EHESP

Master of Public Health - Semester 3

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DECISION ANALYSIS IN PUBLIC HEALTH

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Decision analytic modelling(1): Decision Tree Cost Effectiveness Model

Tuesday 6 December

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Economic evaluation in health care and decision analysis

- **Decision analysis** is an approach used to construct and structure decisions
- Quantitative support for decision-makers in wide range of disciplines

Systematic quantitative approach to decision-making under uncertainty

At least 2 options and their consequences are compared and evaluated in terms of their expected costs and expected outcomes

Decision analysis model for economic evaluation in HC

The aim is to provide decision makers with a guide to health-care resource-allocation questions

Examples: “Should we increase the age range for the national breast screening programme?”, “What is the most cost-effective drug for a particular disease? ”

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Economic evaluation in health care and decision analysis

Randomized clinical trials (RCT) are increasingly used as a framework for the purpose of conducting an economic evaluation.

+ Provide an opportunity to prospectively collect and analyse patient-specific resource use and outcome data
+ Provide an unbiased assessment of the effects of an intervention on the outcomes

BUT :

1. RCTs might not compare all the relevant alternatives;
2. Information from RCTs and others studies may have to be combined;
3. RCTs might not encompass the appropriate time horizon;
4. RCTs might not provide information on final endpoints;
5. RCTs might not provide evidence specific to a particular setting or group of patients.

Uses of decision modelling

- *“ Models and trials can best be seen as complements rather than substitutes in research design: trails and others studies provide data and estimates of particular parameters, while decision models provide an analytical framework within which the evidence can be synthesised to address the decision problem “* (Sculpher et al. 2006)

- The use of decision modelling for the purpose of economic evaluation can:
  1. Structure the economic question;
  2. Provide pre-trial modelling and generate study hypotheses;
  3. Extrapolate beyond observed data;
  4. Link intermediate and final endpoints;
  5. Generalize results to other settings or patient groups;
  6. Synthetize evidence and permit head-to-head comparisons where RCTs do not exist by using indirect and mixed-treatment comparisons (MTC);
  7. Indicate the need for and value of further research;

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When Decision Modelling is Appropriate to Use (NICE 2013)

- All the relevant evidence is not contained in a single trial
- Patients participating in trials do not match the typical patients likely to use the technology
- Intermediate outcome measures are used in trials rather than effect on health-related quality of life and survival
- Relevant comparators have not been used, or trials do not include evidence on relevant subgroups
- Clinical trial design includes crossover (treatment switching) that would not occur in clinical practice
- Costs and benefits of the technologies extend beyond the trial follow-up period

Stages in the development of a decision analytic model

1. Defining the question;
2. Decide on the type of decision model most appropriate for the use in the economic evaluation;
3. Identifying the evidence and populating the model
4. Synthesizing evidence
5. Analysing the model
7. Model evaluation
   - Face of descriptive validity
   - Internal validation and calibration
   - External validation: between-model validation and predictive validity
8. Handling uncertainty

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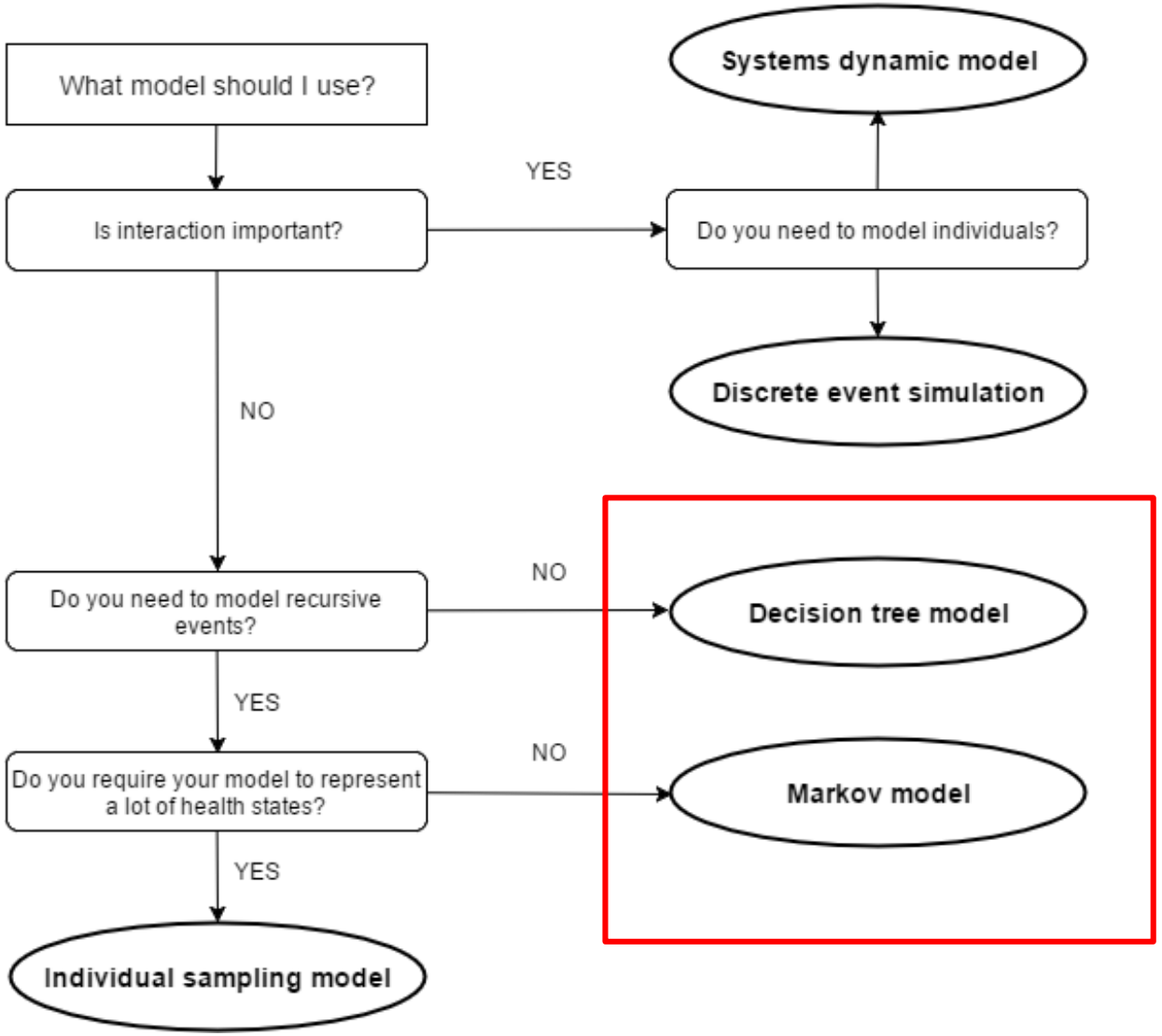
How to decide on the approprate model?



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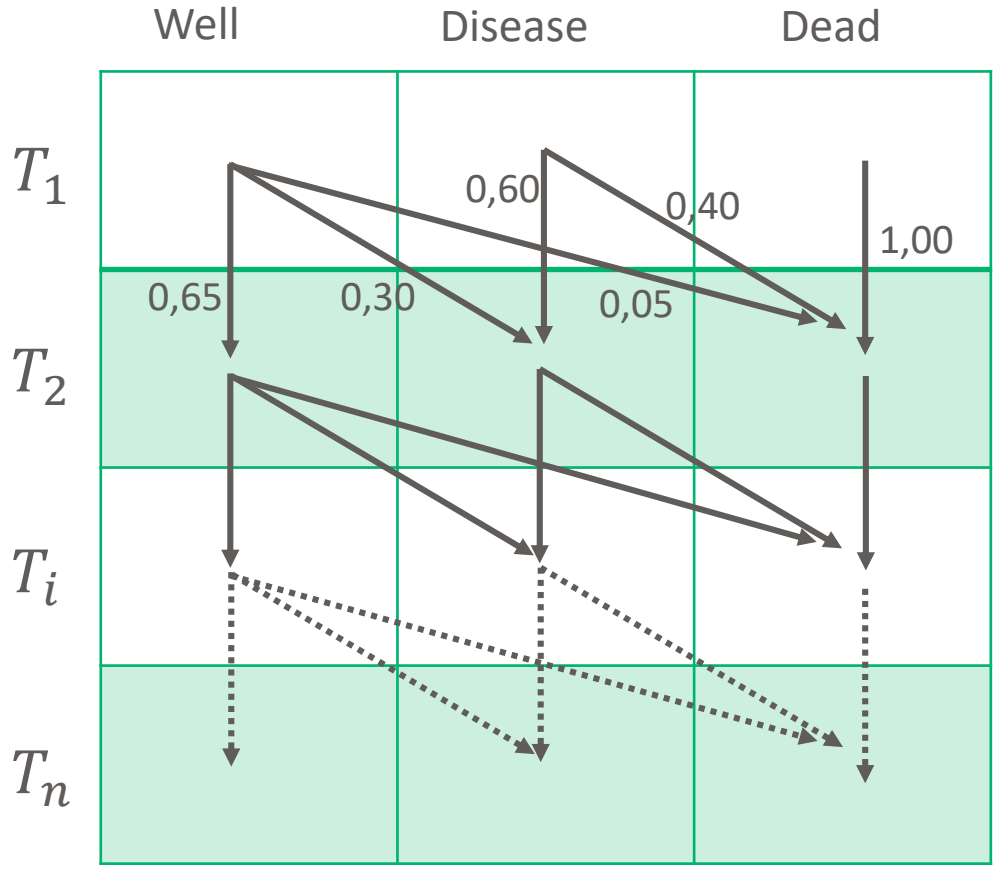
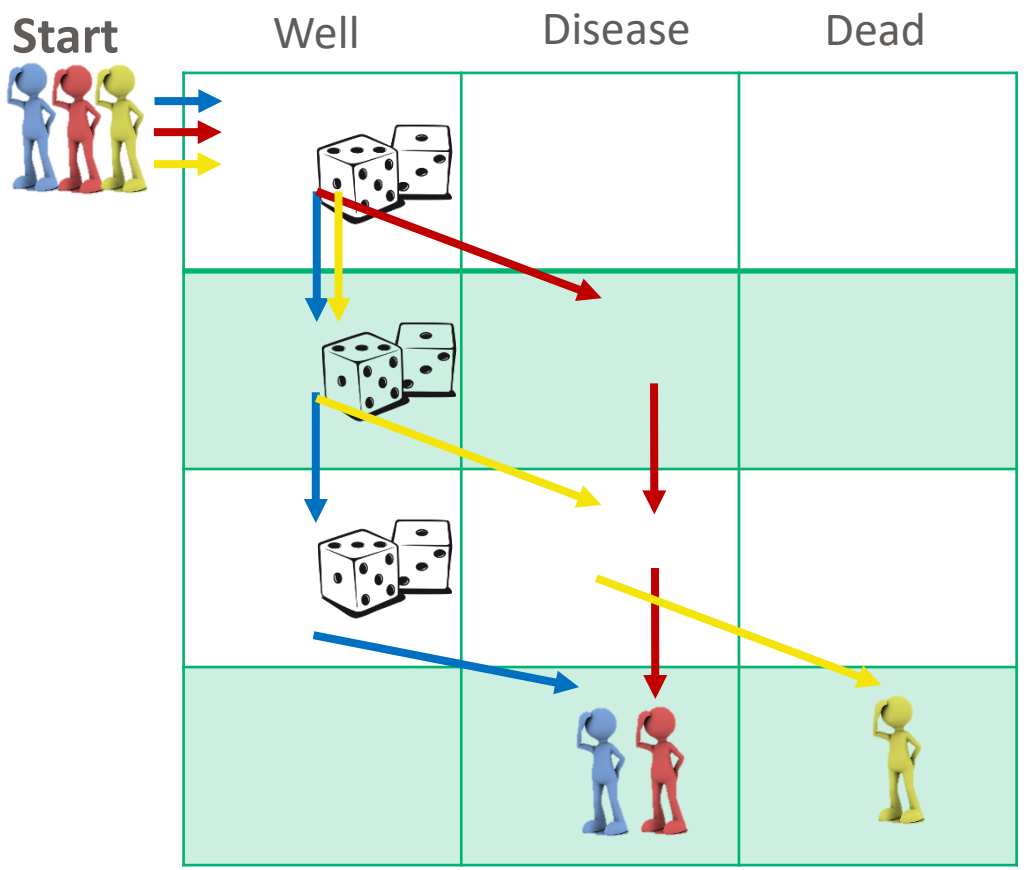
State-Transition Modelling: Markov Model *vs* Microsimulation



Cohort	11,6%	23,0%	65,4%



N=1000	102	234	664

* Siebert et al. 2012 *State-Transition Modeling: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force-3*

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Key elements of a decision tree

Definition: *is a branching structure in which each branch represents an event that may take place in future*

Identifying alternatives and specifying the sequence and linkage of events are essential step in constructing such a model, but are also in themselves of great value in clarifying complex decisions.

- The first step in building a decision tree, and in fact any decision model, is **formulating the decision problem**.
- The decision problem should involve **at least two options** and **at least one outcome** upon which to base a recommendation.

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Key elements of a decision tree (Exemple)

Consider the value of two different types of hip replacement surgery for young people suffering from arthritis: total hip arthroplasty where the whole joint is replaced and resurfacing arthroplasty where part of the joint is replaced, making a smooth surface to allow more normal hip function. We might want to know which type of surgery leads to the best recovery :

Which method of operating on arthritic hips in young patients, total hip arthroplasty or resurfacing arthroplasty provides the likelihood of good recovery?

