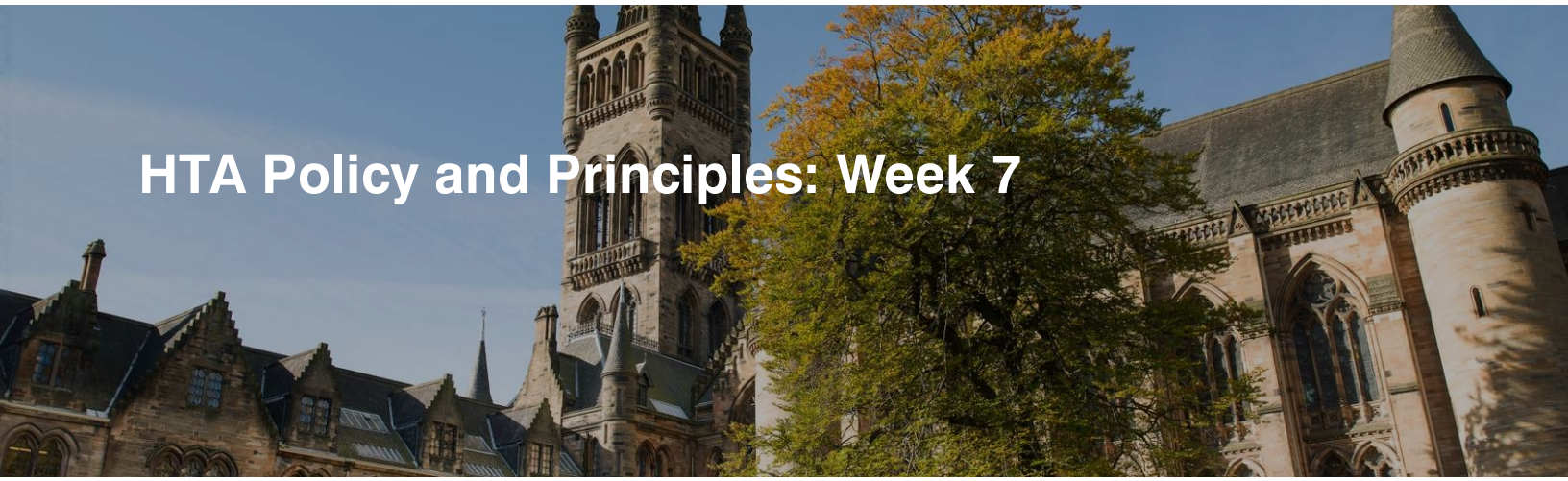


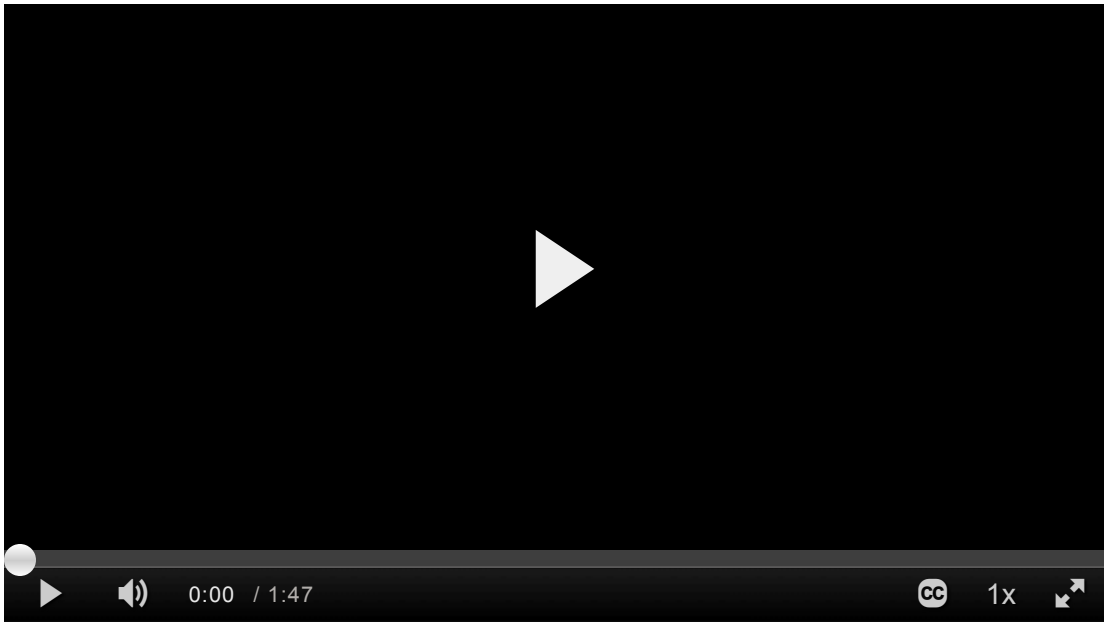
HTA Policy and Principles: Week 7

Frameworks of Decision Making in HTA
Kathleen Boyd

- **Introduction**
- **Session 1: Rationale for Prioritisation & Decision Making**
- **Session 2: Establishing cost-effectiveness and introducing the ceiling ratio or threshold**
- **Session 3: Decision Modelling- overview**
- **Session 4: Implementation: Decision Making in Practice**
- **Resources**

Section 1 of 6

Introduction



Overview

This week's lecture is split into 4 sessions :

- **Session 1: Rational for decision making in HTA & economic analysis**

Introduce the rationale for economic analysis to inform prioritisation and decision making in health care and for HTA. The session will look at cost-effectiveness analysis (the main method of economic

evaluation used to inform decision making) and illustrate how the outcomes of a CEA are most commonly presented as an incremental cost-effectiveness ratio.

- **Session 2: Establishing cost-effectiveness & Introducing the Ceiling Ratio**

The second session will then introduce and discuss decision rules for deciding upon cost-effectiveness.

- **Session 3: Decision Modelling**

The third session will give a brief overview of alternative approaches to decision analytic modelling and when we would se them. It will focus on the commonly used decision tree but provide a summary and links to further details on Markov modelling and discrete event simulation.

- **Session 4: Implementation in Practice**

The fourth session (4) will take a brief look at HTA implementation practices in the UK, giving an overview of the National Institute for Health and Care Excellence (NICE) and Scottish Medicines Consortium (SMC), the approval bodies for new technologies for NHS England and Wales NHS, and NHS Scotland respectively.

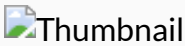
Session 1: Rationale for Prioritisation & Decision Making

Let’s think about the basis for priority setting and decision making in the Health Technology Assessment (HTA). The basic economic problem is that resources are scarce (so we don’t want to waste them), however people and societies have wants and needs which are not limited, and they are infinite. In such a situation, choice is inevitable, so rationing is introduced because we can’t do everything with the given limited resources.

- Finite Resources for Health care

- Increasing Demand for health care
- Demand > Resources = Choices
- Need for Priority Setting

In a health care setting there are limited health care resources (number of nurses, GPs, hospitals etc.) and in publicly provided health settings there are limited financial budgets. The cost of healthcare is also increasing, due both to the labour intensive nature of health care (for example the cost of doctors and nurses), and also the cost of expensive new technologies introduced to the market all the time. Therefore, we have limited healthcare resources and rising healthcare costs, coupled with increasing demand and expectations for healthcare (new technologies, treatments and services emerging on to the market); this leads to the need for priority setting, and particularly where the health care sector is part or fully supported by public funds.



CONTINUE

Here are some approaches to decision making and prioritisation of health care.

Non-economic Approaches

- Historical Allocation
- Decibel / popularity
- Needs assessment
- Burden of disease
- Cost of illness

Historical allocation

The Historical approach – how did we do it last year, and the year before that? Let's use the same budget, or same approach and just do the same again this year!

Decibel/peer pressure approaches

In some cases allocation is based upon whoever shouts the loudest or whichever disease area or illness has the most media attention and appeal!

These two methods are informal, can be misleading and result in unfair, inequitable and inefficient allocation of public money and resources.

However, valid these approaches may seem, they are non-economic approaches and haven't considered efficiency! Information on 'value for money' is still needed to help make decisions on prioritisation fair, transparent and efficient. Economic approaches to decision making are systematic approaches which increase the explicitness and accountability of decision making.

Economic Approaches

Economic approaches can be used to determine value for money for given finite resources, they directly compare alternatives to determine the most desirable solution for equity and efficiency.

Here are three alternative economic approaches to prioritisation.

Economic evaluation

provides a framework to make the best use of clinical information through consideration of both the effects and the health care costs of the available alternatives.

Quality Adjusted Life Years (QALY) league tables

are another economic approach for decision making - where interventions are ranked from lowest to highest cost per QALY gained and decision makers choose based upon this given their overall budget. However, there is a problem with this methods as league tables include QALY estimates from a variety of different studies and there is inherent inconsistency in the methods used for the different evaluations, difficulties in transferability of results, the assumption that point estimates of incremental QALY cost-effectiveness ratios determine rankings, and the implication that all interventions in the table are independent alternatives.

Programme Budgeting and Marginal Analysis (PBMA)

are two planning tools that have become accepted as a consistent approach. It is a pragmatic approach to resource allocation that attempts to divide decision making about priorities into a manageable set of activities.

CONTINUE

Independent vs Mutually Exclusive Interventions

It is important to consider the context for a particular prioritisation question within decision making for HTA. We need to distinguish whether the decision is between independent interventions or mutually exclusive interventions when making decision for HTA

Independent interventions

- More than 1 intervention could be adopted
- ICERs for independent options can be compared

Independent interventions are ones in which the feasibility can be assessed without consideration of any others. For example, independent programmes for different diseases or for different patient groups, such as a smoking cessation programme versus a breast screening programme. In this situation, more than one intervention could be adopted. Therefore, you would compare each independent intervention again

the best alternative treatment in that area, this could even be for example a ‘do nothing’ alternative. This decision is relevant if you have a limited overall health care budget so that you have to choose between independent programmes (do we fund the smoking cessation programme or the breast screening programme?), you could use economic evaluation to compare each independent programme against the current practice within that disease area and the option which represents the best value for money would be chosen.

Mutually exclusive interventions

- Only 1 intervention is adopted for the same population
- Use decision rules:
    - Rank in terms of increasing effectiveness
    - Calculate ICERs

Mutually Exclusive choices reflect a situation where only one of two or more programmes designed for the same purpose can be accepted, for example, within the same disease and population group. In mutually exclusive interventions both alternative treatments cannot occur at the same time – so we need to make a choice, e.g., between different radiotherapy doses and durations in colorectal cancer treatment. Only 1 strategy will be adopted for the relevant population. Economic Evaluation is most commonly used to compare interventions which are mutually exclusive

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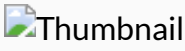
Economic Evaluation

Economic evaluation is the comparative analysis of alternative courses of action in terms of both their costs and their consequences. It is a means of comparing the virtues (benefits) and vices (costs) of different ways of doing things.

Types of economic evaluation

A full economic evaluation must consider both the costs and consequences of an intervention or technology, and also must compare the new technology or intervention to all relevant alternatives. The ‘alternatives’ would typically be current practice or a placebo, but may involve more than one.

