Health economic evaluation: a very Bayesian thing

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Bayes 2014, University College London
Thursday 12 June 2014
That’s us (or is it?)...

Nixon

Jackson

Baio
Outline

- **Health economic evaluation**
  - What is health economics?
  - What does health economics do?
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  - What is health economics?
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- **Statistical modelling**
  - Models for individual-level data
  - Models for aggregated data
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  - Models for individual-level data
  - Models for aggregated data
- **Economic modelling & Decision analysis**
  - Cost-effectiveness/cost-utility analysis
  - Criteria for decision-making in health economics
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  - Criteria for decision-making in health economics
- **Uncertainty analysis**
  - Rationale
  - Main ideas
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  - Cost-effectiveness/cost-utility analysis
  - Criteria for decision-making in health economics
- **Uncertainty analysis**
  - Rationale
  - Main ideas
- **Conclusions**
What is health economics?

Cost analysis

How much does it cost to treat a patient with intervention $i$?

- Financial analysis
- Budgeting
### What is health economics?

A cost analysis is used to determine how much it costs to treat a patient with a specific intervention. This involves financial analysis and budgeting.

<table>
<thead>
<tr>
<th>Cardiovascular system (C)</th>
<th>Expenditure¹</th>
<th>%*</th>
<th>DDD²</th>
<th>%*</th>
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<tbody>
<tr>
<td>Bosentan</td>
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<td>47.9</td>
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<td>11.4</td>
<td>3.5</td>
<td>2.1</td>
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<td>5.5</td>
<td>7.2</td>
<td>15.9</td>
<td>9.9</td>
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<td>0.9</td>
<td>1.1</td>
<td>3.5</td>
<td>2.2</td>
</tr>
</tbody>
</table>

1 Millions €
2 Millions days of therapy
*Percentages are calculated over the total of the ATC category

Source: Osmed (2007)
What is health economics?

- Epidemiology
- Experimental studies
- Cost analysis
- Decision theory
- Causal inference

Health economics

**Generalisation and integration** of **statistics** (methodological & experimental), **epidemiology**, **econometrics** and **financial analysis**

How much does it cost to treat a patient with intervention?  
- Financial analysis  
- Budgeting
What does health economics do?

- **Objective**: Combine costs & benefits of a given intervention into a rational scheme for allocating resources
  - Recently, models have been built upon more advanced statistical foundations
  - This problem can be formalised within a statistical decision-theoretic approach. Rational decision-making is effected through the comparison of expected utilities
  - **Incremental** approach: need to consider at least two interventions
What does health economics do?

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- Increasingly under a **Bayesian framework**, especially in the UK: 5.9.10–12
  Dealing with parameter uncertainty in cost-effectiveness analysis (NICE Methods for Technology Assessment)
  - All inputs used in the analysis will be estimated with a degree of imprecision.
  - Probabilistic sensitivity analysis is preferred for translating the imprecision in all input variables into a measure of decision uncertainty in the cost-effectiveness of the options being compared.
  - Appropriate ways of presenting uncertainty include confidence ellipses and scatter plots on the cost-effectiveness plane (when the comparison is restricted to two alternatives) and cost-effectiveness acceptability curves.
One of the most important characteristic of health economic data is that we have **multivariate outcomes**

- \( e \) = suitable measure of clinical benefit of an intervention
- \( c \) = suitable costs associated with an intervention
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We typically need to assess these quantities **jointly**

- Costs and benefit will tend to be correlated
  - Strong positive correlation — effective treatments are innovative and result from intensive and lengthy research ⇒ are associated with higher unit costs
  - Negative correlation — more effective treatments may reduce total care pathway costs e.g. by reducing hospitalisations, side effects, etc.

- In any case, the economic evaluation is based on both!
Health economic outcome

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- There are different ways in which we can define $(e, c)$ for a specific problem
  - Direct vs indirect vs intangible costs
  - “Hard-” vs utility-based clinical outcomes
  - Public (e.g. NHS) vs private (e.g. insurance) perspective
Health economic evaluations

- Estimates relevant population parameters
- Varies with the type of available data (& statistical approach!)
Health economic evaluations

- Estimates relevant **population** parameters
- Varies with the type of available data (& statistical approach!)