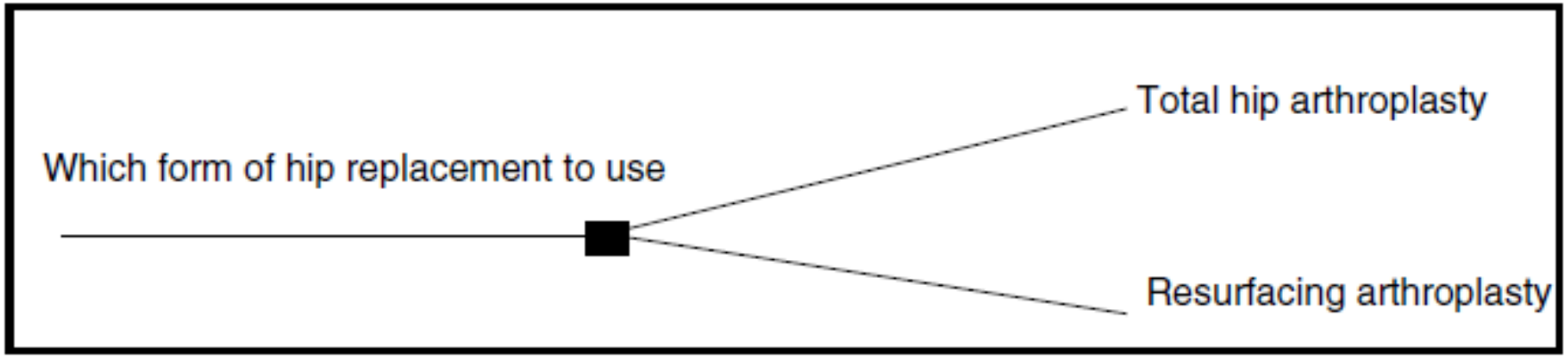
Two different types of hip replacement surgery for young people suffering from arthritis:

- **total hip arthroplasty** where the whole joint is replaced;
- **resurfacing arthroplasty** where part of the joint is replaced, making a smooth surface to allow more normal hip function

Building the decision tree (1)

■ - **decision node**

indicates where a decision is made, and the lines or branches of the decision tree emanating from this node show the options at this point



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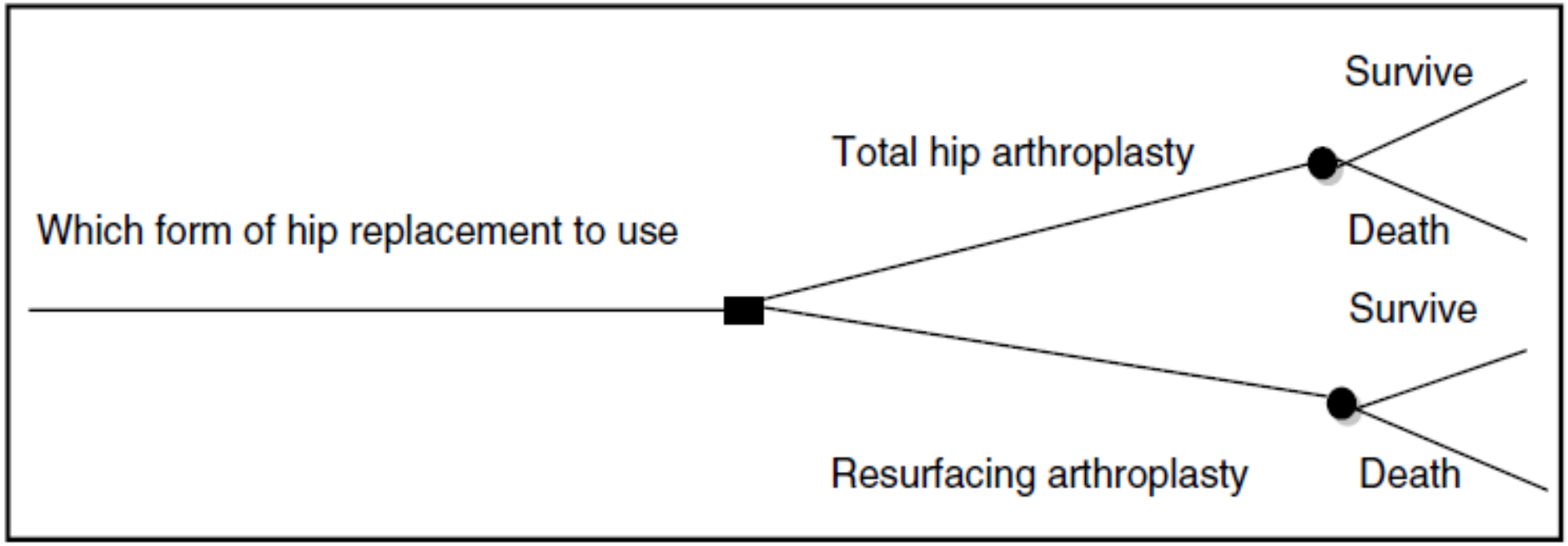
Building the decision tree (2)

● - **chance node**

defines a risk and indicates what will happen as a result of it



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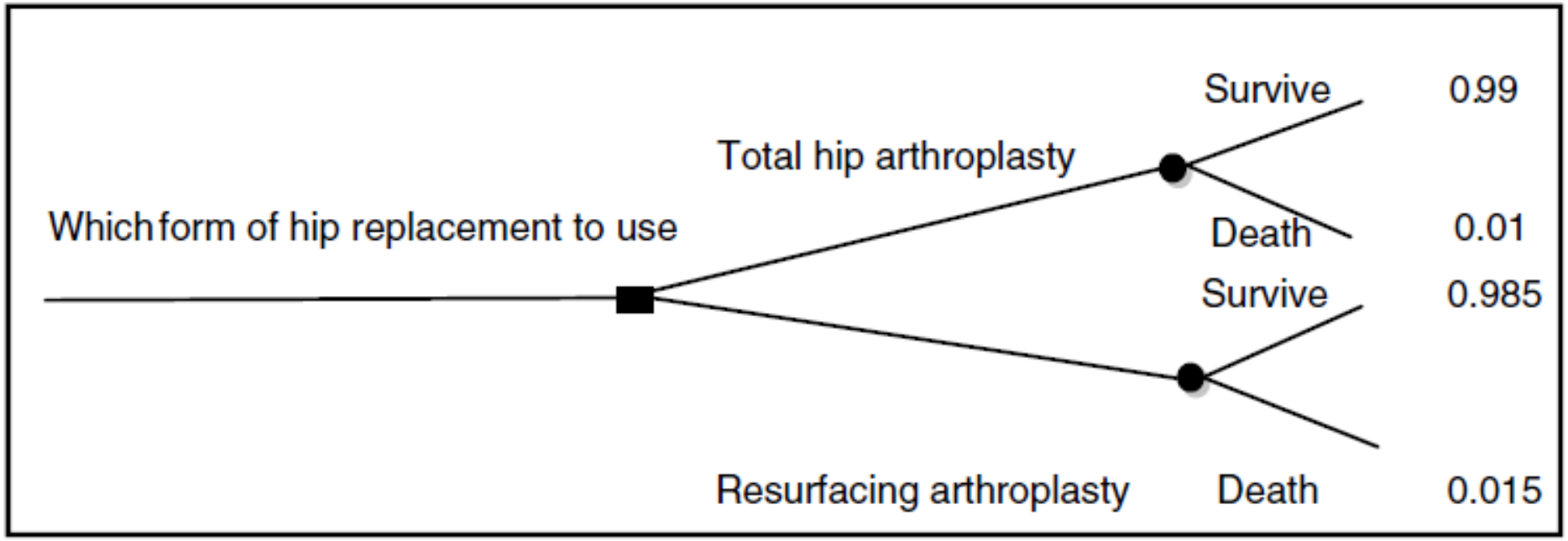
Building the decision tree (3)

Transition probabilities

the probability of transitioning or moving into the survival branch or the perioperative death branch. The probabilities in the branches from each chance node must add to 1.



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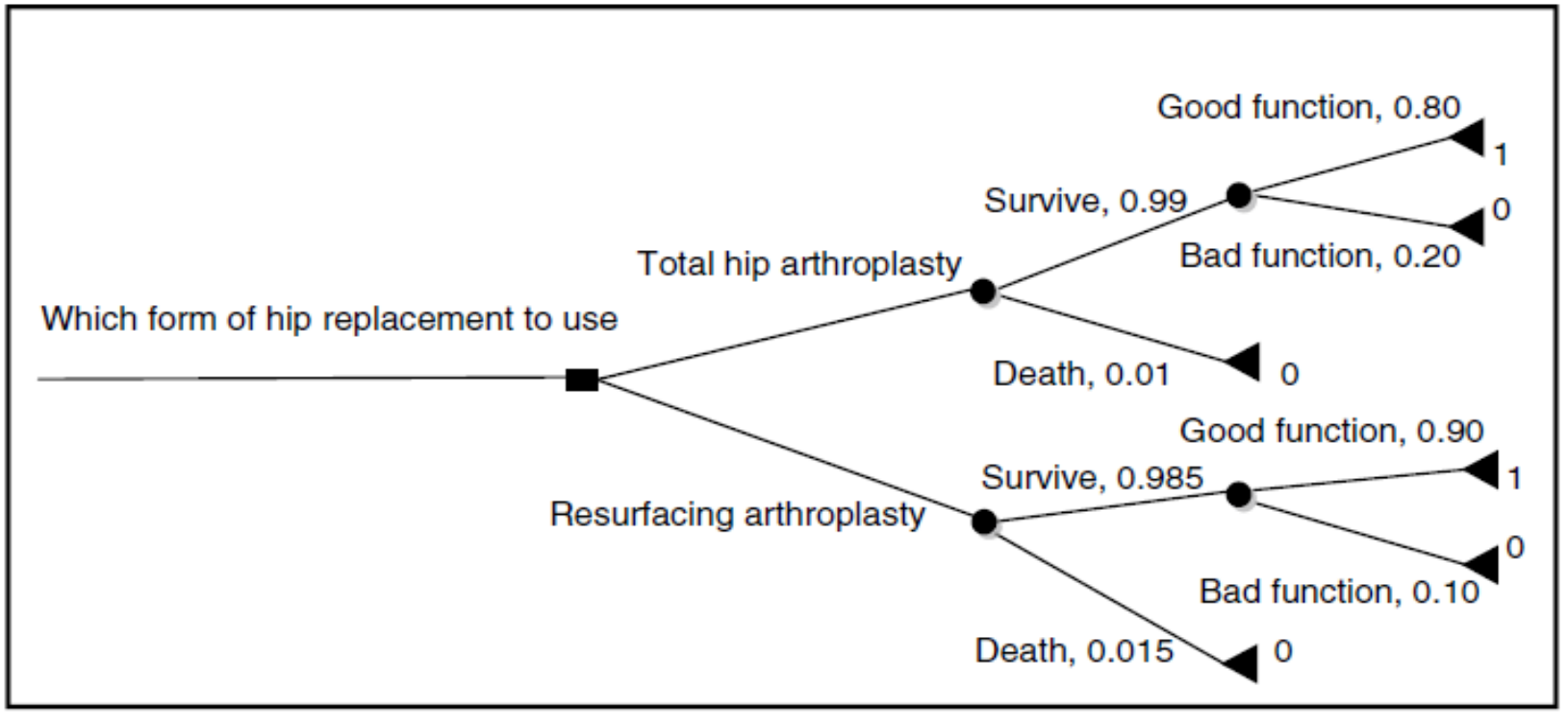
Building the decision tree (4)

◀ - **terminal node**

indicate that we have observed the outcomes, including but not limited to the case when someone has died. At each of the terminal nodes, payoffs are defined.



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Payoffs

- Costs of health care
- Value of the health state

Health care costs:

- costs of the surgery, medications and rehabilitation.

The health outcome:

- measure of quality of life or quality adjusted life years (QALYs).

There is normally more than one payoff (costs and health outcome). However, for this simple example we have assumed single payoffs.

The payoff for a good function is 1, and the payoff for poor function or perioperative death is 0.

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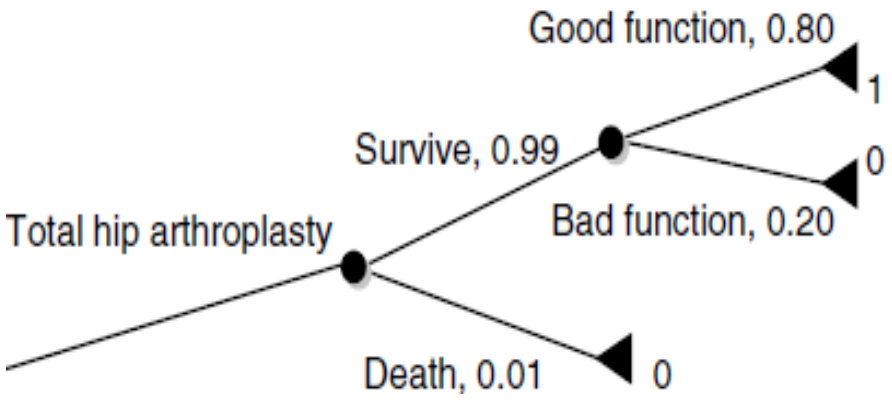
Calculate the expected value of the likelihood

- First consider the total hip arthroplasty branch of the tree :



- Likelihood of payoff for good function
  $= \Pr(survival) \times \Pr(good\ function) \times payoff$
  $= 0.99 \times 0.80 \times 1 = 0.7920$

- Likelihood of payoff for bad function
  $= \Pr(survival) \times \Pr(bad\ function) \times payoff$
  $= 0.99 \times 0.20 \times 0.00 = 0.00$

- Likelihood of payoff for perioperative death
  $= \Pr(perioperative\ death) \times payoff$
  $= 0.01 \times 0.00 = 0.00$

