networks)

◆ Contact: [fjdiez@dia.uned.es](mailto:fjdiez@dia.uned.es)