- Combines the parameters to obtain a population average measure for costs and clinical benefits
- Varies with the type of available data & statistical model used
Health economic evaluations

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Statistical model

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- Varies with the type of available data & statistical model used

Economic model

- Summarises the economic model by computing suitable measures of “cost-effectiveness”
- Dictates the best course of actions, given current evidence
- Standardised process

Decision analysis
Health economic evaluations

Uncertainty analysis

- Assesses the impact of uncertainty (e.g. in parameters or model structure) on the economic results
- Fundamentally Bayesian!

Statistical model

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- Varies with the type of available data (& statistical approach!)

Economic model

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Decision analysis

- Summarises the economic model by computing suitable measures of "cost-effectiveness"
- Dictates the best course of actions, given current evidence
- Standardised process
1. Statistical modelling

- **Sampling variability** for the health economic outcomes is described by a distribution $p(e, c \mid \theta^t)$, which depends on a set of population parameters $\theta^t$
  - Probability of some clinical outcome
  - Duration in treatment
  - Reduction in the rate of occurrence of some event
  - Unit cost of acquisition of a health technology
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- Under the Bayesian approach, **parametric uncertainty** is modelled using a prior distribution \( p(\theta^t) \)
  - This describes the level of knowledge in the value of the population parameters
  - Can be based on subjective information, or existing data
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- The way in which we construct our statistical model, depends on
  - The characteristic of the available data (**individual-level** vs **aggregated** data)
  - The statistical framework (Bayesian vs frequentist)
RCTs vs decision-analytical models

- RCTs are a key component in the evaluation of health care interventions
  - Usually individual-level data are collected for a clinical study and increasingly often complemented by financial outcomes
- However, there may issues with RCTs data
  - Comparator(s) in the trial may not reflect standard of care
  - Limited follow up
  - Small sample size
  - Poor external validity
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- Health economic evaluations should include information from as many sources as possible
  - Evidence synthesis of literature
  - Network meta-analysis

- Bayesian methods ideally placed to deal with these!
Models for individual-level data

• Observe a vector \((e_i, c_i)\) under each intervention being compared
  – May also observe other variables (covariates) — e.g. individual values for age, sex, co-morbidities, etc

• Use observed data to estimate the relevant population parameters
  \(\theta^t = (\theta^t_e, \theta^t_c)\)
  – These are generally vectors, made by several components (e.g. means, variances, rates, etc)

• The main interest is in the population average benefits and costs under treatment \(t\)
  \[\mu^t_e = \mathbb{E}[e \mid \theta^t] \quad \text{and} \quad \mu^t_c = \mathbb{E}[c \mid \theta^t]\]

• NB: Because of underlying correlation, it is necessary to use some form of joint model
  – But: simple models (such as bivariate Normal) are not suitable, as both \(e, c\) tend to be skewed and cost are positive

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Can factorise the joint distribution, for example as $p(e, c) = p(c)p(e | c)$
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For instance, can model

- \( c_{it} \sim \text{Gamma}(\eta_t, \lambda_t) \) [rate & shape] \( \Rightarrow \mu_{ct} = \eta_t / \lambda_t \)
- \( c_{it} \sim \text{logNormal}(\eta_t, \lambda_t) \) [log mean & log sd] \( \Rightarrow \mu_{ct} = \exp(\eta_t + \lambda_t^2 / 2) \)
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Models for individual-level data

Can factorise the joint distribution, for example as \( p(e, c) = p(c)p(e \mid c) \)

Marginal model for \( c \)

\[
\begin{align*}
\eta_t & \quad \lambda_t \\
& \quad \mu_{ct} \\
& \quad c_{it}
\end{align*}
\]

Conditional model for \( e \mid c \)

\[
\begin{align*}
\phi_{it} & \quad \gamma_t \\
& \quad \xi_t \\
& \quad \mu_{et} \\
& \quad e_{it}
\end{align*}
\]