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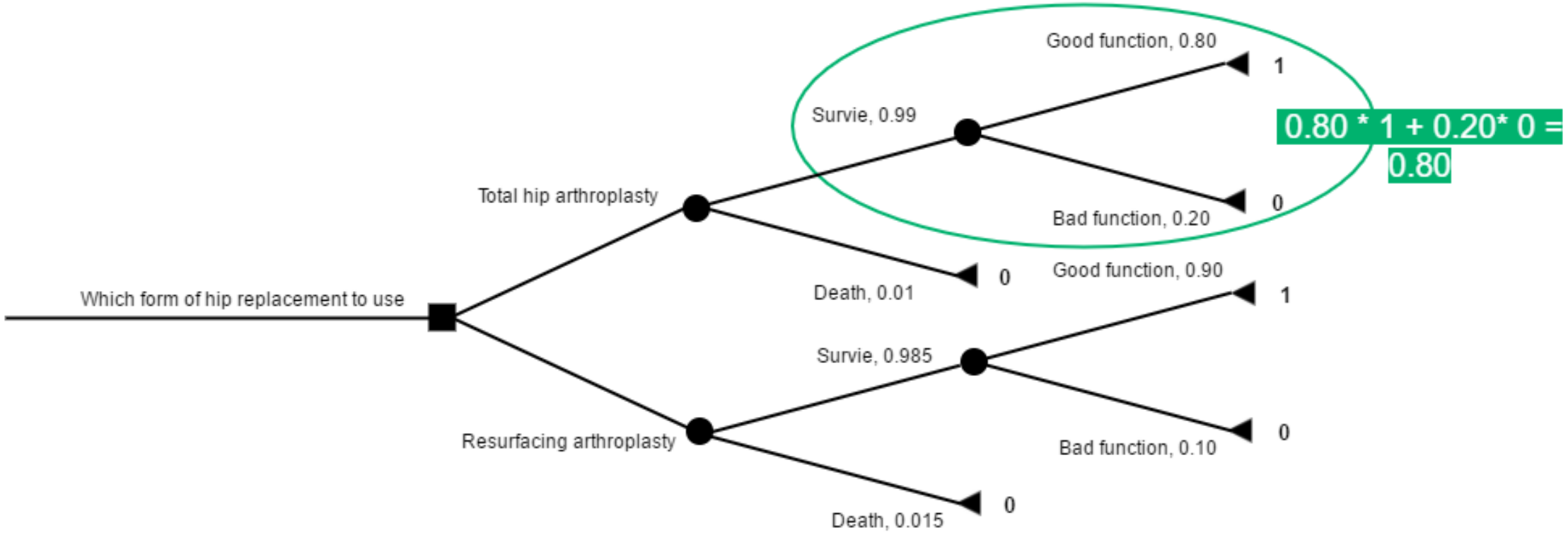
Expected value for patients surviving total hip arthroplasty



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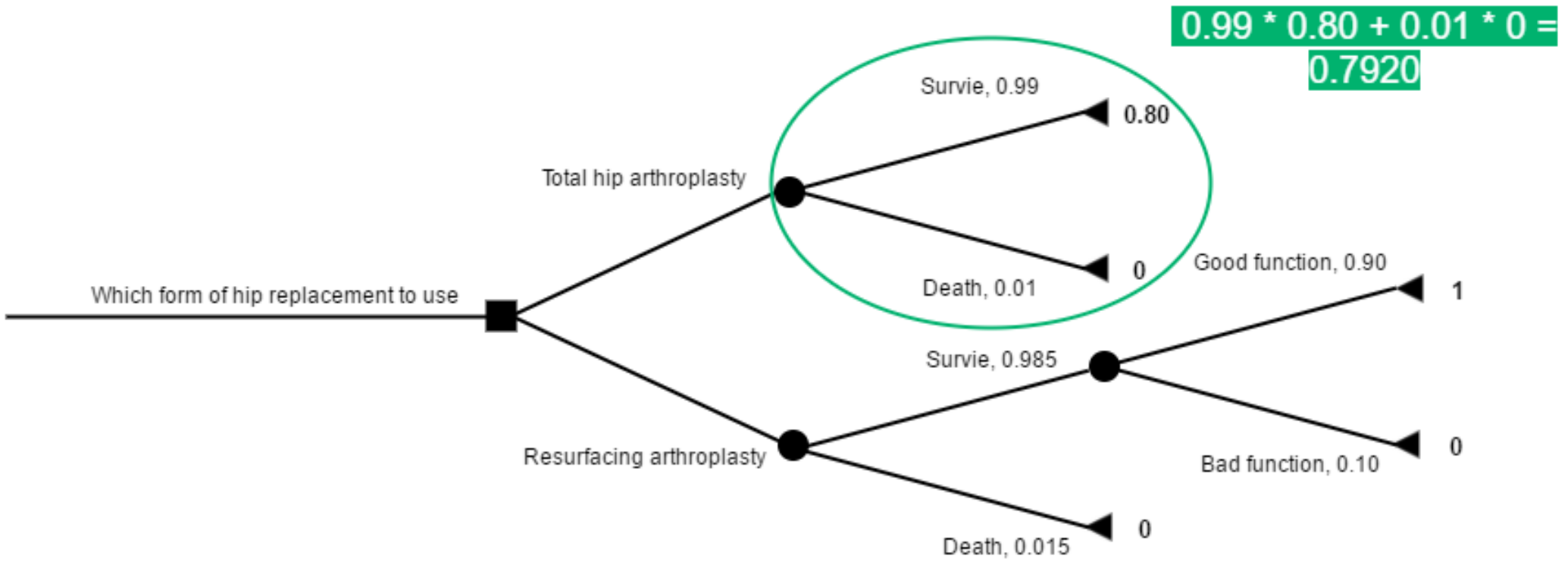
Expected value of total hip arthroplasty



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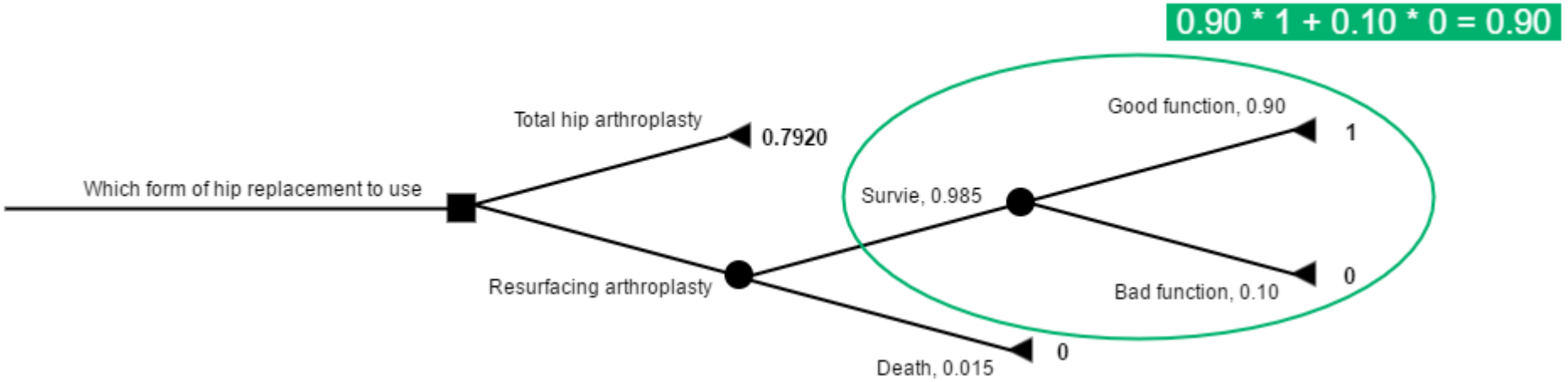
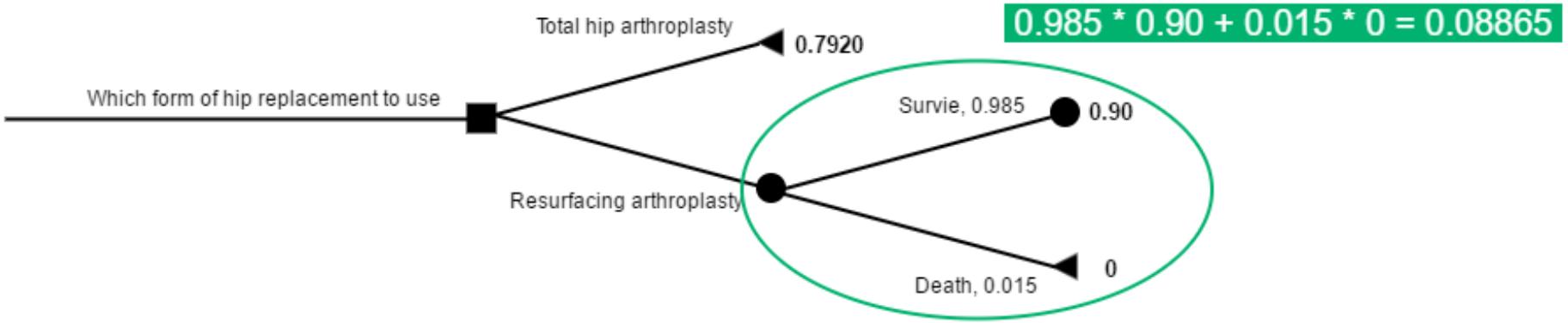
Expected value of resurfacing arthroplasty





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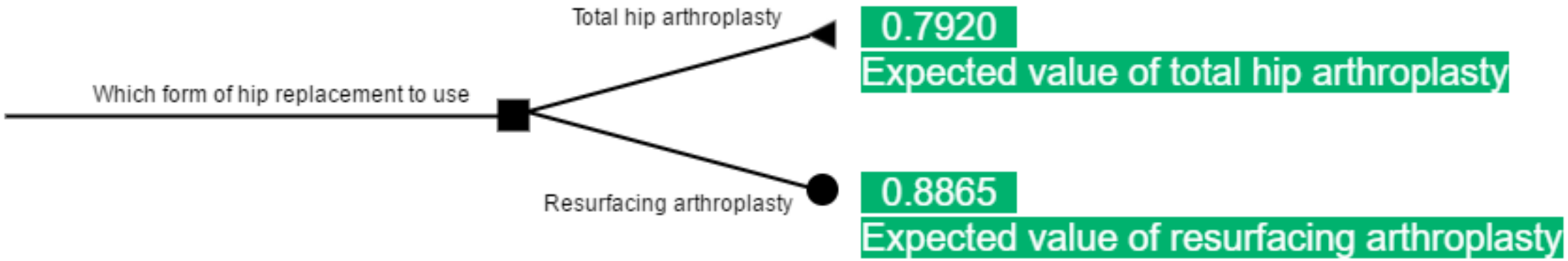
The expected value of a good recovery

- *Which method of operating on arthritic hips in young patients, total hip arthroplasty or resurfacing arthroplasty provides the greater likelihood of good recovery?*



Looking at the expected value from each surgical option, we can see that resurfacing arthroplasty has a higher likelihood of a good recovery.

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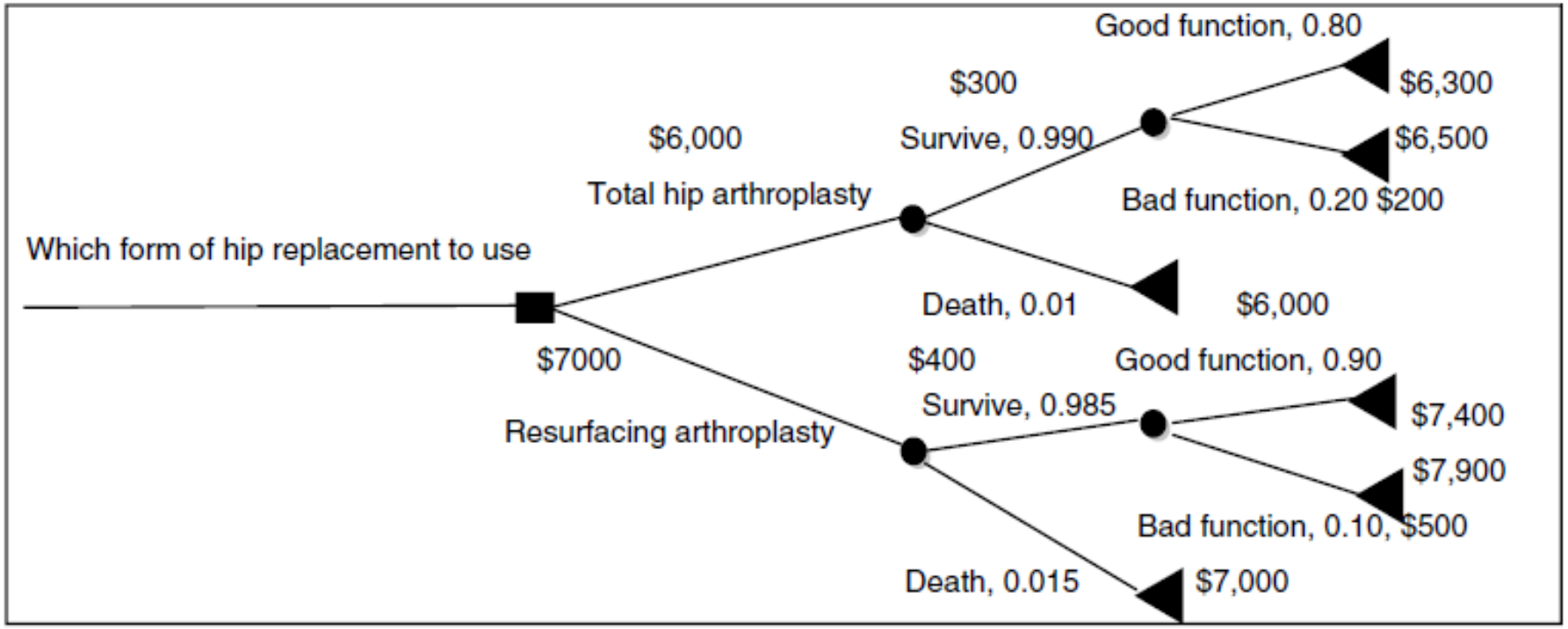
Costs, Benefits and Complexity

- Payoffs will need to include both costs and benefits.
- In line with any economic evaluation, you must consider the perspective the evaluation is taking. This will be informed by the question being asked and the purpose of the analysis.
- **Costs to the health system** might include the costs to secondary, tertiary or primary health care and may in some cases be extended to include costs of personal social care provision.
- If a wider **societal perspective** is taken, this might widen the scope to include not only health and personal social care but also productivity arising from days away from work, the costs of informal care and out-of-pocket expenses accruing to the patient and their family.
- Alternatively the analysis may focus on the impact of a particular intervention in a specified area, for example, hospital admissions.

