DECIDE

Introduction to Health Interventions, Policy and Services

Coordinator:

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DECIDE

Introduction to Health Interventions, Policy and Services

Methods in Decision Analysis and Decision Modelling – Part II
Decision Analysis - Formalization, modelling and quantitative analysis

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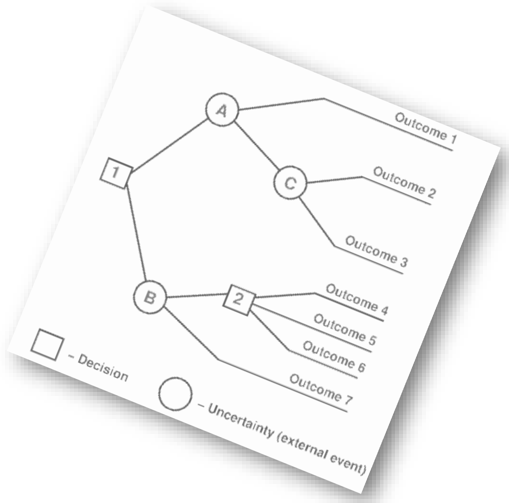
Methods in Decision Analysis and Decision Modelling – Part II:

Decision Analysis – Formalization, modelling and quantitative analysis



Summary

- Decision Analysis – Introduction
- Theoretical Foundations of Decision Analysis
- Decision Analysis – Operational Stages
  - Exploring an example with decision trees
- Uncertainty and Variability in Decision Analysis
  - Exploring analytical approaches through some practical examples
- Some Other Methods and Models Used in Decision Analysis

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Decision Analysis – Introduction

Decision Analysis – Introduction

- Life involves making **decisions**!
  - Decision makers require guidelines and expert support
- Most important decisions involve
  - multiple **uncertainties**
  - multiple **outcomes**, which can often be evaluated using multiple **attributes**
  - Multiple decision-making **stages**
  - **information gathering** at every stage
- Examples in everyday life include business, government policy, medicine, law, and personal decisions

Decision Analysis – Introduction

- **Decision making in health and medicine is a complex and sensible process**
  (1) The **doctor-patient relationship has been subject of a profound paradigm shift** from the classical authority-based model to the modern shared decision-making model
  (2) The **explosion and steady growing in the number of new healthcare technologies**, each one with its **specific associated benefits, risks and costs**
  (3) The **explosion, steady growing and exponential accumulation of scientific evidence in the biomedical area**, with **highly heterogeneous quality and results**
  (4) The **availability and easy access of healthcare professionals** and decision makers to **powerful modern technologies of collection, processing, storage and communication of data, information and knowledge**
  (5) The **easy and indiscriminate access of patients** to **specialized information and knowledge through powerful information and communication technologies**

Decision Analysis – Introduction

- For all these reasons it has become increasingly evident the relevant role of appropriate methods and approaches supporting and helping **healthcare professionals and decision makers** by allowing them to **formalize, model and quantitatively analyse the decision-making process and more appropriately integrate the best available scientific evidence**
- Healthcare professionals and decision-makers are **increasingly interested in using technologies, methods and tools supporting directly or indirectly the decision-making processes**

Decision Analysis – Introduction

- Requires **modeling** the decision
  - Several effective graphical modeling methods
- Provides tools for **quantitative analysis** of decisions with multiple uncertainties and/or conflicting objectives
- Provides decision makers with **insight**, not necessarily a solution
  - Example: Multi-way **sensitivity analysis**
- Benefits from using **computational** tools

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Decision Analysis – Introduction

- **Decision analysis is**
  - **A quantitative and systematic approach**
  - allowing us to **formalize, model and quantitatively analyse the decision-making process**
  - aiming to **compare the relative benefits, risks, outcomes and values associated with different decision alternatives** and
  - the **consideration, evaluation and modelling of several sources of uncertainty and heterogeneity affecting the decision-making process**

- Hunink MGM, Glasziou P, Siegel J, Weeks J, Pliskin J, Elstein A, et al. *Decision making in health and medicine : integrating evidence and values*. Cambridge ; New York: Cambridge University Press, 2001.
- Pauker SG, Kassirer JP. Decision analysis. *N Engl J Med* 1987;316(5):250-8.
- Sox HC, Blatt MA, Higgins MC, Marton KI. *Medical decision making*. Philadelphia: American College of Physicians, 2007.
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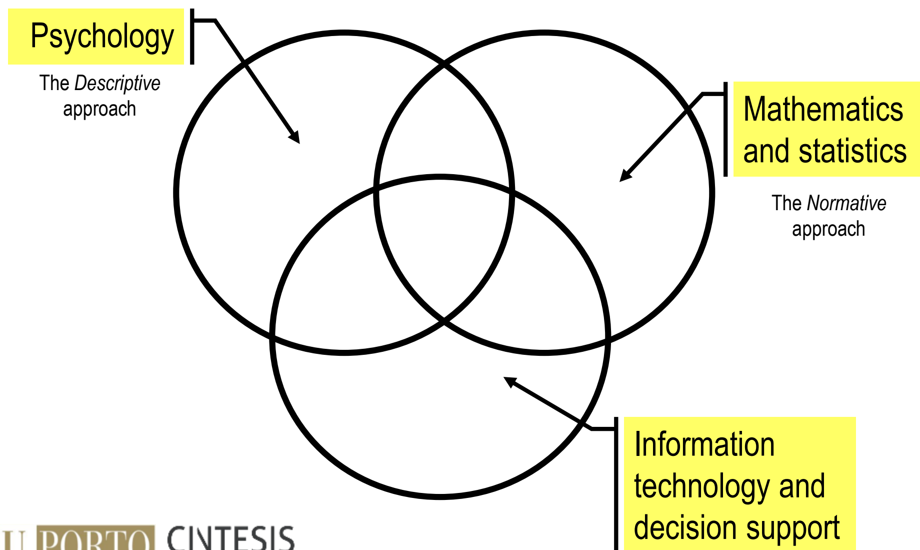
The disciplines of decision making



Disciplinary roots of decision science

	DESCRIPTIVE THEORIES	PRESCRIPTIVE THEORIES
INDIVIDUAL	• Psychology • Marketing • Psychiatry • Literature	• Decision science • Economics • Operations research • Philosophy/logic
GROUP	• Social psychology • Organizational behavior • Anthropology • Sociology	• Game theory • Organizational behavior • Clinical psychiatry/therapy • Finance/economics
ORGANIZATION	• Organization theory • Sociology • Industrial organization • Political science	• Planning/strategy • Control theory/cybernetics • Organization design • Team theory/economics
SOCIETY	• Sociology • Anthropology • Macroeconomics	• Legal philosophy • Political sciences • Social choice

Kleindorfer, P.R., Kunreuther, H.C. and Schoemaker, P.J.H. (1993). **Decision Sciences: An integrative perspective**, Cambridge.

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Decision Analysis – Introduction

- **Decision Analysis** may be **useful in the biomedical area in several different contexts, frameworks and levels of decision-making**:
  - Decisions about **individual patients**
  - Development of **protocols and guidelines**
  - Decisions about **healthcare technologies**
  - **Management and administrative** decisions
  - **Healthcare policy** decisions

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Theoretical Foundations of Decision Analysis

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Decision Analysis – Theoretical Foundations

- The origins of Decision Analysis may be traced back to the decision making axioms proposed by **John von Neumann and Oscar Morgenstern in their classic work on game theory** (1944, 1947)
- These methods and approaches to formalize and quantitatively analyse the decision-making process were **initially used in areas such as economics, management, political sciences and engineering**, but are **now increasingly used by other areas such as law and medicine**
- These methods and approaches are **particularly useful in any area where complex decisions have to be made subjected to different sources of uncertainty and incomplete information**
- The foundations of Decision Analysis in the medical area date back to **1959 with Ledley and Lusted**
- The **first scientific article published making a reference to and applied work of Decision Analysis** dates back to **1967 – a work authored by Henschke and Flehinger** aiming to assess the use of cervical radical dissection in patients with cancer of the oral cavity, without palpable cervical metastasisasis
- The works of **Lusted in 1971 and Kassirer in 1976** also had particular historical relevance
- The use and the number of scientific articles exploring or using Decision Analysis in health and medicine have been **steadily growing since the 70 decade**

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HEADS PhD PROGRAMME IN HEALTH DATA SCIENCE

Rules of Actional Thought

- **Ronald Howard's version of the decision making axioms proposed by John von Neumann and Oscar Morgenstern** in their classic work on game theory (1944, 1947)
- Simple, intuitive guidelines to follow when making decisions
- A set of five rational, consistent rules for a normative decision maker to follow

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Ronald Howard's rules of actional thought

We have seen these rules previously…

- The Probability Rule
- The Order Rule
- The Equivalence Rule
- The Substitution Rule
- The Choice Rule

Lotteries and Normative Axioms

- John von Neumann and Oscar Morgenstern (VNM) in their classic work on game theory (1944, 1947) **defined several axioms a rational (normative) decision maker might follow with respect to preference among *lotteries***
- The VNM axioms **state our rules of actional thought more formally with respect to preferring one lottery over another**
- A **lottery** is a **probability function from a set of states *S* of the world into a set *X* of possible prizes**

The Expected-Utility Maximization Theorem

- Theorem: The **VNM axioms are jointly satisfied iff there exists a utility function *U* in the range [0..1] such that lottery *f* is (weakly) preferred to lottery *g* iff the expected value of the utility of lottery *f* is greater or equal to that of lottery *g***
  - Note: The **proof shows that the preference probability (and its linear combinations) in fact satisfies the requirements**

Implications of Utility Maximization to Decision Making

- Starting from relatively very weak assumptions, VNM showed that there is **always a utility measure that is maximized, given a *normative* decision maker that follows intuitively highly plausible behavior rules**
- **Maximization of expected utility could even be viewed as an evolutionary law** of maximizing some survival function
- However, **in reality (*descriptive behavior*) people often violate each and every one of the axioms**!

Decision Models

- Normative models
  - Decision Trees
  - Influence Diagrams
  - Bayesian/Belief Networks
  - Markov Models
- Descriptive models
  - Fallacies and biases in human decision making and judgment
  - Prospect theory (Tversky and Kahneman)

Decision Analysis – Operational Stages

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Decision Analysis – Operational Stages

1 – **Identification, clarification and simplification of the decision problem**, clear definition of the **decision context and stakeholders**, systematic identification of the **decision alternatives** and the **main factors and components** relevant for the problem

2 – **Structuring, formalizing and representing** the decision problem using **appropriate tools and methods** (e.g.: **Decision Trees**, Influence Diagrams, Bayesian/Belief Networks, Markov Models, etc.) and taking into account the most **relevant events, factors and components of the decision problem**

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Decision Analysis – Operational Stages

3 – Definition of **events and factors** between the alternatives and outcomes

4 – Definition of all possible **outcomes, outcome variables and valuation of each possible outcome**

5 – Finding adequate **evidence to support the estimates of the parameters of the model** and expre**ssing the uncertainty of those estimates**, by **systematically reviewing the scientific evidence** or **discussing with experts**

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Decision Analysis – Operational Stages

6 – Prepare the **final representation of the model** (e.g. a Decision Tree) and **apply the appropriate principles and quantitative methods** to find the best alternative for the decision problem

7 – **Assess and explore the various sources of uncertainty in the model using appropriate methods** (e.g. sensitivity analysis, simulation, statistic modelling, etc.)

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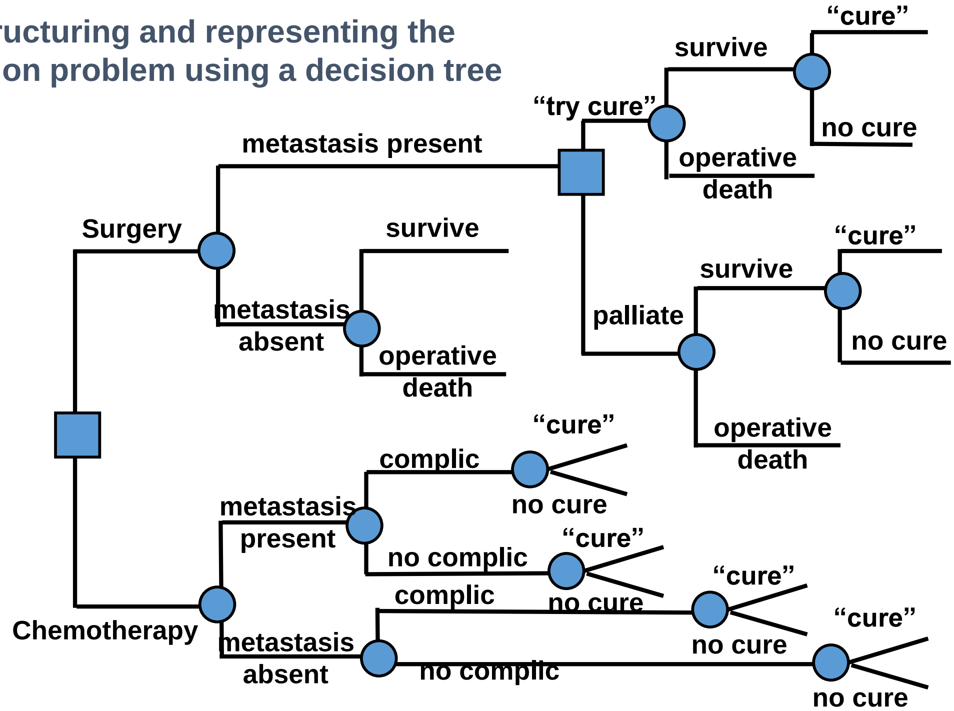
A Practical Example (I)