There are 3 main types of full economic evaluation

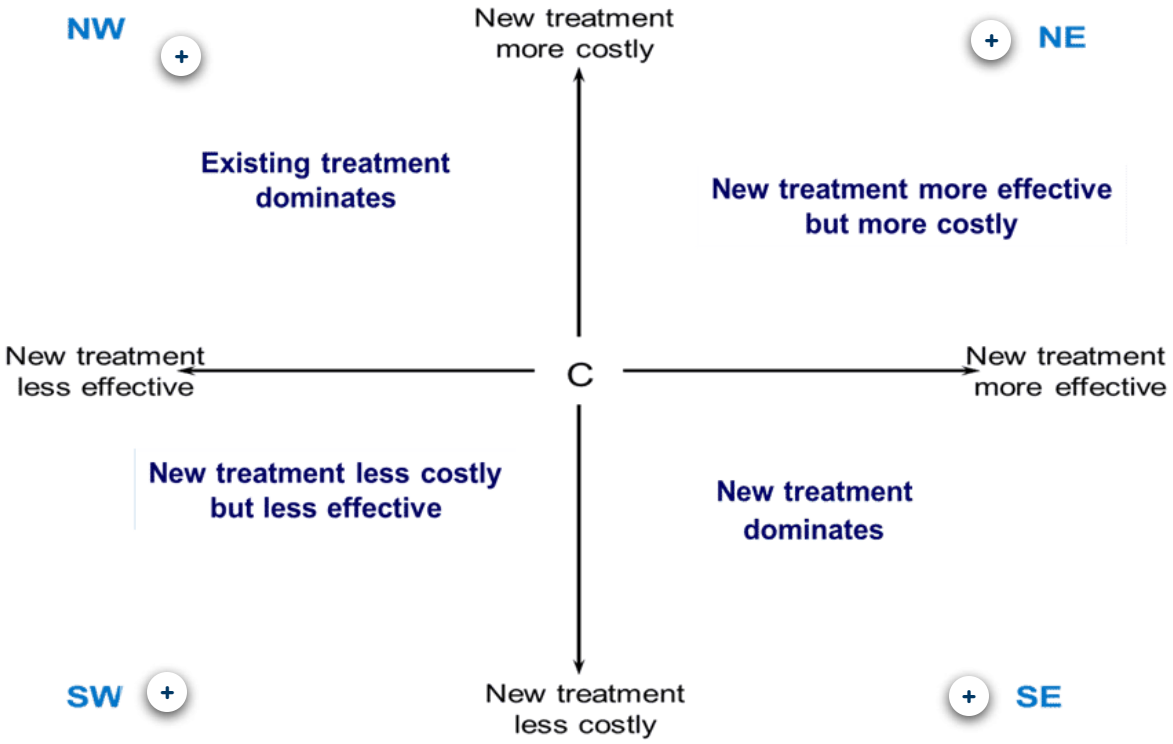


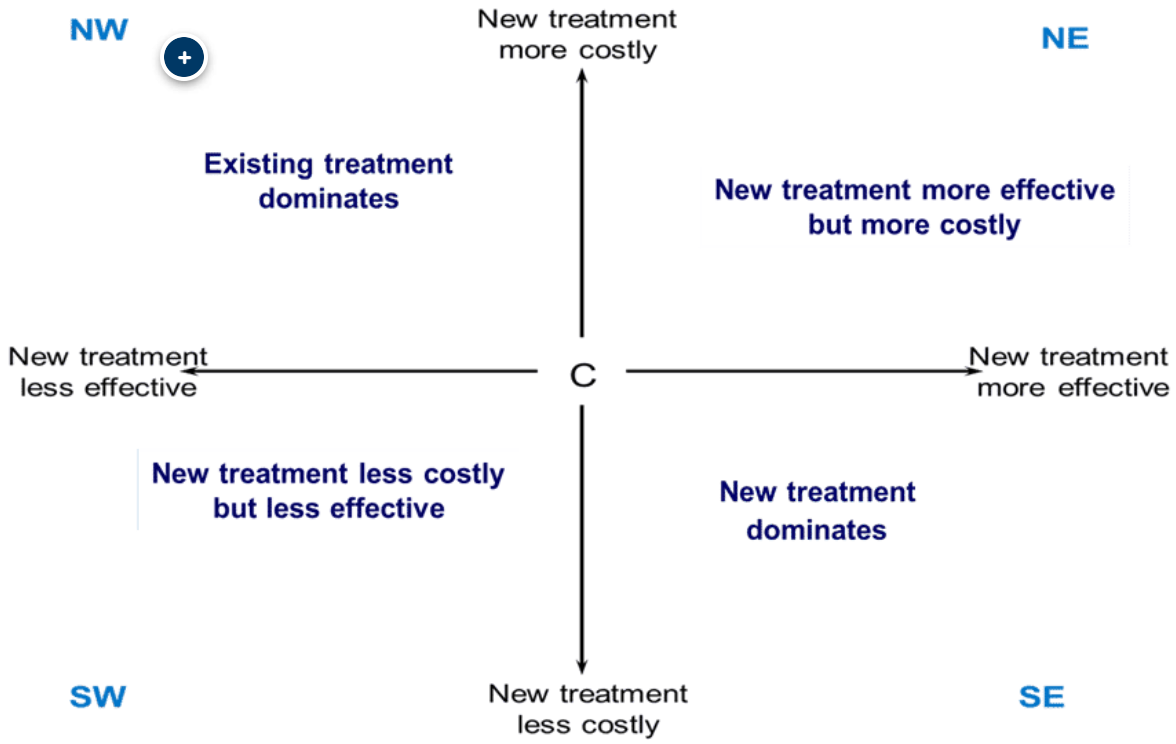
The main reason they differ is in terms of the outcomes. These will be explored in detail in other modules, especially in the Health Economics for HTA module. The key thing to know here is that each of these economic evaluation methods provides a framework for the comparative analysis of costs and ‘outcomes’ to provide the decision maker with evidence on ‘value for money’. **click on each method in the table to find out a little more about them**

Incremental cost-effectiveness plane

The cost-effectiveness plane is often used to illustrate outcomes from a cost-effectiveness analysis. We are interested in the incremental costs and effects of a new treatment compared to an existing comparator treatment. In comparison to the existing treatment, the new treatment may be more or less costly and more or less effective.

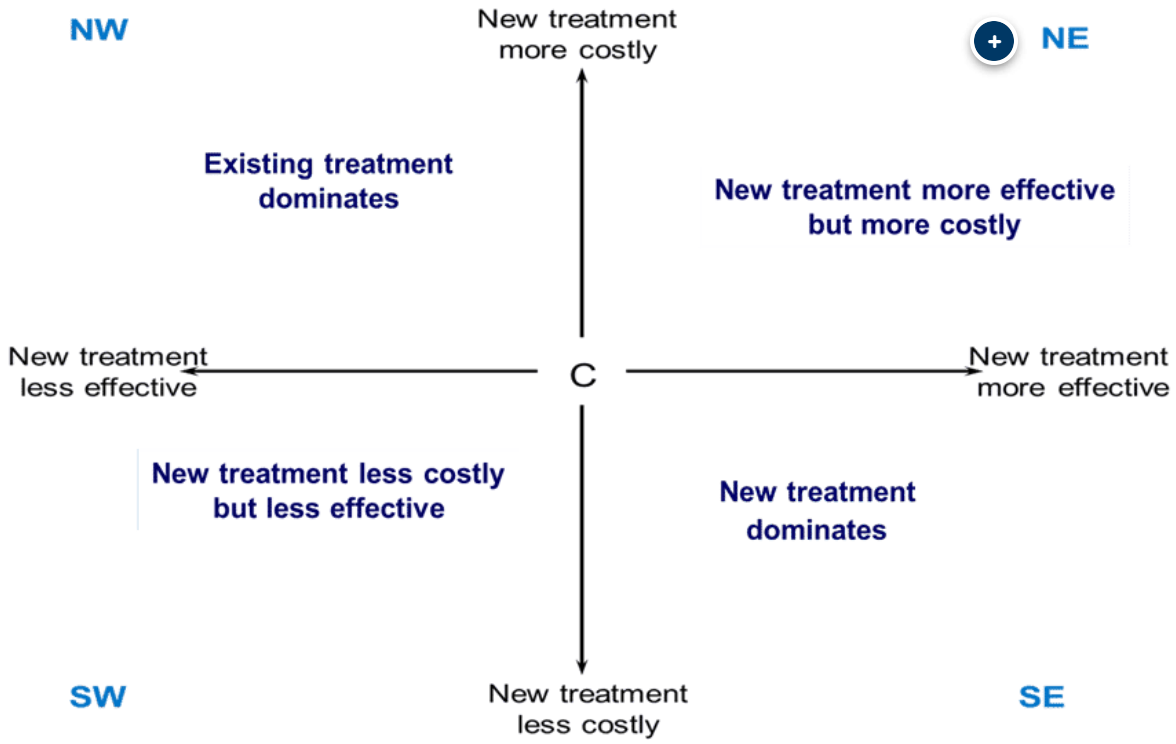
The incremental cost-effectiveness plane illustrates the difference in effectiveness (Intervention minus Control) per patient on the horizontal axis against the difference in cost per patient (Intervention minus Control) on the vertical axis and can then be used to help decision-making regarding cost-effectiveness (Figure 1).





North West (NW) quadrant:

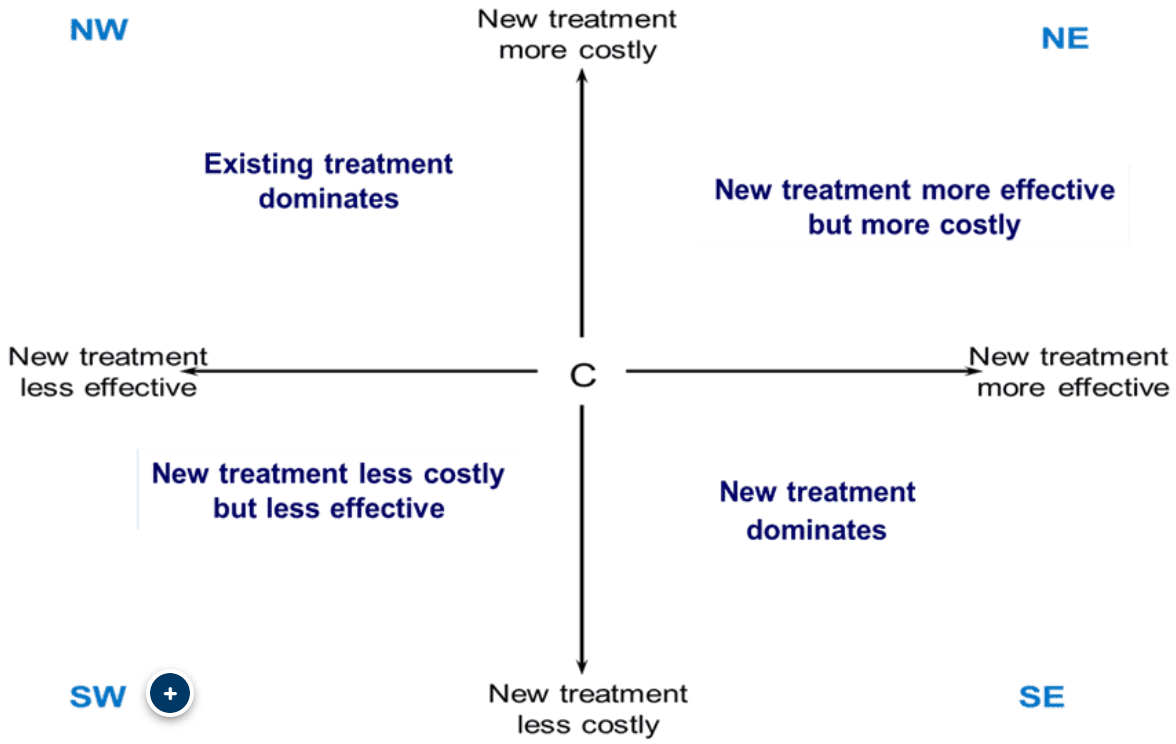
If the cost-effectiveness estimates fall into the North West (NW) quadrant, this demonstrates that the new intervention is less effective than the control, but costs more, and is therefore dominated by the control. In this case the decision about cost-effectiveness is straightforward, we reject the new treatment and adopt the control/old treatment.



North East (NE) or South West (SW):

If the outcomes fall into either the North East (NE) or South West (SW) quadrants this represents a situation where a trade-off is required, as we may have improved effectiveness but at a greater cost in the NE quadrant, or a cost saving but at the expense of reduced effectiveness in the SW quadrant.

In the north east and south west quadrants we need to calculate an ICER, the incremental cost-effectiveness ratio, and apply decision rules regarding cost-effectiveness.



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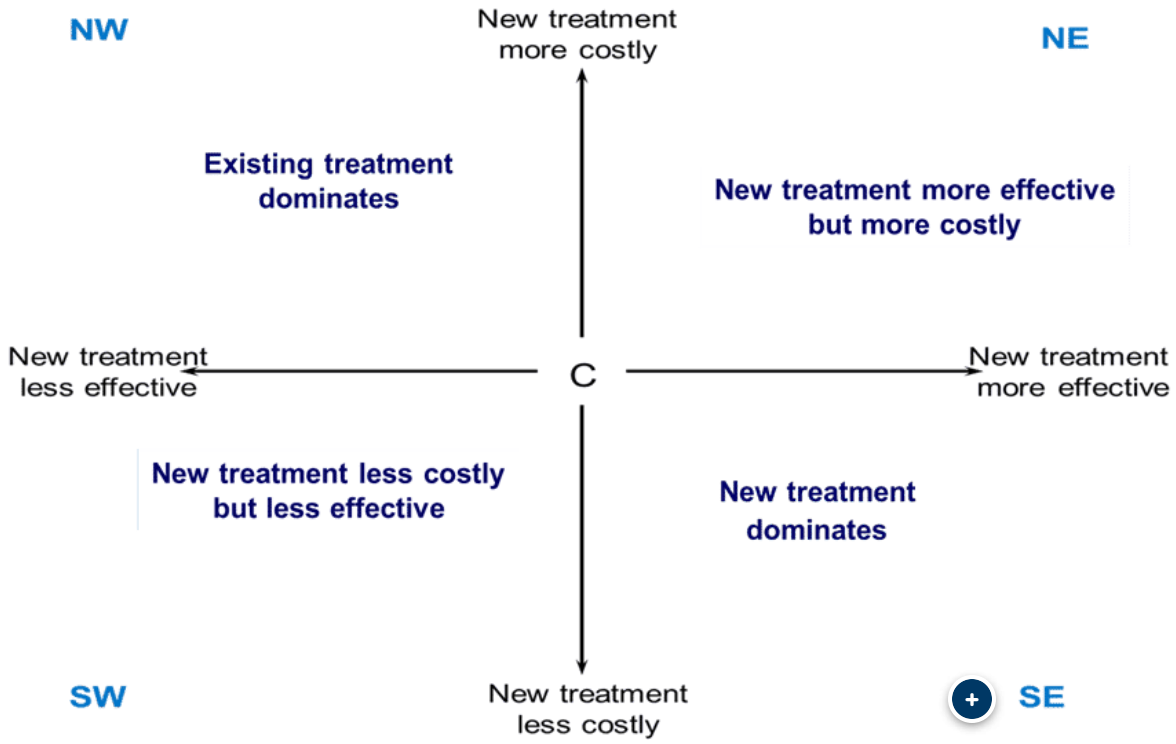


South East (SE) quadrant:

Alternatively if the outcomes fall into the South East (SE) quadrant, this represents improved effectiveness with the new intervention, yet it is also cost saving, and therefore the new intervention is the cost-effective strategy and it dominates the Control. Here the decision is also straightforward: the new intervention dominates the comparator and therefore we adopt the new intervention.

Figure 1

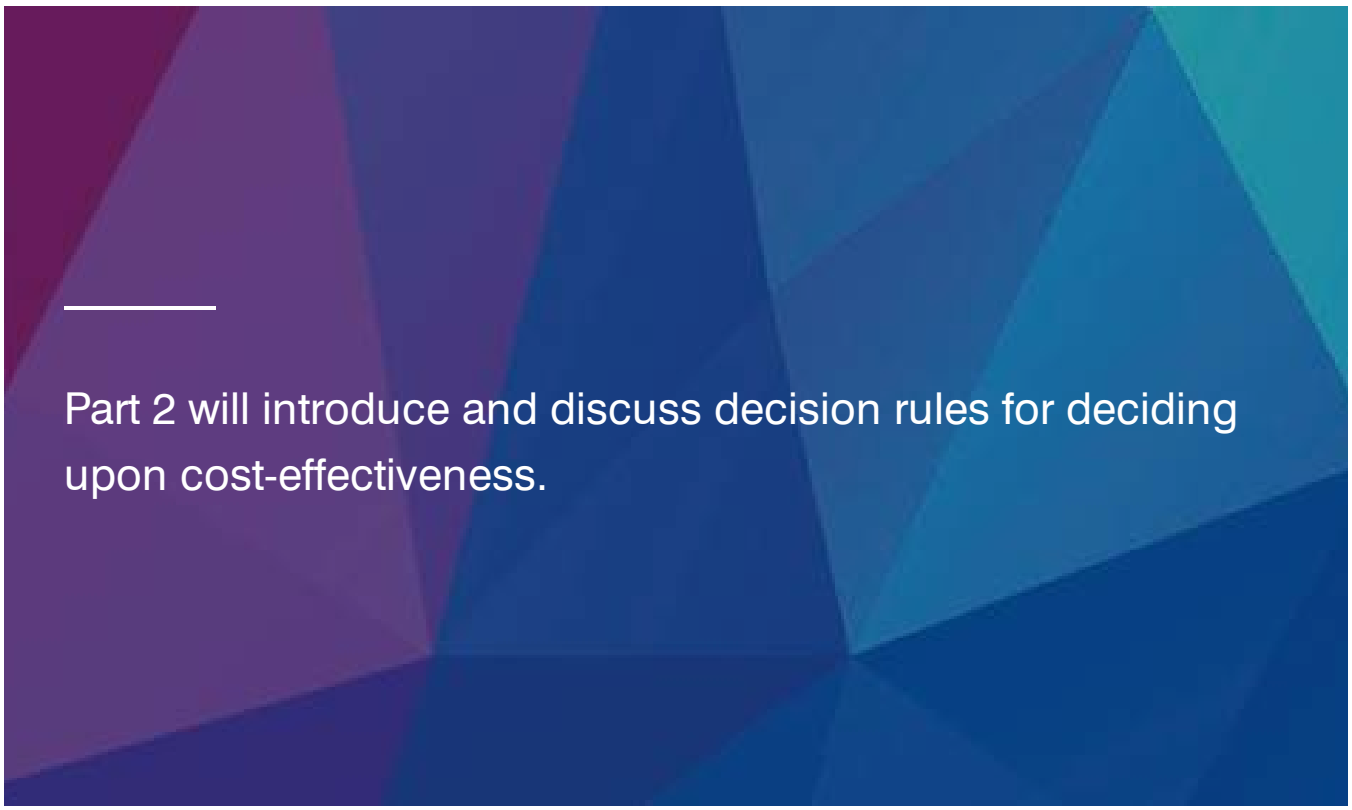
Ceiling Ratio/ willingness to Pay for cost-effectiveness

So what if the results from a cost-effectiveness analysis fall into north east quadrant? How do we decide if a specific ICER value is cost-effective or not?