Decision tree: expected costs

The same process, but this time we have **attached the costs** associated with each option



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Expected costs

- For the total hip arthroplasty arm:

Likelihood of payoff for good function

$$= \Pr(survival) \times \Pr(good\ function) \times payoff = 0.99 \times 0.80 \times \$6{,}300 = \$4{,}989.60$$

Likelihood of payoff for bad function

$$= \Pr(survival) \times \Pr(bad\ function) \times payoff = 0.99 \times 0.20 \times \$6{,}500 = \$1{,}287$$

Likelihood of payoff for perioperative death

$$= \Pr(perioperative\ death) \times payof = 0.01 \times \$6{,}000 = \$60$$

- For the resurfacing hip arthroplasty arm:

Likelihood of payoff for good function

$$= \Pr(survival) \times \Pr(good\ function) \times payoff = 0.99 \times 0.80 \times \$7{,}400 = \$5{,}860.80$$

Likelihood of payoff for bad function

$$= \Pr(survival) \times \Pr(bad\ function) \times payoff = 0.99 \times 0.20 \times \$7{,}900 = \$1{,}564.20$$

Likelihood of payoff for perioperative death

$$= \Pr(perioperative\ death) \times payof = 0.01 \times \$7{,}000 = \$70$$

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Incremental Cost-Effectiveness Ratio (ICER)

- The expected cost of total hip arthroplasty is the likelihood of the payoff of the three pathways added together :

$$\$4\,989{,}60 + \$1\,287 + \$60 = \$6\,336{,}60$$

- The expected cost of resurfacing hip arthroplasty :

$$\$5\,860{,}80 + \$1\,564{,}20 + \$70 = \$7\,495$$

$$ICER = \frac{C_2 - C_1}{E_2 - E_1} = \frac{\$\,7\,795 - \$\,6\,336{,}60}{0.8865 - 0.7920} = \frac{\$\,1\,158{,}40}{0{,}0945} = \$\,12\,258$$

$ 12 258 per Good Functioning Hip

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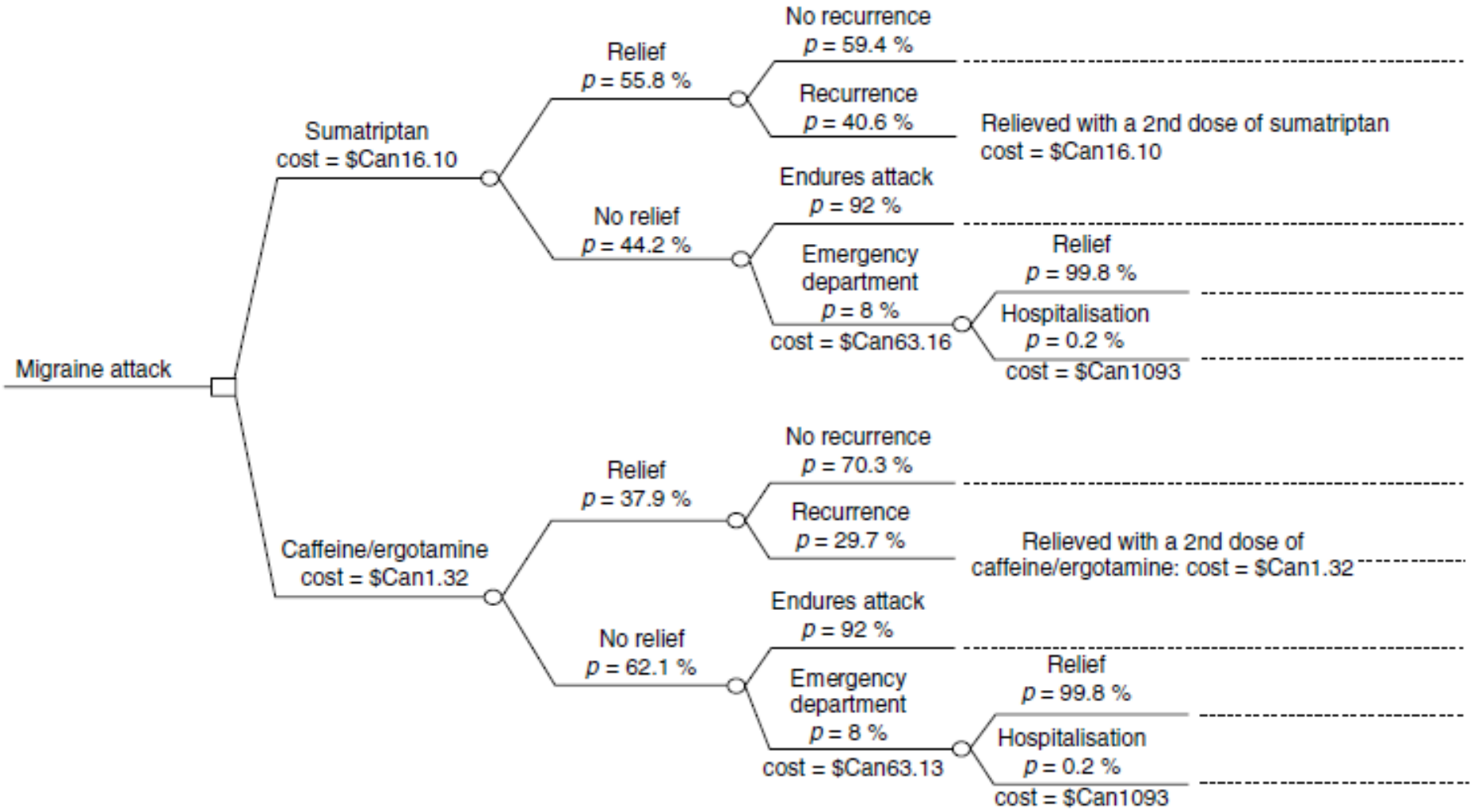
Exercise 1: Building a Decision Tree



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Exercise 2: Completed tables

	Sumatriptan			Caffeine/ergotamine		
	Prob	Cost	Outcomes	Prob	Cost	Outcomes
All cases	1.000			1.000		
Initial relief	0.558			0.379		
No recurrence	0.331452	$ 16.10	1.00	0.266437	$ 1.32	1.00
Recurrence	0.226548	$ 32.20	1.00	0.112563	$ 2.64	1.00
No relief	0.442			0.621		
Endures attack	0.40664	$ 16.10	-	0.57132	$ 1.32	-
ER	0.035			0.050		
Relief	0.035289	$ 79.26	-	0.049581	$ 64.48	-
Hospitalisation	7.07E-05	$ 1,172.23	-	9.94E-05	$ 1,157.45	-

	Sumatriptan			Caffeine/ergotamine		
	Prob	Cost	Outcomes	Prob	Cost	Outcomes
No recurrence	0.331452	$ 16.10	1.00	0.266437	$ 1.32	1.00
Recurrence	0.226548	$ 32.20	1.00	0.112563	$ 2.64	1.00
Endures attack	0.40664	$ 16.10	-	0.57132	$ 1.32	-
Relief	0.035289	$ 79.26	-	0.049581	$ 64.48	-
Hospitalisation	7.07E-05	$ 1,172.23	-	9.94E-05	$ 1,157.45	-
Expected values		$ 22.06	0.56		$ 4.71	0.38

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Exercise 3: Quality of Life outcomes

	Quality of life	Standard deviation
Attack averted with initial treatment	1.0	0
Attack averted with retreatment	0.9	0.01
Attack endured after failed treatment	–0.3	0.10
Emergency room visit after failed treatment	0.1	0.10
Hospitalisation after failed treatment	–0.3	0.10

Exercise 3: Decision tree using QALYs

	Probabilities	Costs			Effectiveness		
Sumatriptan		Health	Societal	Total costs	Cases averted	QALY loss	Total effectiveness
No recurrence	0.331	$ 16.10	$ -	$ 16	1	-	-
Recurrence	0.227	$ 32.20	$ -	$ 32	1	0.0003	0.0003
Endures attack	0.407	$ 16.10	$ 122.52	$ 139	0	0.0036	0.0036
Relief	0.035	$ 79.26	$ 122.52	$ 202	0	0.0025	0.0025
Hospitalisation	0.00007	$ 1,172.26	$ 122.52	$ 1,295	0	0.0036	0.0036
Expected values				$ 76	56%	0.0016	0.0016

		Health	Societal	Total costs	Cases averted	QALY loss	Total effectiveness
Caffeine/ergotamine							
No recurrence	0.266	$ 1.32	$ -	$ 1	1	-	-
Recurrence	0.113	$ 2.64	$ -	$ 3	1	0.0003	0.0003
Endures attack	0.571	$ 1.32	$ 122.52	$ 123	0	0.0036	0.0036
Relief	0.050	$ 64.48	$ 122.52	$ 187	0	0.0025	0.0025
Hospitalisation	0.00010	$ 1,157.48	$ 122.52	$ 1,280	0	0.0036	0.0036
Expected values				$ 81	38%	0.0022	0.0022

Incremental outcomes
Sumatriptan vs. caffeine/ergotamine

-$ 5 for 0.0006 QALYs

-$ 7,768 per QALY

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Decision analytic modelling(2): Markov model

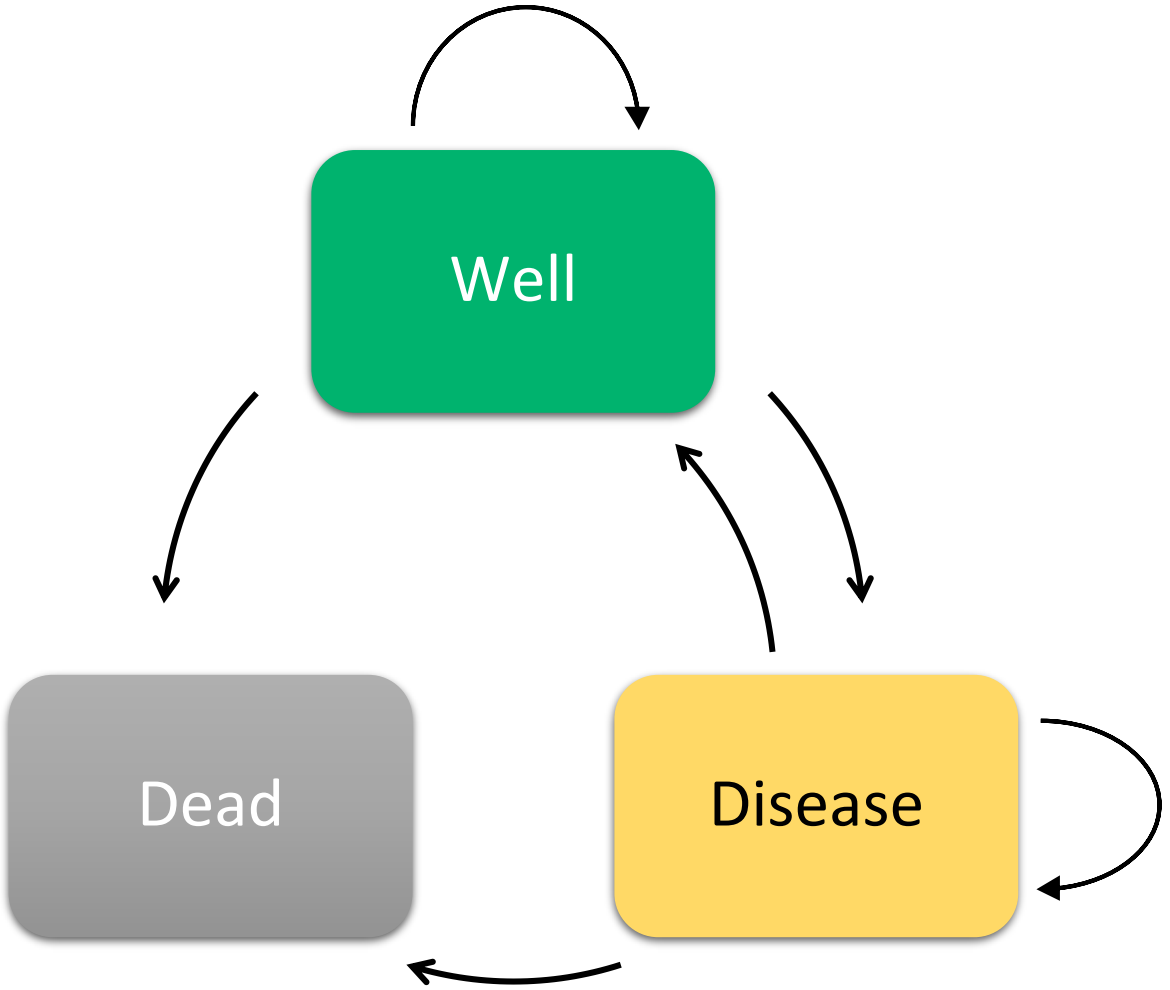
When use Markov Models?

- The most useful when health **events repeat** over time or have **longer-term health effects**;
- When the effect of treatment either stops quickly after an initial treatment or continues at its earlier level;
- When **the risk** of different health events does not **depend on the patient's prior history**;

Why use Markov Models?

