ESF-IfW Conference
New Technology and Medical Decision Making
Salzau Castle, October 7, 2006

Probabilistic graphical models for medical decision making

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OVERVIEW

- Bayesian networks
  - advantages wrt the naïve Bayes model
  - construction of Bayesian networks
- Influence diagrams
  - advantages wrt decision trees
  - influence diagrams vs. (for) clinical practice guidelines
  - new model: decision analysis networks (DANs)
- Temporal PGMs
  - new models: event networks (non-Markovian) and dynamic LIMIDs (Markovian)
  - advantages wrt Markov decision trees

Elvira

- Research project of several Spanish universities
- Supported by national research agencies
    - Elvira I (1997-2000), Elvira II (2001-2005)
- Elvira program
    - written in Java (advantage: portability; drawback: slowness)
    - ~120.000 lines of source code, publicly available on Internet: `www.ia.uned.es/~elvira`
    - advanced graphical interface for editing and evaluating models
        - in Spanish and English; easy to translate to other languages
    - several algorithms for inference and for learning from databases
    - weaknesses
        - still buggy
        - no on-line help yet
- Used for tuition and research in at least 8 countries

1. Bayesian networks

Old method: naïve-Bayes for probabilistic diagnosis

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

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

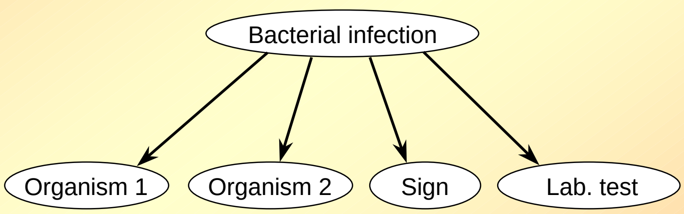
- Bayes' theorem (naïve method)

$$P(d_i|f_1, \ldots, f_m) = \frac{P(f_1|d_i) \cdot \ldots \cdot P(f_m|d_i) \cdot P(d_i)}{\sum_j P(f_1|d_i) \cdot \ldots \cdot P(f_m|d_i) \cdot P(d_j)}$$

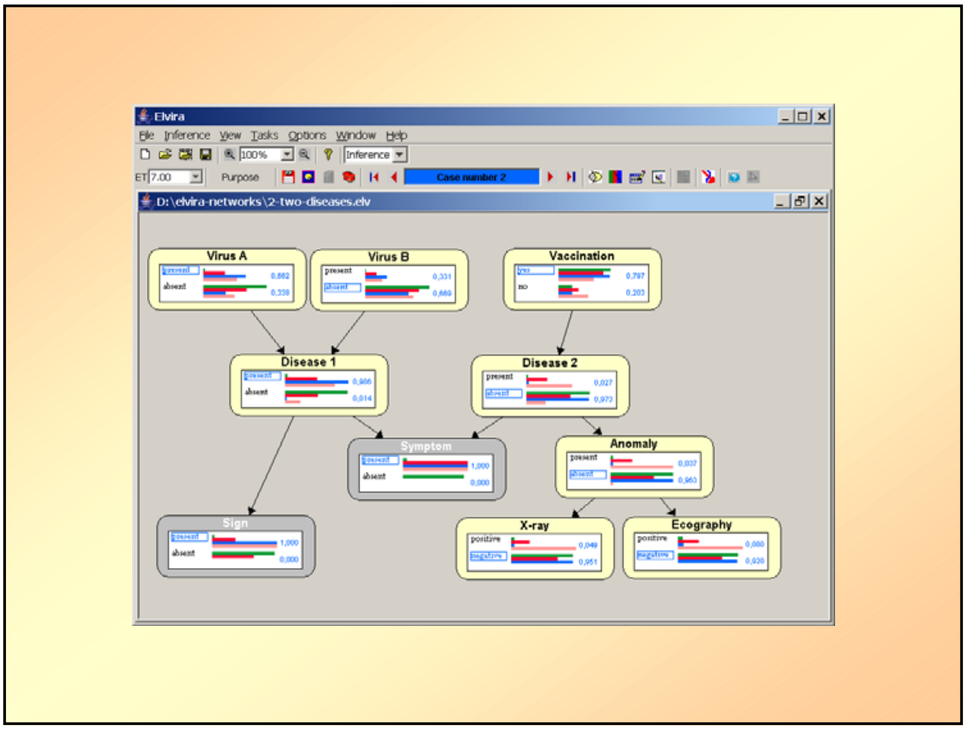
$$P(f_m \mid f_1, \ldots, f_{m-1}) = \frac{\sum_j P(f_1|d_i) \cdot \ldots \cdot P(f_m|d_i) \cdot P(d_j)}{\sum_j P(f_1|d_i) \cdot \ldots \cdot P(f_{m-1}|d_i) \cdot P(d_j)}$$

