Decision analytic modelling for economic evaluation of new diagnostic tests

Jane Wolstenholme
Outline of Session

- What is economic evaluation
- Rationale for modelling
- Stages in model development
- Decision trees
- Markov models
Why Economic Evaluation?

- Increasing acceptance that effectiveness information is necessary but not sufficient for decision making
  - Need to explicitly consider costs and opportunity costs of different courses of action

- Economic methods can contribute to the decision making process

- Offer a coherent, explicit and theoretically based approach to:
  - Identifying, measuring and valuing resource use, costs and outcomes
  - Handling uncertainty
What is Economic Evaluation?

- Economic evaluation: a comparison of alternative diagnostic or treatment options in terms of their costs and outcomes
  - **Costs** – the value of the resources involved in providing treatment and managing side-effects, symptoms and disease-related events
  - **Outcomes** – the health effects of the intervention
- Comparative methodology – interested in **incremental costs and outcomes**
- Can be expressed as an incremental cost-effectiveness ratio (ICER):

\[
ICER = \frac{Cost_A - Cost_B}{Effect_A - Effect_B}
\]
Incremental Costs and Outcomes: Example


“The Cost-Effectiveness of a Novel SIAscopic Diagnostic Aid for the Management of Pigmented Skin Lesions in Primary Care: A Decision-Analytic Model”

\[
\frac{\text{£1133}}{15.108 \text{ QALYs}} - \frac{\text{£1115}}{15.098 \text{ QALYs}} = \text{£1,896 per QALY}
\]
# Types of Economic Evaluation

<table>
<thead>
<tr>
<th>Type</th>
<th>Outcome measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost-consequence analysis (CCA)</td>
<td>Multiple outcomes reported in disaggregated manner</td>
</tr>
<tr>
<td>Cost-minimisation analysis (CMA)</td>
<td>None (evidence or assumption of equivalent outcomes)</td>
</tr>
<tr>
<td>Cost-effectiveness analysis (CEA)</td>
<td>Natural units (e.g. life years, cases detected)</td>
</tr>
<tr>
<td>Cost-utility analysis (CUA)</td>
<td>QALYs (longevity and quality of life)</td>
</tr>
<tr>
<td>Cost-benefit analysis (CBA)</td>
<td>Monetary valuation placed on health outcomes</td>
</tr>
</tbody>
</table>
The cost-effectiveness plane

New treatment more costly

Existing treatment dominates

New treatment less costly but less effective

New treatment more effective but more costly

New treatment dominates

New treatment less costly

Maximum acceptable incremental cost-effectiveness ratio = CE threshold
Scatterplot of incremental cost and QALY pairs: MoleMate v Best practice (5000 Monte Carlo samples)

---: threshold of £30,000 per QALY gained
Where can we obtain evidence about cost-effectiveness?

- A good source is randomised controlled trials
  - Unbiased estimates of treatment effects
  - Can collect outcome and resource use information prospectively
  - Obtain patient-specific data

SO WHY USE A MODEL TO CONDUCT AN ECONOMIC EVALUATION?

- Trials do have limitations:
  - Patients may not be representative
  - May be unsuitable for population interventions
  - May not compare all the relevant alternatives
  - Trial duration may not be long enough
    - We are interested in long-term/lifetime costs and effects
RCTs: Patients may not be representative

- Trials tend to provide evidence specific to a particular setting or group of patients, and this may not represent patients commonly seen in clinical practice or reflect the requirements for the particular decision problem being posed.

- If there is a need to generalise to other settings or patient sub-groups, additional modelling of the trial baseline risks and resource usage informed by other sources may be required to make the results generalisable.
RCTs might not compare all the relevant alternatives

- Economic evaluation is a comparative methodology for assessing the value of one course of action compared to another (or range of options).

- A randomized trial may provide evidence on two or three options, but is unlikely to be able to provide evidence on all the relevant options available.
Information from RCTs and other studies may have to be combined.

- A single trial is unlikely to provide all the information required, and it might be necessary to combine evidence from a range of sources.
- It is important that all available evidence is scrutinised and assessed for its applicability to the evaluation being undertaken.
- In the case of economic evaluation this means evidence on resource utilisation, unit costs, effectiveness and where available health–related quality of life.
- The range of sources from which this information could be drawn may include trials but also cohort studies, surveys or patient records, expert opinion.
- Decision models can provide an organizing framework within which these different types of data can be synthesised.
Decision models: combining evidence

Epidemiological evidence

Absolute risk (e.g. Control group)

Relative treatment effect

Tx effect

Policy decisions: clinical benefit and cost-effectiveness

Individual RCT

Systematic review of trial evidence

Associated resource use, costs & utility

Absolute risk difference

Size of benefits/harms
RCTs might not encompass the appropriate time horizon.