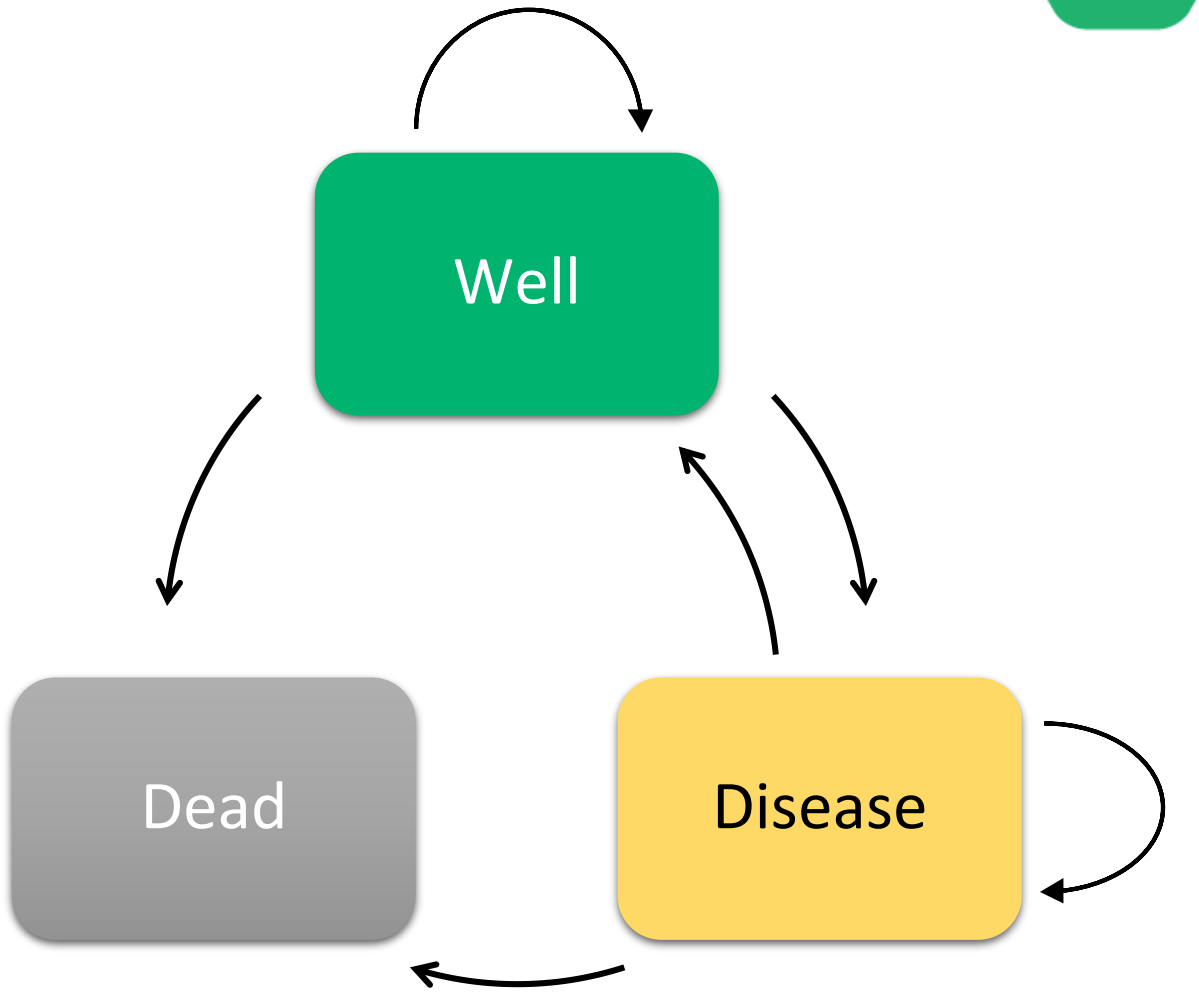
- Decision trees are limited in as much as they are designed to capture what happens at a point in time ; there is no explicit sense of time passing.
- But, Markov models enable us to incorporate the passage of time.
- However, decision trees are good for considering transitory health conditions.
- But what alternatives are open to us when decision models became very complex – when the trees became *bushy* ?
- The way that Markov models are structured gets round this problem as the model has health **states that individuals can transition between** (forwards and backwards); whereas decision trees are unidirectional, the individual can only move from left to right in the model.

Model with 3 States



Health States

- Within Markov models, health is split into distinct categories.
- These categories or **health states** must be mutually exclusive and cover all the people in the model (everyone must fit into a health state at any point in time).
- **Individuals can only be in one state at a time** and will stay in that state for a specified or fixed period of time.
- This period of time is known as a **cycle**, and at the end of each cycle, the patient can stay in the same health state or move to another health state.



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Transition Probabilities

What is the chance of an individual who is well contracting the specified disease represented in the model, i.e. moving from the Well health state to the Disease health state?

Transition probabilities are a key element of a Markov model;
Transition probability predicts how people will move from one health state to another.
The probability of moving to disease at the end of period, given that you started in the period t in Well, is summarised as ***P (Disease$_{t+1}$ | Wellt)***.

		End of period t (start of period $t+1$)		
		Well	Disease	Dead
Start of period t	**Well**	$P(\text{Well}_{t+1} \mid \text{Well}_t)$	$P(\text{Disease}_{t+1} \mid \text{Well}_t)$	$P(\text{Dead}_{t+1} \mid \text{Well}_t)$
	Disease	$P(\text{Well}_{t+1} \mid \text{Disease}_t)$	$P(\text{Disease}_{t+1} \mid \text{Disease}_t)$	$P(\text{Dead}_{t+1} \mid \text{Disease}_t)$
	Dead	$P(\text{Well}_{t+1} \mid \text{Dead}_t)$	$P(\text{Disease}_{t+1} \mid \text{Dead}_t)$	$P(\text{Dead}_{t+1} \mid \text{Dead}_t)$

Transition Matrix

- **Transition Matrix** is a way of combining conditional probabilities together.

Thinking about the transition between health states, what can we say about the transition $P\,(Well_{t+1} \mid Dead_t\,)$?

Quite simply this will always have a transition probability of **zero**. If a person is Dead in time period 1, then he/she cannot transition to Disease in the next time period.

		End of period t (start of period $t+1$)		
		Well	Disease	Dead
Start of period t	**Well**	0.7	0.2	0.1
	Disease	0.1	0.6	0.3
	Dead	0	0	1

Markov **Assumption**

- Markov **property** : process can make predictions for the future based solely on its present state i.e., conditional on the present state of the system, its future and past are independent.

- The Markov assumption states that you **use the same transition matrix every time**; however, this assumption is relaxed for transition changes by time.

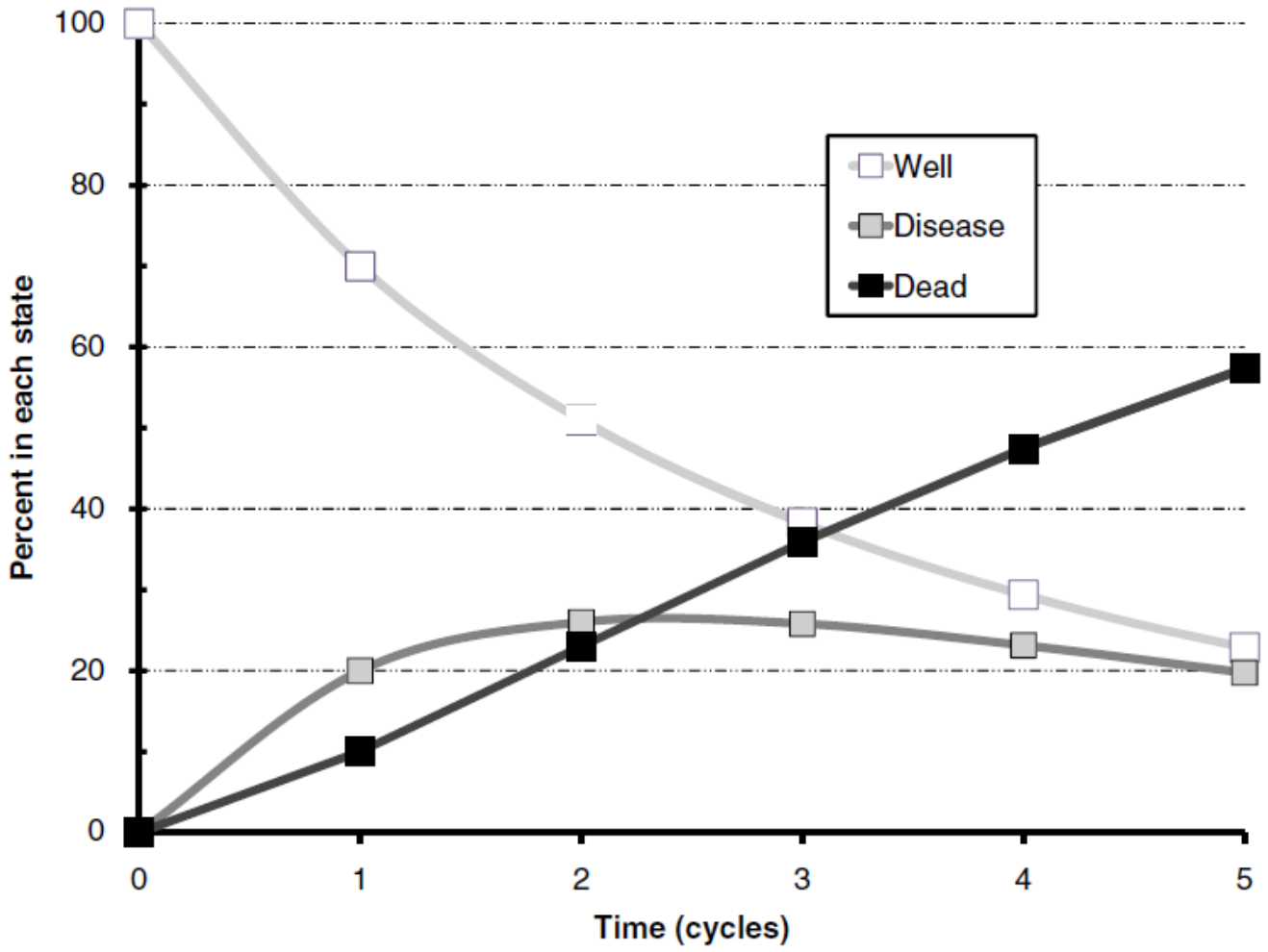
- A Markov model can allow the transition matrix to change; the transition probabilities can depend on the period, but the same figures apply for everyone.

Markov Trace

- The Markov trace captures the numbers or proportion of people in each health state in each time period and how that changes over time.
- The Markov trace uses the transition probabilities to calculate the movement between groups.

	Well	Disease	Dead
$T=0$	100	0	0
$T=1$	70	20	10
$T=2$	51	26	23
$T=3$	38.9	25.3	35.9
$T=4$	29.39	23.14	47.47
$T=5$	22.887	19.762	57.351

Graphical depiction of the Markov trace for a simple Markov model



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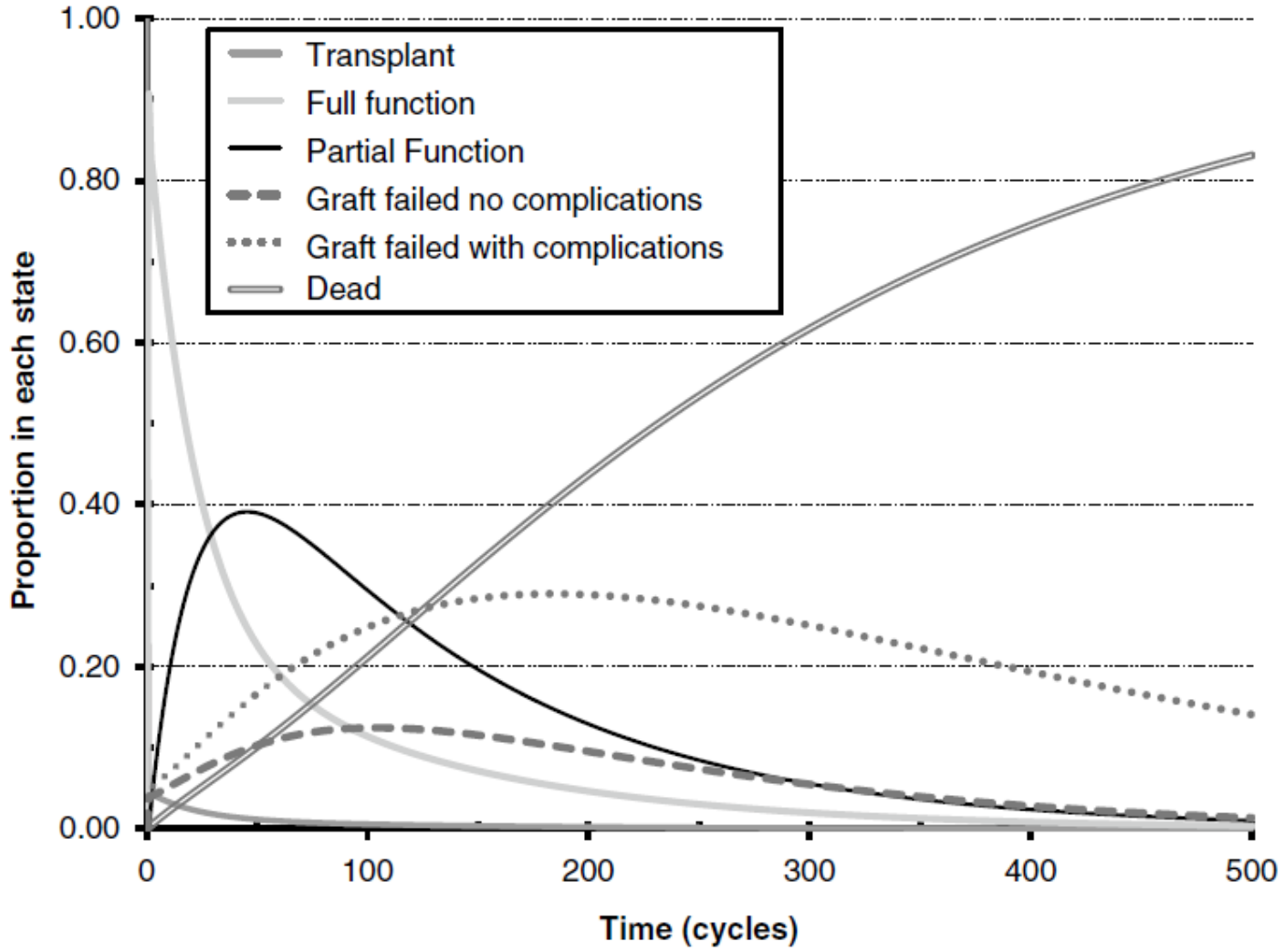
Graphical depiction of a Markov trace for a more complex Markov model



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Cycle Length

- The **cycle length** is the minimum time people spend in a state (all members of the cohort will spend at least one cycle in the state they begin the model in). This is often informed by the smallest clinically meaningful item included as a distinct event.
- Transition probabilities depend in part on the cycle length :
  - If the chance of dying in 1 year is 25 % ;
  - we have a corresponding cycle length of 1 year;

$$P(Dead_{t+1} \mid Well_t) = 0.25$$

But if the cycle length is only, for example, 6 months ?