Limitations of the naïve-Bayes method

- In general diagnoses are not mutually exclusive.
- In general findings are not conditionally independent.



- In the 70s, probability was discarded in artificial intelligence
- ... but came back in the 80s with Bayesian networks


Elvira
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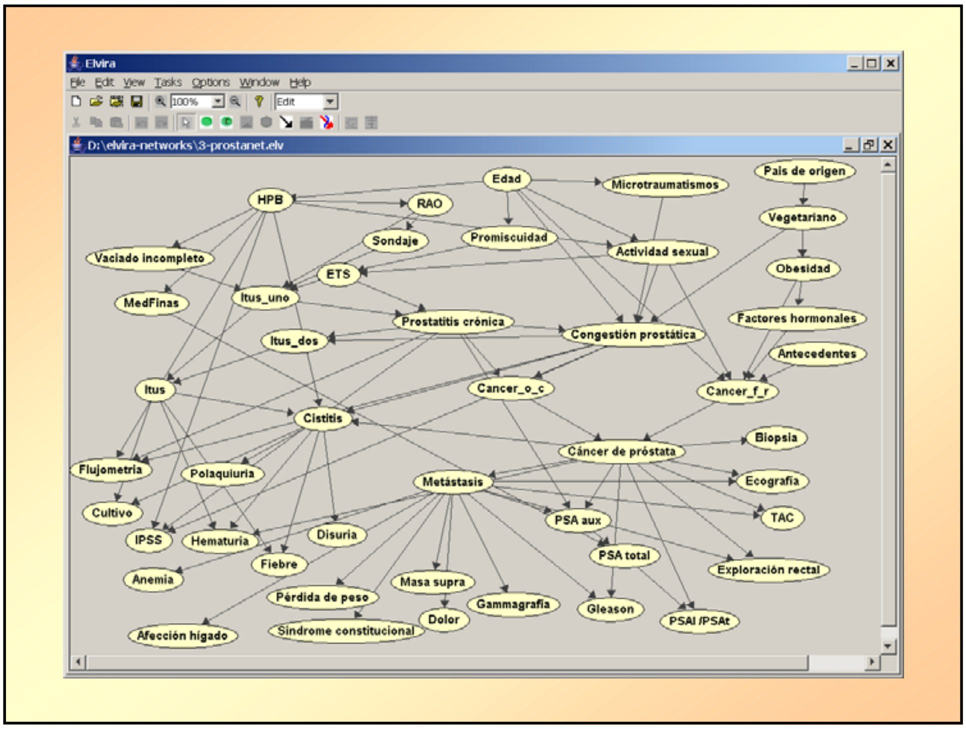
Virus A
Virus B
Vaccination
Disease 1
Disease 2
Symptom
Anomaly
Sign
X-ray
Ecography