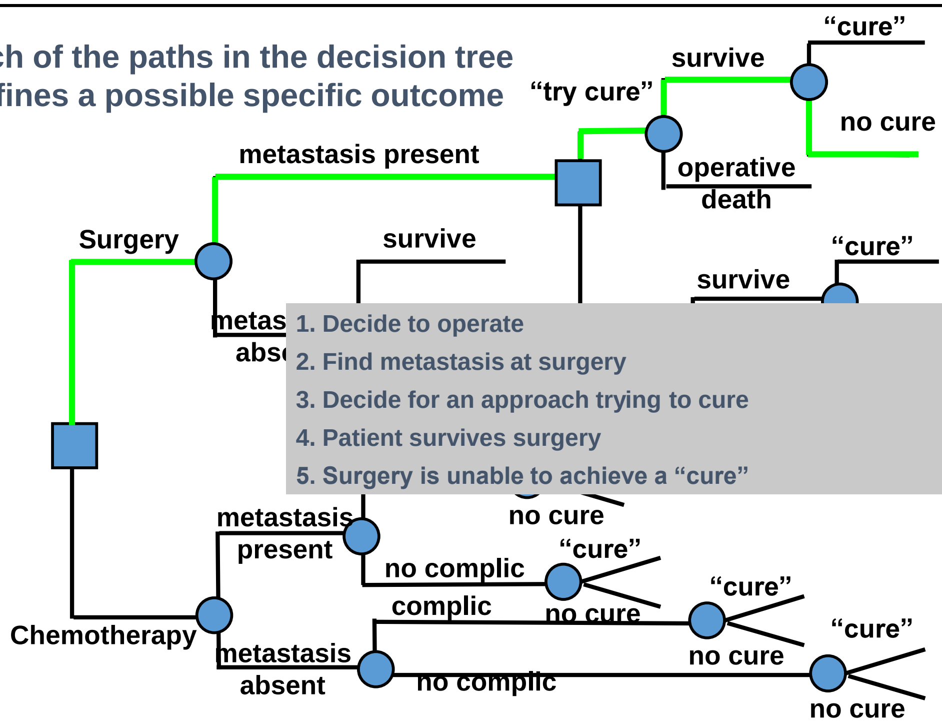
Clinical Scenario

- A symptomatic patient suspected of having a metastasisatic cancer:
  - Surgery [SUR] (higher risk but higher probability of "cure")
  - Medical treatment [chemotherapy – CT] (lesser risk but lesser probability of "cure")
- Confirmation of presence and disease extension during surgery will allow the additional decision between a surgery with "curative" or palliative intention
- The alternative of chemotherapy also has some risk of complictions
- We aim to decide between the alternatives SUR or CT in order to maximize the expected overall survival of the patient

Structuring and representing the decision problem using a decision tree



Each of the paths in the decision tree defines a possible specific outcome



1. Decide to operate
2. Find metastasis at surgery
3. Decide for an approach trying to cure
4. Patient survives surgery
5. Surgery is unable to achieve a "cure"

Decision Analysis – Operational Stages

- **Decision Tree**
  - Structured **from left to right**
  - In general, most often the alternatives, events and outcomes are organized in chronological sequence; however, this is not mandatory
  - The decision tree has **nodes**, **branches** and **outcomes**
  - **There are two types of nodes:**
    - **Decision node**
    - **Probability node**

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Decision Analysis – Operational Stages

- **Decision Tree**
  - **Decision nodes are represented by squares** and usually are at the beginning of the tree and define all the alternatives in the decision problem
  - **Probability nodes are represented by circles** and define the relevant events between alternatives and outcomes and the respective probabilities for each possible branch

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Decision Analysis – Operational Stages

Decision Tree

- The **sum of the probabilities of the branches initiating in a given probability node should total 1**; thus, each probability node defines a **mutually exclusive** and **jointly exhaustive** set of possible events
- **Branches** link nodes and link nodes with outcomes

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Decision Analysis – Operational Stages

Decision Tree

- The **outcomes, utilities or payoffs** at the end of each path are represented by **terminal nodes in the form of triangles or rectangles** at the right side of the decision tree
- The **outcome variables** considered will **dependent on the clinical context and decision problem analysed** (e.g.: mortality, morbidity, disability, utility, survival time, quality adjusted life years, etc.)

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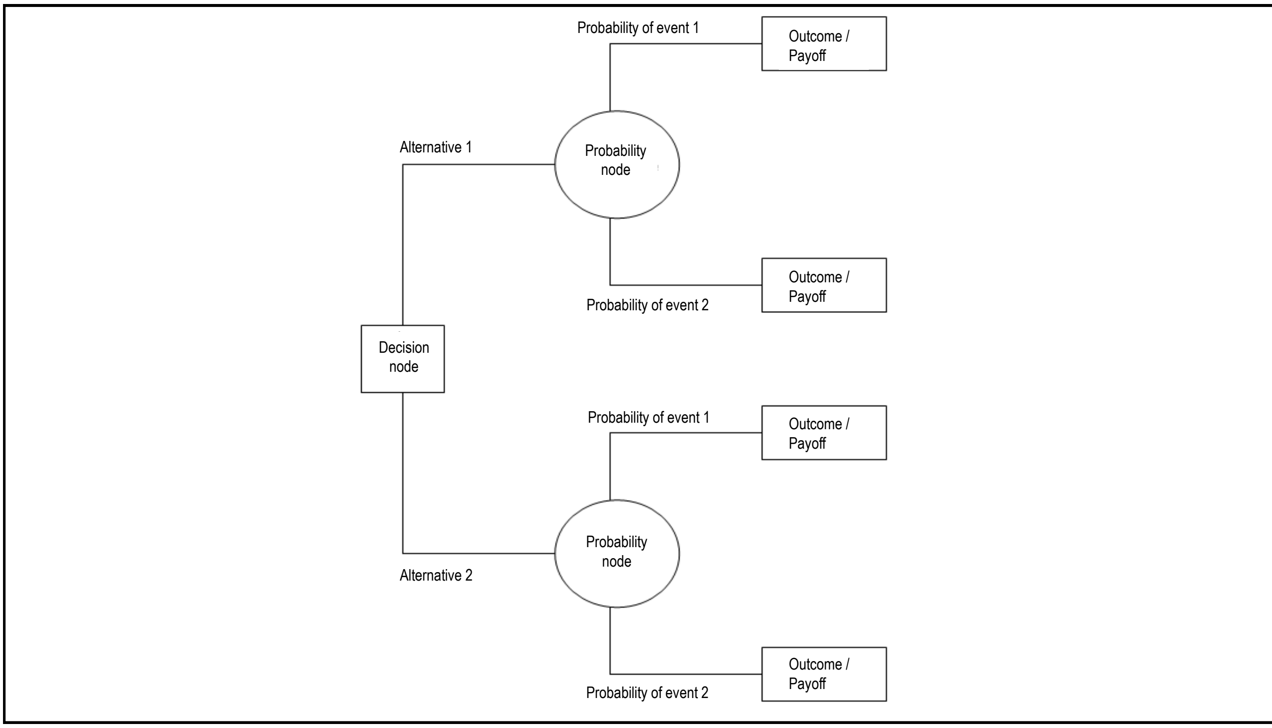
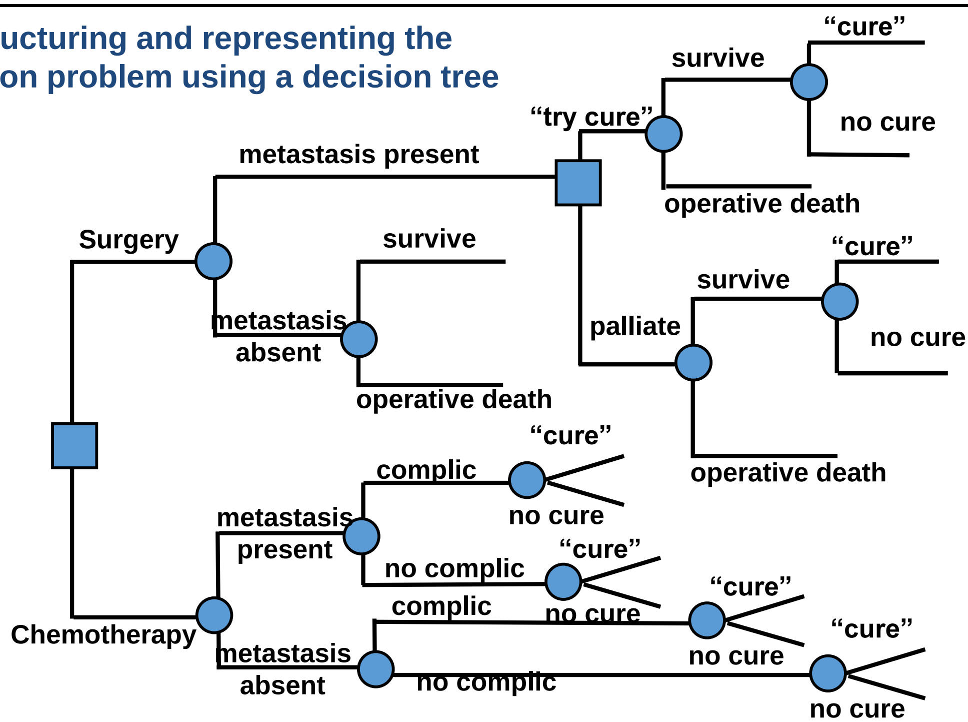
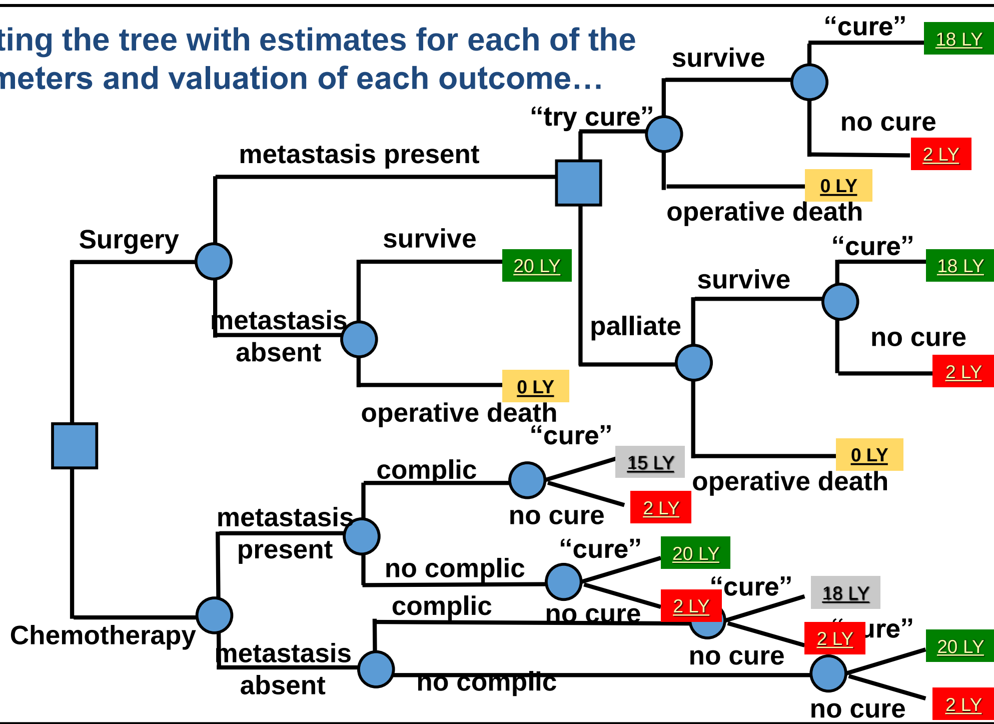


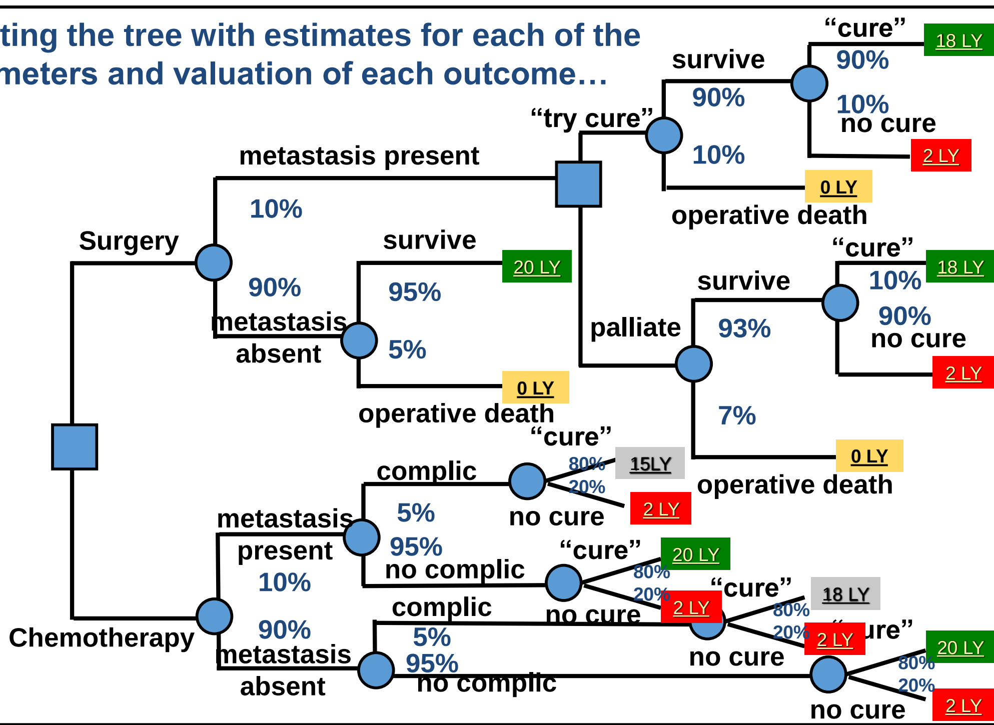
Structuring and representing the decision problem using a decision tree