It is left to the decision maker to decide if spending the amount implied by the ICER to reach the next most expensive alternative is worthwhile.

The analyst doesn't put a value on the ICER, it is up to the decision maker or society to set this value, either implicitly or explicitly.

Decision makers can set a value to reflect societies' 'willingness-to-pay' for an ICER and if they do so this is known as the 'ceiling ratio' or 'maximum threshold'.



Session 2: Establishing cost-effectiveness and introducing the ceiling ratio or threshold

In part 1 we finished off thinking about the ICER outcome from a cost-effectiveness analysis. In this session we will explore how decision makers decide if the ICER is acceptable to them. What are the decision rules for deciding upon cost-effectiveness?

To determine cost-effectiveness we need a value to reflect our or societies' 'willingness-to-pay' for an ICER, this is known as the 'ceiling ratio' or 'maximum threshold'.

What is an appropriate threshold?

How do we decide if spending the amount implied by the ICER is worthwhile?

Consider this hypothetical example of a cost-effectiveness analysis of diagnostic tools for cancer screening. Take a moment to look through the table and outcomes from a cost-effectiveness analysis.

Diagnostic tool	Cost	QALYs
MRI scan + CT scan	£15,151	9.42
MRI scan + CT scan + PET/CT scan	£17,418	9.43

Diagnostic tool	Cost	QALYs
Difference	£2,267	0.01
Incremental Cost Effectiveness Ratio (ICER)	£226,700 per QALY	

The addition of the PET/CT scan costs an extra £2,267 per person with a QALY gain of 0.01 leading to an ICER of greater than £ 226,700 per QALY.

Is this acceptable? How do we know? Should the analyst make this decision on whether £431,000/QALY is cost-effective or not?

What are we willing to pay per QALY? 1,000? 100,000?

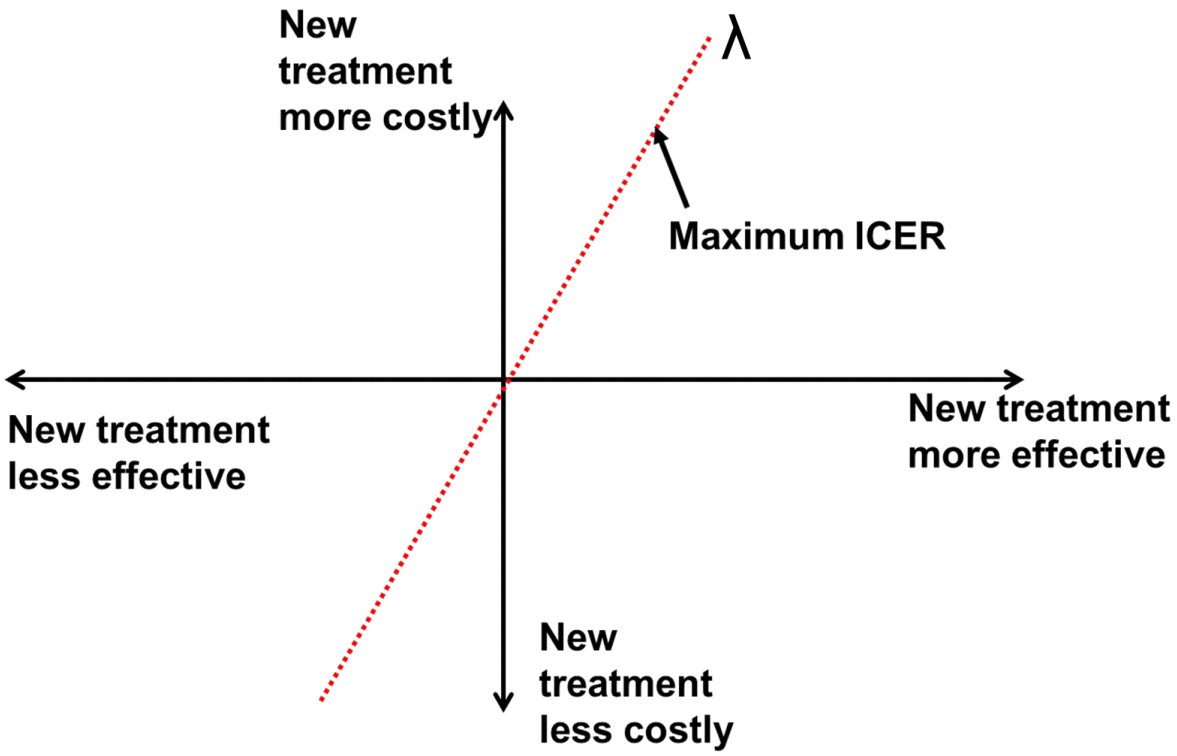
Celling ratio and cost-effectiveness plane

Now let's look at how this would be represented on the cost-effectiveness plane.

Celling ratio for cost-effectiveness

The figure below illustrates what setting such a threshold could look like on the cost-effectiveness plane.

If we set a maximum threshold for which we are willing-to-pay for an ICER, this can be represented by the symbol lambda (λ) which is the red dotted line on the cost-effectiveness plane.



Below such a threshold a new treatment may be deemed cost-effective (anything which falls to the right of the red dotted line on the slide). Above such a threshold is considered unacceptable (any treatment with an ICER which falls to the left of the red dotted line).

This maximum ICER threshold (which is also often referred to as a ceiling ratio) is of use when the incremental costs and effects fall in the NE and SW quadrants of the CE plane, where the new treatment is not dominated or dominant and we need to make a decision regarding cost-effectiveness.

If we can obtain an estimate of the maximum willingness to pay by decision-makers for an additional unit of effect then we can use this ceiling ratio to make this trade-off. We can represent this decision rule on the CE plane by a line passing through the origin with positive slope equal to the ceiling ratio.

The analyst doesn't make the decision on cost-effectiveness, it is up to the decision maker or society to set this value, either implicitly or explicitly.

UK cost-effectiveness decision threshold

The analyst doesn't put a value on the ICER, it is up to the decision maker or society to set this value, either implicitly or explicitly. It is left to the decision maker to decide if spending the amount implied by the ICER to reach the next most expensive alternative is worthwhile.

The threshold can be set either explicitly by an HTA agency or decision making body, or it may be implicitly applied with no formal statement on a hard cut-off value.

National Institute for Health & Care Excellence (NICE): £20,000 – £30,000 / QALY

$$\text{ICER} : \frac{\text{Cost}_A - \text{Cost}_B}{\text{Effect}_A - \text{Effect}_B} \leq £20{,}000 \quad \text{per QALY}$$

Currently in the UK the National Institute for Health and Care Excellence (NICE) uses a threshold range of £20,000–30,000 per QALY gained, and this has remained the case in the NICE methods guidance since 2004. Interventions with an ICER greater than £30,000/QALY are deemed not cost-effective and won't be available on the NHS. Those between £20-£30,000/QALY are considered potentially cost-effective, and those under £20,000/QALY are cost-effective and will likely to accepted for use in NHS.

The NICE methods manual is available at this link for further reference

Many countries such as the UK set such a value explicitly so that pharmaceuticals and service providers know outright that their products, treatments and technologies must reach this cost-effectiveness threshold if they want to be available on the NHS, while other countries use a range or don't explicitly set any limit, yet they may still use one implicitly.

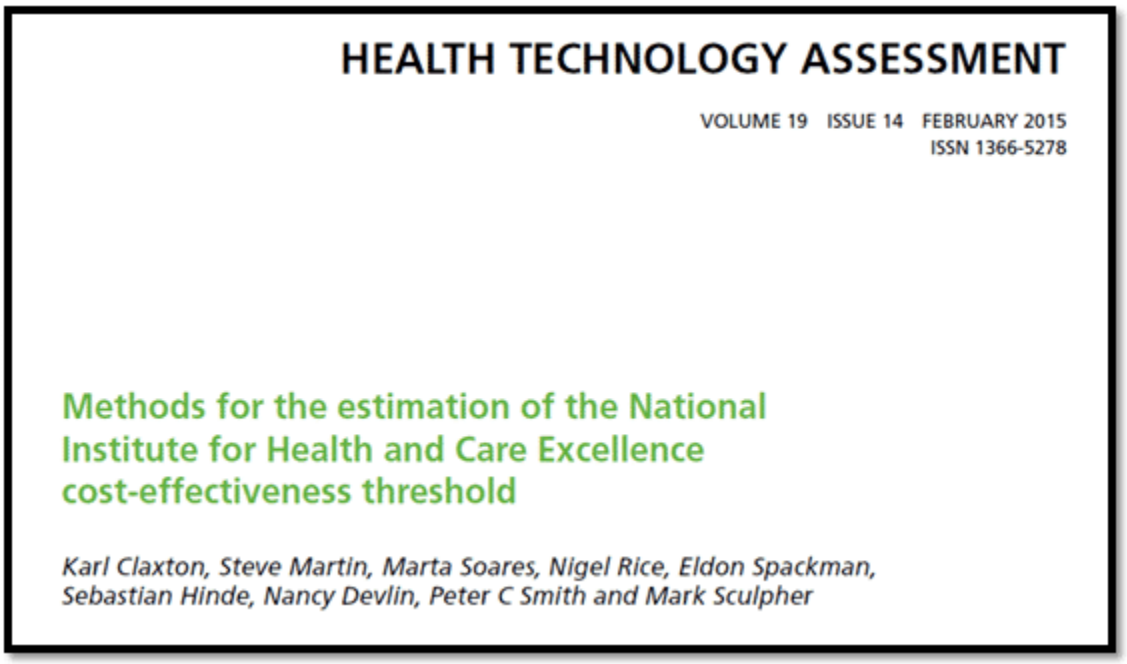
In recent years there have been a number of calls for further research on how the UK value is set and the actual value itself. At the end of this session I have provided some further reading on this for you to consider and reflect upon.

CONTINUE

Some examples of Decision Rules

UK: NICE £20,000-30,000 of threshold is not based on empirical evidence

Research has shown that the NICE threshold has been set on a case history basis rather than on a transparent empirical evidence and this has led to some controversy and methodological discussion on how it could/should be set. Claxton et al. 2015 estimated the most relevant 'central' threshold to be £12,936 per QALY for UK context.



Available online at: https://www.journalslibrary.nihr.ac.uk/hta/hta19140/

However, it is not just the threshold alone that is taken into consideration for decision making in practice. There are many other factors that decision making bodies take into consideration alongside the ceiling ratio.

For example NICE decision committees will consider uncertainty in the cost-effectiveness analysis, equity issues related to the patient population of interest, social value judgements, ethical issues. Therefore, although the ceiling ratio is set at £20,000 - £30,000 per QALY in the UK this is one of multiple factors which will be discussed in the decision making process. More detail on these issues will be discussed in your other lectures for this course.

Beyond the UK

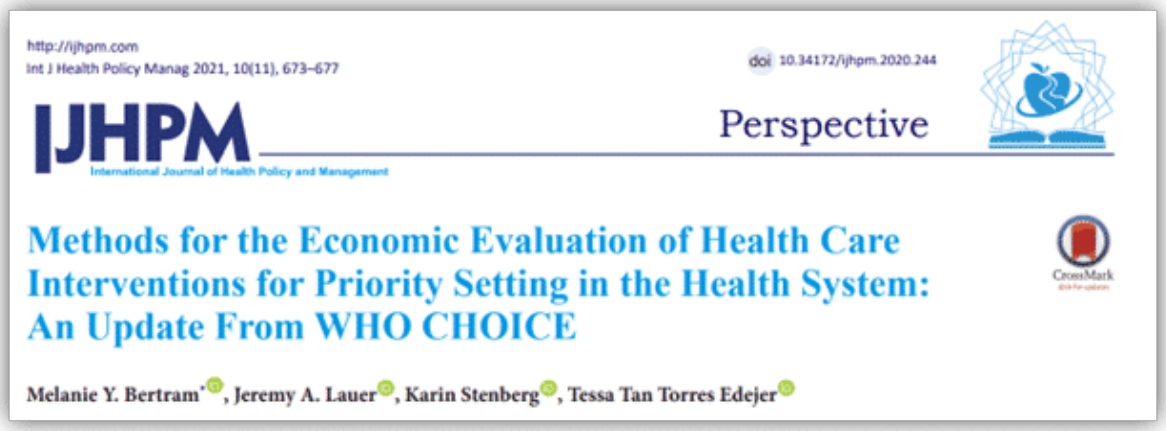
In the low and middle income country context, the World Health Organisation WHO (WHO-CHOICE) recommended that a per capita Gross domestic product (GDP) should be used to indicate the ceiling ratio. This was the method for many years but has recently changed:

WHO GDP thresholds:

- Highly cost-effective (< GDP per capita)
- Cost-effective (1 to 3 times GDP)
- Not cost-effective (> times GDP per capita)

The WHO have issued guidance to stipulate that an intervention will be considered highly cost-effective if the ICER is less than per capita GDP, cost-effective if it is between 1-3 times per capita GDP, and not cost-effective if greater than 3 times per capita GDP.