For instance, can model

- \( c_{it} \sim \text{Gamma}(\eta_t, \lambda_t) \) [rate & shape] \( \Rightarrow \mu_{ct} = \frac{\eta_t}{\lambda_t} \)
- \( c_{it} \sim \log\text{Normal}(\eta_t, \lambda_t) \) [log mean & log sd] \( \Rightarrow \mu_{ct} = \exp\left(\eta_t + \frac{\lambda_t^2}{2}\right) \)
- \( E[e_{it}] = \phi_{it}; g(\phi_{it}) = \xi_t + \gamma_t(c_{it} - \mu_{ct}) \Rightarrow \mu_{et} = g^{-1}(\xi_t) \)
Decision-analytic models

- Often, we do not have access to individual data and all we have is a set of aggregated data on relevant quantities
- These can in turn be used to construct a “population model” to describe the disease history and its implications
  - Decision trees
  - Markov (multistate) models
- Often, we do not have access to individual data and all we have is a set of aggregated data on relevant quantities.
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**Example:** influenza

```
Prophylactic NIs?

Yes → Influenza?
   Yes → (p₁) → Cost with NIs +
        → cost influenza
   No → (1 - p₁) → Cost with NIs

No → Influenza?
   Yes → (p₀) → Cost influenza
   No → (1 - p₀) → Cost with no NIs
```
Decision-analytic models

- Data sources for a decision-analytic model include
  - Published literature (e.g. probability of influenza in the range $[0.2 - 0.4]$)
  - Evidence synthesis/meta-analysis
  - Expert opinions
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  – Published literature (e.g. probability of influenza in the range \([0.2 - 0.4]\))
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• We need to combine the parameters of the population model to derive suitable measures of costs and benefits
  \[ c_0 = (1 - p_t)c_{GP}^G + p_t (c_{GP}^G + c_{Inf}^I) \Rightarrow \text{avg cost for } t = 0 \]
  \[ c_1 = (1 - p_t) (c_{GP}^G + c_{NI}^{NI}) + p_t (c_{GP}^G + c_{NI}^{NI} + c_{Inf}^I) \Rightarrow \text{avg cost for } t = 1 \]
  \[ e_t = l p_t \Rightarrow \text{avg measure of clinical benefit} \]

• NB: Again, under the Bayesian framework, all the parameters are modelled and the uncertainty is fully accounted for!
Decision-analytic models

\[ \mu \gamma \quad \sigma^2 \gamma \quad \mu \delta \quad \sigma^2 \delta \]

\[ \gamma_h \quad \beta_h \quad \beta_h \quad \beta_h \]

\[ \mu \gamma \quad \sigma^2 \gamma \quad \mu \delta \quad \sigma^2 \delta \]

\[ h = 1, \ldots, H \quad s = 1, \ldots, S \]

\[ p_1 \quad p_0 \quad \rho \]

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2. Economic modelling (types of evaluations)

- **Cost minimisation**
  - Assumes that the benefits produced by two interventions are identical \(\Rightarrow\) the only dimension of interest is costs

- **Cost-benefit analysis**
  - Requires that costs and benefits are converted and analysed into monetary terms \(\Rightarrow\) difficulties in valuing health outcomes in monetary units
2. Economic modelling (types of evaluations)

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- **Cost-effectiveness analysis** (CEA)
  - Evaluates cost-per-outcome gained
  - Outcomes are usually “hard” measurements (eg death) ⇒ easy to understand for clinicians, but difficult to compare across diseases (may have different main outcome)

- **Cost-utility analysis** (CUA)
  - Considers a common health outcome unit (= QALYs), so easy to compare across diseases
  - Often interchangeable with CEA (common methodology!)
2. Economic modelling

Can think of this step as the process of obtaining relevant population summaries for the measures of cost & clinical benefits. For example, when comparing two interventions $t = 0, 1$, the main focus is on

- The **increment in mean benefits**

\[
\Delta_e = \underbrace{\mathbb{E}[e \mid \theta^1]}_{\mu_e^1} - \underbrace{\mathbb{E}[e \mid \theta^0]}_{\mu_e^0}
\]

- The **increment in mean costs**:

\[
\Delta_c = \underbrace{\mathbb{E}[c \mid \theta^1]}_{\mu_c^1} - \underbrace{\mathbb{E}[c \mid \theta^0]}_{\mu_c^0}
\]

- **NB**: In a Bayesian context, these are functions of $\theta$ and thus random variables!