Elvira
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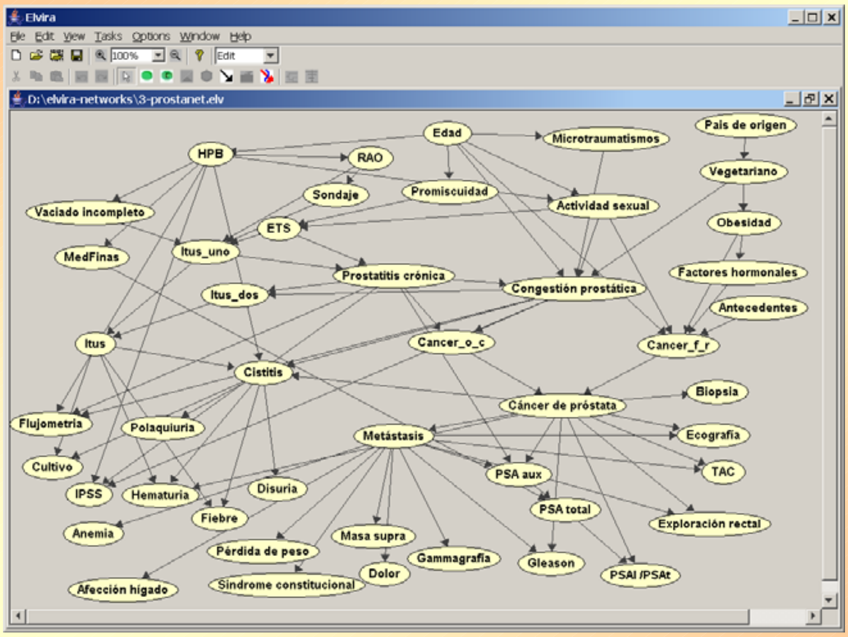
Edad
HPB
RAO
Microtraumatismos
País de origen
Vegetariano
Sondaje
Promiscuidad
Actividad sexual
Vaciado incompleto
ETS
Obesidad
MedFinas
Itus_uno
Prostatitis crónica
Factores hormonales
Itus_dos
Congestión prostática
Antecedentes
Itus
Cancer_o_c
Cancer_f_r
Cistitis
Biopsia
Cáncer de próstata
Flujometría
Polaquiuria
Metástasis
Ecografía
Cultivo
PSA aux
TAC
IPSS
Hematuria
Disuria
PSA total
Fiebre
Exploración rectal
Anemia
Masa supra
Pérdida de peso
Gammagrafía
Gleason
Dolor
PSAl /PSAt
Afección hígado
Síndrome constitucional



Advantages of Bayesian networks (1/2)

- BNs are usually causal models
  - closer to doctors' reasoning: explanation of reasoning
  - probabilities are in general easier to obtain
- BNs can diagnose several diseases simultaneously
- BNs do not assume conditional independence
- BNs can be learnt from databases
- BNs can combine objective probabilities (frequencies) with subjective estimates
- Specific methods for sensitivity analysis in BNs

Advantages of Bayesian networks (2/2)

- Canonical models facilitate the construction of BNs
  - when the BN is built from human knowledge (subjective estimates)
  - and also when a BN is learnt from a database
    - Díez, Druzdzel. Canonical probabilistic models for knowledge engineering. 2005
- Canonical models lead to more efficient inference
    - Díez, Galán. Efficient computation for the noisy-MAX. 2003
- Several methods for the explanation of reasoning in BNs
    - Lacave, Díez. A review of explanation methods for Bayesian networks. 2002.
  - useful for building and debugging Bayesian networks
    - Lacave, Onisko, Díez. Use of Elvira's explanation facility for debugging. 2006.
  - useful for avoiding human reluctancy to accept expert systems
  - useful for using BNs as tutoring systems (e.g. for students of medicine)

Use of BNs in real world applications

- BNs are more and more popular in artificial intelligence, not only in Academy but also in industry
- Many applications:
  - medicine: diagnostic expert systems
  - genetics: modeling gene interactions
  - epidemiology: detecting and quantifying causal influences
    - Program on Causal Inference in Epidemiology (Harvard; director: J. Robins)
  - agriculture, computer security, e-commerce, etc., etc.
- In contrast, BNs are almost unknown in medicine
  - Textbooks only describe the naïve Bayes method (and quite superficially, by the way)
- Why?