- The appropriate time period for the purpose of an economic evaluation is the time period that is long enough to capture in full the differences in resource use, unit costs and benefits between the alternative options being evaluated.

- Often, as is the case for interventions for chronic disease, this requires a time horizon that captures the patients’ lifetime.

- Trials rarely provide evidence over the lifetime of all patients (except in cases of interventions for terminal illness).

- There is therefore a need to extrapolate beyond the trial evidence, and decision models can provide a vehicle to extrapolate evidence from trials to a longer, more appropriate, time horizon.
RCTs might not provide information on final endpoints.

- Trials often provide evidence on intermediate clinical endpoints such as numbers of events or changes in risk factors. For example, a trial may collect or even have as its pre-defined endpoint information on HbA1c levels in patients with type 2 diabetes.

- It is unlikely that they will collect comprehensive information for all patients on final outcomes such as mortality, or that they will collect detailed health–related quality of life data that could be combined with survival data to provide quality adjusted life years (QALYs).

- As a result there will often be a need to link these intermediate endpoints to the long-term outcomes of interest to health economists, and this usually involves combining evidence from a number of sources.

- In the example given above, clinical trials may provide information on changes in HbA1c levels in patients with type 2 diabetes subsequent to an intervention, and the analyst would then have to extrapolate this information into life expectancy and quality adjusted life expectancy using a survival model incorporating data from a range of sources including other trials and cohort studies.
What happens next?
The need for extrapolation

- New intervention
- Old intervention

End of trial follow-up
Limited extrapolation
No continuing treatment effect
Lifetime horizon
Rationale for Modelling

- **Decision models can be used to**
  - Structure the economic question and compare all relevant alternatives
  - Extrapolate beyond observed data
  - Link intermediate and final endpoints
  - Generalise results to other settings/patient groups
  - Use synthesised evidence and facilitate head-to-head comparisons where RCTs don’t exist
  - Indicate the need for further research
Why model?

- To inform decisions about resource allocation
- Integral to the NICE DAP (Diagnostics Assessment Programme) process
- Hence models should deliver:
  - Expected costs and health effects
  - For all options
  - Relating to appropriate population and sub-populations
  - Based on full range of existing evidence, throughout care (dx and tx) pathway
  - Quantification of the decision uncertainty (model structure, parameters inputs etc)
  - Valuation of further research

In a timely manner to support decisions
<table>
<thead>
<tr>
<th>Topic</th>
<th>Publication Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>The EOS 2D/3D imaging system (DG1)</td>
<td>October 2011</td>
</tr>
<tr>
<td>Elucigene FH20 and LIPOchip for the diagnosis of familial hypercholesterolaemia (DG2)</td>
<td>December 2011</td>
</tr>
<tr>
<td>New generation cardiac CT scanners (Aquilion ONE, Brilliance iCT, Discovery CT750 HD and Somatom Definition Flash) for cardiac imaging in people with suspected or known coronary artery disease in whom imaging is difficult with earlier generation CT scanners (DG3)</td>
<td>January 2012</td>
</tr>
<tr>
<td>Adjunctive colposcopy technologies for examination of the uterine cervix – DySIS and the Niris Imaging System (DG4)</td>
<td>August 2012</td>
</tr>
<tr>
<td>SonoVue (sulphur hexafluoride microbubbles) – contrast agent for contrast-enhanced ultrasound imaging of the liver (DG5)</td>
<td>August 2012</td>
</tr>
<tr>
<td>Depth of anaesthesia monitors – Bispectral Index (BIS), E-Entropy and Narcotrend-Compact M (DG6)</td>
<td>November 2012</td>
</tr>
<tr>
<td>SeHCAT (tauroselcholic [75 selenium] acid) for the investigation of diarrhoea due to bile acid malabsorption in people with diarrhoea-predominant irritable bowel syndrome (IBS-D) or Crohn's disease without ileal resection (DG7)</td>
<td>November 2012</td>
</tr>
<tr>
<td>EGFR-TK mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer (DG9)</td>
<td>August 2013</td>
</tr>
<tr>
<td>Intraoperative tests (RD-100i OSNA system and Metasin test) for detecting sentinel lymph node metastases in breast cancer (DG8)</td>
<td>August 2013</td>
</tr>
<tr>
<td>Gene expression profiling and expanded immunohistochemistry tests for guiding adjuvant chemotherapy decisions in early breast cancer management: MammaPrint, Oncotype DX, IHC4 and Mammostrat (DG10)</td>
<td>September 2013</td>
</tr>
<tr>
<td>Faecal calprotectin diagnostic tests for inflammatory diseases of the bowel (DG11)</td>
<td>October 2013</td>
</tr>
<tr>
<td>Measuring fractional exhaled nitric oxide concentration in asthma: NIOX MINO, NIOX VERO and NObreath (DG12)</td>
<td>April 2014</td>
</tr>
<tr>
<td>Detecting, managing and monitoring haemostasis: viscoelastometric point-of-care testing (ROTEM, TEG and Sonoclot systems) (DG13)</td>
<td>August 2014</td>
</tr>
</tbody>
</table>
Decision Analytic Models