Populating the tree with estimates for each of the parameters and valuation of each outcome…



Populating the tree with estimates for each of the parameters and valuation of each outcome…



Decision Analysis – Operational Stages

Analysing and solving the decision tree

- The analysis of the decision tree will follow the principle of **maximization of expected utility (or minimization of expected disutility)**
- The calculations throughout the process are based on **the rules of multiplication and summation of probabilities** and on the **Bayes' theorem** and assume the **conditional independence** of events
- The calculations will estimate the **probability of each path** (***folding back***); and this will **weight the outcome, payoff, utility or disutility associated with that path**

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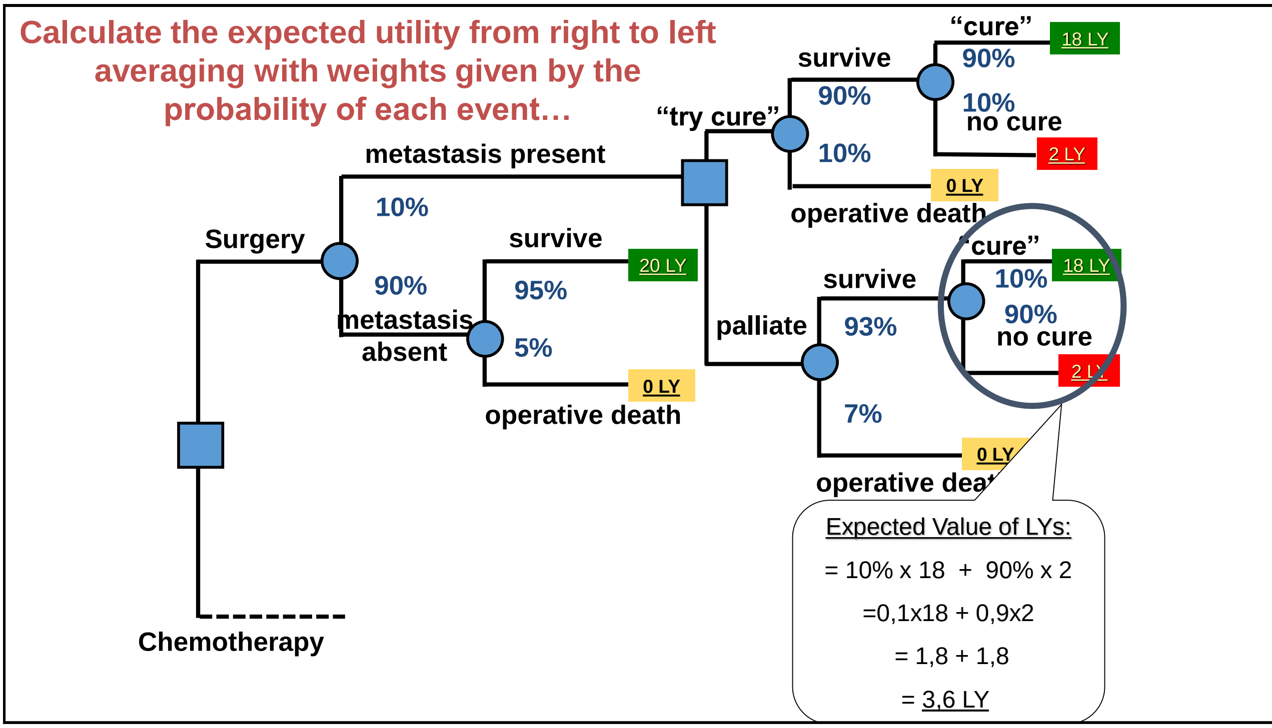
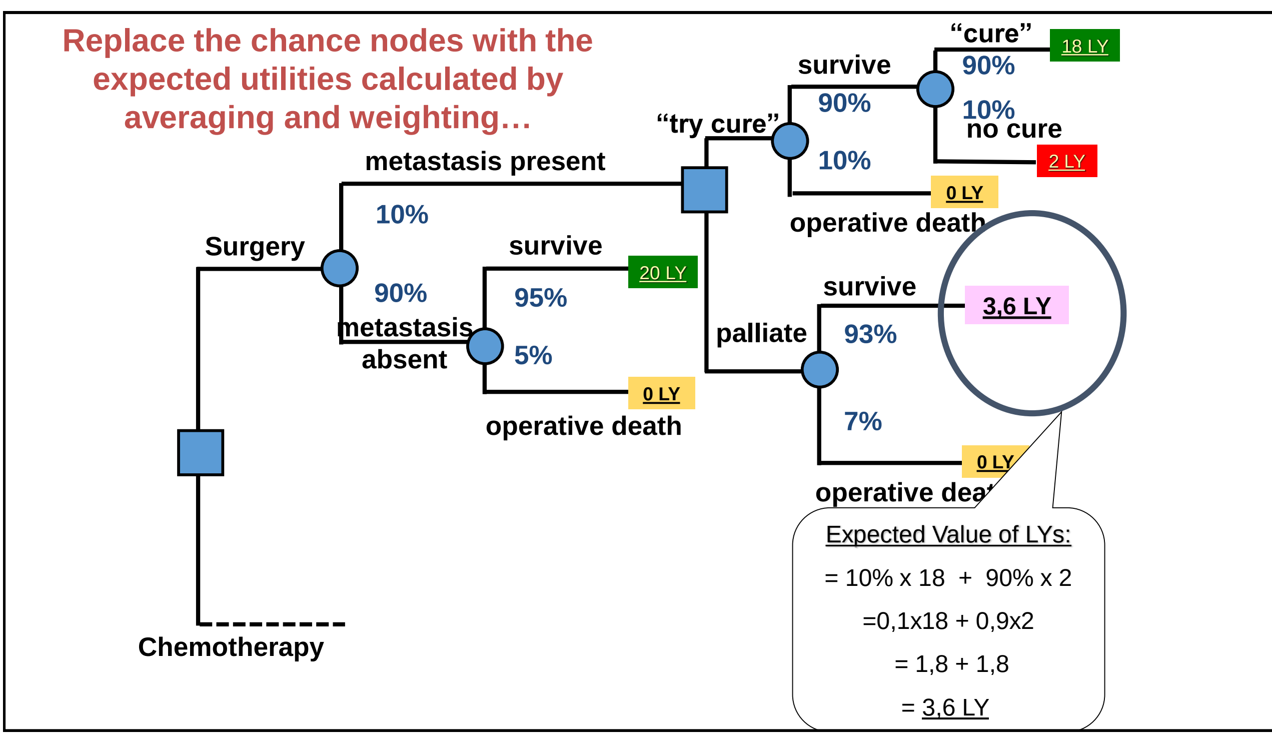
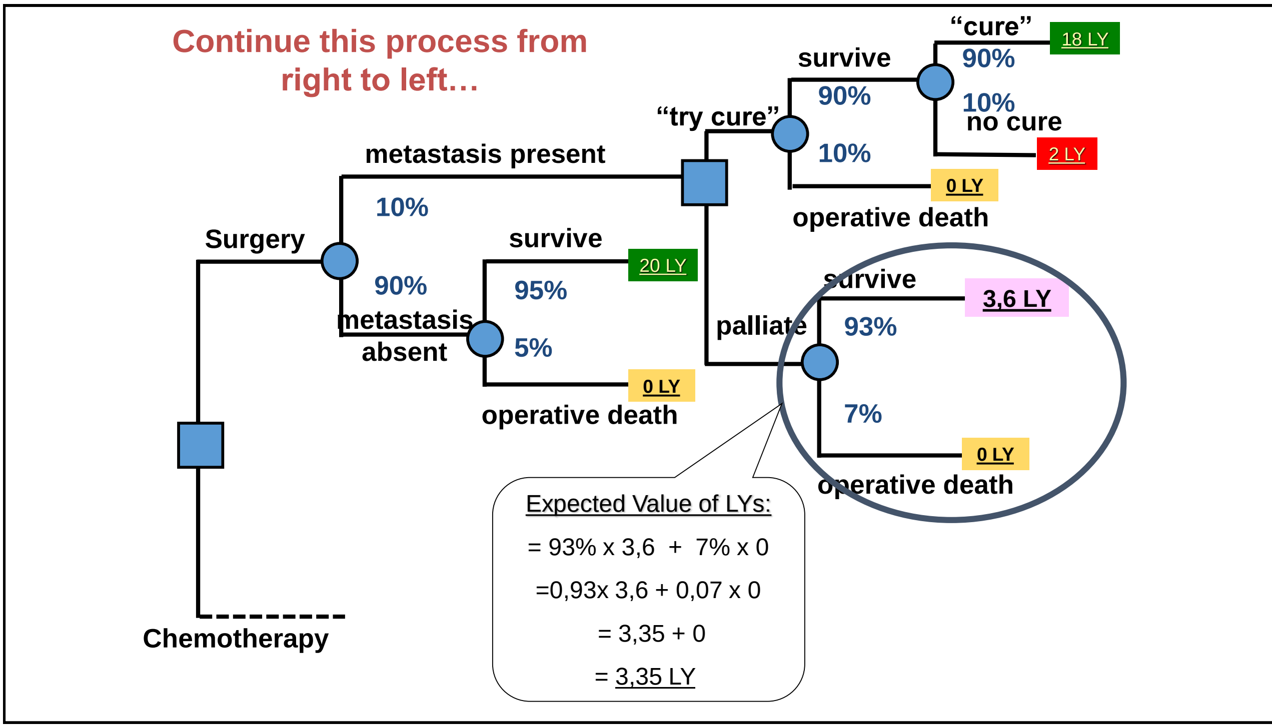
Decision Analysis – Operational Stages