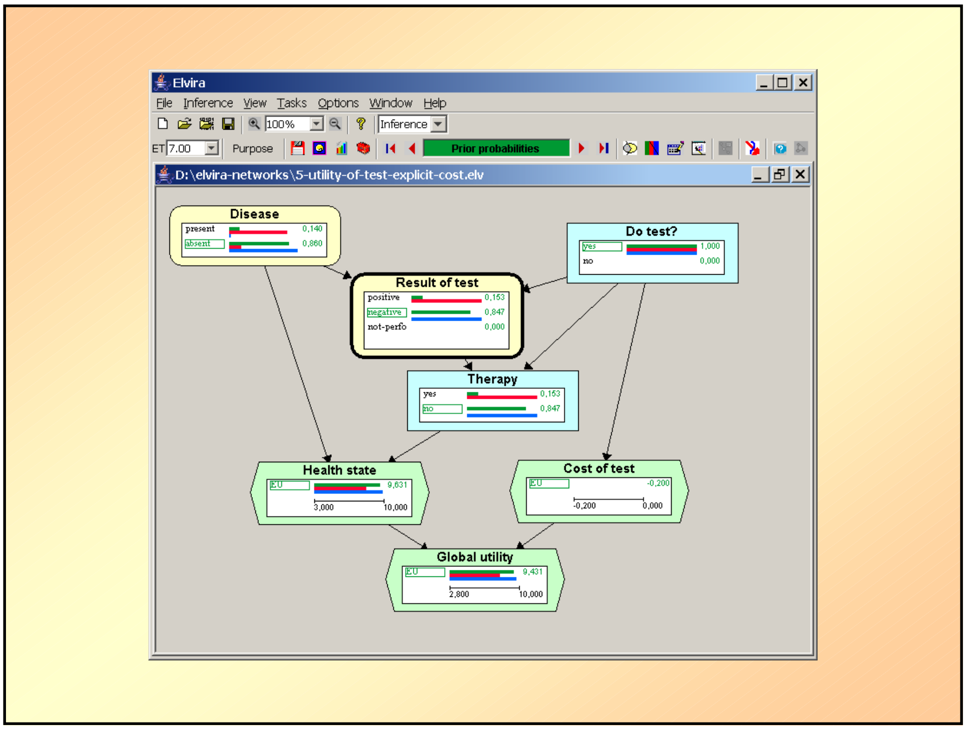
2. Influence diagrams

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 worthy to do the test?
  - In what cases should we apply the therapy?