In 2021 the WHO CHOICE program has changed the recommendation due to criticism and debate in the literature on the GDP approach. The WHO-CHOICE GDP thresholds set such a low celling ration (e.g. for a country with very low GDP per capita) for cost-effectiveness that very few interventions with evidence of efficacy could be ruled out. WHO CHOICE now recommend using league tables and no threshold is used to define interventions as cost-effective or not. The current recommendation of WHO CHOICE threshold is detailed in paper below,



Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9278384/

Many countries including some low and middle income group have their own threshold or ceiling ratio. For example, Thailand (an upper middle income country) has a threshold 160,000 Baht (~$5000) per QALY, as set by the Thai government in 2013.

CONTINUE

Methods which can be used for setting a ceiling ratio or decision threshold

Let's take a look at the various methods which can be used for setting a ceiling ratio or decision threshold. There are six key approaches in determining the threshold or ceiling ratio.

Determining the critical ratio/ceiling ratio: Six approaches (from Weinstein, 1995):

- Rules of thumb
- Shadow price of an explicit budget constraint
- Opportunity cost
- Comparison with other health care interventions
- Inference from previous decisions
- Cost-benefit methods

You can read more in-depth about these methods from the indicated reading at the end of this session

Let's have a quick overview of the two key methods – rule of thumb and shadow price of a budget constraint.

Rules of thumb

is an easily applied means of determining a value, however, it is not based on theory but rather on practical experience, for example, what was done in previous years. Therefore, there are many criticisms of this approach as it has no empirical basis.

Criticisms of rules of thumb:

- Completely arbitrary
  - CAN $20,000-CAN$100,000 (Laupacis et al, 1992)
  - US $20,000-US$100,000 (Kaplan & Bush, 1981)

- Will lead to growth in expenditure
- Fixed price per QALY violates welfare economic theory

Shadow price of a budget constraint

used to rank interventions in terms of increasing cost per QALY. This introduce interventions down the list until the available funds are exhausted. The ceiling ratio is then equivalent to the point where the budget runs out.
"Procedures should be ranked so that activities that generate more gains to health for every £ spent of resources take priority over those that generate less"

QALY league table

Table 2 below presents an example of a QALY league table of interventions with their cost per QALY gain (ICER), listed from lowest to highest. So, if we are given an explicit set budget constraint you would introduce interventions down this list until the available funds are exhausted.

Table 2. QALY league table with total cost

Intervention	ICER	ANNUAL COST (£'000)	TOTAL COST (£'000)
A	100	45	45
B	200	80	125
C	450	25	150
D	700	100	250
E	900	40	290
F	1,200	600	890
G	2,500	30	920
H	4,000	400	1,320
I	4,600	180	1,500
J	4,900	10	1,510
K	6,200	45	1,555
L	7,400	600	2,155
M	8,800	800	2,955
N	12,000	400	3,355
O	16,000	150	3,505
P	23,000	20	3,525

Maximum acceptable ICER = £8,800

Budget constraint = £3 million

Issues with using League tables

One of the major issues with using a league table approach to deciding upon a ceiling ratio is that within a QALY league table we are implicitly assuming we are comparing like with like. However, most of the time in healthcare this assumption may not be true and we end up making inappropriate comparison. Each of the ICER values in a league table are likely to have come from different studies, with different comparators, populations etc, and therefore we end up in this way making inconsistent choices.

The third session will give a brief overview of alternative approaches to decision analytic modelling and when we would se them. It will focus on the commonly used decision tree but provide a summary and links to further details on Markov modelling and discrete event simulation.

Session 3: Decision Modelling- overview

In the last session we considered decision rules for establishing whether an ICER can be considered to be cost-effective or not – determining the ceiling ratio.

This session will now look at approaches to decision analytic modelling. We will consider various reasons for decision modelling and then look at the different types of decision models, focusing in detail

on the commonly used decision tree. We will also provide a brief overview of Markov models and their key features and a brief summary of another type of model, discrete event simulations.

The objective of this session is to provide you with some insight into decision modelling methods, it is not intended as an in-depth session on decision modelling. Some of the other online modules available, such as 'Decision Analytic Modelling and early HTA' will take a much deeper more detailed look at these techniques.

What is decision analytic modelling and why do we undertake it?

A decision-analytic model is a mathematical system which provide a framework for compiling clinical and economic evidence in a systematic fashion – under conditions of uncertainty. It is used in HTA to determine a health technologies value, and communicate that value to decision makers. Decision analysis is a systematic approach to decision making under conditions of uncertainty!

How and why do we undertake them?

As part of a clinical trial to overcome trial limitations

- **Limited data (follow-up inadequate)**

Decision models are often undertaken as part of an economic evaluation alongside a clinical trial. The clinical trial information is often used for economic analysis, however, they have some limitations which can be overcome by the use of decision modelling. A decision model can be used to represent and model the trial pathway, and also they are often used to extrapolate the analysis beyond the trial time horizon.
Trials have truncated / short time horizons as it is extremely expensive to have long trial follow-up and even very well-funded trials will likely be limited to a maximum of three to five years follow-up.
Economic analysis often requires a lifetime time horizon, so again decision models are used to extrapolate beyond the trial.

- **Limited comparators**

Some other clinical trial limitations include failure to compare all relevant options (they are often focused on establishing efficacy of one new technology in comparison to a control), whereas it may be appropriate for the economic analysis to include numerous alternative technologies.
Lack of relevance to the decision context, failure to incorporate all evidence, and inadequate quantification of uncertainty are also limitations of clinical trials which can be dealt with in decision models.

As a stand alone Decision analytic modelling

- **Based purely on existing 'secondary' data**

Decision modelling can also be employed to undertake an economic analysis purely based on previously published, currently existing evidence as opposed to based on a single clinical trial.
Systematic literature reviews can be undertaken to help the design of the model and to inform the various parameters for the decision model. In this fashion decision models are a systematic approach to synthesising data from numerous sources.

As a combination - synthesising key trial evidence with other sources

- Specific trial info synthesised with wider evidence base
- Role of trial is complimentary

Throughout the 1980's the stand alone model based evaluation was often the approach taken for economic analyses, and then in the 1990's it became popular to undertake economic analyses based solely alongside a clinical trial. These days it is more widely recognised that it is more appropriate to utilise prospective trial information supported by a wider secondary evidence to provide a more robust analysis. Sculpher et al. 2006 have an interesting article discussing this in more detail:
Sculpher, M. 2006. Whither trial-based economic evaluation for health care decision making? Health Economics , 2006; 15:7; pp 677–687. Available at: *https://pubmed.ncbi.nlm.nih.gov/16491461/*

Therefore these days the role of a trial is seen as complementary to an economic model, providing data inputs which can also be synthesised with external secondary data.

CONTINUE

Decision models

Decision models are mathematical systems which aim to provide a simplified version of reality. They can be as simple or as complex as required without losing credibility. A simple model may well be more fit for purpose and more credible than a complex model with many parts and features.

The first paper plane picture is simple, yet much more accurate and is clearly defined.

The more complex paper plane which has additional features, yet is less accurate/defined

---

Decision analysis is a systematic approach to decision making under conditions of uncertainty. It involves 4 key steps:

1 Identifying and bounding the decision problem

2 Structuring the decision problem over time

3 Characterising the information needed

4 Choosing a preferred course of action

The key requirements of a decision model are that it is a mathematical prediction of health-related events, where we usually compare mutually exclusive interventions for a particular patient group. The events have cost and health implications. In the modelling process data is synthesized from various sources. There is uncertainty in data inputs used in the model, which can be formally addressed in the model. The decision model should incorporate all the clinically and economic important aspects in order to address the question at hand and enable appropriate decision making.

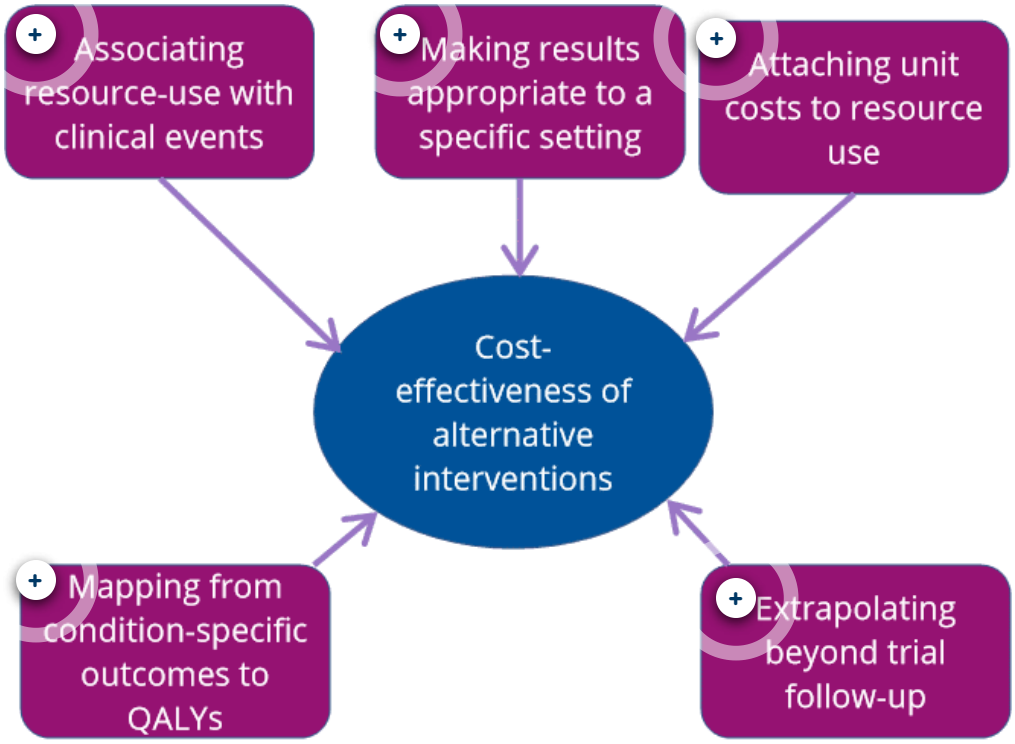
Decision models

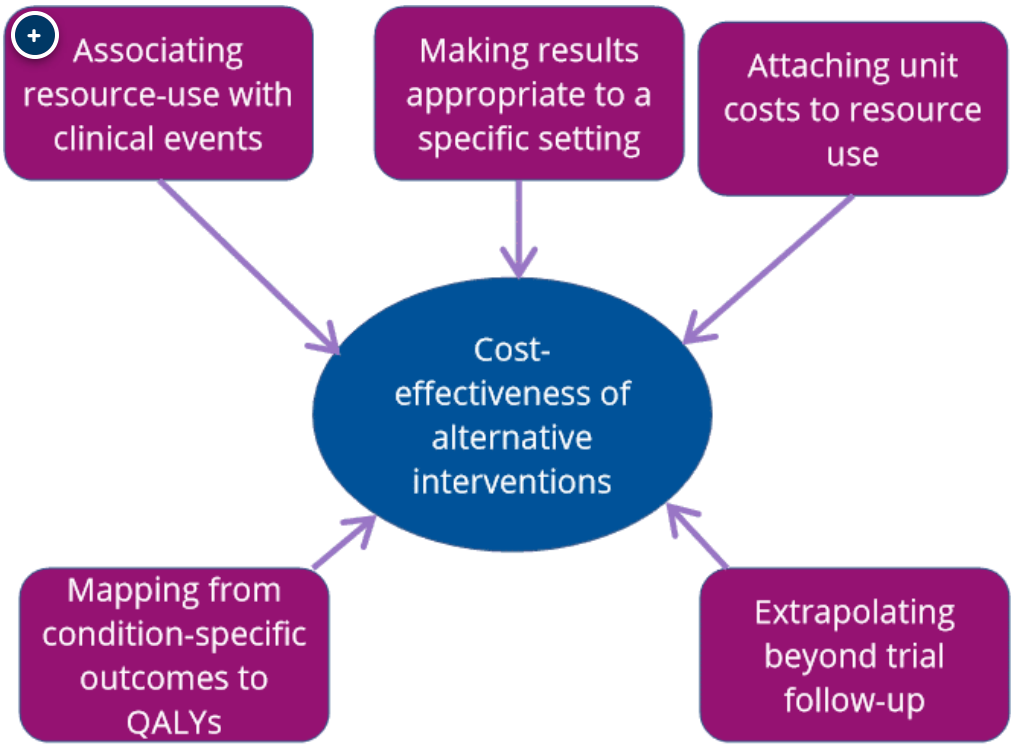
- Simplified versions of reality
- Mathematical prediction of health-related events
- Events have cost and health implications
- Data is synthesized from various sources
- Uncertainty in data inputs
- Focus on appropriate decision

Evidence synthesis for decision modelling

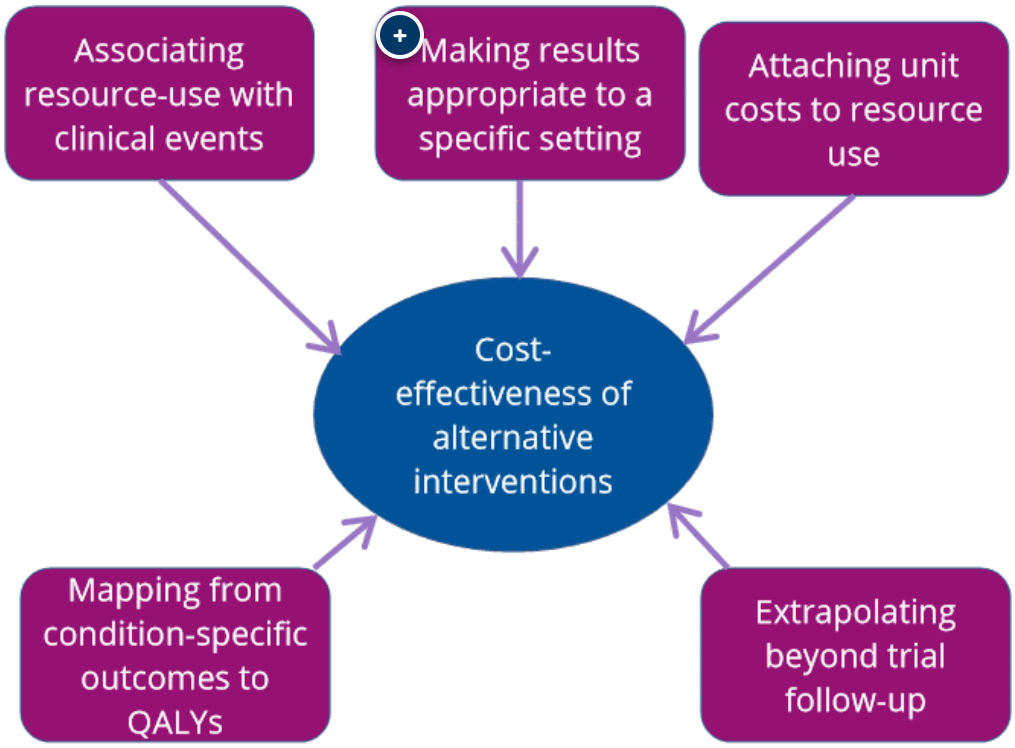
A decision model will syntheses evidence from a variety of sources, and undertake 5 key processes as depicted in the graph illustrated in figure below.