- Decision analysis (DA) is an explicit quantitative approach to decision making under uncertainty
  - Mathematical representation of a series of possible events that flow from a set of alternative options being evaluated
    - DA compares at least two alternatives
    - Likelihood of each event is expressed as probability
    - Each event has associated values/outcomes
  - DA is based on the concept of expected value (EV)
    - For a given option, EV is the sum of the values of each event weighted by the probability of the event.
Stages in the Development of a Decision Model

- Conceptualise model
  - Define the question/decision problem
  - Decide on model structure and type of decision model
- Identify the evidence
  - Synthesise evidence (where possible)
- Populate the model with evidence
- Analyse the model (inc. costs, outcomes and ICERs)
- Validate the model
- Explore uncertainty
Model development process: feedback from HTA modellers

Chilcott, J. et al *Health Technology Assessment* 2010; 14[25].
Conceptualising the model

- **Decision problem**
  - Disease, perspective, target population, interventions, outcomes, and time horizon

- **Modelling objective and scope**

- **Model structure according to natural history of disease**
  - Impact of disease on HRQoL and other outcomes
  - Impact of disease on resource use
  - Relevance of risk subgroups
  - Impact of intervention on disease process
  - Type of model (e.g. decision tree, Markov model, etc)

- Chilcott, J. et al Health Technology Assessment 2010; 14[25].
Decide on Appropriate Model Type

What model should I use?

Is interaction between patients important e.g. queuing / infection?
- NO
- YES

Do you need to model recursive events?
- NO
- YES

Do you require your model to represent a lot of health states?
- NO
- YES

- Systems Dynamic Model
- Discrete Event Simulation
- Decision Tree Model
- Markov Model
- Individual Sampling Model
Identifying the evidence

  
  • Systematic, transparent and justified such that it is clear that sources of evidence have not been identified serendipitously, opportunistically or preferentially.
  
  • All sources of information used to support the conceptualisation, specification or parameterisation of a model should be identified and supported by appropriate referencing.
  
  • The factors influencing the choice of evidence source should be identified and justified.
Types of evidence to inform models

- Clinical effectiveness review
- Prevalence epidemiology co-morbidities Natural history
- Cost-effectiveness model
- Current Tx Comparator Tx effect
- Adverse events, relapse rates
- Resource use Unit costs Outcomes

Unit costs
Outcomes
A specific model input parameter might be based on a number of sources of evidence

- Evidence synthesis using acceptable methods (e.g. meta-analysis, meta-regression)

Well formulated for use with measures of effectiveness but is less so for other cost-effectiveness parameter inputs

Useful source for further reading

- Evidence synthesis technical support documents (TSD) series
  - Medical Decision Making (July 2013)
Evidence from research conducted by Cooper et al. suggests that reporting of the structure, data inputs and outputs of health care decision models have in the past been poor, and that a more structured, transparent, reproducible format for analysing and reporting should be developed (Cooper et al. 2005).

