A real clinical decision problem supported by an influence diagram model: IctNeo DSS

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Background (1/4)

Neonatal Jaundice $\rightarrow$

- situations with a high level of serum bilirubin such that the skin and/or the ocular sclerotic are at least slightly yellow; physiologic vs pathologic (toxic effects in the central nervous system, even death)
- Neonatal Jaundice is treated daily at all hospitals
- Doctors should take into account many factors, their experience and skill that should be modeled to set out the many uncertainties involved in the decision-making process
- Here we show a complex DSS for Neonatal Jaundice management for Neonatology Service of Gregorio Marañón Hospital in Madrid (Over the past 4 years, the hospital attended an average of 3720 births and 522 admissions, 15% of which were due to jaundice)

Background (2/4)

Clinical protocols $\rightarrow$

- Infants born at hospital with more than 4 days old
- Recommendations have increased the minimum level of risk
- 50's: blood exchange
- 60's,70's,80's: phototherapy, observation and a less blood exchange than before
- 90's: Newman & Maisels92: gentler and conservatives approaches, but not clear help in frontier situations and based on few factors

Background (3/4)

Clinical practice guideliness show some lacks →

- there is no consensus on the circumstances under which each treatment should be administered
- there is a need to take into account different doctors's points of view and, more interestingly, parents's opinions
- better decisions will decrease not only treatment risks but also the costs of diagnostics and therapeutics

Background (4/4)

Requirements and Objectives of the IctNeo DSS: a Decision Analysis based protocol for neonatal jaundice management $\rightarrow$

- New recommendations
- Much more (uncertain) variables, including related pathologies which may cause jaundice
- Preferences of parents and doctors
- Decrease diagnostic and therapeutic costs and risks
- Help in frontier situations, where various treatments could be considered
- A tool for evaluating the current protocol
- Aid for interns and residents
- Automatic support to store information

Influence Diagram

The decision model is an influence diagram, a probabilistic graphical model which represents a decision-making problem under uncertainty $\rightarrow$

- Problem representation: admission and treatment decision
- Uncertainty model: influence among historical data and subjetive judgments variables
- Preference model: multiatribute utility function of parents and doctors
- DSS validation: sensitivity analysis and explanations of results

IctNeo DSS

Conclusions and outputs →

- IctNeo DSS construction and use have induced changes in medical practice avoiding aggressive treatments and reducing the lengths of stay at the hospital
- More useful information available to make decisions
- Comparisons between real cases and DSS proposals reveal nonexperts doctors biases.
- IctNeo DSS helps novice neonatologists to avoid unnecessary treatments
- The system aggregates different points of view: doctors, parents, hospital administration
- The system can be easily adapted to other hospitals and clinical problems

Decision Model

Knowledge sources →

- 4 analysts lead 3 neonatologists acting as domain experts to the model.
- The experts contribute with the clinical guideline about neonatal jaundice and their clinical experience
- The analysts suggest the Decision Analysis methodology and an Influence Diagram as problem representation
- The team need to find: Objetives; Scope; Variables for decisions, clinical facts, factors and specific objetives; Constraints;. . .

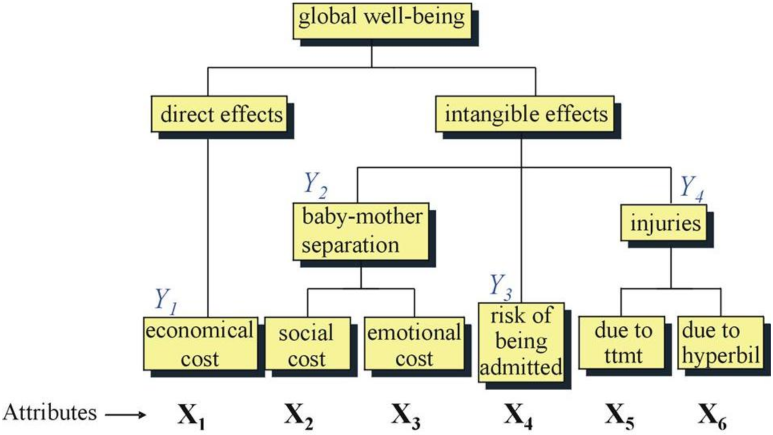
Definition of the Problem

Conceptualization and formulation of model (chance, decision and utility attributes) variables $\rightarrow$