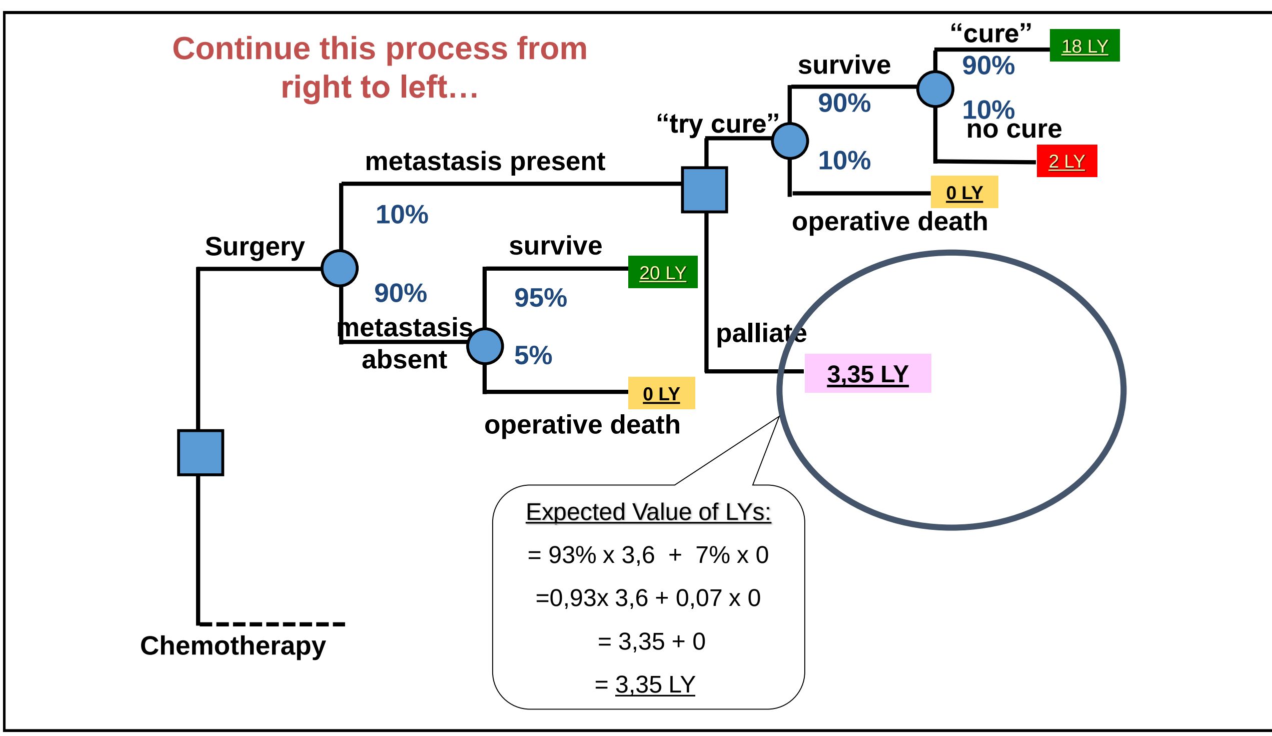
Analysing and solving the decision tree

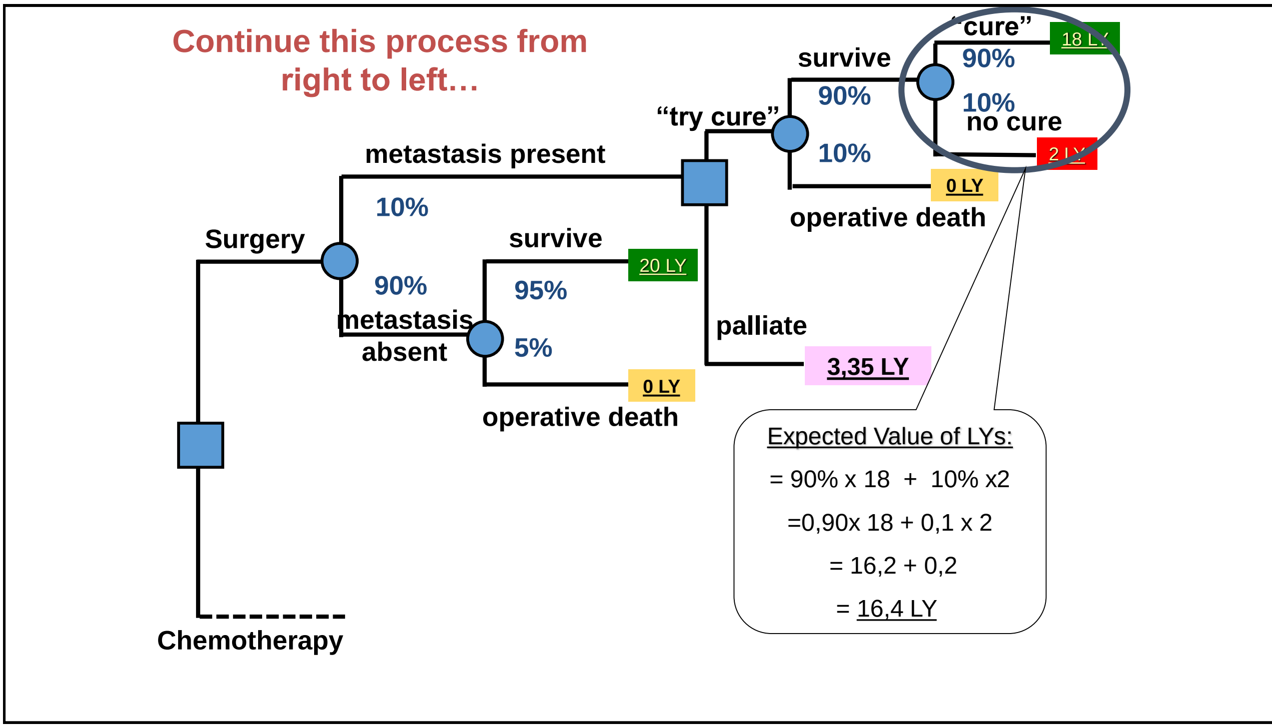
- From the calculation of the probability of each path as the weight of the outcome, payoff or utility of each path we are able to estimate the **expected utility (or disutility) for each alternative** in the decision node
- The **expected utility for each alternative is calculated as the weighted (by the probability of each path) average of the outcomes, payoffs or utilities** of each path (***averaging***)


Calculate the expected utility from right to left averaging with weights given by the probability of each event…
Surgery
Chemotherapy
metastasis present
10%
90%
metastasis absent
survive
95%
20 LY
5%
0 LY
operative death
"try cure"
survive
90%
"cure"
90%
18 LY
10%
no cure
2 LY
10%
0 LY
operative death
palliate
survive
93%
"cure"
10%
18 LY
90%
no cure
2 LY
7%
0 LY
operative death
Expected Value of LYs:
= 10% x 18 + 90% x 2
=0,1x18 + 0,9x2
= 1,8 + 1,8
= 3,6 LY

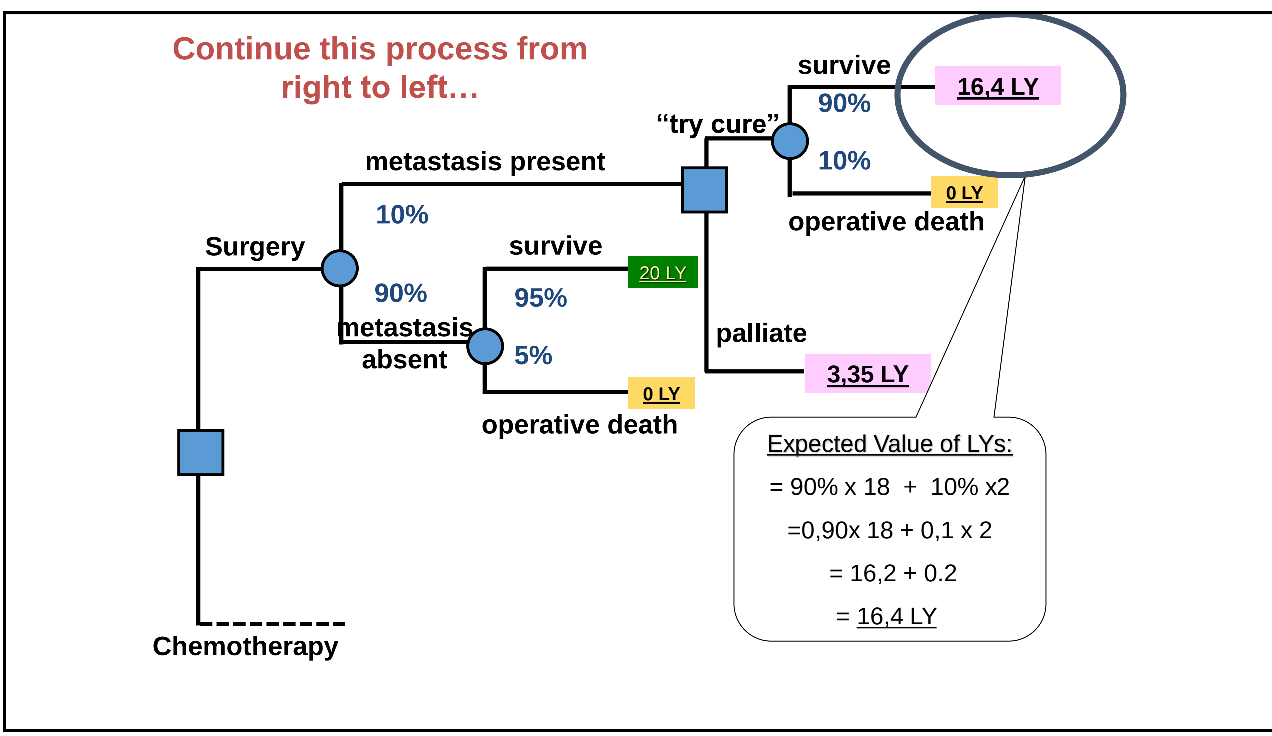

Replace the chance nodes with the expected utilities calculated by averaging and weighting…
Surgery
Chemotherapy
metastasis present
10%
90%
metastasis absent
survive
95%
20 LY
5%
0 LY
operative death
"try cure"
survive
90%
"cure"
90%
18 LY
10%
no cure
2 LY
10%
0 LY
operative death
palliate
survive
93%
3,6 LY
7%
0 LY
operative death
Expected Value of LYs:
= 10% x 18 + 90% x 2
=0,1x18 + 0,9x2
= 1,8 + 1,8
= 3,6 LY


Continue this process from right to left…
"cure"
18 LY
survive
90%
10%
no cure
2 LY
"try cure"
90%
10%
0 LY
operative death
metastasis present
10%
Surgery
survive
20 LY
90%
95%
metastasis absent
5%
0 LY
operative death
survive
3,6 LY
palliate
93%
7%
0 LY
operative death
Chemotherapy
Expected Value of LYs:
= 93% x 3,6 + 7% x 0
=0,93x 3,6 + 0,07 x 0
= 3,35 + 0
= 3,35 LY

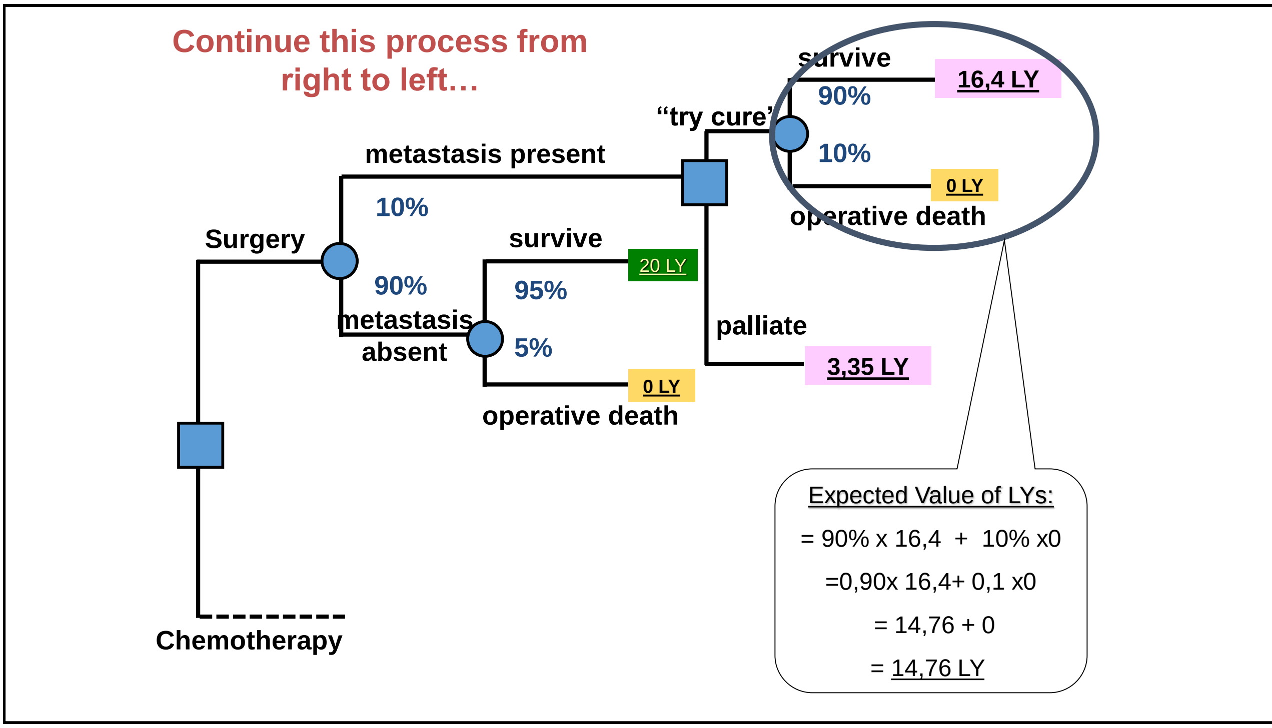

Continue this process from right to left…
"cure"
18 LY
survive
90%
10%
no cure
2 LY
"try cure"
90%
10%
0 LY
operative death
metastasis present
10%
Surgery
survive
20 LY
90%
95%
metastasis absent
5%
0 LY
operative death
palliate
3,35 LY
Chemotherapy
Expected Value of LYs:
= 93% x 3,6 + 7% x 0
=0,93x 3,6 + 0,07 x 0
= 3,35 + 0
= 3,35 LY

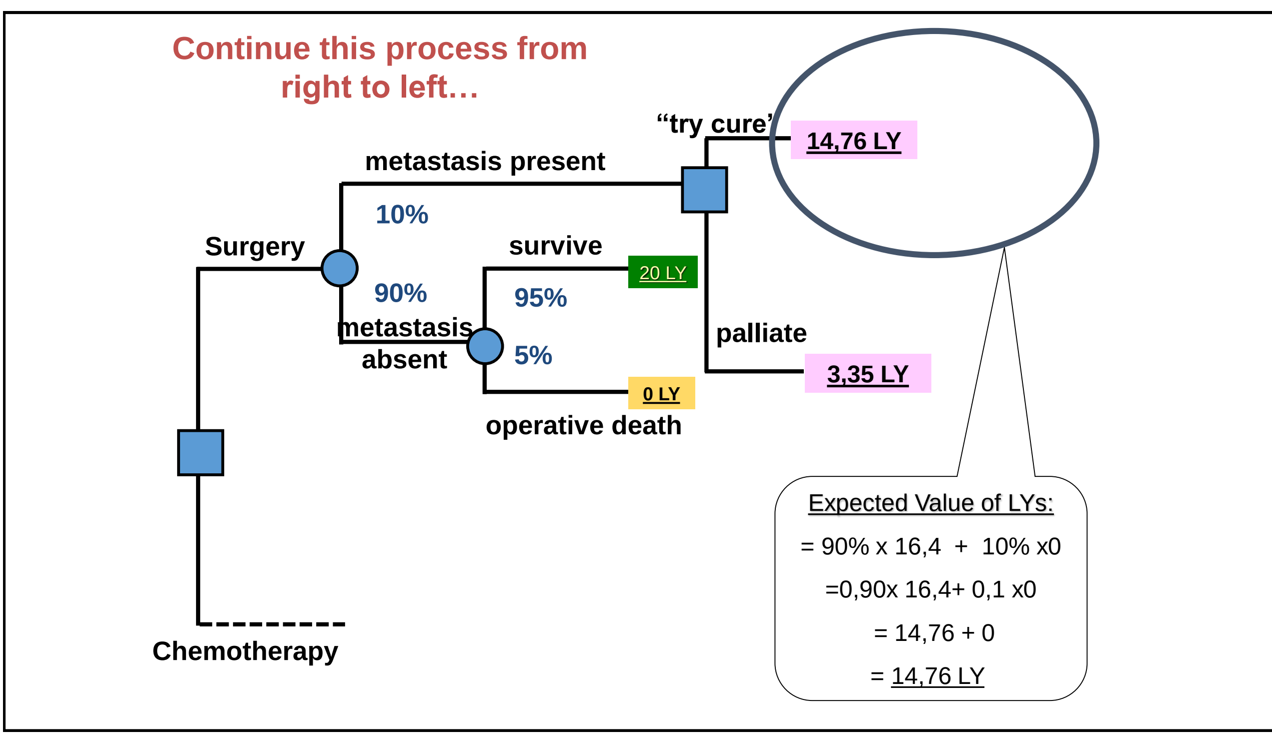


Continue this process from right to left…
"cure"
18 LY
survive
90%
10%
no cure
2 LY
"try cure"
90%
10%
0 LY
operative death
metastasis present
10%
Surgery
survive
20 LY
90%
95%
metastasis absent
5%
palliate
3,35 LY
0 LY
operative death
Expected Value of LYs:
= 90% x 18 + 10% x2
=0,90x 18 + 0,1 x 2
= 16,2 + 0,2
= 16,4 LY
Chemotherapy