Philips and colleagues, in developing a synthesised best practice guideline for decision analytic modelling in health technology assessment, used major themes that emerged from fifteen previously published guidelines as a basis for their best practice guideline (Philips et al. 2004; Philips et al. 2006)
Outline of Session

- What is economic evaluation
- Rationale for modelling
- Stages in model development
- Decision trees
- Markov models
Steps in Constructing and Analysing Decision Trees

- A decision tree is a visual representation of a decision analysis
  1. Structure the tree
  2. Estimate probabilities
  3. Estimate payoffs (assign values to costs and outcomes)
  4. Analyse the tree
- Evaluate the tree
- Explore uncertainty
1. Structuring the Tree

- A decision tree is made up of nodes, branches and outcomes
- **Nodes:**
  - Decision node – describes the problem
  - Chance node – represents the point at which several possible events can occur
  - Terminal node – represents the end of a tree with a payoff attached
- Branches issuing from a chance node represent possible events patients may experience at that point in the tree
- Branch probabilities represent the likelihood of each event
- The sequence of chance nodes from left to right usually follows the sequence of events
- The events stemming from a chance node must be mutually exclusive and probabilities should sum to 1
Problem: Mole Mate vs Best Practice

- Decision problem
  - Pigmented skin lesions (moles) presenting in a primary care setting
  - How to diagnose malignant melanoma?

- Mole Mate vs Best Practice
  - Mole Mate – diagnostic aid comprising handheld SIAscopy scanner (noninvasive scanner) incorporating an algorithm to be used in primary care
  - Best practice – clinical history + naked eye exam + 7-point checklist

- Outcome Measure: Referral from primary to secondary care
  - Referral
  - Non referral
Structure of decision tree

MoleMate

1. Clinically significant mole (D+)
   - Refer (T+/D+)
   - Not refer (T-|D+)

2. Not clinically significant (D-)
   - Not refer (T-|D-)

Best Practice

1. Clinically significant mole (D+)
   - Refer (T+/D+)

2. Not clinically significant (D-)
   - Not refer (T-|D-)
# Structuring the Tree

- **Dependent on available probabilities**
- **Classification of diagnostic outcomes:**

<table>
<thead>
<tr>
<th>Diagnostic verdict</th>
<th>True diagnosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>No cancer</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>True positive (A)</td>
<td>False positive (B)</td>
</tr>
<tr>
<td>Negative</td>
<td>False negative (C)</td>
<td>True negative (D)</td>
</tr>
<tr>
<td>Total</td>
<td>A + C</td>
<td>B + D</td>
</tr>
</tbody>
</table>

- Sensitivity = $A/(A+C)$
- PPV = $A/(A+B)$
- Specificity = $D/(B+D)$
- NPV = $D/(C+D)$
- Prevalence = $(A+C)/(A+B+C+D)$
Structuring the Tree: Process-Ordered

- Test positive
  - True positive: \( p(D^+|T^+) \), \( PPV \)
  - False positive: \( p(D^-|T^+) \)

- Test negative
  - True negative: \( p(D^-|T^-) \), \( NPV \)
  - False negative: \( p(D^+|T^-) \)

\( P = probability \)
\( T = test \)
\( D = disease \)
\( PPV = positive\ predictive\ value \)
\( NPV = negative\ predictive\ value \)

{Diagnostic verdict} {Disease status}
Structuring the Tree: According to Disease Status

Test

Cancer

\[ p(D+) \]

Test positive

True positive

\[ p(T+|D+) \]

Sensitivity

Test negative

False negative

\[ p(T-|D+) \]

No cancer

\[ p(D-) \]

Test positive

False positive

\[ p(T+|D-) \]

Test negative

True negative

\[ p(T-|D-) \]

Specificity

\{Disease status\} \quad \{Diagnostic verdict\}

\( P = \) probability

\( T = \) test

\( D = \) disease
2. Estimating Probabilities

- Probabilities need to be assigned to the events in the tree
- Identify data sources in a consistent manner
- Specify base case, range of reasonable estimates and measures of precision for each probability
Entering Probabilities

Probabilities are entered after the chance nodes as shown
3. Estimating Payoffs

- Payoffs include:
  - Costs
  - Utilities
  - Life years
  - Quality-adjusted life years

- Payoffs should be identified in a systematic manner as for probabilities
  - Kaltenthaler E. et al. NICE DSU Technical Support Document 13
    [http://www.nicedsu.org.uk](http://www.nicedsu.org.uk)

- Payoffs are entered at terminal nodes
Entering Payoffs

Payoffs entered at terminal nodes as shown.
4. Analysing the Decision Tree

- The decision tree is averaged out and folded back to get the expected payoffs for each strategy
  - Estimated separately as the sum of products of the probability of events and their payoffs i.e. weighted average of the outcome values