Elvira
File Inference View Tasks Options Window Help
Inference
Purpose
Prior probabilities
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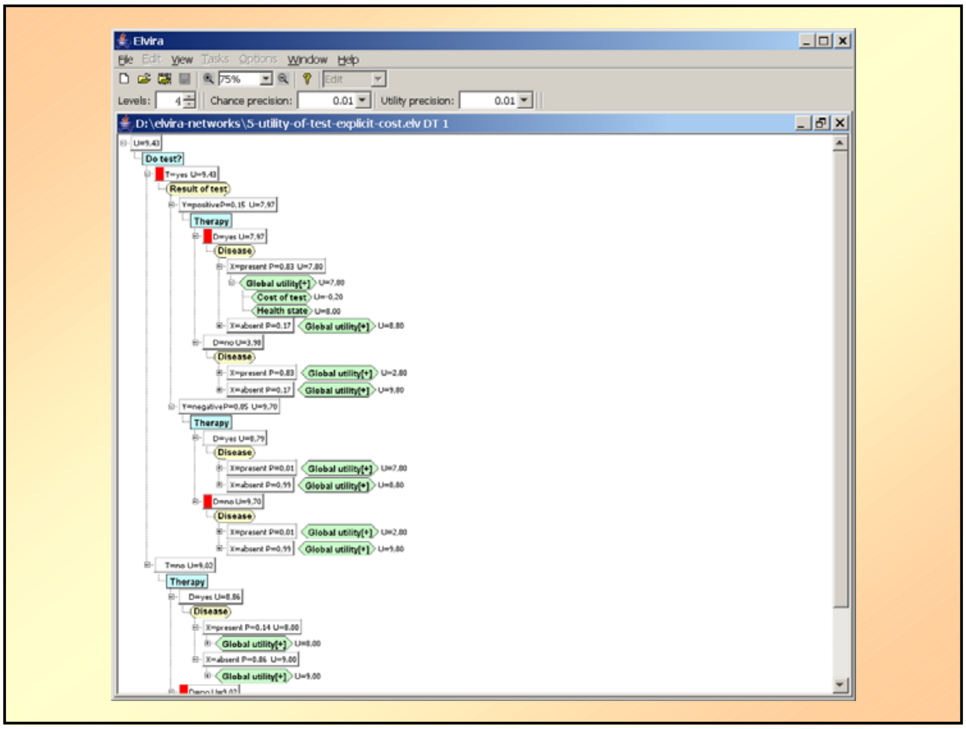
Disease
present 0,140
absent 0,860
Do test?
yes 1,000
no 0,000
Result of test
positive 0,153
negative 0,847
not-perfo 0,000
Therapy
yes 0,153
no 0,847
Health state
EU 9,631
3,000 10,000
Cost of test
EU -0,200
-0,200 0,000
Global utility
EU 9,431
2,800 10,000


Elvira
File Edit View Tasks Options Window Help
Levels:
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Utility precision:
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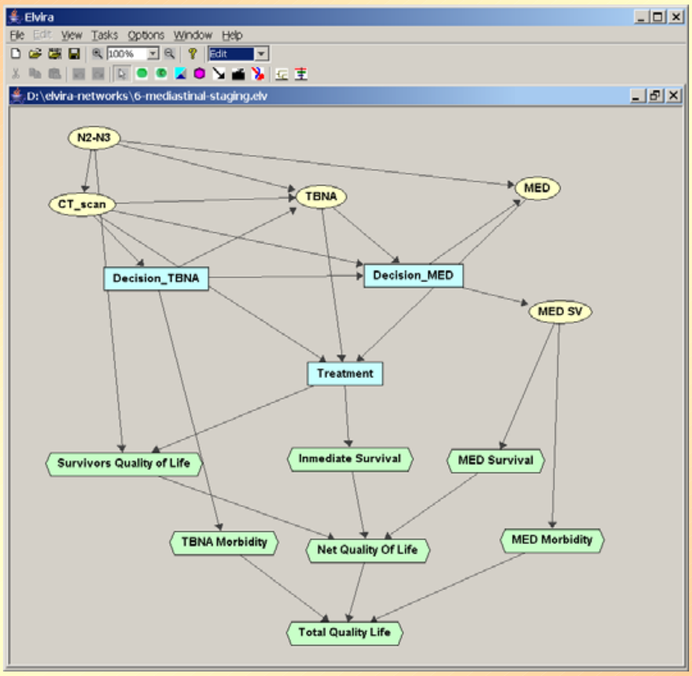
Do test?
Result of test
Therapy
Disease
Global utility(+)
Cost of test
Health state



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
- Explicit representation of <u>causality</u>
  - a link indicates causal influence
  - the absence of a link means “no causal influence” (hypothesis)
- IDs are much easier to <u>build</u> than decision trees
  - IDs use direct probabilities (prevalence, sensitivity, specificity...) and costs (mortatility, morbidity, economic cost...)
  - No external pre-calculation of probabilities is required
  - IDs can use super-value nodes: explicit combination of utilities
  - Each parameter appears only once in the ID
    - in many cases it is not necessary to have parametric variables

Advantages of influence diagrams (2/3)

- Having all the information, no debugging is usually needed
  - On the contrary, "all trees have bugs" (*Primer on MDA*)
- Parametric sensitivity analysis is much easier
- IDs are much easier to modify than decision trees
  - Refine the model with new decisions and chance variables
  - Structural sensitivity analysis is incomparably easier
  - Can adapt to different regional settings
  - Can adapt to patient's medical characteristics and preferences
- 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, with much less effort.