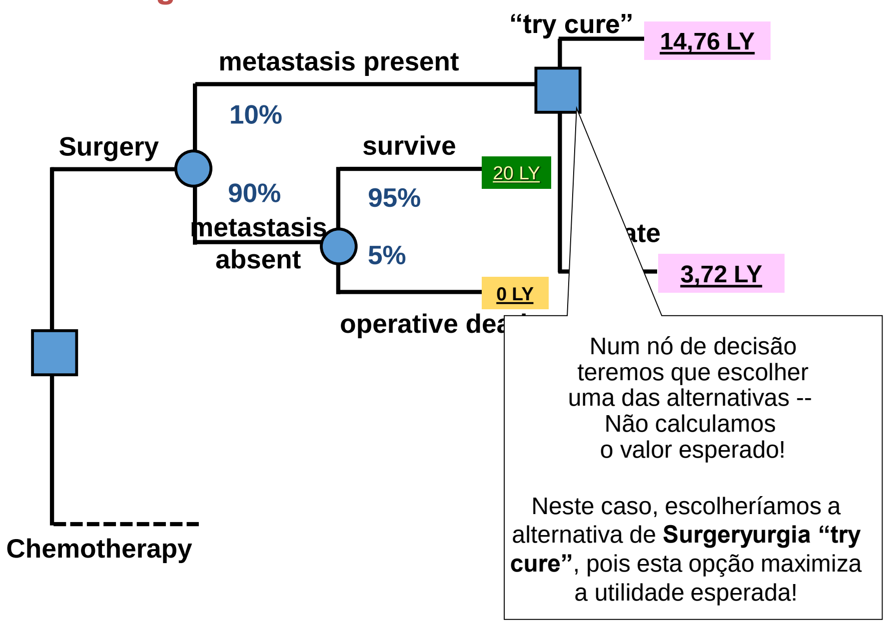


Continue this process from right to left…
survive
16,4 LY
90%
"try cure"
10%
0 LY
operative death
metastasis present
10%
Surgery
survive
20 LY
90%
95%
metastasis absent
5%
palliate
3,35 LY
0 LY
operative death
Expected Value of LYs:
= 90% x 18 + 10% x2
=0,90x 18 + 0,1 x 2
= 16,2 + 0.2
= 16,4 LY
Chemotherapy

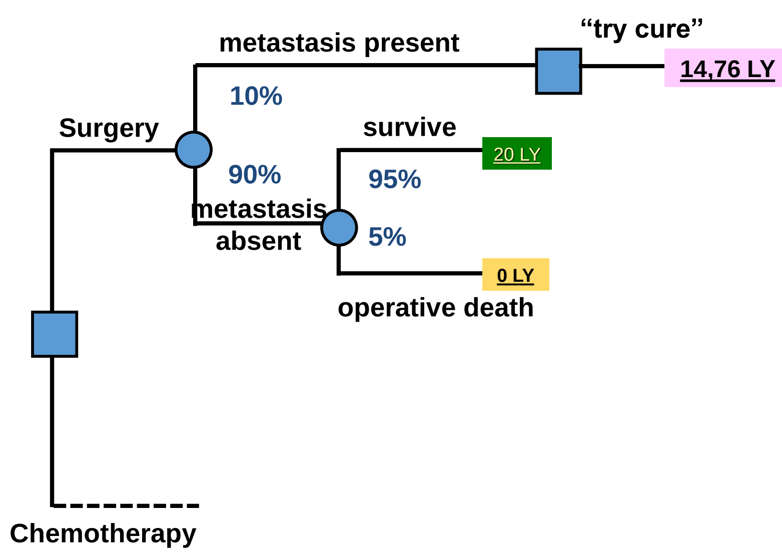

Continue this process from right to left…
survive
16,4 LY
90%
"try cure"
10%
metastasis present
0 LY
10%
operative death
Surgery
survive
20 LY
90%
95%
metastasis absent
palliate
5%
3,35 LY
0 LY
operative death
Expected Value of LYs:
= 90% x 16,4 + 10% x0
=0,90x 16,4+ 0,1 x0
= 14,76 + 0
= 14,76 LY
Chemotherapy


Continue this process from right to left…
"try cure"
14,76 LY
metastasis present
10%
Surgery
survive
20 LY
90%
95%
metastasis absent
palliate
5%
3,35 LY
0 LY
operative death
Expected Value of LYs:
= 90% x 16,4 + 10% x0
=0,90x 16,4+ 0,1 x0
= 14,76 + 0
= 14,76 LY
Chemotherapy

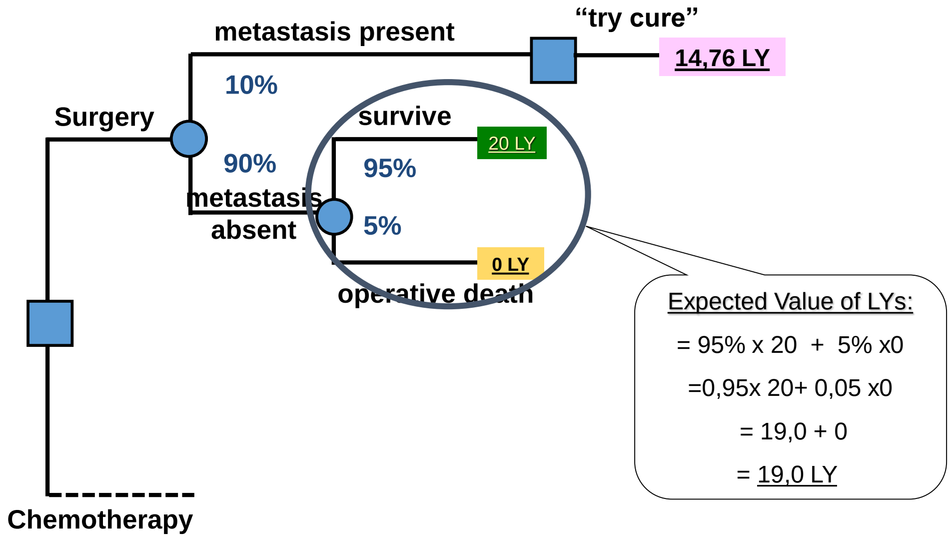
Continue this process from right to left…



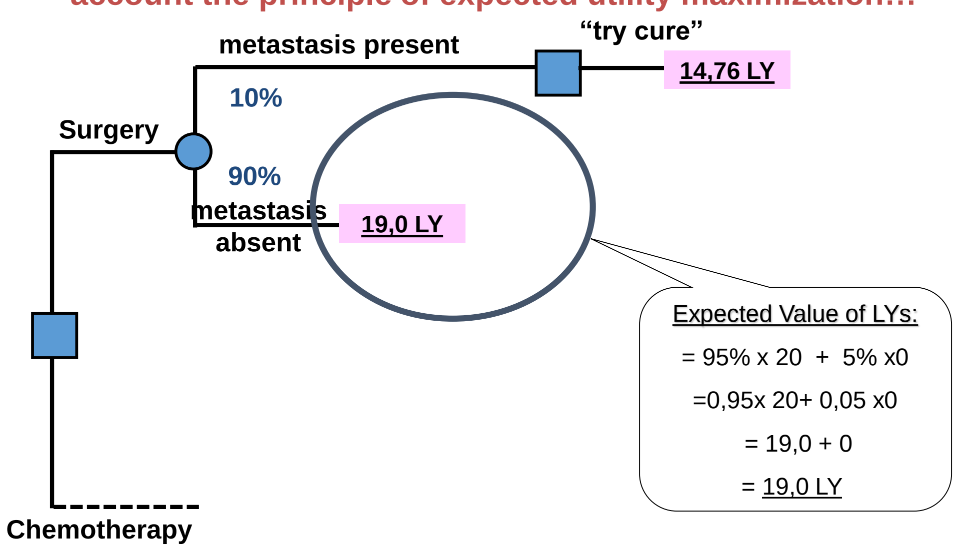
Continue this process from right to left…

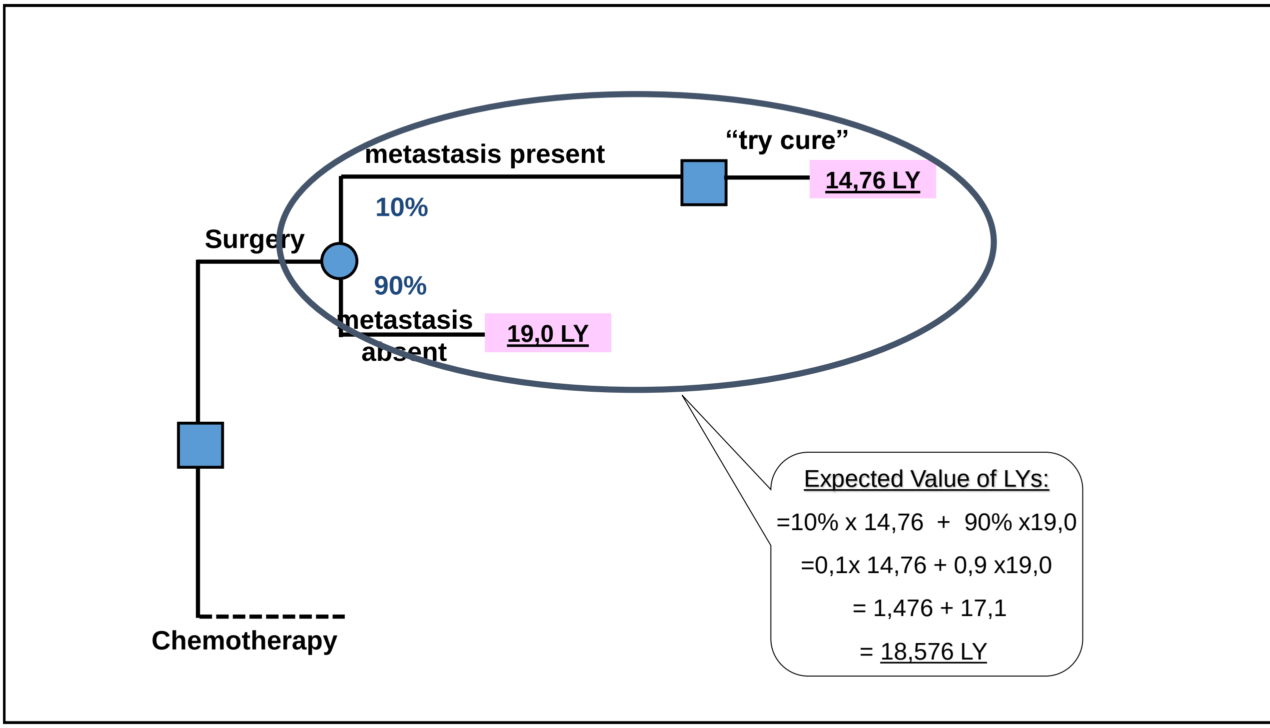


Continue this process from right to left… Calculating the expected value for each probability node and selecting an alternative in the decision nodes, taking into account the principle of expected utility maximization…

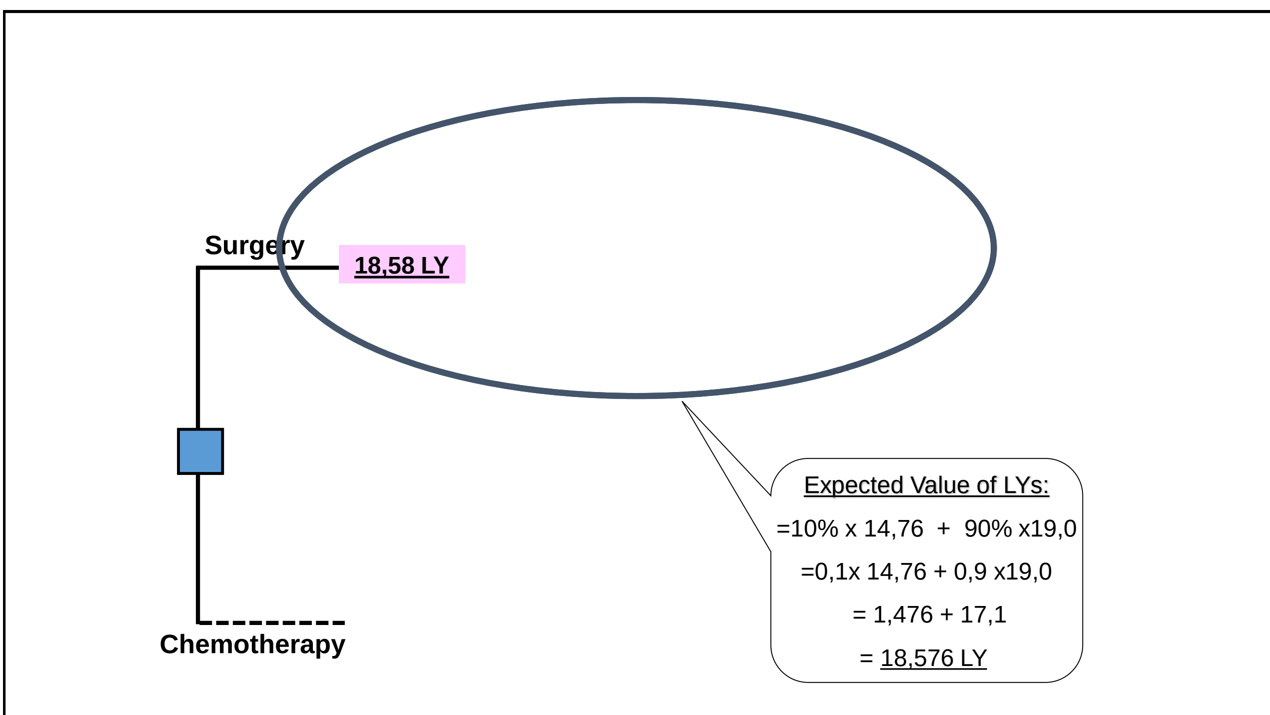


Continue this process from right to left… Calculating the expected value for each probability node and selecting an alternative in the decision nodes, taking into account the principle of expected utility maximization…