- Objectives of the systems and hierarchy
- Admision, teraphy, medical test, clinical history, socio-economic environment,...
- Valid chains of treatment decisions

Definition of the Problem

Objetives Hierarchy



Structure of the Problem

Connections and (in)dependences among variables $\rightarrow$

- Decision sequence, evidence sequence
- Information available at each decision-making time
- Uncertain events, causality, correlation, conditional independences,...
- Preferences of the agents over the decision-making proccess direct result

Model Structure

Modelization difficulties $\rightarrow$

- Decision Definition: complex domains, model time, global constraints
- Constraints of chains of treatments: less than 3 exchanges per treatment, exchange followed and preceded by phototherapy
- Reaching the final diagram (graph drawing)

Model Structure

Domains decision variables

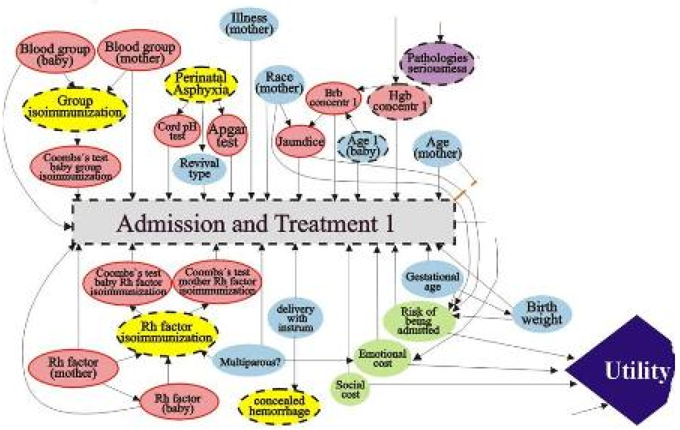
1st Decision	2nd and 3rd Decision	4th Decision	5th Decision
No admission	Null	Null	Null
Admission + 6-phototherapy	Observation + discharge	Observation + discharge	Observation + discharge
Admission + 12-phototherapy	Observation	Observation + outside treatment	Observation + outside treatment
Admission + 24-phototherapy	Observation + outside treatment	6-phototherapy	
Admission + outside treatment	6-phototherapy	12-phototherapy	
	12-phototherapy	24-phototherapy	
	24-phototherapy		
	6-phototherapy + exchange transfusion + 6-phototherapy		
	12-phototherapy + exchange transfusion + 12-phototherapy		