Five key processes for evidence syntheses for decision model

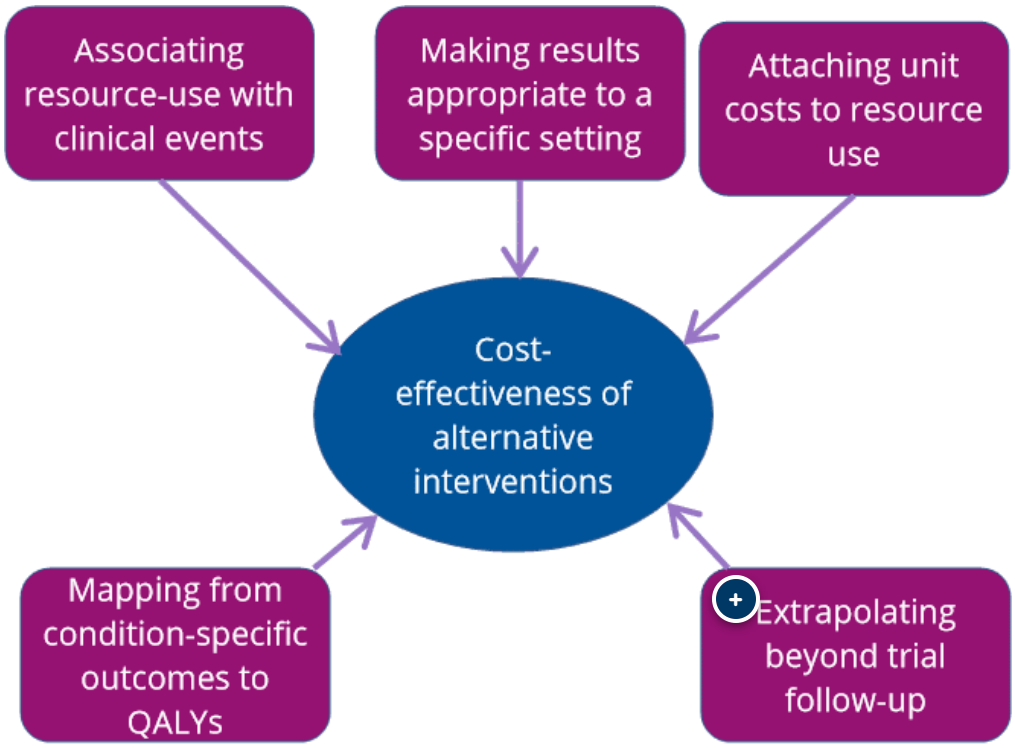




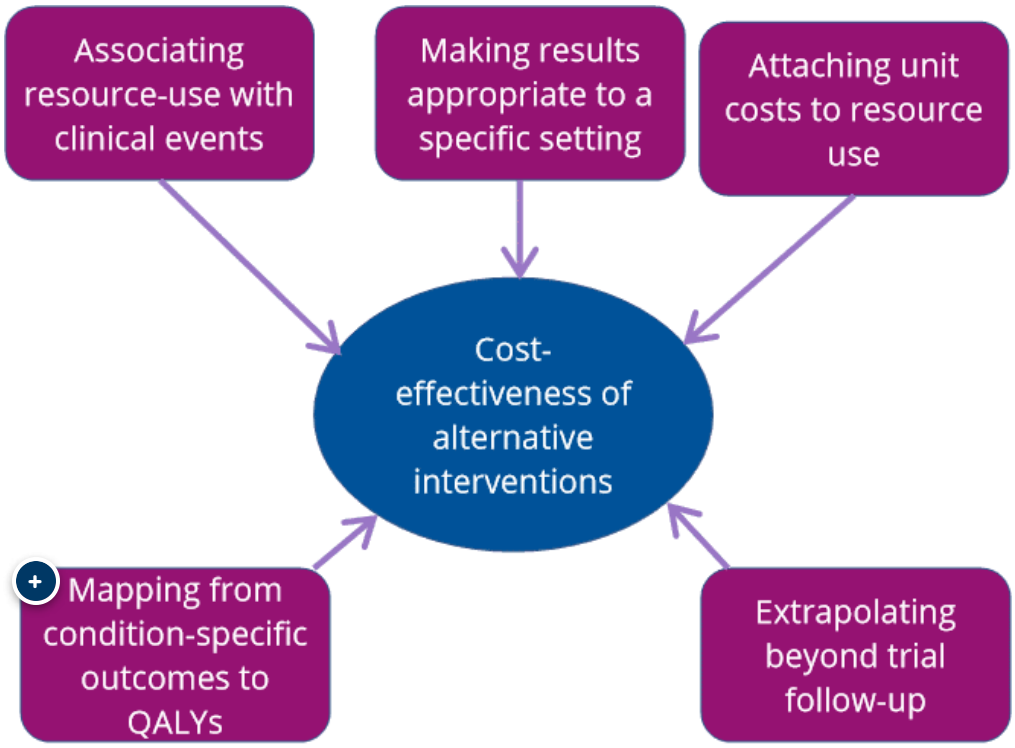
Synthesise data on resource use associated with clinical events



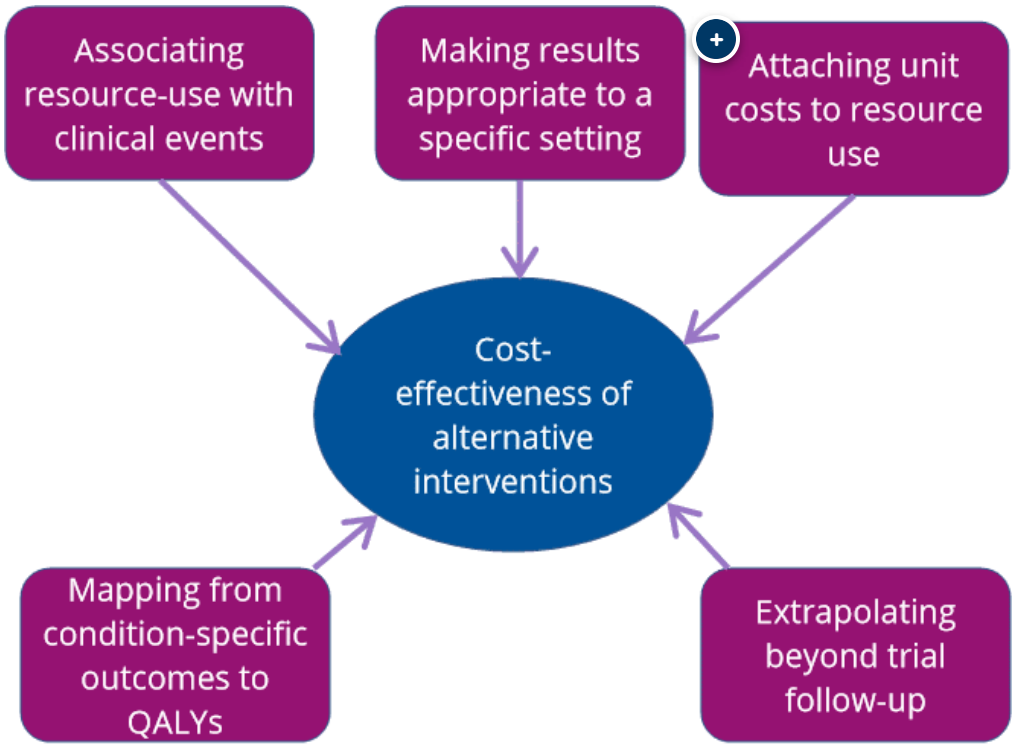
Make results appropriate to specific settings.



extrapolate data into the long term to calculate outcomes over a lifetime time horizon



It will utilise evidence on quality of life and utilities and synthesise this with outcome and life expectancy data to calculate QALYs,



Synthesise data on resource use associated with clinical events and combine this with unit cost information to calculate costs.

CONTINUE

Here are 3 types of commonly used decision modelling methods.

- Decision trees
- Markov models
- Discrete Event simulations

The most commonly used are decision trees and Markov models. We will discuss each of these in turn, focusing on decision tress, with some summary description for the other two and links to additional reading. The '*Decision Modelling and Early HTA*' module will cover the different modelling methods in more detail.

CONTINUE

The decision tree

So how do we go about constructing and analysing a decision tree? The name indicates it involves drawing trees, but how do we draw them?

1. Structure the tree
2. Estimate probabilities
3. Estimate payoffs
4. Analyse the tree
5. Verify the tree
6. Explore uncertainty

We need to identify the alternatives (e.g. the comparator), and the information required. Then establish a logical and temporal sequence of events, including in this the choices to be made, any probabilistic events and resulting outcomes. We then characterise the uncertainties, and valued outcomes. Finally

synthesis the structure, solve the problem and undertake sensitivity analysis. Depending on what text you read they may be some variation on the steps.

Decision tree construction: A decision tree is made up of nodes, branches and leaves

Nodes

- Decision nodes are represented by squares
- Chance nodes are represented by circles
- First node is the decision tree's root

There are three types of nodes:

- decision node – represents a decision being made
- chance node – reflects the probability of events
- terminal node – represents the outcome or payoff.

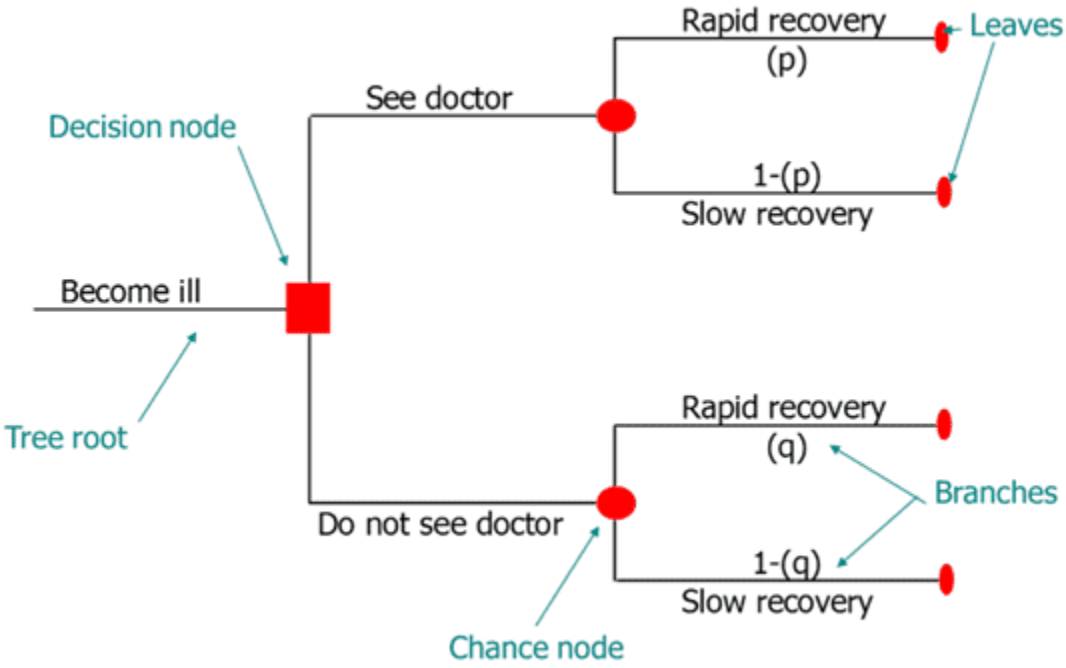
Branches

Interconnect the decision and chance nodes

Leaves

Outcomes (sometimes called terminal nodes)

The Figure below shows a simple example of decision tree. The red box (a decision node) depicts the first decision: do you see a doctor or not, then given your decision the next is a chance node (red circle), reflecting the chance of either rapid or slow recovery. The chance or probability of recovery associated here will depend on whether or not you saw a doctor.



Desicion Tree

Generally decision nodes are represented by square boxes and chance nodes by circles.

Terminal nodes, can be anything, e.g., triangles, open rectangles or leaves (like in Figure). As the name reflects, the terminal nodes signifies the end point of the decision tree.

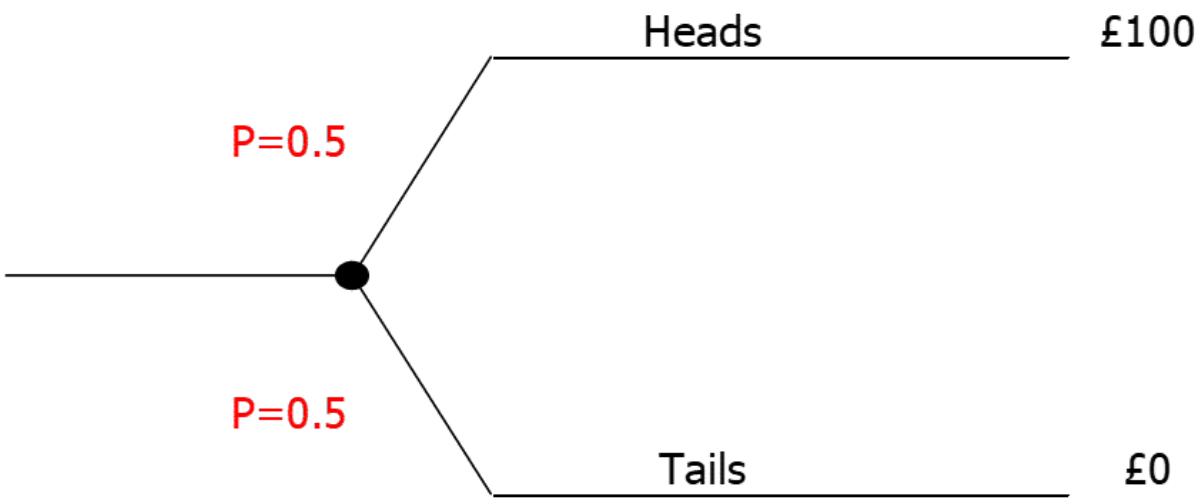
How do we solve a decision tree?

This is a relatively simple process. The process is always the same no matter how complex the tree is. We work from backwards, from right to left pruning the tree back from the terminal node back to a decision node. The aim is to maximise the expected value.

We will consider how to prune in a moment, but first let's discuss expected value.