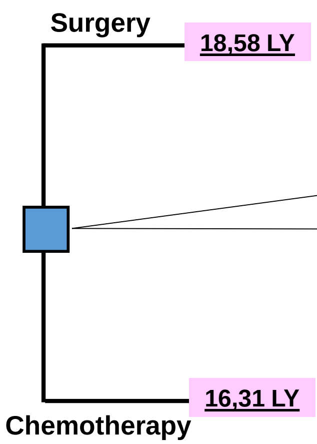


metastasis present
"try cure"
14,76 LY
10%
Surgery
90%
metastasis absent
19,0 LY
Chemotherapy
Expected Value of LYs:
=10% x 14,76 + 90% x19,0
=0,1x 14,76 + 0,9 x19,0
= 1,476 + 17,1
= 18,576 LY



Surgery
18,58 LY
Chemotherapy
Expected Value of LYs:
=10% x 14,76 + 90% x19,0
=0,1x 14,76 + 0,9 x19,0
= 1,476 + 17,1
= 18,576 LY

The outcome for each decision is more apparent now:



Surgery (intending cure) produces an average outcome / expected utility of 18,58 LY

The incremental benefit of **Surgery** versus **Medical Management with Chemotherapy** is:

18,58 – 16,31 = ***2,27 LY***

Chemotherapy produces an average outcome / expected utility of 16,31 LY

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Decision Analysis – Operational Stages

- **Exploring and assessing the uncertainty and model assumptions**
  - The **exploration of structural assumptions** in the decision tree (e.g.: tree structure, outcomes, etc.) and the **exploration of uncertainty in the estimation of the model's parameters** is a crucial step in decision analysis and allows to **test the robustness of the model and the robustness of the results and conclusions**

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Decision Analysis – Operational Stages

- **Exploring and assessing the uncertainty and model assumptions**
  - The most frequently used method in this context to assess and explore the uncertainty in the model is the **sensitivity analysis**
  - **Sensitivity analysis** is a method where the robustness of the estimates of parameters is assessed using simulation and modelling techniques

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Uncertainty and Variability in Decision Analysis

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Uncertainty and Variability in Decision Analysis

- There are **five essential sources of variability and potential uncertainty that should be taken into account, assessed and explored** no in the context of any decision analytic model:
  1. **Variability and uncertainty associated with the model structure and assumptions**
  2. **Variability associated with the uncertainty affecting the model parameters**
  3. **Variability associated with the stochastic nature of events and outcomes/utilities in the target population**
  4. **Variability associated with the heterogeneity in the target population**
  5. **Variability associated with the existence of subgroups in the target population**

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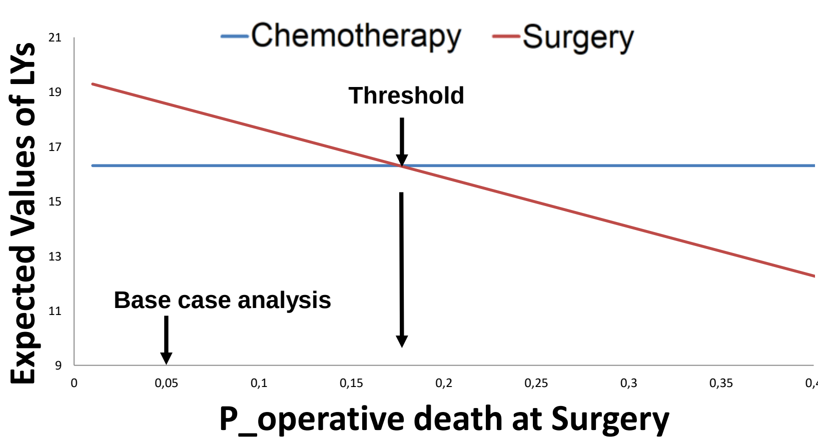
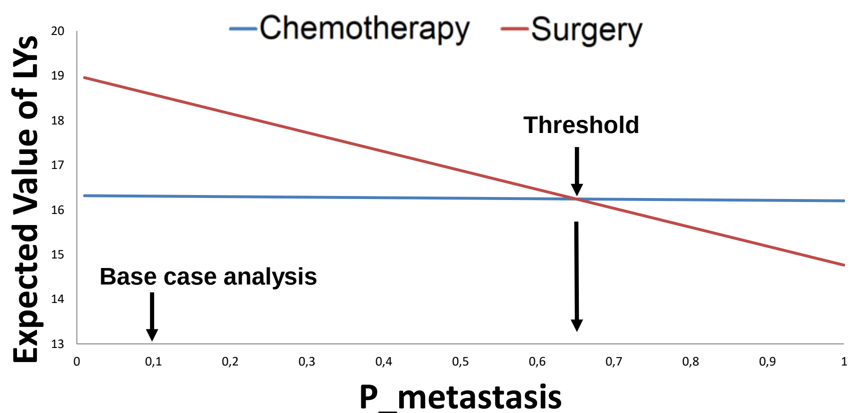
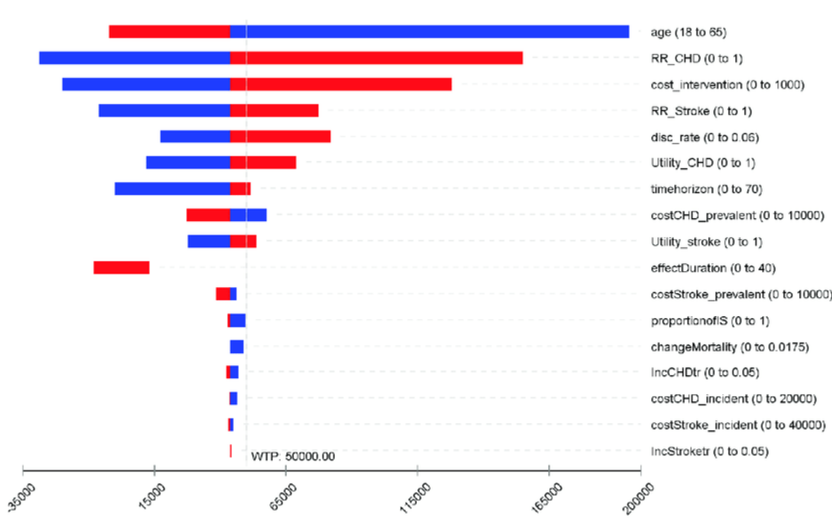
Deterministic Sensitivity Analysis: Probability of operative death at Surgery



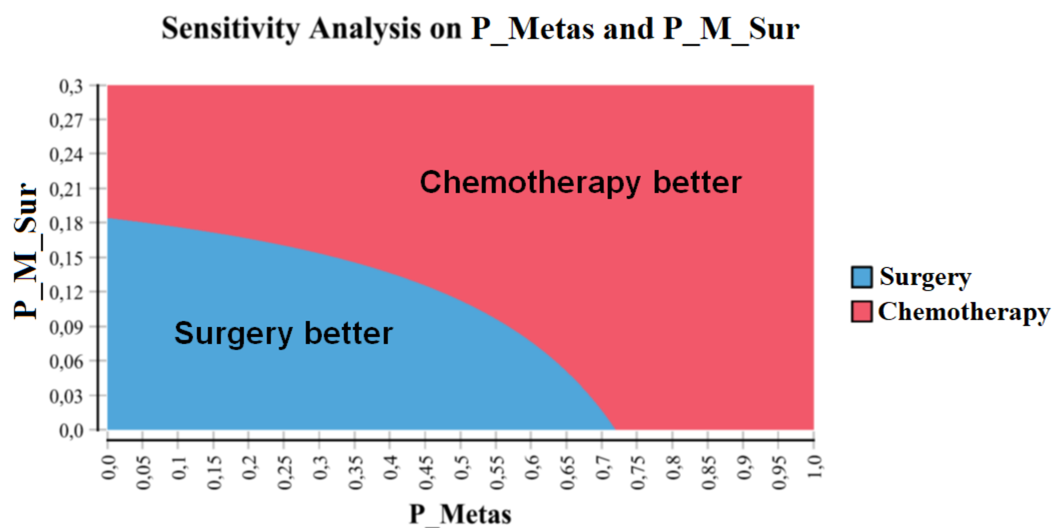
Deterministic Sensitivity Analysis: Probability of metastasis



Deterministic Sensitivity Analysis: Tornado diagrams



Bivariate Deterministic Sensitivity Analysis: p(metastasis) vs. p(operative death / mortality at surgery)



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Practical Example (II): Rao et al. 2007

- Rao C, Aziz O, Panesar S, et al. **Cost effectiveness analysis of minimally invasive internal thoracic artery bypass versus percutaneous revascularisation for isolated lesions of the left anterior descending artery**. BMJ. 2007;334:621.
- Aim: Compare
  - ***Coronary artery bypass grafting* – CABG**

    vs.
  - ***Percutaneous transluminal coronary angioplasty with stenting* – PTCA**
- Clinical Context:

  "We have **fewer symptoms recurrences with CABG**, but **less procedure related mortality with PTCA**. In this context, **which is the best alternative?** In this example we will be using a **simplified version of the original decision analytic model used in the study above referenced.**

Athanasiou T, Darzi A (Editors). Evidence Synthesis in Healthcare: A Practical Handbook for Clinicians. London: Springer-Verlag, 2011.

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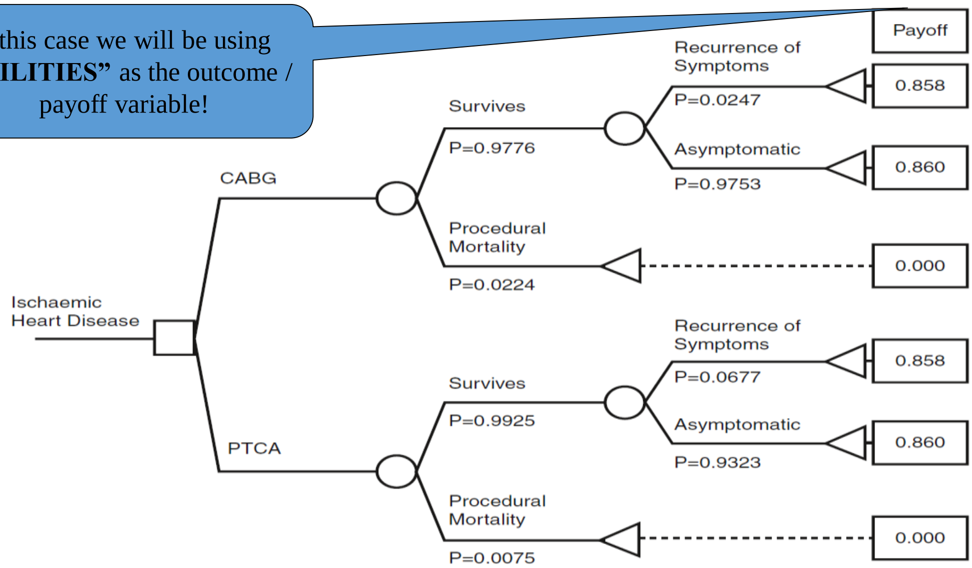
Practical Example (II): Rao et al. 2007

In this case we will be using **"UTILITIES"** as the outcome / payoff variable!