- Cost-effectiveness analysis
  - Decision rules should be followed
  - Strongly and extendedly dominated strategies removed and ICERs estimated
## Example: Probabilities for Diagnostic Test

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Base case</th>
<th>Low estimate</th>
<th>High estimate</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>0.829</td>
<td>0.744</td>
<td>0.897</td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td>0.855</td>
<td>0.839</td>
<td>0.901</td>
<td></td>
</tr>
<tr>
<td>Prevalence</td>
<td>0.004</td>
<td>0.002</td>
<td>0.006</td>
<td></td>
</tr>
</tbody>
</table>
# Example: Payoffs for Diagnostic Test

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Cost (£)</th>
<th>Resources included</th>
<th>Utility</th>
</tr>
</thead>
<tbody>
<tr>
<td>True positive</td>
<td>4,974</td>
<td>(test, assess, tx early C)</td>
<td>0.48</td>
</tr>
<tr>
<td>False negative</td>
<td>9,108</td>
<td>(test, assess, tx late C)</td>
<td>0.45</td>
</tr>
<tr>
<td>False positive</td>
<td>96</td>
<td>(screen, assess)</td>
<td>0.79</td>
</tr>
<tr>
<td>True negative</td>
<td>12</td>
<td>(screen)</td>
<td>0.94</td>
</tr>
</tbody>
</table>

Also payoffs for best practice arm
Example: Folding back

\[(4974 \times 0.829) + (9108 \times 0.171) = \£5681\]

Test positive

Test negative

Cancer

\[0.829\]

\[0.004\]

Test negative

Test positive

No cancer

\[0.996\]

\[0.171\]

\[0.145\]

\[0.855\]

\[(5681 \times 0.004) + (24 \times 0.996) = \£46.81\]

\[(96 \times 0.145) + (12 \times 0.855) = \£24\]

\[\£4974\]

\[\£9108\]

\[\£96\]

\[\£12\]
### Example: Analysing the Tree (CEA)

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost (£)</th>
<th>Incr Cost (£)</th>
<th>Eff</th>
<th>Incr Eff</th>
<th>C/E (£)</th>
<th>Incr C/E (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best Practice</td>
<td>36.4</td>
<td></td>
<td>0.888</td>
<td></td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>Diagnostic Test</td>
<td>46.8</td>
<td>10.4</td>
<td>0.917</td>
<td>0.028</td>
<td>51</td>
<td>369</td>
</tr>
</tbody>
</table>
Once the base case analysis has been undertaken, the model should be subjected to:

1. Evaluation in the form of checking for model validity and consistency
2. Exploration of uncertainty using sensitivity analysis

These techniques will be introduced in greater detail later in the session
Advantages of Decision Trees

- They enable the economic question to be structured in a meaningful and visual manner.
- They allow data informing the model parameters to be assimilated and, where appropriate, synthesised.
- They are relatively simple to undertake and suitable for:
  - Diseases that occur only once
  - Decisions about acute care
  - Decisions with short time frames
Limitations of Decision Trees

- They do not explicitly account for passage of time:
  - Passage of time accounted for by outcome measure
- Limited ability to account for long term outcomes
  - Possible to add branches but results in a complex model
  - Other modelling techniques can handle repeated events better
- Structure of tree only allows for one-way progression of patient through model: not movement back and forth between states
- Decision trees can still be useful as a sub-model see Wilson et al (2012)
Decision tree used to model the test and referral process. Disease process modelled using a Markov model.

True positives: model (a).
False negatives: model (b) and for those detected (a)
Non-clinically significant lesion: model (c)
Outline of Session

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Markov Modelling

- Models uncertain processes over time
- Useful for computing long term outcomes
- Useful for sequential or repetitive outcomes
- Estimates life expectancy/ life years gained and QALYs
- Commonly used for economic evaluation
  - Extrapolation from trial endpoints (Johannesson et al. 1995, Karnon et al. 2006, Mihaylova et al. 2006)
  - Progression of disease (Fenn & Gray 1999, Hawkins et al. 2005)
  - Screening (Legood et al. 2006, Wordsworth et al. 2010)
  - Recurrent events (Moermans & Annemans 2008)
  - Disease management (Palmer et al. 2005, Steuten et al. 2007)
Basic Features of a Markov Model