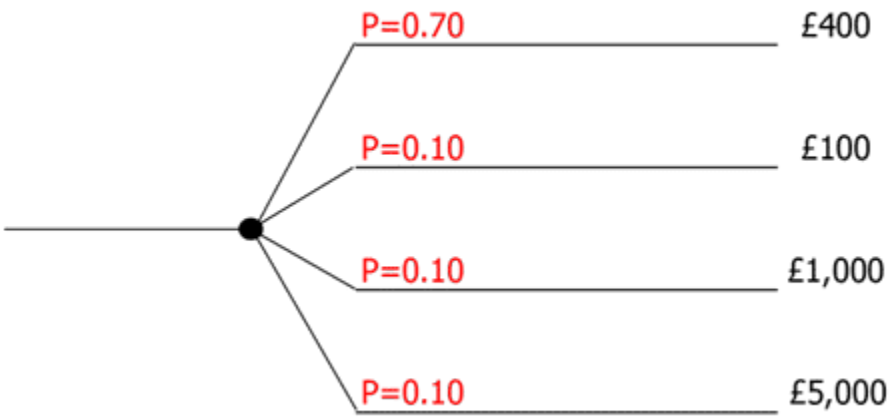
Expected Value

Toss of a coin, if it's heads you win £100, if its tails you win nothing. What's the expected value (EV)? The EV depends on the chance of a heads or a tails. Tossing a coin, generally 50:50 chance, so expected value is £50. 50% of the time you'll get £100, whereas for the rest of the time you'll get nothing, average this out and you get your expected value.



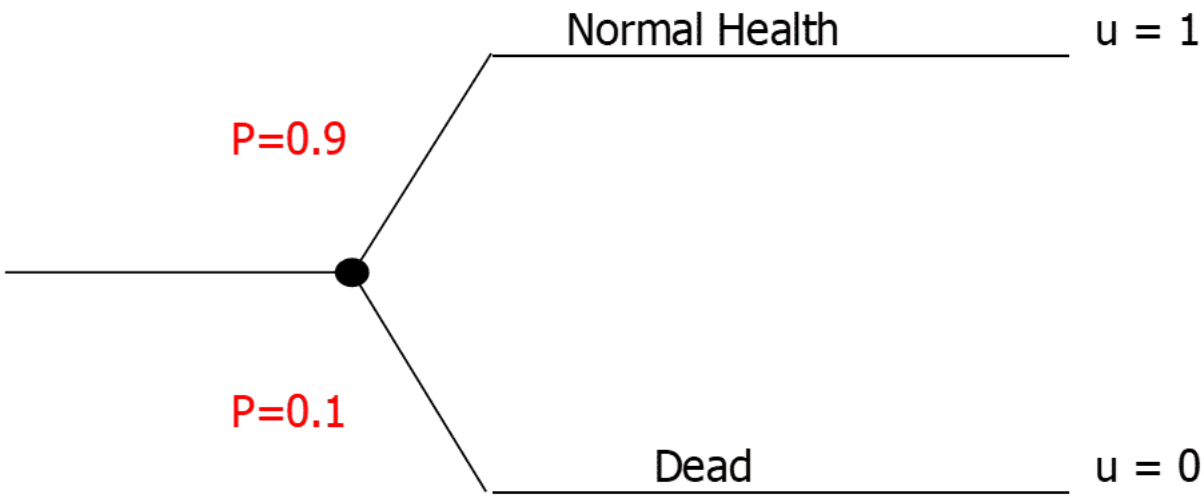
Expected value (EV) = 0.5×£100 + 0.5×£0 = £50

Here are some more examples of expected value:



EV = 0.70*£400 + 0.10*£100 + 0.10*£1000 + 0.10*£5000 =£890

Expected utility: For an outcome, e.g. utility we can solve for expected utility, in exactly the same manner.



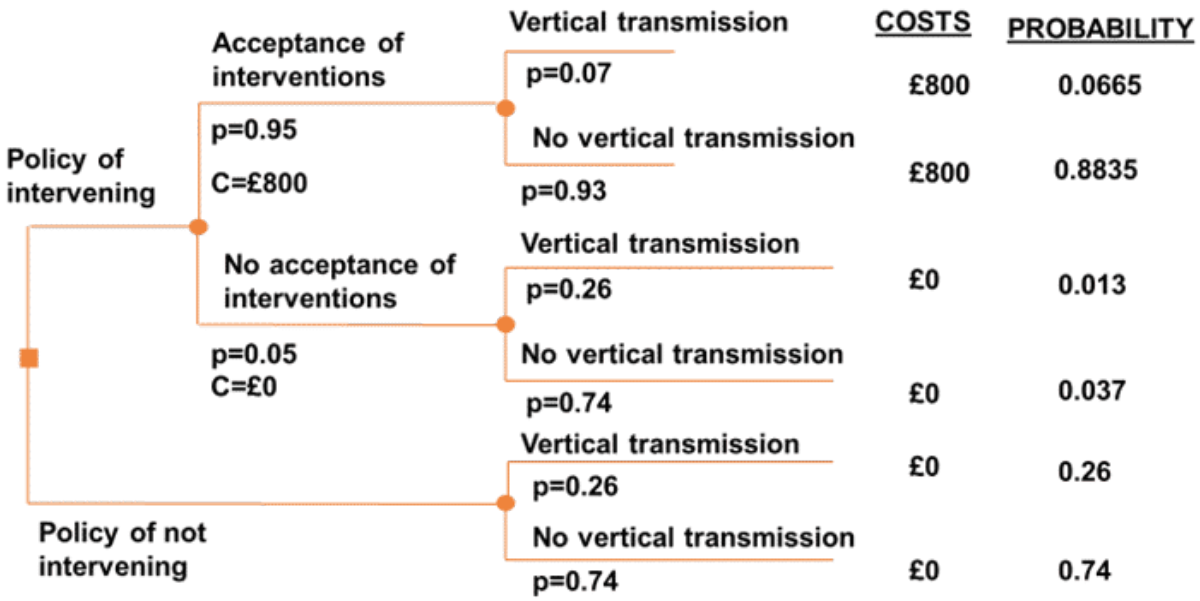
EU = 0.9x1 + 0.1x0 = 0.9

CONTINUE

Decision Trees: Example of vertical transmission of HIV

This is an example of Decision tree to examine the cost-effectiveness of a policy intervention to prevent HIV transmission. The policy decision (at the decision node) is whether to intervene or not. In the intervention arm, the intervention can be accepted or not, which leads to transmission of disease or not.

In the no policy intervention comparator arm the final branch is transmission or no transmission of disease.



Adapted from Ratcliffe *et al.* *AIDS* 1998;12:1381-1388

The probabilities of each decision are detailed at the decision node, as are the costs at each decision. At the end of the tree the overall costs and probability of being in each leave or terminal node are detailed.

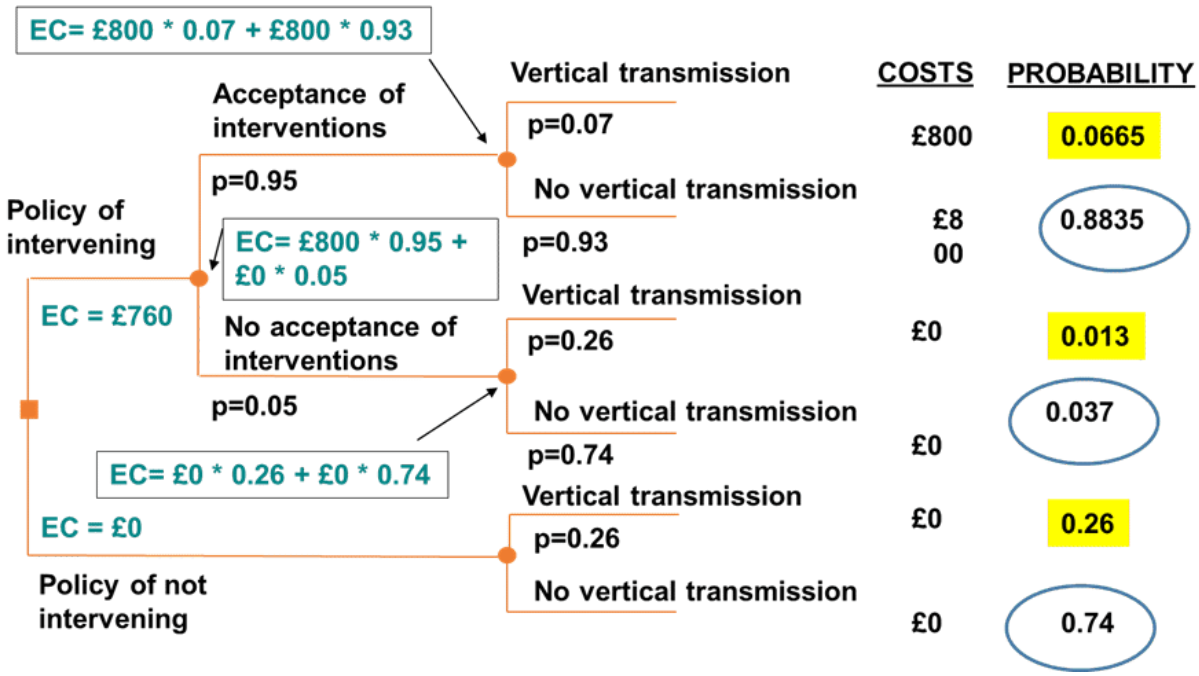
This example is from a published decision tree by Ratcliffe and colleagues 1998. Available online at:

Ratcliffe, Julie1,4; Ades, A E.2; Gibb, Diana2; Sculpher, Mark J.1; Briggs, Andrew H.3. Prevention of mother-to-child transmission of HIV-1 infection: alternative strategies and their cost-effectiveness. AIDS 12(11):p 1381-1388, July 30, 1998

CONTINUE

Decision Trees: Roll back calculation

The same decision tree illustrates how the expected costs and expected utilities are calculated:



We roll-back the tree to calculate the expected costs for Intervention £760 and the Expected risk of no transmission 0.8835+0.037 = 0.9205 (health gain), and for the control arm the expected cost £0, and expected risk of no transmission (health gain) = 0.74

Calculating the ICER from decision tree

Intervention: Expected cost: £760

Avoiding vertical transmission: 0.9205

No intervention: Expected cost: £0

Avoiding vertical transmission: 0.74

Incremental cost of interventions per HIV-infected child avoided:

Differential cost : 760 - 0 = 760

Differential risk : 0.9205 - 0.74 = 0.1805

ICER= £4,210

In our example, the incremental costs effectiveness ratio can be calculated as shown in this slide, where the differential costs is divided by the differential risk., is equal to an ICER of £4210.

At the end of this session there is a decision tree exercise for you to undertake - to give you a chance to do this process yourself.

For further information, the full article including background, depiction of the tree, analysis and results are available online

CONTINUE

Limitations of decision tree

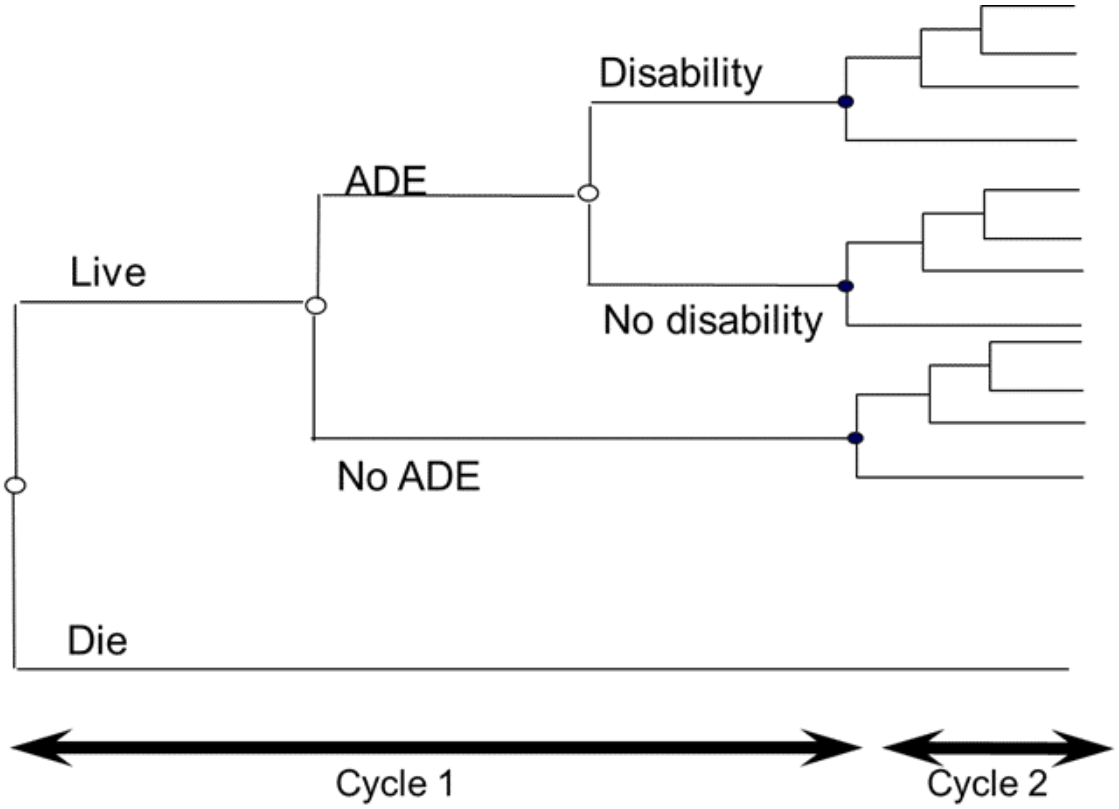
- Present sequence of events over a particular time period
- Unable to differentiate between earlier and later events or determine when events occur
- Inflexible when events recur over time

- Particular difficulty in modelling chronic diseases: complications, recurrence, remission, mortality
- Leads to excessively ‘bushy’ decision trees
- Problems with assigning outcomes over time and discounting

Decision trees provide a simple method to sequence events over a particular time period. However, they do not handle time very well. Within a decision tree it is difficult to distinguish between events that happen at different times. Where this is important information, or where events recur over time (e.g. surgery, recovery, complication, repeat surgery, recovery etc.) the inclusion of timeframe can lead to a large number of branches on the tree. This is particularly an issue when modeling chronic diseases.

‘Bushy’ decision tree

This decision tree represents the experience of patients on a long term drug treatment. Some patients might die as a result of treatment. Those who don’t can experience an adverse drug event, or not. Those that experience an adverse drug event may be disabled as a result, or not. As this is a long term treatment, patients may experience these outcomes at any point over the course of their treatment.