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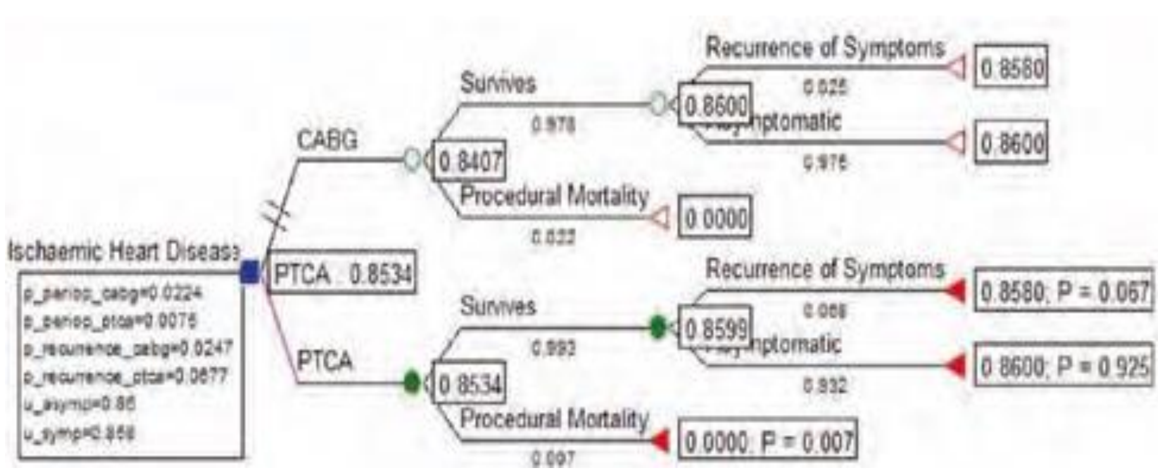
Practical Example (II): Rao et al. 2007

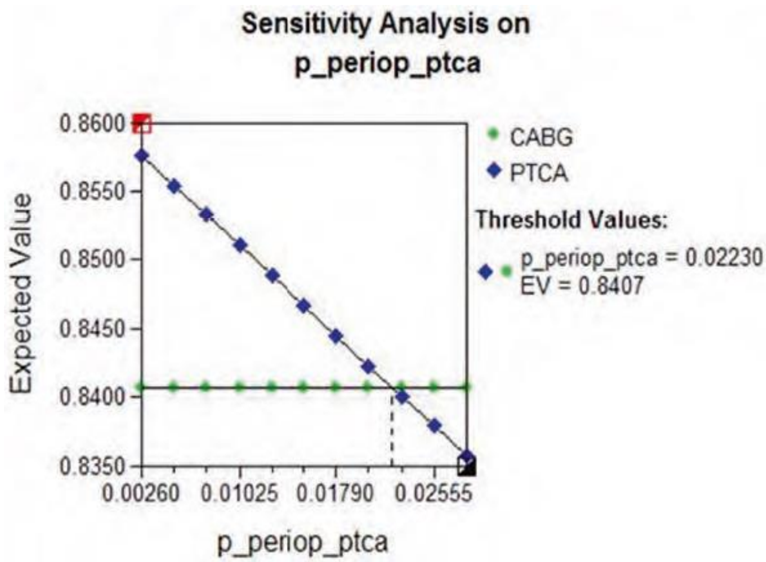


Athanasiou T, Darzi A (Editors). Evidence Synthesis in Healthcare: A Practical Handbook for Clinicians. London: Springer-Verlag, 2011.

Practical Example (II): Rao et al. 2007

Univariate Deterministic Sensitivity Analysis

NOTE:
In the **base case analysis PTCA had higher expected utility**, however **the increase of the probability of procedure related operative death may change the outcome and its expected value**. Specifically, **when the operative death with PTCA is higher than 2.23% (see graph in the right) the alternative of CABG has higher expected utility and becomes the better alternative**.

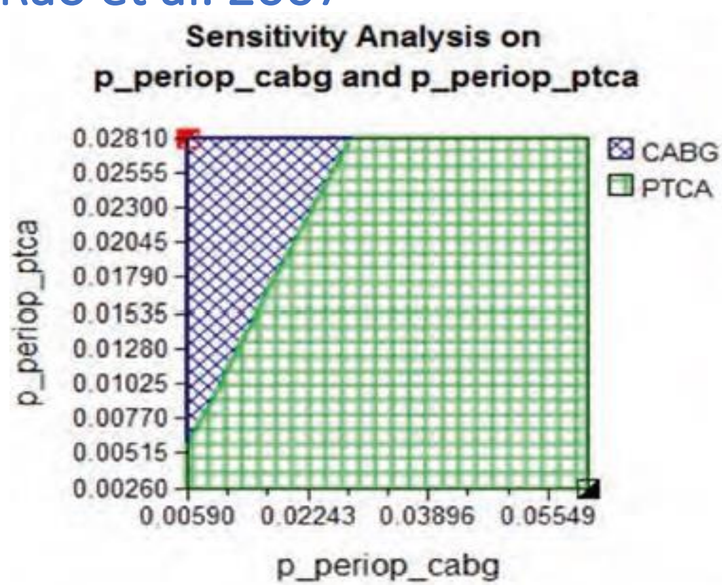


Athanasiou T, Darzi A (Editors). Evidence Synthesis in Healthcare: A Practical Handbook for Clinicians. London: Springer-Verlag, 2011.

Practical Example (II): Rao et al. 2007

Bivariate Deterministic Sensitivity Analysis

NOTE:
For each **pair of values of procedure related perioperative mortality for CABG and PTCA** we have in the graph on the right the indication of **which of the alternatives has higher expected value (expected utility)** and should thus be selected as the preferred alternative (in the **blue area the preferred alternative is CABG** and in **the green area the preferred alternative is PTCA**).



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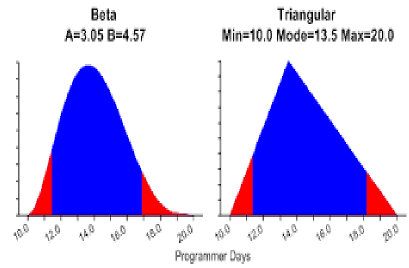
Exemplo: Rao et al. 2007

Probabilistic Sensitivity Analysis via Monte Carlo

Table 10.1 Model parameters used in Example 1

Parameter	Value	Range	Distribution
Utility parameters			
Asymptomatic utility	0.860	0.774–0.946	Triangular
Symptomatic utility	0.858	0.772–0.944	Triangular
Path probabilities			
PTCA symptom recurrence rate	0.0677	0.0284–0.1535	Triangular
CABG symptom recurrence rate	0.0247	0.0098–0.0573	Triangular
PTCA procedural mortality	0.0075	0.0026–0.0281	Triangular
CABG procedural mortality	0.0224	0.0059–0.0610	Triangular



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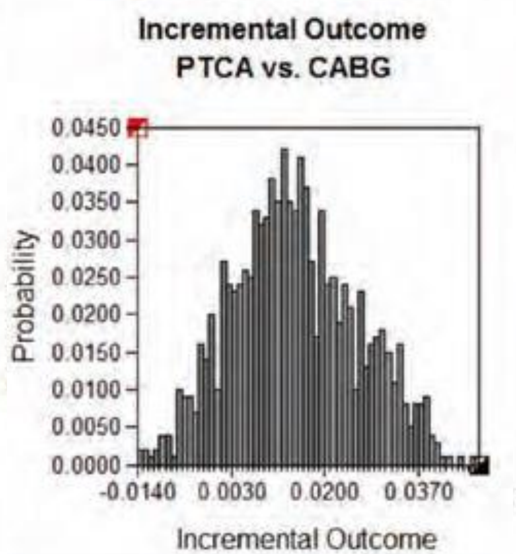
Practical Example (II): Rao et al. 2007

Probabilistic Sensitivity Analysis

TreeAge Pro Monte Carlo Simulation
Statistics for 1000 outputs

Statistic	CABG	PTCA	Dist(1)	Dist(2)	Dist(3)	Dist(4)	Dist
Mean	0.8369	0.8513	0.029724998	0.012667775	0.030762718	0.083624277	0.8
Std Dev	0.0347	0.0330	0.011415299	0.005600076	0.009680487	0.027147918	0.0
Minimum	0.7453	0.7710	0.007221237	0.002715927	0.010919591	0.028959601	0.7
2.5%	0.7710	0.7877	0.011348178	0.004200189	0.013871343	0.040843253	0.7
10%	0.7907	0.8058	0.015717303	0.005933483	0.018969903	0.049934914	0.8
Median	0.8354	0.8510	0.028348466	0.011729053	0.030097261	0.079477609	0.8
90%	0.8852	0.8955	0.045869853	0.021016324	0.044262835	0.122932096	0.9
97.5%	0.9018	0.9131	0.053460417	0.024394502	0.051055497	0.138594093	0.9
Maximum	0.9263	0.9316	0.060330843	0.027193426	0.05663658	0.152403305	0.9

Notes:
Dist(1) - d_periop_cabg
Dist(2) - d_periop_ptca
Dist(3) - d_recurrence_cabg
Dist(4) - d_recurrence_ptca
Dist(5) - d_asymp
Dist(6) - d_symp



Athanasiou T, Darzi A (Editors). Evidence Synthesis in Healthcare: A Practical Handbook for Clinicians. London: Springer-Verlag, 2011.

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Monte Carlo Methods – Simulation

- **Probabilistic Sensitivity Analysis via Monte Carlo**
  - There is **uncertainty associated with the estimation of model parameters**
  - This method allow us to **integrate in the model the uncertainty associated with the estimation of model parameters** using for **each parameter a probability distribution** (with a **set of possible values of the parameter associated with different probabilities**) **instead of a single point estimate**. The probability distribution is **selected taking into account the best available knowledge / scientific evidence regarding the parameter, its behaviour and its most probable values**.

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Monte Carlo Methods – Simulation

- **Probabilistic Sensitivity Analysis via Monte Carlo**
  - To perform Probabilistic Sensitivity Analysis (PSA) we should use the **Monte Carlo Methods (MCM)**
  - The MCM are a **broad class of computational algorithms that rely on repeated random sampling to obtain numerical results** for operations dependent upon the model parameters and **allowing us to stochastically estimate the expected values of each alternative.** These methods rely on successive simulations of random processes similar to what we would see gambles in a casino (the reason behind the name Monte Carlo)

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Micro-simulation

Sensitivity Analysis using Microsimulation

- The **International Association of Microsimulation** defines microsimulation as a **modelling technique that operates at the level of individual units such as persons, households, vehicles or firms**
- Within these models each **unit** is represented by a record containing a **unique identifier** and a set of **associated attributes** (e.g. age, sex, marital and employment status). A **set of rules (transition probabilities)** are then applied to these units leading to **simulated changes in state and behaviour**. These rules may be **deterministic or stochastic** (e.g. chance of dying within a given time period). In either case the result is an estimate of the outcomes of applying these rules, possibly over many time steps, including both **total overall aggregate change and, crucially, the distributional nature of any change**.

Paul Williamson, 2007. The role of the International Journal of Microsimulation. International Journal of Microsimulation, vol. 1(1), pages 1-2.

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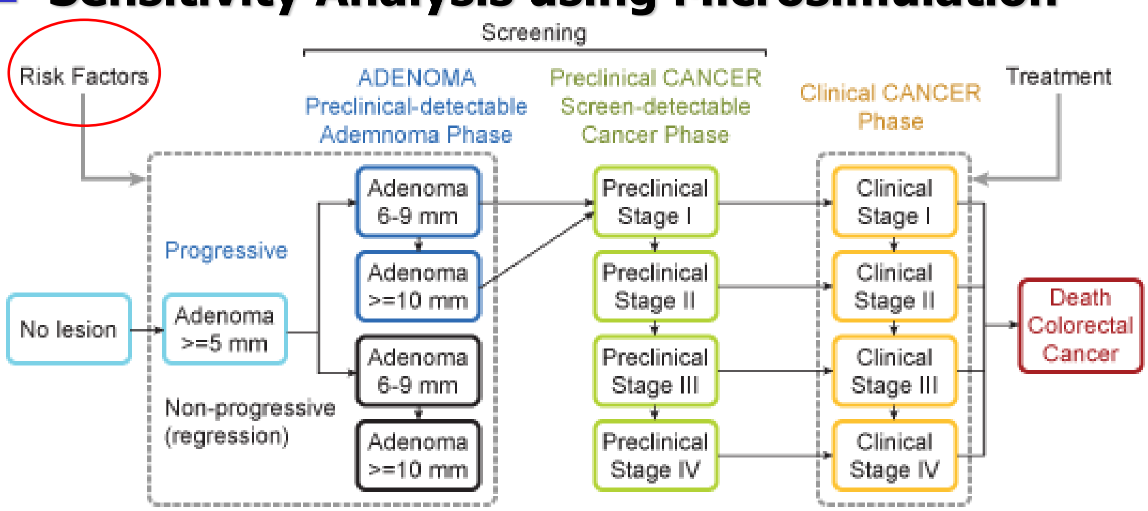
Micro-simulation

Sensitivity Analysis using Microsimulation



Some Other Methods and Models Used in Decision Analysis

Influence Diagrams

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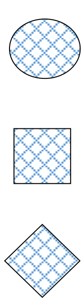
Node Conventions

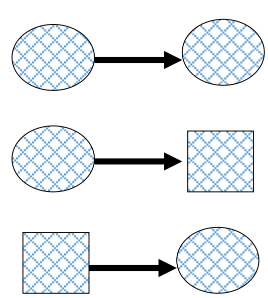


Chance node

Decision node

Utility node

Link Semantics



Dependence link

Information link

Influence link

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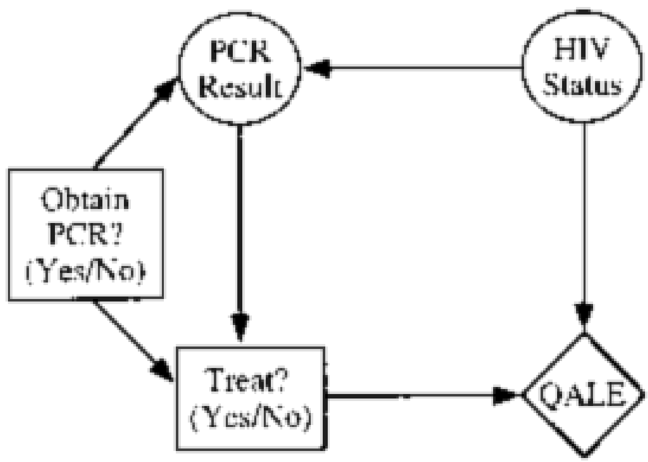
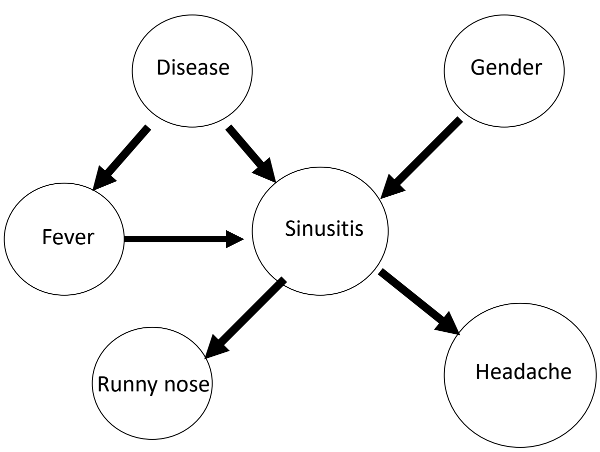
Influence Diagrams: An HIV Example