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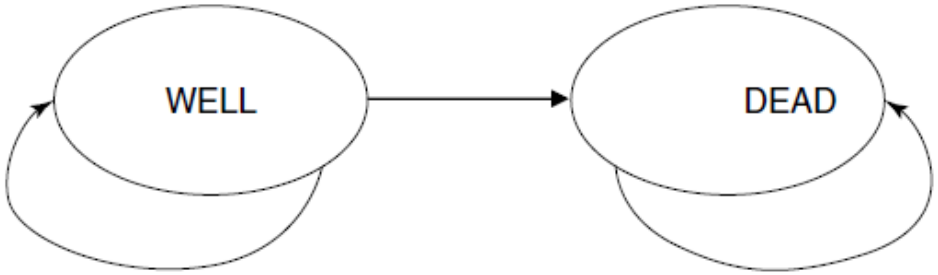
Transition probabilities and Cycle Length

Assuming constant hazards, the equations we need are

$r = \ln(1 - p)$

$p = 1 - e^{-r}$

where r is the rate and p is the probability.



- The 12 month rate is $\ln(1 - 0.25) = 0.288$
- The 6 month rate is $0.288/2 = 0.144$
- The 6 month probability is $1 - e^{-0.143841} = 0.134$

Assuming constant hazards, find the per cycle probability if we have a cycle length of 1 month and the 12-month probability is 50 %.

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Time Horizon

- The **time horizon** is the total period of time over which the models runs.
- It should be long enough to capture meaningful differences in costs and outcomes between the intervention and comparator (CADTH 2006; NICE 2013).
- In general a lifetime horizon is thought to be the default position and will be best for most chronic conditions.
- Some types of question will have a shorter horizon for a variety of reasons: it might be because costs and benefits stop accruing, because this is in line with decision makers' requirements or that there is such limited evidence for the longer term that the decision maker chooses a shorter time horizon.

Half Cycle Correction

- On average, the events will occur approximately halfway through the cycle.
- However in discrete state models, such as Markov state models, all the patients in each state accrue the full costs and health for each cycle. This means that the Markov trace for costs and outcomes will overstate the underlying continuous processes that we are trying to model.

shift the allocation of patients by **half a cycle**, so that the costs and outcomes attributed to each state in each cycle are based on half the state membership from the current cycle and half the state membership from the next cycle.

To implement this correction : in calculating the *total* costs and outcomes, we replace the first period result with the total of 50 % of the first period result and 50 % of the final period result.

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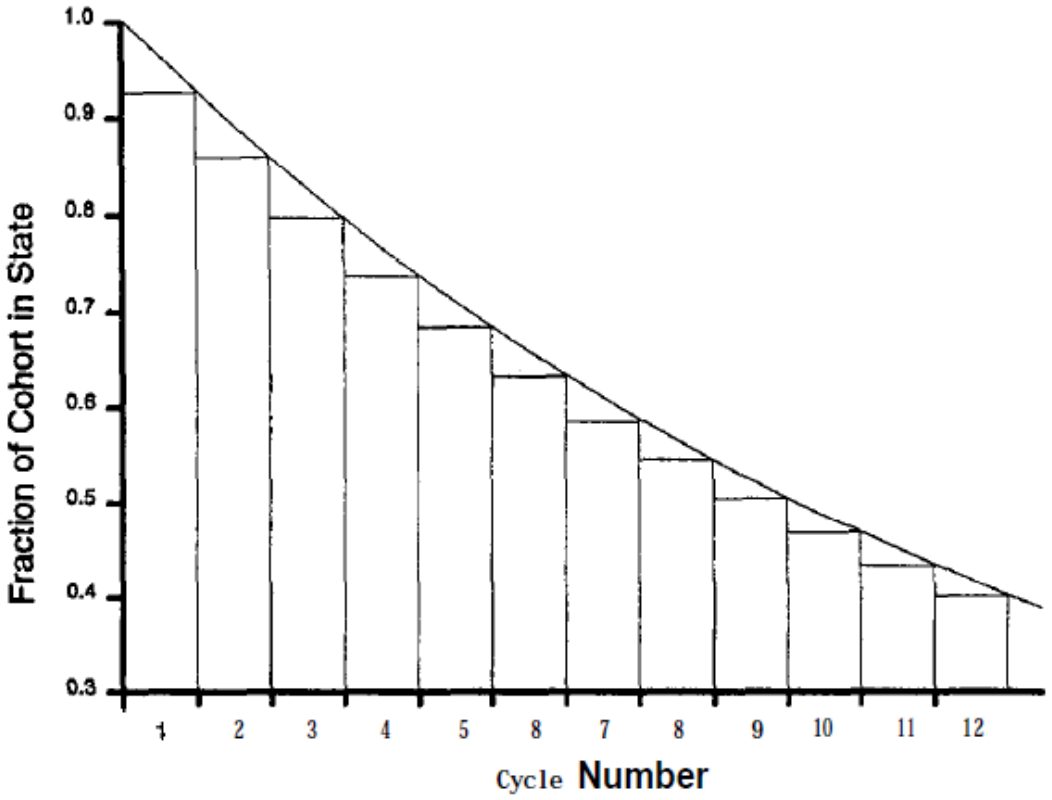
Counting cohort membership

Counting cohort membership **at the end** of each cycle



Counting cohort membership **at the beginning** of each cycle

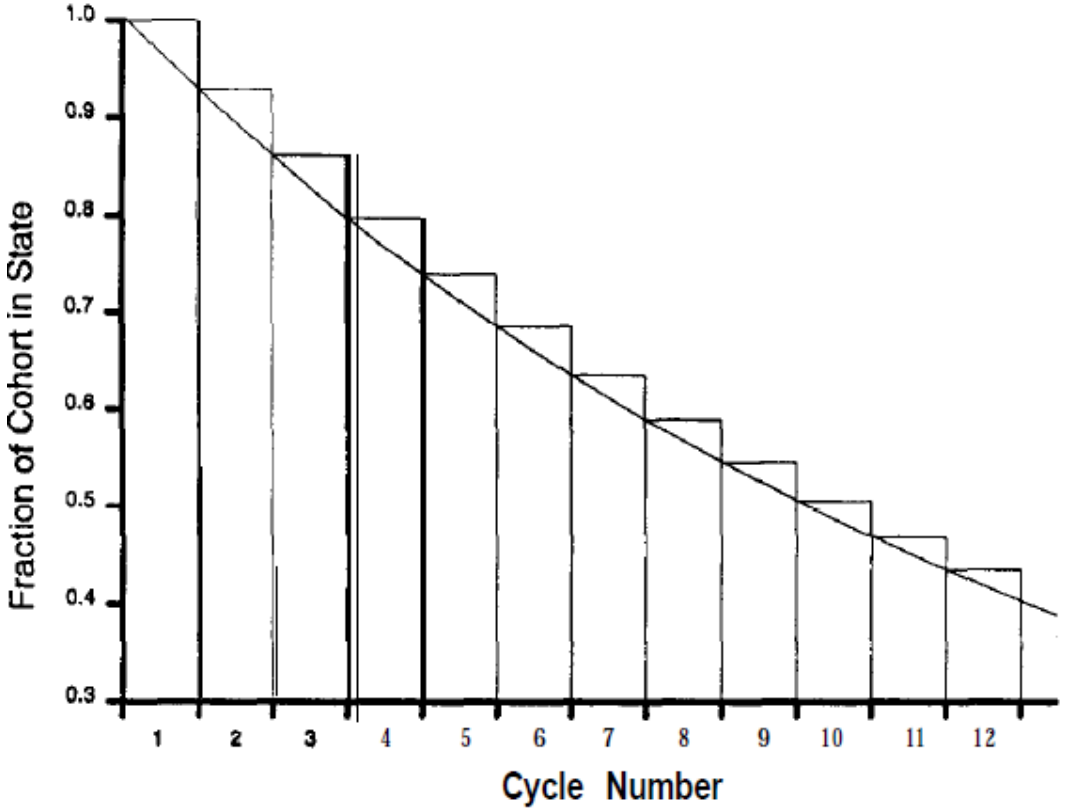


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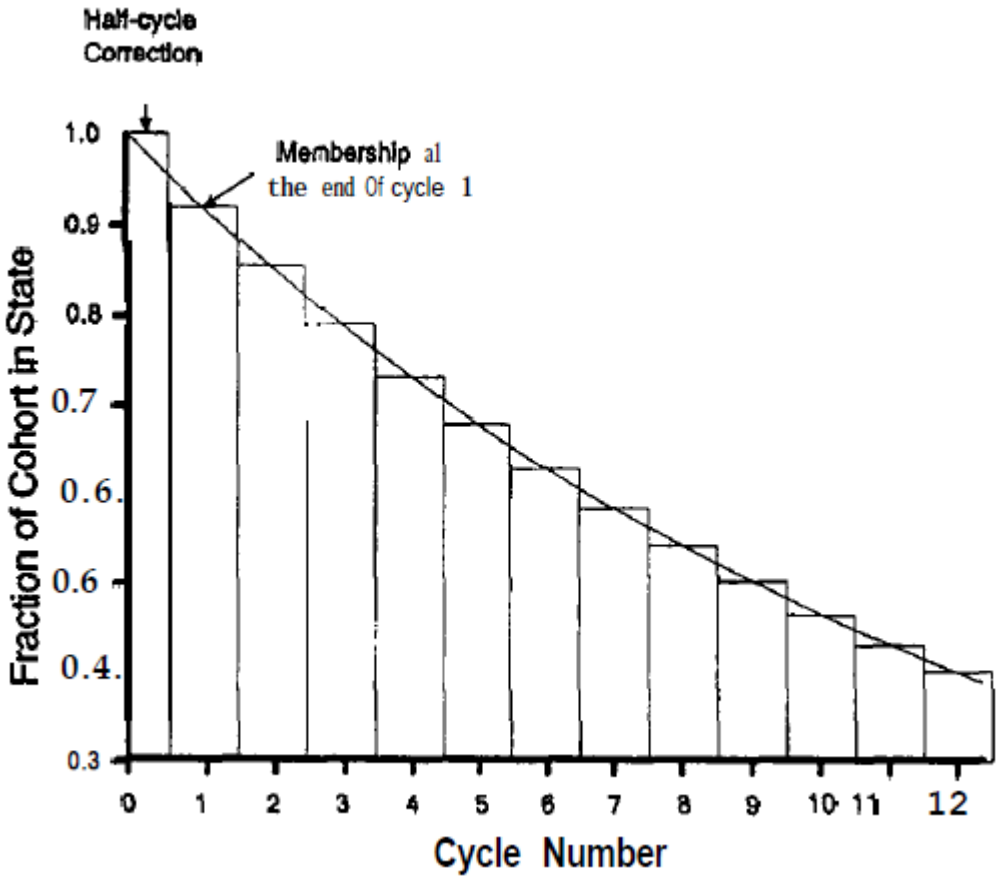
Illustration of the half-cycle correction



- To more accurately reflect the continuous nature of the state transitions, we make the assumption that state transitions occur, on average, ***halfway through*** each cycle
- There is no way to determine the state membership in the middle of the cycle.
- However, if we consider the count at the end of each cycle to be in the middle of a cycle that begins halfway through the previous cycle and ends halfway through the subsequent cycle, then the under- and overestimations will be balanced.

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Discounting

A **discount factor** : the value of costs and benefits depends on both their ***value*** and ***when*** they occur.

- A consistent ***value*** for costs is obtained by using costs adjusted to refer to the same currency/year.
- In respect of ***when*** they occur, the value of future costs and benefits decreases if they occur further into the future.

$$1/(1 + r)^n$$

$\boldsymbol{r}$ is the discount rate

$\boldsymbol{n}$ is the number of years from now.

Time (years)	Calculation	$
0	$1/(1+0.05)^0$	1
1	$1/(1+0.05)^1$	0.9524
2	$1/(1+0.05)^2$	0.9070
3	$1/(1+0.05)^3$	0.8638
4	$1/(1+0.05)^4$	0.8227

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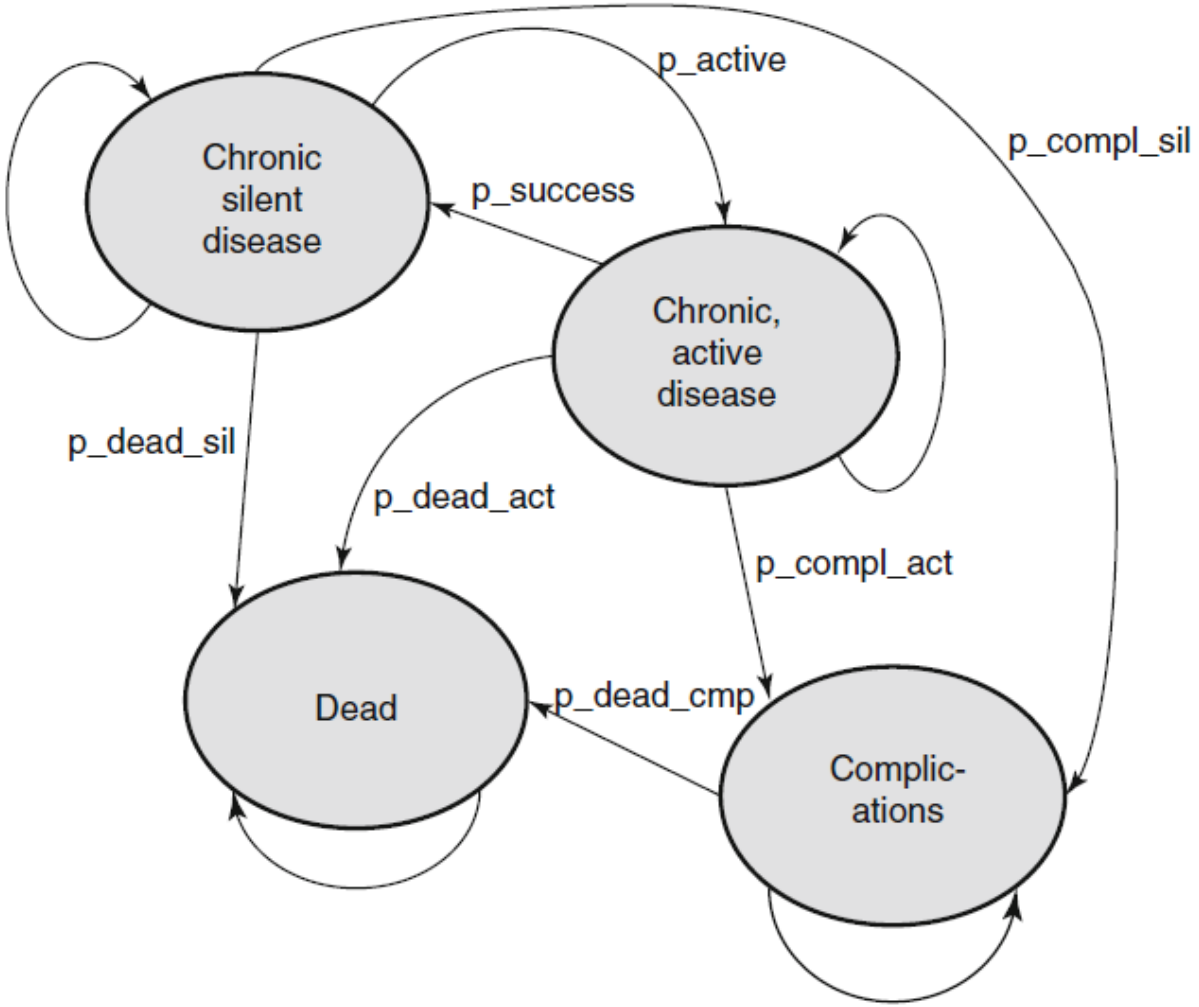
Summary