- Patient is in one of a finite number of health states
- The model is run for several cycles in which there are transitions between health states over time
- Transition probabilities determine movements between states
- Rewards (costs and outcomes associated with being in each state) are earned at the end of each cycle
For patients who have had breast cancer in the past but who are still at risk of recurrence now, should we implement a treatment that has been shown to reduce the number of recurrences?
1. Defining States and Allowable Transitions

Possible in this model to return to ‘well’ state
## Transition Matrix

<table>
<thead>
<tr>
<th>Transition from:</th>
<th>Transition to:</th>
<th>Well</th>
<th>Recurrence</th>
<th>Dead</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well</td>
<td></td>
<td>1-(0.3+0.1) (#)</td>
<td>0.3</td>
<td>0.1</td>
</tr>
<tr>
<td>Recurrence</td>
<td>0.2</td>
<td>1-(0.2+0.2) (#)</td>
<td>0.2</td>
<td></td>
</tr>
<tr>
<td>Dead</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
5. Determining Rewards

- **Types of reward:**
  - Incremental (state)
  - One-time rewards at beginning or end – used for half cycle correction
  - Transition

- **Rewards:**
  - Costs
  - Utilities
  - Life years
  - Period should correspond to cycle length
  - Discount at the point in time when costs or outcomes occur
6. Analysing Markov Models

- **Cohort analysis**
  - Proportions of the starting cohort transit between states from cycle to cycle
  - The model averages the ‘experience’ of the patients in the cohort
  - Hence, cohort size is arbitrary as the same result will be reached regardless of size
Analysing Markov Models

WELL

Cycle 0

RECURRENCE

Cycle j

Cycle j+1

DEAD

Cycle K
Analysing Markov Models

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Well</th>
<th>Recurrence</th>
<th>Dead</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10,000</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>0.806=8060</td>
<td>0.004=40</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>8060</td>
<td>1900</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>0.786=7860</td>
<td>0.21=1693</td>
<td>0.104=198</td>
</tr>
<tr>
<td>3</td>
<td>6335</td>
<td>3395</td>
<td>270</td>
</tr>
<tr>
<td></td>
<td>0.755=4783</td>
<td>0.24=1520</td>
<td>0.105=347</td>
</tr>
<tr>
<td></td>
<td>4783</td>
<td>4559</td>
<td>658</td>
</tr>
</tbody>
</table>
### Example: Cohort Analysis

<table>
<thead>
<tr>
<th>Cycle (Stage)</th>
<th>Stage Cost</th>
<th>Stage Eff</th>
<th>Cum Cost</th>
<th>Cum Eff</th>
<th>P(Well)</th>
<th>P(Rec)</th>
<th>P(death)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>884</td>
<td>0.8</td>
<td>884</td>
<td>0.8</td>
<td>0.8</td>
<td>0.2</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>1,262</td>
<td>0.7</td>
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**Markov Trace: No intervention**

**Proportion of cohort in states**

- Average total cost
- Average total effect
## Example: Cohort Analysis

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<th>Strategy</th>
<th>Cost (£)</th>
<th>Incr Cost (£)</th>
<th>Eff (QALY)</th>
<th>Incr Eff (QALY)</th>
<th>C/E (£)</th>
<th>Incr C/E (£)</th>
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**Average cost-effectiveness ratio**: Incremental cost-effectiveness ratio
Limitations of Markov Models

- Transition probabilities and rewards cannot vary with patient history (Markovian assumption)
  - Can be overcome with use of more complex models or tunnel states
Decision Models Should:

- Represent a simplification of the real world
- Encourage decision-makers to be explicit
- Reflect current clinical practice and use appropriate comparators
- Be based on the best quality data available
- Cover the appropriate time period
- Include sensitivity analysis to explore uncertainty of data inputs and model structure
- Be transparent and reproducible
- Have internal and external validity
- Adhere to good practice guidelines (e.g. NICE, ISPOR)
Software packages available for decision modelling

- Modelling specific:
  - TreeAge

- Generic software:
  - MS Excel and other spreadsheet software

- Statistical packages:
  - R, Stata and SAS
  - WinBUGS
Handbook provides more background, references, and information on cost-effectiveness analysis

One of a series, edited by Alastair Gray and Andrew Briggs and co-authored by members of HERC

http://www.herc.ox.ac.uk/courses