IctNeo DSS Influence Diagram

Nodes of Pathology

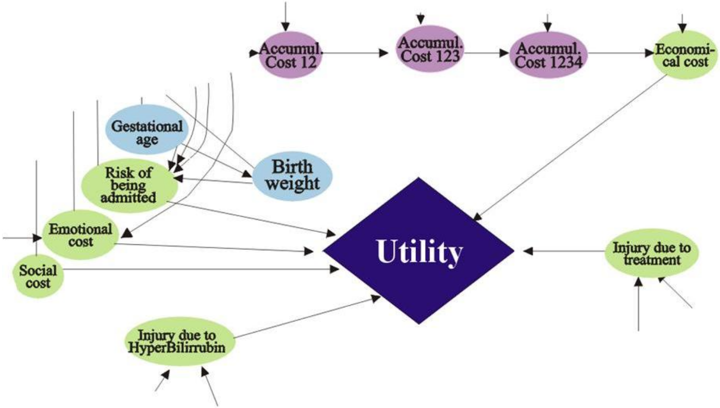
IctNeo DSS Influence Diagram

Admission node



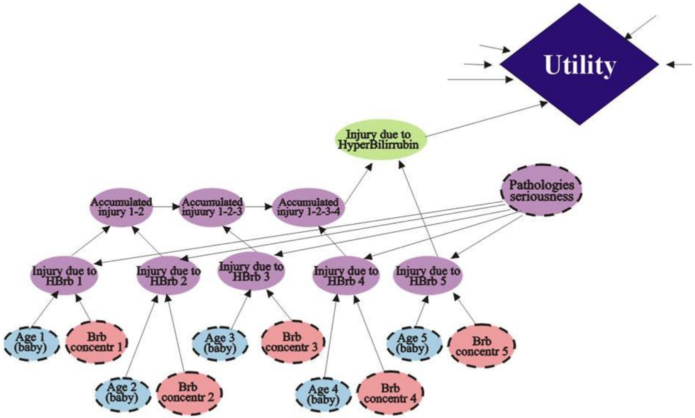
IctNeo DSS Influence Diagram

Utility node and its attributes



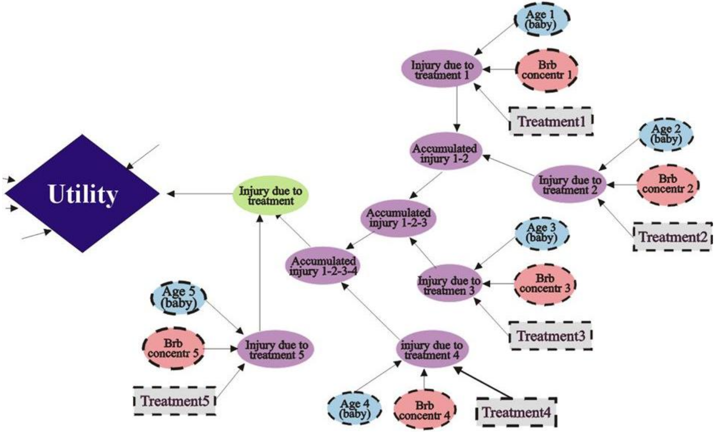
IctNeo DSS Influence Diagram

Injury of Hyperbilirrubin



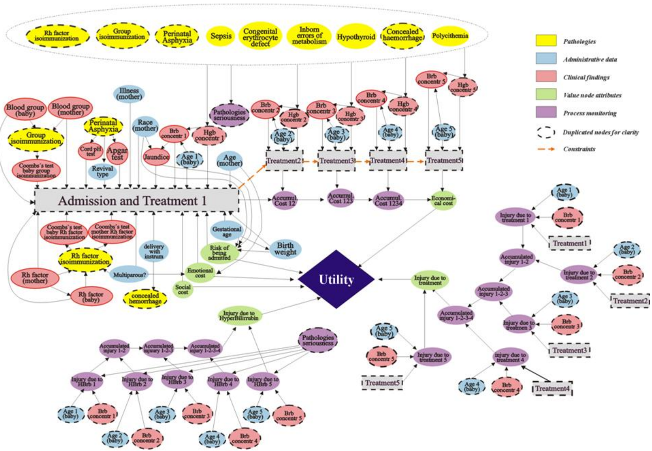
IctNeo DSS Influence Diagram

Injury of Treatment



IctNeo DSS Influence Diagram

Full diagram



Elicitation of Probabilities

Probabilities $\rightarrow$

- 68 random variables. Finally, 13,521 parameters
- Discretization (age, weight, bilirubin concentration,...)
- Historical data (3.12%)
- Subjective judgments (standard encoding process)
- Formal protocol of probability elicitation: SRI protocol