- Markov models are most useful when health events repeat over time or have longer-term health effects; when the effect of treatment either stops quickly after an initial treatment or continues at its earlier level; and when the risk of different health events does not depend on the patient's prior history.
- The clinical pathway is fundamental given Markov models are structured around health states and movements between them. Influence diagrams are a great way to visually represent your model.
- Transition probabilities predict how people will move from one health state to another.
- The Markov trace captures the numbers or proportion of people in each health state over time. The Markov trace uses the transition probabilities to calculate the movement between groups within your model.
- The cycle length is the minimum period of time that people spend in a health state. This is often informed by the smallest clinically meaningful item included as a distinct event.
- The time horizon is the total period of time we follow the cycles and should bechosen to reflect when relevant costs or benefits of the model stop happening.
- For models following a cohort for >1 year, a discount factor should be applied.

5

Building a Markov Cost Effectiveness Model in Excel

Influence diagram for the Markov model



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Parameter table

Transition probabilities	**Utility parameters**
Chronic silent to chronic active (p_active)	Utility in chronic silent disease (u_silent)
Chronic silent to complications (p_compl_sil)	Utility in chronic active disease (u_active)
Chronic silent to death (p_dead-sil)	Utility in complications (u_comp)
Chronic active to chronic silent (p_success)	Utility in death (u-death)
Chronic active to chronic complications (p_compl_act)	
Chronic active to death (p_dead_act)	
Complications to death (p_dead_cmp)	
Cost parameters	
Cost in chronic silent (c_silent)	Cost in complications (c_comp)
Cost in chronic active (c_active)	Cost in death (c_death)

Does your parameter table look like this Table? If it doesn't, what parameters did you miss and why? Did you have any parameters that we have not listed? What type of state is Dead in this model?

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Model transition matrix

		Outcome at end of period/start of next period			
		Silent	Active	Compl	Dead
Outcome at start of period	Silent	1-(p_silent + p_compl_sil + p_dead_sil)	p_silent	p_compl_sil	p_dead_sil
	Active	p_success	1 – (p_success + p_compl_act + p_dead_act)	p_compl_act	p_dead_act
	Compl	0	0	1-p_dead_cmp	p_dead_cmp
	Dead	0	0	0	1

Parameter table structure

Model control				opt_modeltype						
opt_modeltype	Model Type	Deterministic		Deterministic						
				Stochastic						
Transition parameters								Distribution		
Parameter	**Description**	**Refers to**	**Value used**	**Deterministic**	**Stochastic**	**Random**	**Dist**	**Param 1**		**Param 2**
p_active	Probability of active disease from silent disease	Treatment A								
		Treatment B								
p_success	Probability of silent disease from active disease	Treatment A								
		Treatment B								
p_compl_sil	Probability of complications from silent disease	Treatment A								
		Treatment B								
p_compl_act	Probability of complications from active disease	Treatment A								
		Treatment B								
p_dead_sil	Probability of death from chronic, silent disease	Treatment A								
		Treatment B								
p_dead_act	Probability of death from chronic, active disease	Treatment A								
		Treatment B								
p_dead_cmp	Probability of death from complications state	Common								
Cost parameters										
Parameter	**Description**	**Refers to**	**Value used**	**Deterministic**	**Stochastic**	**Random**	**Dist**	**Param 1**		**Param 2**
Chronic,silent disease	Health state specific costs	Common								
Chronic,active disease	Health state specific costs	Common								
Complications	Health state specific costs	Common								
c_TxA	Cost of treament A	Treatment A								
c_TxB	Cost of teament B	Treatment B								
Utility parameters										
Parameter	**Description**	**Refers to**	**Value used**	**Deterministic**	**Stochastic**	**Random**	**Dist**	**Param 1**		**Param 2**
Chronic,silent disease	Health state specific Utility	Common								
Chronic,active disease	Health state specific Utility	Common								
Complications	Health state specific Utility	Common								

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Deterministic Sensitivity Analysis

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Probabilistic Senstivity Analysis & Monte-Carlo Simulation

6

Outputs from Probabilistic Sensitivity Analysis

Formulas for Outputs from Cost Effectiveness Analysis

$$\text{ICER} = \frac{\bar{C}_2 - \bar{C}_1}{\bar{E}_2 - \bar{E}_1} = \frac{\overline{\Delta C}}{\overline{\Delta E}}$$

$\bar{C}_2$ is the cost under the intervention of interest (the new intervention).
$\bar{E}_2$ is the effectiveness under the intervention of interest (the new intervention).
$\bar{C}_1$ is the cost under the comparator or control.
$\bar{E}_1$ is the effectiveness under the comparator or control.
λ is the cost effectiveness threshold/willingness to pay for health.

$$\overline{\text{NHB}_i} = \bar{E}_i - \bar{C}_i / \lambda$$

$$\overline{\text{NMB}_i} = \bar{E}_i \lambda - \bar{C}_i$$

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PSA Tools

There are two reasons for using PSA:

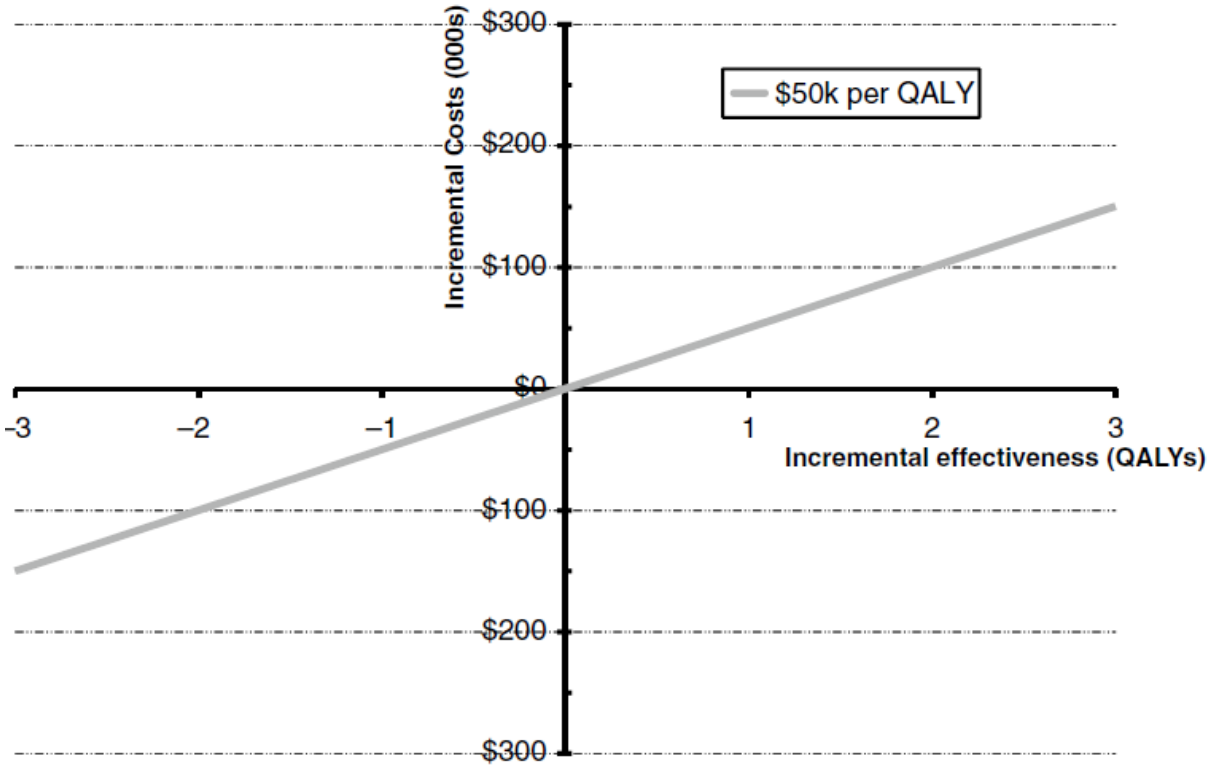
1. to ensure that the estimate of the ICER, and by extension the Net Benefit, is unbiased if the model is non-linear;
2. to characterise the uncertainty in the inputs to the model and thereby quantify the resulting uncertainty in the model outputs.

Key mechanisms for summarising the uncertainty in the ICER and Expected Net Benefit from cost effectiveness models:

- scatter plot on the cost effectiveness plane (Black 1990)
- cost effectiveness acceptability curve (CEAC) (Van Hout et al. 1994)
- cost effectiveness acceptability frontier (CEAF) (Barton et al. 2008)

Cost Effectiveness Plane

- In the *North East* quadrant, we locate ICERs where the new technology produces more health but also costs more than the comparator.
- In the *South East* quadrant, we locate ICERs where the new technology produces more health and costs less than the comparator.
- In the *South West* quadrant, we locate ICERs where the new technology produces less health but also costs less than the comparator.
- In the *North West* quadrant, we locate ICERs where the new technology costs more and produces less health than the comparator.



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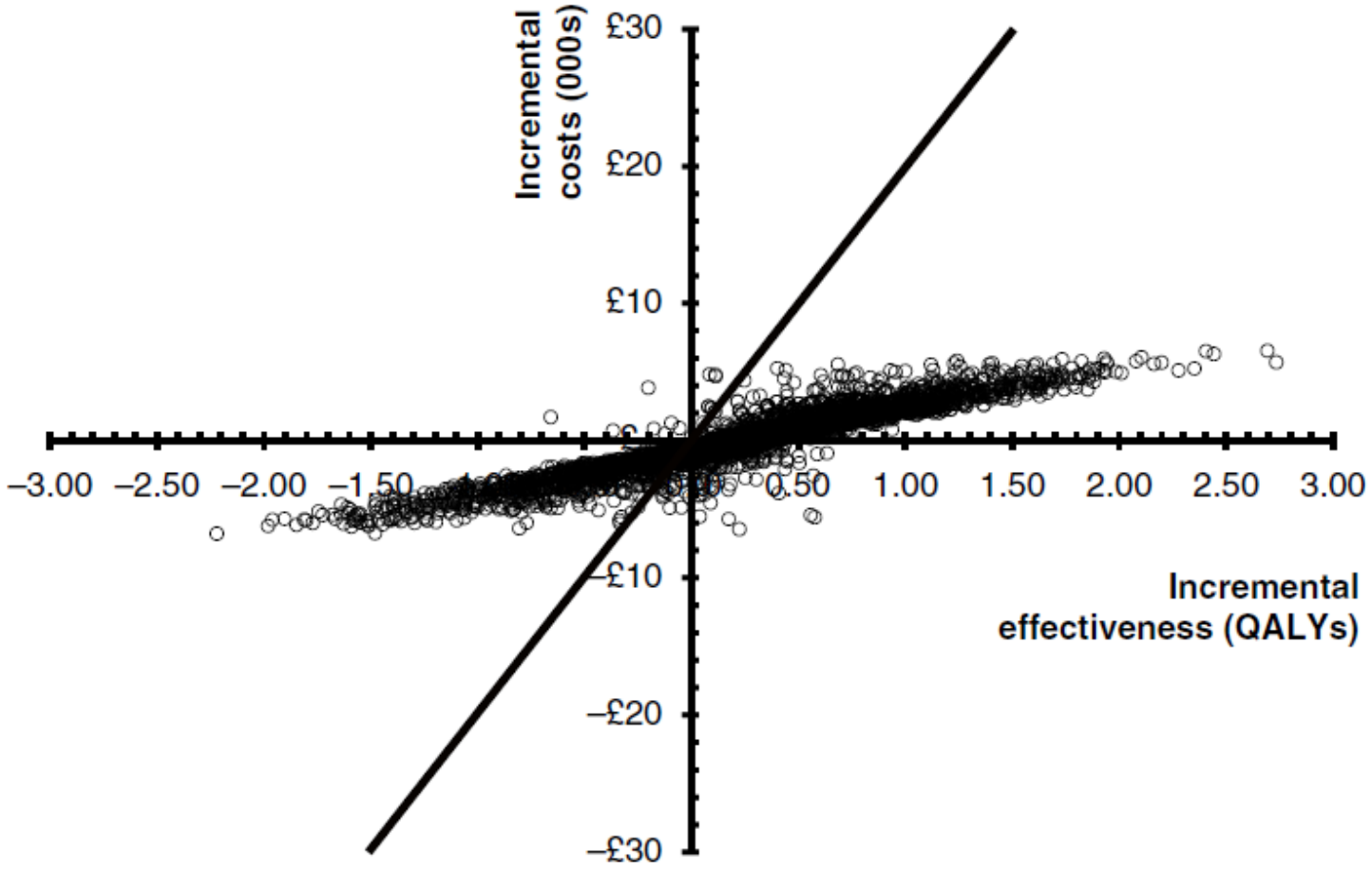
Scatterplot on the Cost Effectiveness Plane



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Problems and Solutions

- On the basis of this diagram alone, it is not possible to tell if Oncotype Dx is likely to be cost effective;
- The decision maker needs to consider whether the incremental cost is justified by the magnitude of the incremental QALYs across all four quadrants.