The model represents two time periods ‘cycles’ of treatment (e.g. 2 months). As you can see the model is already very “bushy”. The number of branches will continue to grow with the addition of each time period (1st period = 4 branches, 2nd period = 13 branches, 3rd period = 28 branches…) and will quickly become unmanageable.

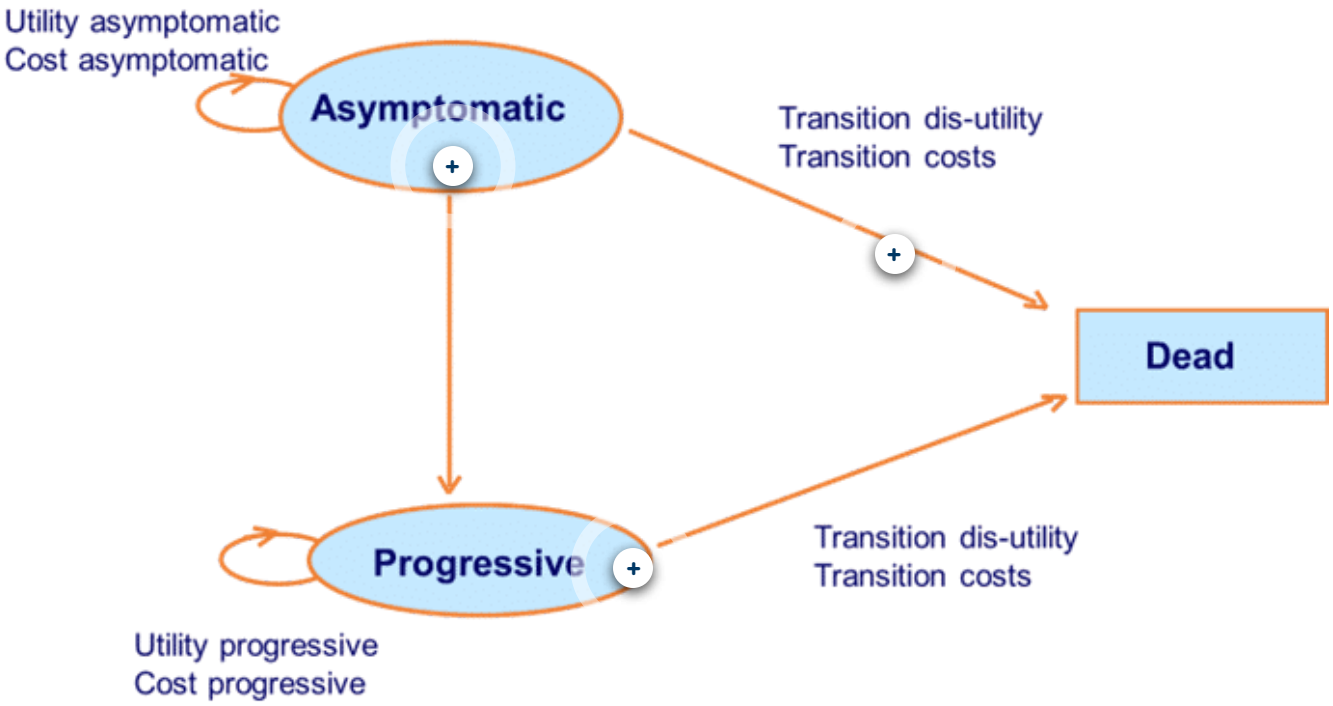
CONTINUE

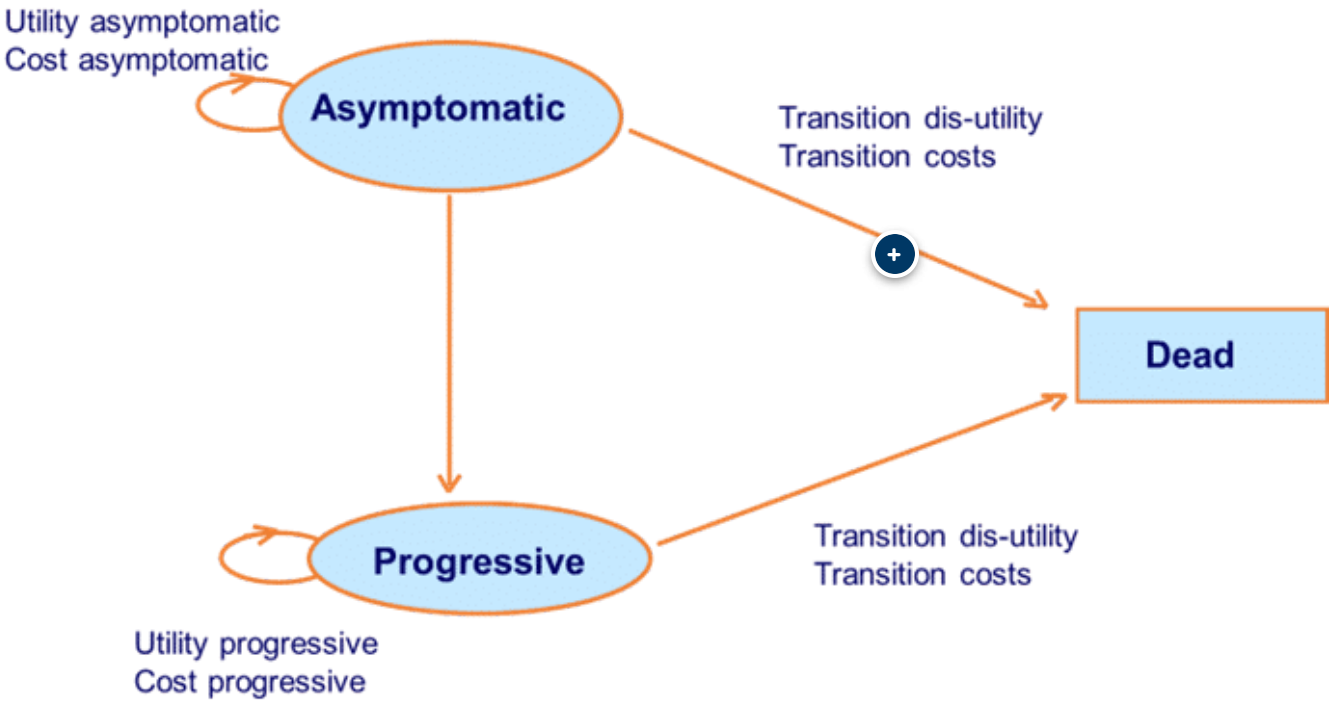
Markov model

Within health economic evaluation, Markov models tend to be undertaken where decision trees are inappropriate – typically over long time horizons or where a lifetime analysis is required.

A Markov model involves a notional group of patients who progress through a series of health states (each of which represents a different level of disease, prognosis or event) accumulating costs and outcomes as time progresses in discrete steps or cycles (e.g. months, years). The speed of the progression through the model depends on the cycle length and the transition probabilities.

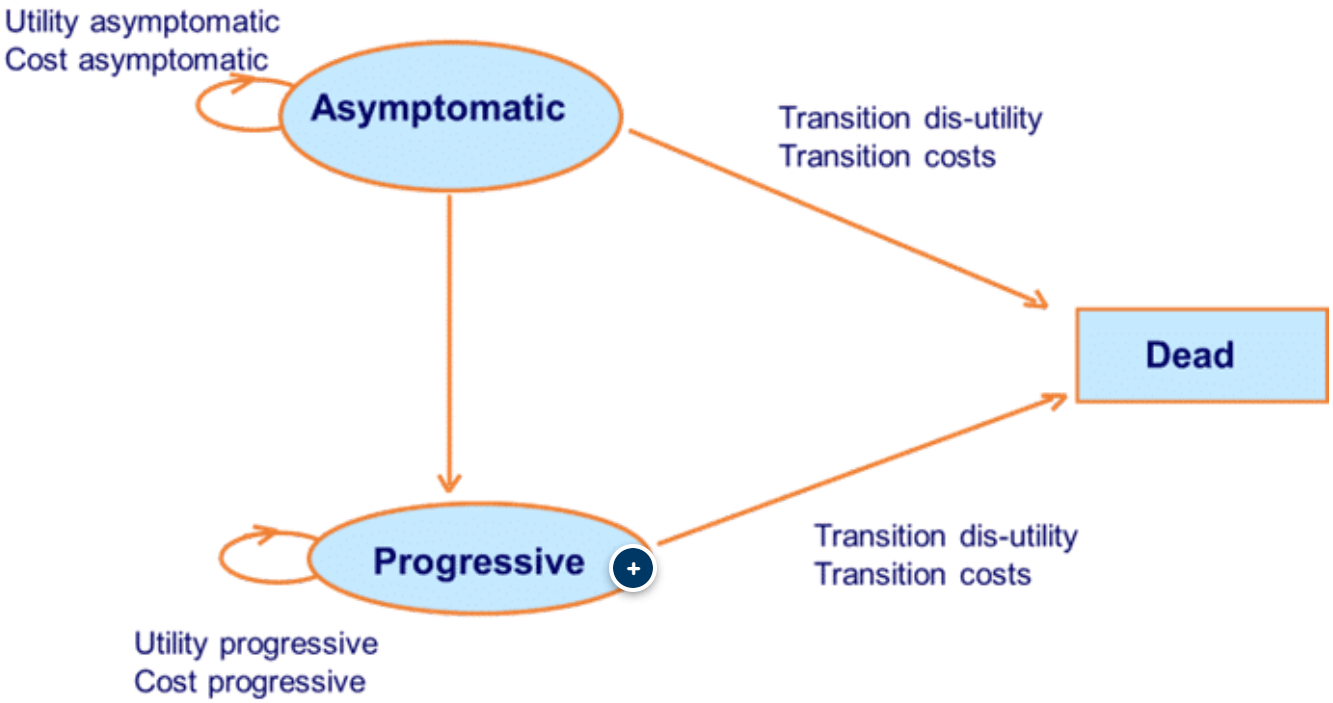
This figure below details the key features of a Markov model.



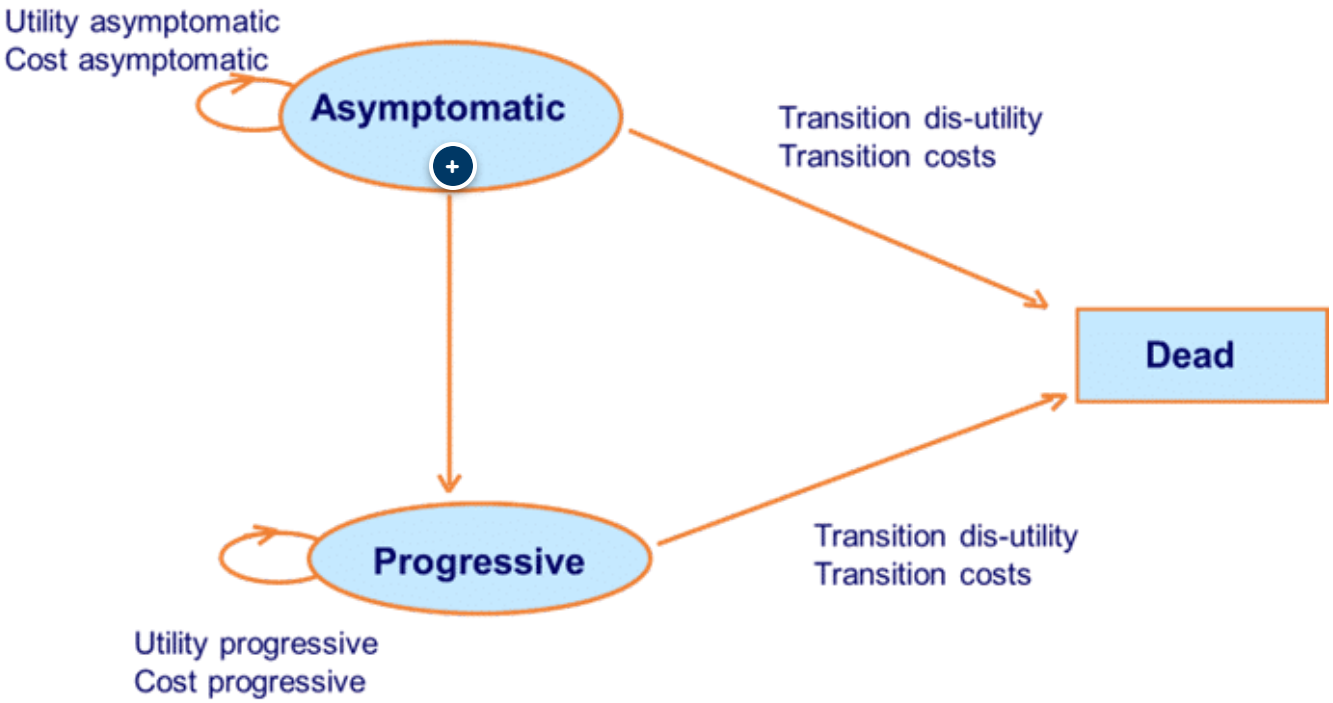


Item 1

Arrows indicate the allowable transitions between health states. Back-bending arrows indicate that individuals can stay within the current health state.



Once progressive, individuals either stay progressive or die in each cycle. Dead is the absorbing state.



At each cycle – individuals within the asymptomatic health state can either stay asymptomatic; develop progressive disease or die.

This diagram depicts a simple three state markov model where patients can be asymptomatic, progressive or dead.

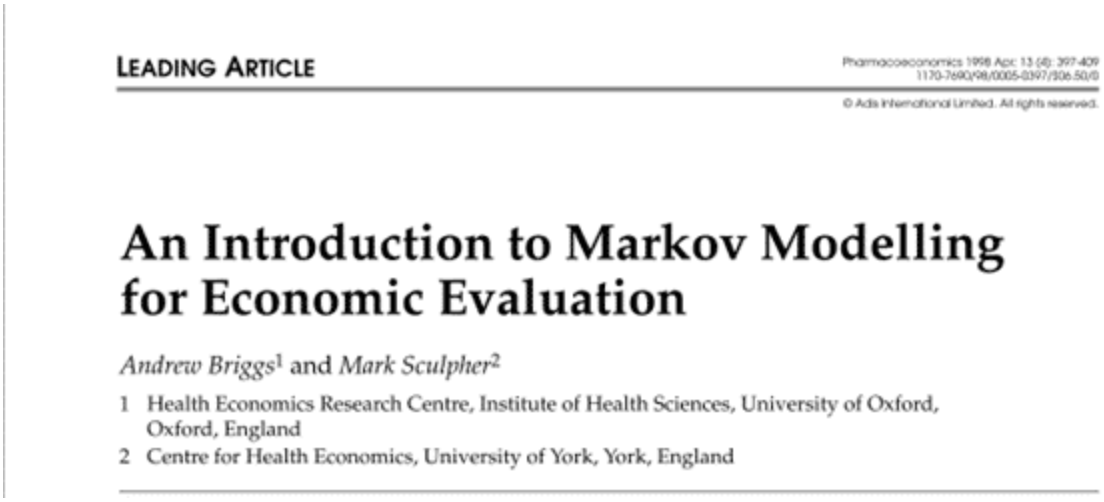
Costs and utilities can be applied to health states, or to transitions within the model.