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.

Clinical practice guidelines (CPGs)

- Construction of CPGs
  - Usually: expert opinion or consensus of experts
  - Another possibility: influence diagrams
    - Sanders, Nease, Owens: several papers on building CPGs from IDs.
- Advantages of an ID wrt a CPG
  - explicit decision model
    - easily combine expert opinions and evidence (statistical data)
    - help in difficult cases, in which the policy is not evident
  - flexibility: can be extended and adapted, as mentioned above
  - can include patients' preferences
  - the physician plays an active role,
    he/she is not a passive user of CPGs developed by others

A proverb

- Don't give a man a fish;
  give him a rod
  and teach him how to fish.
- Don't give a doctor a written CPG;
  give them an influence diagram
  and teach them how to use Elvira.

IDs in the literature on MDM

- Journal: *Medical Decision Making*
  - very few papers using IDs in their analyses
- Books that mention decision trees and do not mention IDs
  - Weinstein, Fineberg. *Clinical Decision Making*. 1980.
    [Influence diagrams were first published in (Howard and Matheson, 1984)]
  - Sox et al. *Medical Decision Making*. 1988.
  - Sloan (ed.). *Valuing Health Care*. 1995.
  - Gold et al. *Cost-Effectiveness in Health and Medicine*. 1996.
  - Sacket et al. *Evidence-Based Medicine*. 1997
    (and three other books on EBM).
  - Petiti. *Meta-Analysis, Decision Analysis and Cost-Effectiveness Analysis*. 2nd ed., 2000.
  - Drummond, McGuire (eds.). *Economic Evaluation in Health Care Programs*. 2001.
  - Hunink, Glasziou. *Decision Making in Health and Medicine*. 2001.

IDs in the literature on MDM (cont.)

Books that mention decision trees and do not mention IDs (cont.)

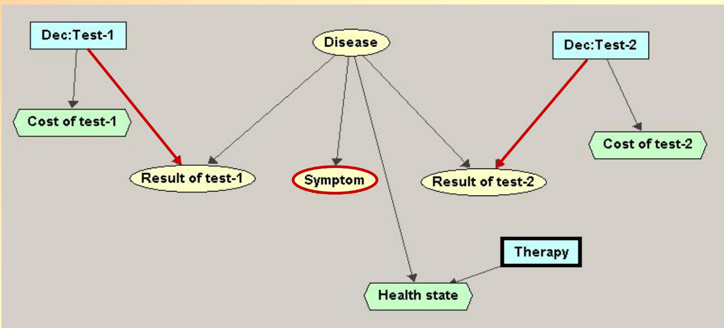
- Haddix et al. *Prevention Effectiveness*. 2nd ed., 2003.
- Drummond et al. *Methods for the Economic Evaluation of Health Care Programmes*. 3rd ed., 2005.

- One book that mentions IDs
  - Chapman, Sonnenberg (eds.). *Decision Making in Health Care*. 2000
    (5 pages out of 421).
- Another book that mentions 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]
- Conclusion: informal survey of books on MDM and EBM
  - 10 books on MDM and several on EBM published after 1984
  - All of them mention DTs but only one mentions IDs, quite briefly

Limitations of IDs

- Dealing with asymmetric problems
  - Standard IDs are symmetric
  - Some software tools (e.g., TreeAge) allow asymmetry
    - but sometimes "arcs of asymmetry" are not intuitive
  - Many asymmetric problems can not be solved with IDs
- Limitations of current software packages
  - Very few packages allow sensitivity analysis directly on IDs.
  - No package allows cost-effectiveness analysis directly on IDs.
- Solutions
  - More powerful software tools (e.g., future versions of Elvira)
  - More flexible representation models for asymmetric problems
    - Jensen, Nielsen, Shenoy. Sequential influence diagrams. Proc. of PGM-04.