- To compare two or more technologies, we simply compare Net Monetary Benefit (NMB); whichever intervention has the higher positive NMB will be the preferred intervention.
- The **probability** that the new technology is cost effective compared to the current technology is calculated by comparing the NMB figures for each simulation run, *counting how many times the new technology has the greater NMB* and *dividing this by the total number of simulations*.

Example: NMB, λ=24 000€

	Traitement 1		Traitement 2		BMN		Probabilité que l'innovation soit efficiente		
Simulation	**QALY**	**Cost**	**QALY**	**Cost**	**Txt 1**	**Txt2**	$Max\,(BMN_{Txt1})^*$	$Max(BMN_{Txt2})^*$	**Traitement optimal**
1	1,28	9 223	0,94	4 001					
2	1,36	9 275	0,81	4 303					
3	1,53	10 744	1,14	5 365					
4	1,51	11 220	1,11	6 242					
5	1,34	10 209	0,87	4 716					
…	…	…	…	…					
81	2,28	15 373	2,01	8 140					
…	…	…	…	…					
1000	1,20	8 576	0,97	4 233					
Moyenne	**1,55**	**10 881**	**1,15**	**5 710**					

$$BMN = \lambda * E - C$$

$$BMN_{Txt1} >?< BMN_{Txt2}$$

Cost Effectiveness Acceptability Curves (CEACs)

- CEAC is a graphical representation of the quantification of the uncertainty around the expected cost effectiveness.
- It is also the first graphical output from PSA that is understood most easily in the Net Benefit Framework

Chemotherapy for all			Oncotype DX		
QALYs	Costs	NMB	QALYs	Costs	NMB
8.664	£14,813	£245,107	8.937	£16,410	**£251,689**
8.578	£14,587	£242,757	8.729	£14,757	**£247,121**
8.620	£16,172	**£242,428**	9.769	£58,432	£234,623
8.497	£19,583	£235,326	8.622	£16,152	**£242,520**
9.137	£26,555	£247,554	10.516	£51,953	**£263,522**
8.859	£14,319	£251,444	8.968	£14,511	**£254,537**
9.335	£17,943	**£262,107**	10.023	£65,120	£235,570
9.101	£19,845	**£253,176**	10.325	£57,333	£252,416
9.032	£27,397	£243,569	10.779	£65,485	**£257,891**
8.828	£19,556	£245,274	9.649	£37,124	**£252,352**

In this data we can see that there is a **XX**% chance that Oncotype Dx would be cost effective and a **XX** % chance that it would not be, given a cost effectiveness threshold of £30,000 per QALY.

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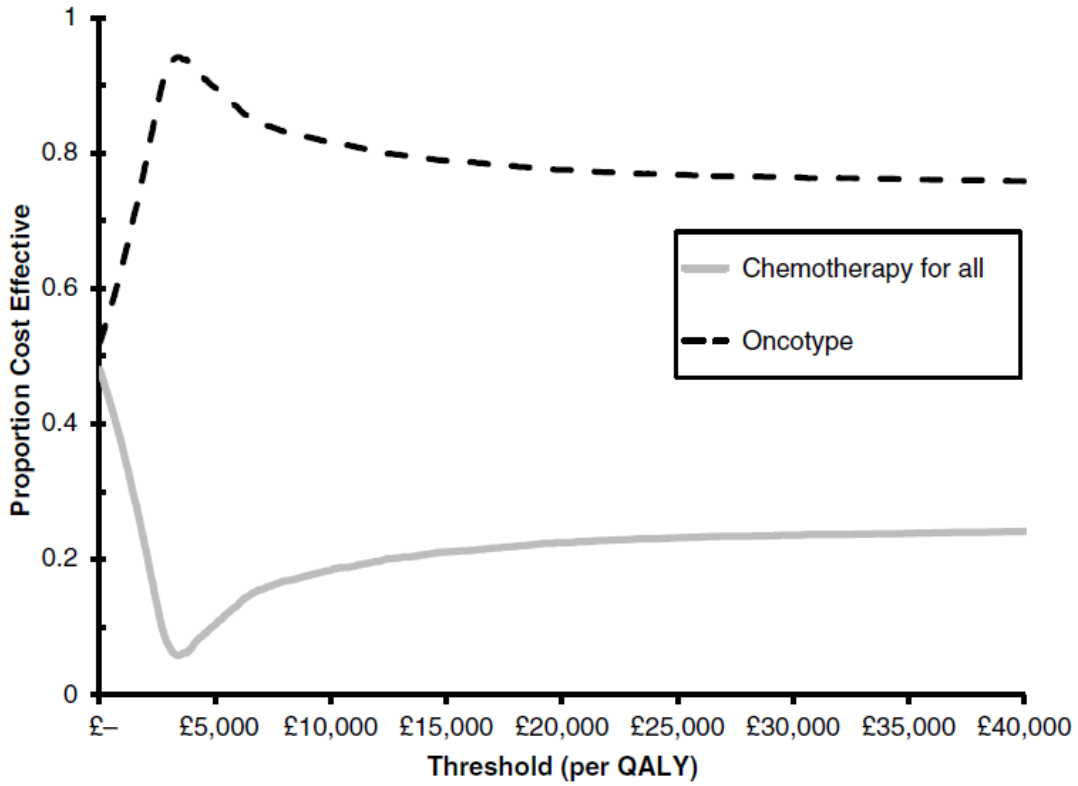
Cost effectiveness acceptability curve



- The CEAC displays this type of information across a range of values for lambda.
- The CEAC is plotted with probability on the vertical axis and willingness to pay (WTP)/cost effectiveness threshold (λ) on the horizontal axis.
- For each value of lambda (λ), we calculate the proportion of the simulations for which the intervention has the highest NMB.

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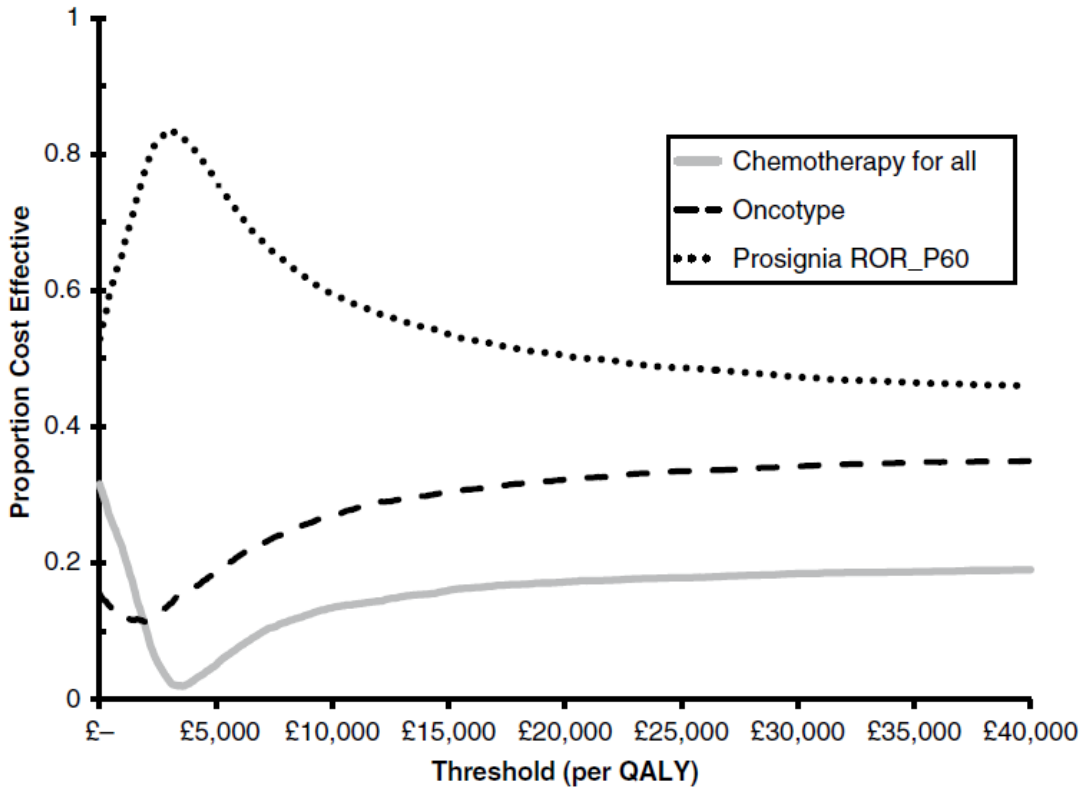
Cost effectiveness acceptability curves for multiple technologies



- Oncotype Dx, Prosignia and chemotherapy for all
- CEAC does not suffer from the same interpretation problems as the scatter plot on the cost effectiveness plane.
- Example for λ = £30,000:
  - P(Prosignia is cost effective) - 47 %
  - 34 % for Oncotype DX-guided therapy
  - 18 % for chemotherapy for all.
- CEACs allow us to clearly differentiate the decision uncertainty regarding each of the comparator technologies and how it varies over a range of values for health.

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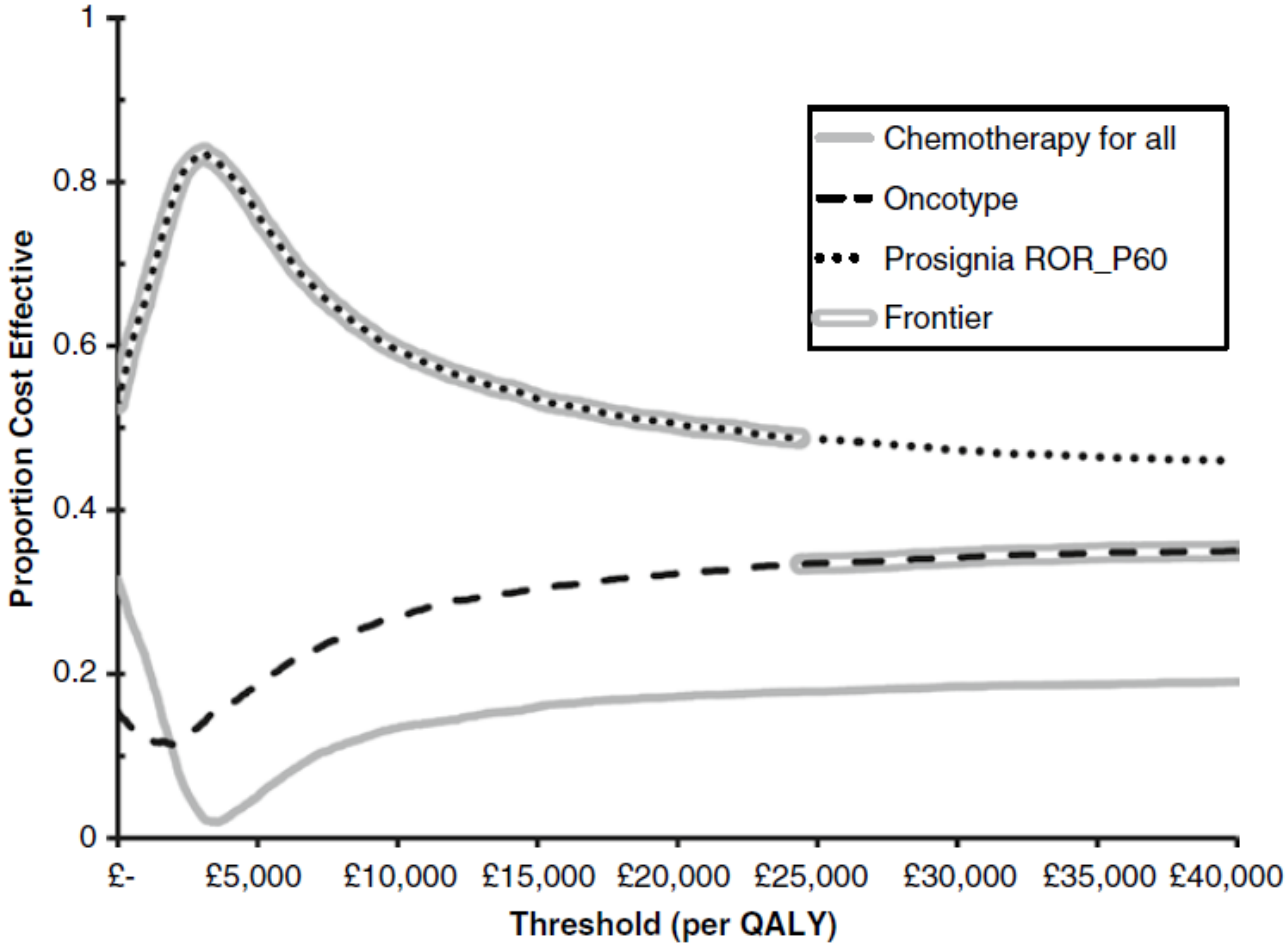
Cost Effectiveness Acceptability Frontiers (CEAFs)

$$\overline{\text{NMB}_2} = \overline{\text{NMB}_1}$$

$$\bar{E}_2\lambda^* - \bar{C}_2 = \bar{E}_1\lambda^* - \bar{C}_1$$

$$\bar{E}_2\lambda^* - \bar{E}_1\lambda^* = \bar{C}_2 - \bar{C}_1$$

$$\lambda^* = \frac{\bar{C}_2 - \bar{C}_1}{\bar{E}_2 - \bar{E}_1} = \text{ICER}$$



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