A cohort of patients are run through the model and then the state payoffs are calculated by multiplying the applicable cost or utility by the number of individuals occupying the state. The transition payoffs are calculated by multiplying the applicable cost or utility by the number of individuals making the transition. The total payoffs are determined by summing the state and transition payoffs for all states over all cycles. The average cost and average utility from the model are then calculated. The model is run for the intervention and then for the control and the cost and QALY outcomes are compared incrementally.

The steps that are involved in constructing a Markov Models are:

- Select a finite number of mutually exclusive health states
- specify cycle length
- specify the number of cycles/stopping rules
- identify allowable transition
- assign transition probabilities
- seeding: specify how we are spreading the notational patients across the health states in the model initially.

In following articles Briggs et al summarize application of Markov modelling for economic evaluation



LEADING ARTICLE

Pharmacoeconomics 1998 Apr; 13 (4): 397-409
1170-7690/98/0005-0397/$06.50/0

An Introduction to Markov Modelling for Economic Evaluation

Andrew Briggs[1] and *Mark Sculpher*[2]

1 Health Economics Research Centre, Institute of Health Sciences, University of Oxford, Oxford, England
2 Centre for Health Economics, University of York, York, England

Available at: https://link.springer.com/article/10.2165/00019053-199813040-00003

CONTINUE

Discrete event simulations (DES)

Discrete event simulations (DES) are more complex models than Markov Models. They describe the progress of individuals through healthcare process or systems, affecting their characteristics and outcomes over unrestricted time periods. Unlike markov models, they allow for memory in the simulation of each individual through the model.

The benefits of this simulation relate to the greater flexibility around the implementation and population of complex models, which may provide more accurate or valid estimates of the incremental costs and benefits of alternative health technologies.

Discrete event simulations (DES)

- DES is not restricted to the use of equal time periods (like the cycle length in Markov model)
- Not limited by Markovian assumption/ memoryless property: the probability of a state is independent of its history, but only depends upon its immediately previous state
- Allow individuals to interact with each other -for example, in a transplant programme where organs are scarce and transplant decisions and outcomes for any individual affect everyone else in the queue

Use of discrete event simulations

Karnon, et al. 2014 describe when it is appropriate to use discrete event simulations. They undertook a literature review found four factors that are associated with the use of DES

- Heterogeneity in the baseline characteristics of the eligible population (e.g., age, sex, disease severity)
- Disease progression as a continuous process (e.g., each patients has different experience with the health condition)
- Time-varying event rates
- The effect of prior events on subsequent event rates

For further information have a read of their article:

Karnon J, Haji Ali Afzali H. When to use Discrete Event Simulation (DES) for the economic evaluation of health technologies? A review and critique of the costs and benefits of DES. Pharmacoeconomics. 2014;32(6):547-558. doi:10.1007/s40273-014-0147-9.

Some additional reading on decision modelling and how to select which method is as follows:

Review article

Modelling in the economic evaluation of health care: selecting the appropriate approach

Pelham Barton, Stirling Bryan, Suzanne Robinson
Health Economics Facility, University of Birmingham, Birmingham, UK

Available at: https://doi.org/10.1258/135581904322987535

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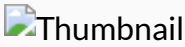


Resources

Barton, Pelham, Stirling Bryan, and Suzanne Robinson, 'Modelling in the Economic Evaluation of Health Care: Selecting the Appropriate Approach', Journal of Health Services Research and Policy, 9.2 (2004), 110–18 https://doi.org/10.1258/135581904322987535

Briggs A, Sculpher M. An introduction to Markov modelling for economic evaluation. Pharmacoeconomics (1998) 13: 397-409.

Caro. et al.2012. Modeling Good Research Practices—Overview: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force-1, Value in Health, 15:796-803 Available at: https://pubmed.ncbi.nlm.nih.gov/22999128/

Karnon J, Haji Ali Afzali H. When to use Discrete Event Simulation (DES) for the economic evaluation of health technologies? A review and critique of the costs and benefits of DES. Pharmacoeconomics. 2014;32(6):547-558. doi:10.1007/s40273-014-0147-9. Available at: https://pubmed.ncbi.nlm.nih.gov/24627341/

Petrou, Stavros, and Alastair Gray, 'Economic Evaluation Using Decision Analytical Modelling: Design, Conduct, Analysis, and Reporting', Bmj, 342.7808 (2011), 1–6 https://doi.org/10.1136/bmj.d1766

Ratcliffe, Julie1,4; Ades, A E.2; Gibb, Diana2; Sculpher, Mark J.1; Briggs, Andrew H.3. Prevention of mother-to-child transmission of HIV-1 infection: alternative strategies and their cost-effectiveness. AIDS 12(11):p 1381-1388, July 30, 1998

Sculpher, M. 2006. Whither trial-based economic evaluation for health care decision making? Health Economics , 2006; 15:7; pp 677–687. Available at: https://pubmed.ncbi.nlm.nih.gov/16491461/

Siebert U, Alagoz O, Bayoumi A, Jahn B, Owens D, Cohen D, Kuntz K. “State-transition modelling: A report of the ISPOR-SMDM Modelling Good Research Practices Task Force-3 ”, Med Decis Making (2012) 32:690-700. Available at: https://pubmed.ncbi.nlm.nih.gov/22999130/

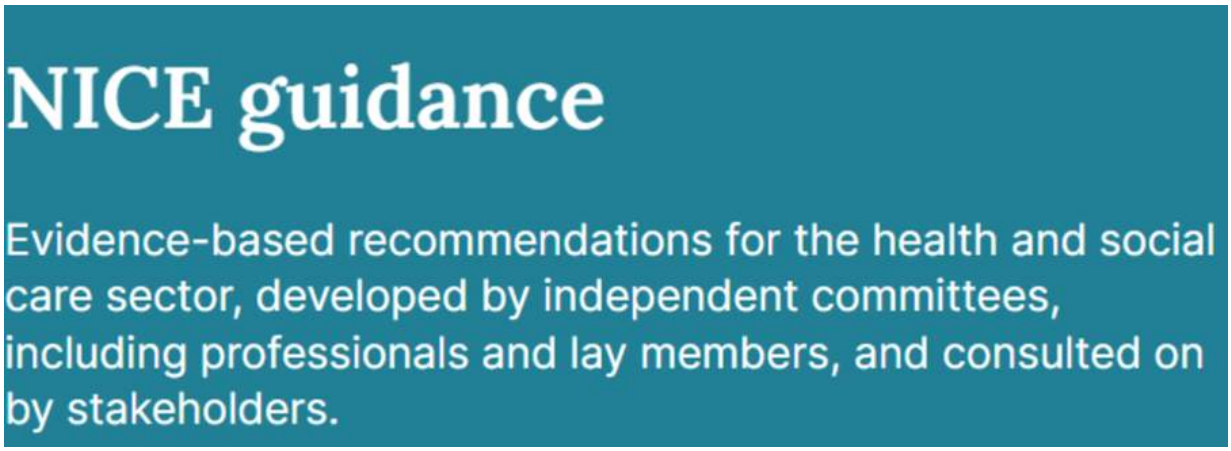
The fourth session will take a brief look at HTA implementation practices in the UK, giving an overview of the National Institute for Health and Care Excellence (NICE) and Scottish Medicines Consortium (SMC), the approval bodies for new technologies for NHS England and Wales NHS, and NHS Scotland respectively.

Session 4: Implementation: Decision Making in Practice

National Institute for Health & Care Excellence (NICE)

The National institute for Health and Care Excellence (NICE) is the reimbursement agency for England and Wales in the UK. They act on behalf of the NHS to assess and issues guidance on new technologies, treatments and services for the NHS. They develop guidance standards and information on high quality health and social care services.

NICE guidance



https://www.nice.org.uk/guidance

NICE guidelines are based upon the concept of a reference case where preferred methods are outlined for companies to adhere to. The purpose is to achieve standardisation and consistency in submissions to NICE.

The key guidelines for economic appraisal for submissions to NICE are detailed below:

What NICE decisions are based on

- Evidence - NICE reviews each treatment or new technique and bases their decision on the best available evidence
- Value for money - NICE looks at the Quality Adjusted Life Years (QALYs) to assess the benefit and quality of life a treatment will provide
- Input from experts - lay members and members from clinical practice, public health, social care and industry
- Public involvement - patients, carers, service users and the general public

The most recent guideline was published in 2022. Available online at: https://www.nice.org.uk/process/pmg36/chapter/economic-evaluation

NICE consider an additional QALY to be of equal value regardless of other characteristics of the individuals, such as their age, socio-demographic details, or their pre- or post-treatment level of health.

The Committee has discretion to consider a different equity position, and may do so in certain circumstances and when instructed by the NICE Board or the Department of Health

NICE Reference Case (Published Jan 2022)

Element of Health Technology Assessment	Section Providing Details

Defining the Decision Problem	Scope Developed by NICE (All relevant for NHS)
Comparator(s)	As Listed in the Scope Developed by NICE
Perspective on Outcomes	All Health Effects, Whether for Patients or, When Relevant, Carers
Perspective on Costs	NHS and Personal Social Services (PSS)
Types of Economic Evaluation	- Cost-Utility Analysis with Fully Incremental Analysis - Cost-Comparison Analysis
Time Horizon	Long Enough to Reflect All Important Differences in Costs or Outcomes Between the Technologies Being Compared
Synthesis of Evidence on Health Effects	Based on Systematic Review
Measuring and Valuing Health Effects*	Health Effects Should Be Expressed in Quality-Adjusted Life Years (qalys). The EQ-5D Is the Preferred Measure of Health-Related Quality of Life in Adults
Source of Data for Measurement of Health-Related Quality of Life*	Reported Directly by Patients or Carers, or Both
Source of Preference Data for Valuation of Changes in Health-Related Quality of Life*	Representative Sample of the UK Population

Equity Considerations*	An Additional QALY Has the Same Weight Regardless of the Other Characteristics of the Individuals Receiving the Health Benefit, Except in Specific Circumstances
Evidence on Resource Use and Costs	Costs Should Relate to NHS and PSS Resources and Should Be Valued Using the Prices Relevant to the NHS and PSS
Discounting	The Same Annual Rate for Both Costs and Health Effects (Currently 3.5%)

Source: https://www.nice.org.uk/process/pmg36/chapter/economic-evaluation

NICE decision threshold for England and Wales

NICE set the decision threshold for England and Wales. They explicitly set a value of £20,00-£30,000 per QALY. Anything below £20,000per QALY is considered cost-effective. Anything costing between £20,000-£30,000 is possibly cost-effective, and anything above the £30,000 is not cost-effective. NICE has difference decision threshold for special needs (e.g., end of life, rare disease). This is discussed further in the *health economics for HTA* module.

$$\text{ICER} : \frac{\text{Cost}_A - \text{Cost}_B}{\text{Effect}_A - \text{Effect}_B} \leq £20{,}000 \quad \text{per QALY}$$

Decision Making in Scotland

In Scotland there are various bodies – all under Health Improvement Scotland (HIS) - which focus on different types of health technologies in terms of health care guidance and decision making.

The Scottish medicines Consortium (SMC)

SMC is the Scottish decision making body, focussed on decisions for new medicines. Their remit is to provide advice to NHS boards and drug committees across Scotland about clinical and cost-effectiveness of new medicines. The SMC Committee takes a range of factors into consideration when deciding whether to accept a new medicine under review. The committee considers the clinical and health economic evidence provided by the submitting company as well as evidence submitted by patient groups to decide whether the medicine provides value for money.
https://www.scottishmedicines.org.uk/

The Scottish Health Technologies Group (SHTG)

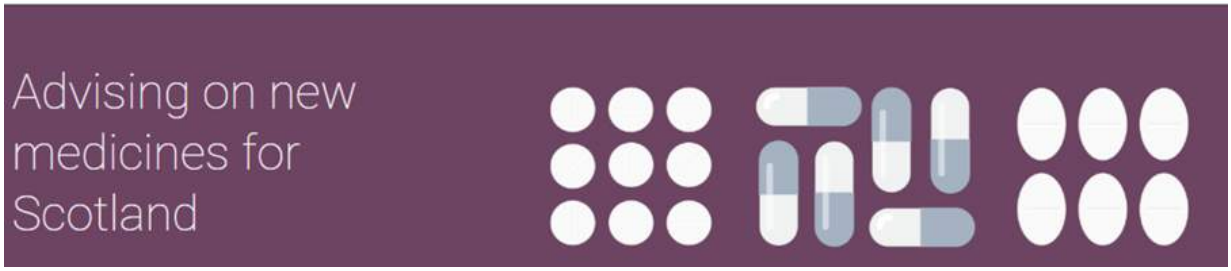
https://shtg.scot/

SHTG is an advisory group set up to provide assistance to NHSScotland boards when considering selected health technologies, they cover all technolgies excluding medicines which are the remit of the SMC. https://shtg.scot/

The Scottish Intercollegiate Guidelines Network (SIGN)

SIGN develops evidence based clinical practice guidelines for the National Health Service (NHS) in Scotland. SIGN guidelines are derived from a systematic review of the scientific literature and are designed to translate new knowledge into fast practice to improving patient-important outcomes as fast as possible. https://www.sign.ac.uk/

The Scottish medicines Consortium (SMC)



- Rapid appraisals of medicines only
- Shortly after licensing
- Faster process than NICE
- Routine availability
- Ensure recommended drugs are available to patients

SMC assessment process and time frame is more straightforward and shorter than NICE – aim to provide advice within 3 months of launch of all new drugs to enable early access as soon as possible to Scottish patients. https://www.scottishmedicines.org.uk/

Decision threshold

For a medicine with a cost per QALY between £20,000 and £30,000 SMC might accepted by SMC if the medicine gives significant benefits over existing treatments.

NICE and SMC

The SMC assessment process and Time frame is less involved and shorter than NICE – aim to provide advice within 3 months of launch of all new drugs to enable early access ASAP to Scottish patients.

NICE approved for new drugs/medicines don't apply to Scotland, however the Multiple medicine assessment from NICE are reviewed by the SMC to enable them to make decisions for Scotland, using the NICE evidence.

END OF THIS WEEK'S SESSION

Resources

Session 1

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Session 4

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