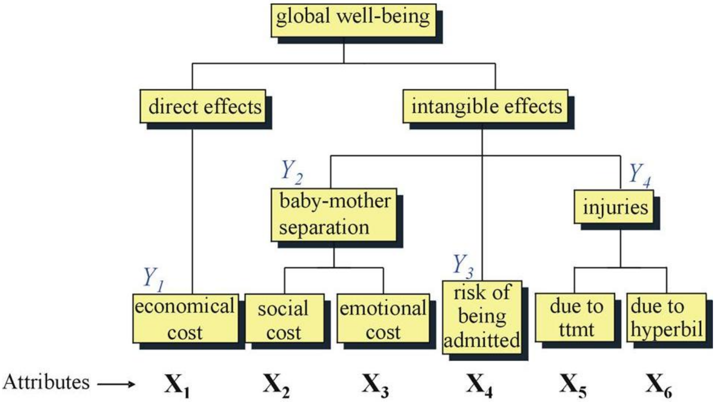
Elicitation of Probabilities

Conditional probability distribution $\rightarrow$

- Use of noisy OR-gates (from 9,216 parameters to 163), assign $P(\text{effect}|\text{all causes but one are absent})$ and derive the others
- Include more nodes to represent progressive accumulation
- Logical constraints about the accumulated costs and injury due hyperbiblirubin and treatment: qualitative rules: e.g. Cost 1-2-3 $\geq$ Cost 1-2

Preferences Structure

Objetives Hierarchy



The Multiattribute Utility Function Assessement Procedure

Objectives, Components and Assessement

- Min $\{$patient risk and worries, cost$\}$
- Attributes and scales, 5400 parameters, Multiattribute utility function assignament: $u(y_1, y_2, y_3, y_4) = f[u_1(y_1), u_2(y_2), u_3(y_3), u_4(y_4)]$
- Assign utility functions u_i, scaling constants k, k_i, k_i^x : imprecise

The Multiattribute Utility Function Assessement Procedure

Independence assumptions about decision-maker attitudes to risk $\rightarrow$

- Additive utility function: $u(y_1, y_2, y_3, y_4) = \sum_{i=1}^{4} k_i u_i(y_i)$
- Multiplicative utility function:

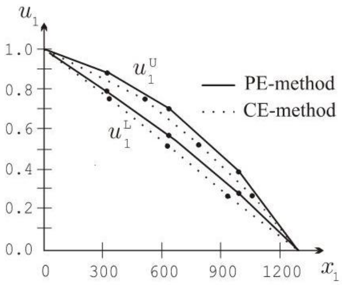
$$u(y_1, y_2, y_3, y_4) = \sum_{i=1}^{4} k_i u_i(y_i) + k \sum_{i=1, i>j}^{4} k_i k_j u_i(y_i) u_j(y_j) +$$

$$k^2 \sum_{i=1, j>i, l>j}^{4} k_i k_j k_l u_i(y_i) u_j(y_j) u_l(y_l) + k^3 \prod_{i=1}^{4} k_i u_i(y_i)$$

- $u_2(x_2) = k_2^x u_2^x(x_2) + k_3^x u_3^x(x_3)$
- $u_4(x_4) = k_5^x u_5^x(x_5) + k_6^x u_6^x(x_6)$

Component Utility Function Assessement Procedure

Utility functions for attribute X_1. PE = probability equivalent; CE = certainty equivalent



a) Upper and lower bounds for utility function u_1

b) Range for the DM's utility function u_1

Component Utility Function Assessement Procedure

Single-Attribute Utility Functions

Attribute	u_i	Range
X_1	$u_1(x_1) = 1.604 - 0.604\exp(0.00077x_1)$	[0, 1260]
X_2	$u_2^x(x_2) = -0.1108 + 1.111\exp(-1.153x_2)$	[0, 2]
X_3	$u_3^x(x_3) = -0.225 + 1.225\exp(-0.8473x_3)$	[0, 2]
X_4	$u_4(x_4) = 1.277 - 0.2766\exp(0.5098x_4)$	[0, 3]
X_5	$u_5^x(x_5) = 1.361 - 0.361\exp(0.3316x_5)$	[0, 4]
X_6	$u_6^x(x_6) = 1.408 - 0.4083\exp(0.2476x_6)$	[0, 5]