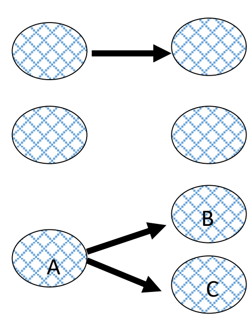
Belief Networks

(Bayesian/Causal Probabilistic/Probabilistic Networks, etc)

Influence diagrams (DAGs) without decision and utility nodes



Link Semantics



Dependence

Independence

Conditional independence of B and C, given A

Markov Models

- In a **Markov Model** we represent a **theoretical imaginary subject** (e.g. a patient) that may exist in several different and mutually exclusive **health "states"**. At the end of each pre-defined **time period** or **"cycle"** (e.g. a year, a month or a week) the subject will be allowed to a change or not change in health state with given probabilities for each alternative.
- The probabilities of changing health state at the end of each cycle are called **"transition probabilities (TP)"**.
- There are two main types of Markov Models: **Markov chains** (discrete time, stationary when TP are constant in all cycles) and **Markov processes** (continuous time).
- Markov Models are particularly useful to **model clinical scenarios represented by recursive decision trees**, where recursive events are modelled.
- A **Markov process** is a random process in which the future is independent of the past, given the present. The Markov property refers to the **memoryless property** of a stochastic process. A stochastic process has the Markov property if the **conditional probability distribution of future states of the process depends only upon the present state, not on the sequence of events that preceded it**

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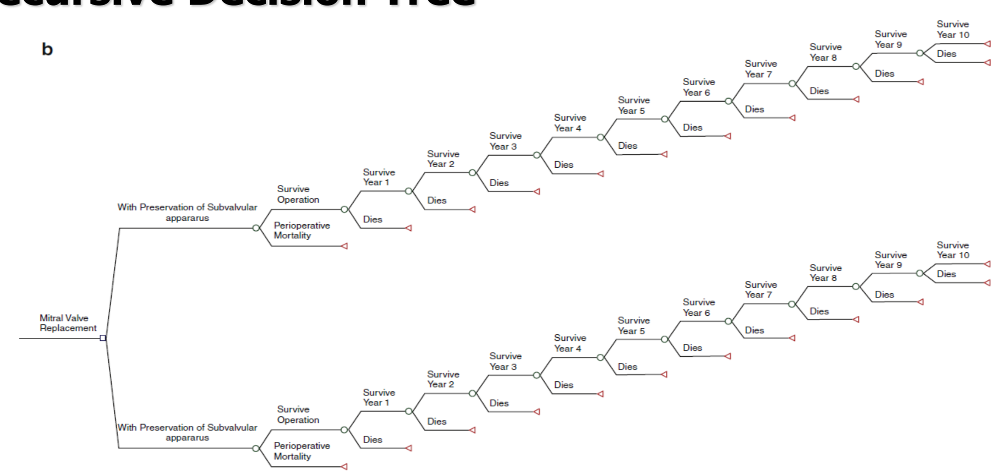
Markov Models

Recursive Decision Tree



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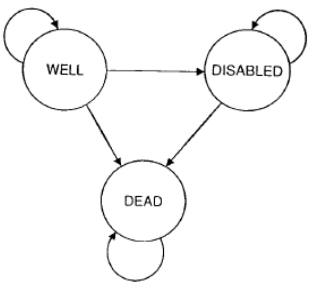
Markov Models

Markov states diagram



Transition probabilities matrix

		To		
		WELL	DISABLED	DEAD
From	WELL	0.6	0.2	0.2
	DISABLED	0	0.6	0.4
	DEAD	0	0	1

A Markov process is a stochastic process where the **probability of the system (each subject) being in the state I in the time period (n+1) depends only on the present state of the system at period n**. Thus, Markov process are so called memoryless. **The main elements in a Markov process** are: **(1) the probabilities $p_i[n]$ of occurring state I at the period n or n^{th} cycle; (2) the transition probabilities p_{ij}, representing the probability of being in the state "i" in the $(n+1)^{th}$ cycle given that the subject is presently in the state "j" in the n^{th} cycle**. These probabilities are normally represented in a matrix – the **transition matrix, stochastic matrix or Markov matrix**.

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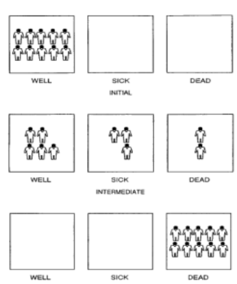
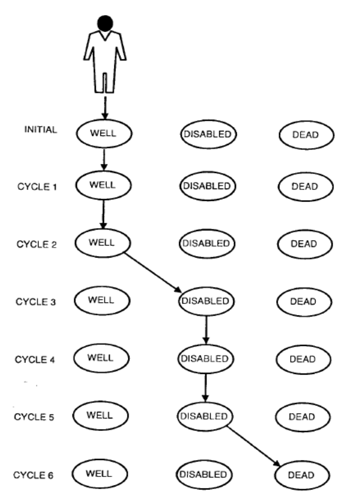
Markov Models

Markov Cohorts Simulation



Cycle	WELL	DISABLED	DEAD	Cycle Sum	Cumulative Utility
Start	10,000	0	0	—	—
1	6,000	2,000	2,000	7,400	7,400
2	3,600	2,400	4,000	5,280	12,680
•	•	•	•	•	•
•	•	•	•	•	•
23	0	1	9,999	7	23,752
24	0	0	10,000	<1	23,752
Total	15,000	12,500		23,752	23,752

Markov Transitions Simulations via Monte Carlo



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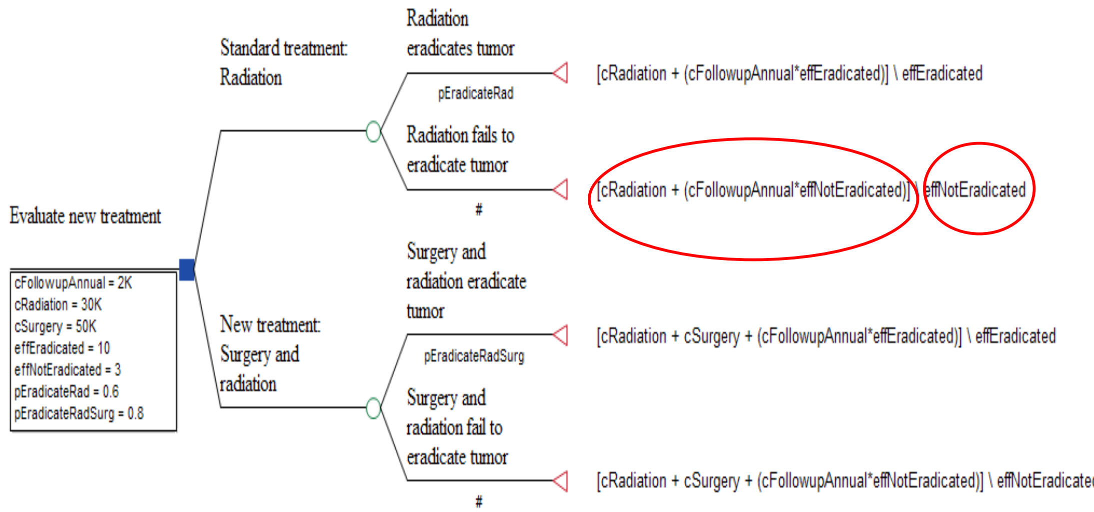
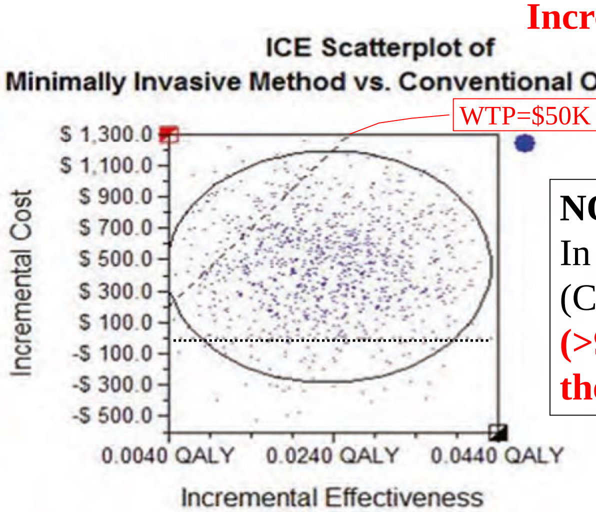
Economic Evaluation with Decision Analysis



Economic Evaluation with Decision Analysis

Incremental Cost-Effectiveness plane!



NOTE:
In this incremental cost-effectiveness (CE) plane **most of the simulations (>90%) result in an ICER below the WTP threshold of $ 50.000.**

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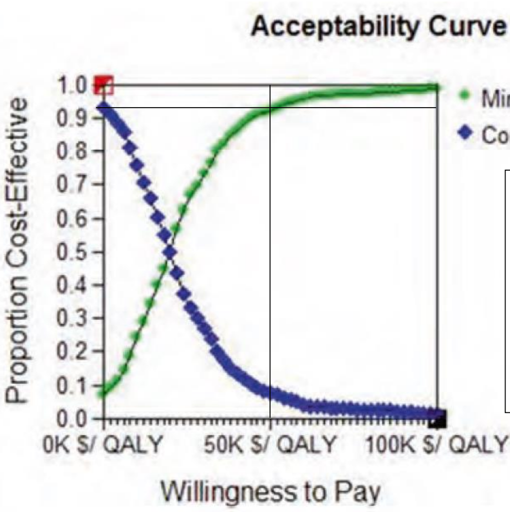
Economic Evaluation with Decision Analysis

Cost-Effectiveness Acceptability Curve!



NOTE:
In this cost-effectiveness (CE) acceptability curve it is possible to see that **for a CE threshold of $ 50.000 the probability of the minimally invasive intervention being cost-effective when compared with the conventional method is 93%!!!**

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Economic Evaluation with Decision Analysis: Implementation in R

```
library(rjags)

cat("model{
    cost_bypass ~ dgamma(38.83,0.006231)
    cost_endoscop ~ dgamma(55.13,0.0743)
    cost_hosp_day ~ dgamma(37.68,0.06138)
    cost_min_op ~ dgamma(18.97,0.871)
    time_minv_incr ~ dgamma(9.315,0.6105)
    time_conv_incr ~ dgamma(4.326,4.16)
    util_bypass ~ dbeta(40.5576,6.6024)
    util_minv_incr ~ dbeta(21,884.46)

    cost_minv <- cost_bypass+cost_endoscop+(cost_min_op*time_minv_incr)-(cost_hosp_day*time_conv_incr)
    diff_costs <- cost_minv-cost_bypass
    util_minv <- util_bypass+util_minv_incr
    diff_util <- util_minv-util_bypass

    icer <- diff_costs/diff_util
    n_simul <- step(50000-icer)
    }", file="teste.txt")

jags.m <- jags.model(file="teste.txt",n.chains = 2,n.adapt=500) #Set up the JAGS model

params <- c("icer","diff_costs","diff_util","n_simul") #Specify the parameters of interest

samps <- coda.samples( jags.m, params, n.iter=50000) #Run JAGS model and save the samples
inp <- window(samps, start=15001)
inp_list <- do.call(rbind.data.frame, inp)
summary(window(inp))
quantile(inp_list[,4],probs=seq(from=0,to=1,by=0.01))
```

```
1. Empirical mean and standard deviation for each variable,
   plus standard error of the mean:

               Mean        SD  Naive SE Time-series SE
diff_costs 4.365e+02 3.686e+02 1.393e+00      1.393e+00
diff_util  2.319e-02 5.016e-03 1.896e-05      1.896e-05
icer       1.975e+04 1.770e+04 6.691e+01      6.692e+01
n_simul    9.646e-01 1.848e-01 6.986e-04      6.986e-04

2. Quantiles for each variable:

                2.5%       25%       50%       75%     97.5%
diff_costs -3.998e+02 2.246e+02 4.780e+02 6.902e+02 1.049e+03
diff_util   1.441e-02 1.967e-02 2.283e-02 2.632e-02 3.406e-02
icer       -1.803e+04 9.620e+03 2.050e+04 3.074e+04 5.340e+04
n_simul     0.000e+00 1.000e+00 1.000e+00 1.000e+00 1.000e+00
```

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Recommended readings

- **Highly recommended (Moodle)**
  - Chapters 5 and 6 of the book "Athanasiou T, Darzi A (Editors). ***Evidence Synthesis in Healthcare: A Practical Handbook for Clinicians.*** London: Springer-Verlag, 2011."
- **Additional papers (Moodle)**
  - Principles of Medical Decision Making
  - What is a clinical decision analysis study?

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