Decision-analysis networks (DANs)



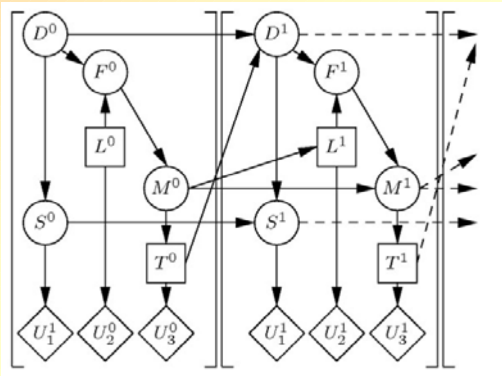
- Very similar to IDs, but:
  - DANs do not have information arcs
  - DANs do not require a total ordering of decisions
  - Some nodes are marked as "*always known*" (for instance, symptoms)
  - DANs may have *revelation arcs*: "Dec:Test"→"Result of test"

3. Temporal PGMs

Temporal PGMs

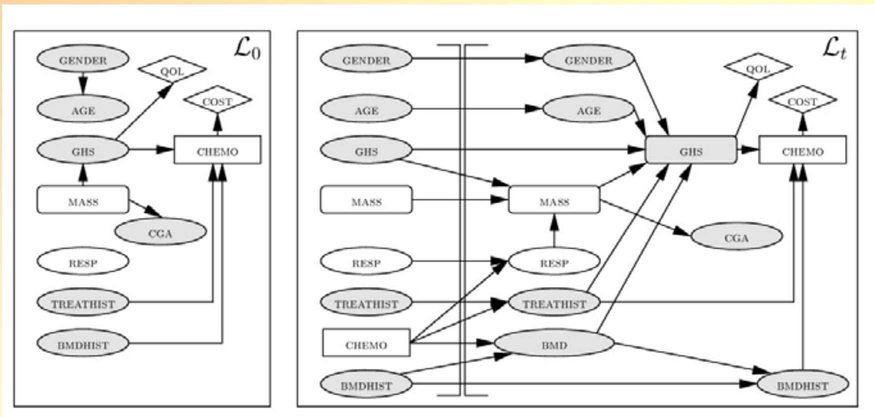
- Non-Markovian models
  - For instance, birth delivery happens 9 months after conception
  - New model: networks of events (temporal Bayesian networks)
    - Galán, Aguado, Díez, Mira. NasoNet: Modelling the spread of nasopharyngeal cancer with temporal Bayesian networks. AI in Med, 2002.
- Markovian models
  - Influence diagrams with Markov nodes
    - A node in an ID that represents a (small) Markov model
  - Other models: factored MDPs, factored POMDPs…
  - New model: 2TLIMIDs
    - van Gerven, Díez, Taal, Lucas. Selecting treatment strategies with dynamic LIMIDs. Submitted to AI in Med, 2006.

2TLIMID for a simplified medical example



- It would be difficult to build a Markov decision tree for this problem.

2TLIMID for a real-world example



- It would be <u>impossible</u> to build a Markov decision tree for this problem.

Conclusion

- Advantages of PGMs
  - Bayesian networks vs. naïve Bayes method
  - Influence diagrams vs. decision trees
  - Influence diagrams vs. (for) clinical practice guidelines
  - Temporal PGMs (2TLIMIDs, etc.) vs. Markov decision trees
- Nevertheless, PGMs are almost unknown in medicine
- Our research
  - new types of models (representation)
  - algorithms for "old" and new models
  - public software tool, Elvira (`www.ia.uned.es/~elvira`)
  - real-world models for several medical problems
- Our interest
  - collaborating with other groups doing research on medical decision analysis