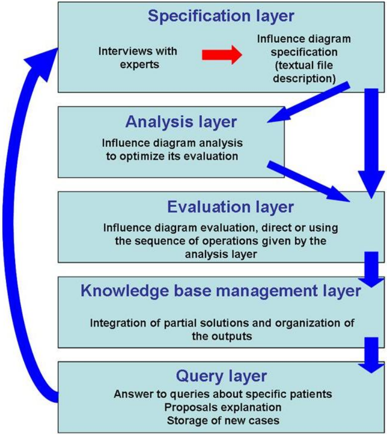
Implementation and Computational Issues

5-layer architecture $\rightarrow$

- Reconsideration of the model: changes, stepwise refinement, tuning of parameters,. . .
- Modularity of the system: clinical knowledge domain and decision analysis knowledge domain

Implementation and Computational Issues

IctNeo Architecture



Implementation and Computational Issues

The complexity related to the development of a decision support system such as IctNeo $\rightarrow$

- Optimal decison tables very huge: instantiation and aggregation of results
- *KBM2L* list to aggregate results, compact the storage of tables and synthesize high-level explanations of DSS proposals

Implementation and Computational Issues

IctNeo Output Complexity

	D_1	D_2	D_3	D_4	D_5
Relevant variables	20	23	26	29	32
States for D_i	5	9	9	7	3
Numbers to be computed	1.9×10^9	6.1×10^{10}	1.1×10^{12}	1.5×10^{13}	1.2×10^{14}

Sensitivity Analysis

Sensitivity analysis techniques were applied to gain confidence about the models behavior $\rightarrow$

- Focused on several critical parameters: probabilities and weights used for the utility function
- 1-way sensitivity analyses, mainly using tornado diagrams
- Multiway sensitivity analyses to explore the impact of several parameters at a time and find out possible interrelationships
- Simulationbased method based on the expected value of perfect information
- Parameter interactions are important

Results (1/2)

Beyond de DSS $\rightarrow$

- This introspection into the jaundice problem that has made such a profound impact on the daily clinical practice
- Centralize information about patients
- IctNeo reports matches or discrepancies between its recommended treatments and the treatments actually administered
- IctNeo gives proposals to doctors and trainig.
- IctNeo is available on a common PC where the (partial) evaluation of the model is stored

Results (2/2)

Comparison between the decision support system proposals and the experts decisions based on 50 clinical histories

Issue	IctNeo	Experts	Comments
Admissions	46 admissions, 4 not admitted	49 admissions, 1 not admitted	6% of difference
Outside treatments	4 cases, 1 at the 1st decision, 3 for the rest		100% match
Phototherapies	9 of short duration, 23 of average duration, 13 of long duration	8 of short duration, 21 of average duration, 16 of long duration	6% of difference; the 3 categories take into account the total phototherapy duration all over the stay; short duration (up to 24 h), average duration (24–48 h), long duration (more than 48 h)
Exchange transfusions	0		The experts took into consideration this alternative for only 1 patient
Total length of stay at hospital	35 with shorter stays, 10 with the same stay length		78% of the cases with shorter stays; this is measured by adding the actual duration of every patient treatment and computing the difference with respect to physician proposals

Discussion

- The state of art includes decision trees, expert systems and formal logic-based approaches
- Our proposal is a novel idea in this field: we use decision analysis
- The influence diagram model has many valuable capabilities for guiding the clinical decision-making process
- The optimal treatments is derived according to the maximum expected utility principle
- It is very difficult and time-consuming to add new knowledge

Conclusions

- Influence diagrams (ID) have proven to be powerful for communicating ideas in decision-making problems
- We had to tackle difficulties related to problem structuring (C), knowledge acquisition (P&U) and computational limitations
- IctNeo plays a role in automating medical decision making by means of which the knowledge of 1st-class experts can be made available to the rest of the health care community
- Multiattribute utility analysis made it possible to combine the point of view of patients, doctors, and the hospital
- Our tool allows the representation and refinement of the ID, consistency tests, data acquisition, ID evaluation, presentation of system proposals and explanations, and clinical data storage and use

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- In memory of Professor Sixto Ríos-Insua.

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