- Also, when using individual-level data, estimation typically directly available from the statistical model
3. (Bayesian) Decision analysis

Based on the precepts of expected utility theory

1. Characterise variability in the observable outcomes and uncertainty in the parameters using a model \( p(e, c, \theta^t) = p(e, c \mid \theta^t)p(\theta^t) \)

2. Value the consequences of decisions through the future outcomes, using a suitable utility function \( u(e, c; t) \)
   - Typically choose the monetary net benefit \( u(e, c; t) := ke - c \)
   - \( k \) = “willingness to pay” = cost per extra unit of effectiveness gained

3. For each intervention \( t \), compute the expected utility \( U^t = E[u(e, c; t)] \)

4. Choose the intervention that maximises the expected utility
   - It is possible to prove that this is equivalent to maximising the chance of obtaining the preferred outcome
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**NB:** When only two interventions are being compared, this is equivalent to assessing whether

\[ EIB = U^1 - U^0 > 0 \]

So, if \( EIB > 0 \) then \( t = 1 \) is more cost-effective than \( t = 0 \)
EIB vs ICER

- Alternative criterion for making decisions

\[
\text{ICER} = \frac{E[\Delta_c]}{E[\Delta_e]} = \text{Additional cost to gain 1 unit of benefit}
\]

\[
\Delta_e = E[e | \theta^1] - E[e | \theta^0] = \text{increment in mean benefits}
\]

\[
\Delta_c = E[c | \theta^1] - E[c | \theta^0] = \text{increment in mean costs}
\]

- When the MNB is used as utility function and \( T = (0, 1) \)

\[
\text{EIB} = \mathcal{U}^1 - \mathcal{U}^0 = E[k \Delta_e - \Delta_c] = kE[\Delta_e] - E[\Delta_c]
\]

and thus

\[
\text{EIB} > 0 \Rightarrow k > \frac{E[\Delta_c]}{E[\Delta_e]} = \text{ICER}
\]
Cost-effectiveness plane vs ICER

Cost-effectiveness plane

Δ\text{c}

Δ\text{e}

Cost differential

Effectiveness differential

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Cost-effectiveness plane vs ICER

Cost-effectiveness plane

\[ \text{ICER} = \frac{E[\Delta_c]}{E[\Delta_e]} = \text{Cost per QALY} \]
Another criterion for making decisions is based on

\[
\text{ICER} = \frac{E[\Delta_c]}{E[\Delta_e]} = \text{Additional cost to gain 1 unit of benefit}
\]

- \( \Delta_e = E[e | \theta^1] - E[e | \theta^0] = \text{increment in mean benefits} \)

- \( \Delta_c = E[c | \theta^1] - E[c | \theta^0] = \text{increment in mean costs} \)

- When the MNB is used as utility function and \( T = (0, 1) \)

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\]
Cost-effectiveness plane vs EIB vs ICER

Cost effectiveness plane
New Chemotherapy vs Old Chemotherapy

\[ \text{ICER} = 6497.10 \]
Cost-effectiveness plane vs EIB vs ICER

Cost effectiveness plane
New Chemotherapy vs Old Chemotherapy

• ICER=6497.10

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Health economic evaluation based on EIB

Expected Incremental Benefit

Willingness to pay

EIB

\( k^* = 6700 \)
4. Uncertainty analysis

So: problem solved?
4. Uncertainty analysis

So: problem solved?... Well, not really!
4. Uncertainty analysis

So: problem solved?... Well, not really!

- The quality of the current evidence is often limited
  - During the pre-market authorisation phase, the regulator should decide whether to grant reimbursement to a new product — and in some countries also set the price — on the basis of uncertain evidence, regarding both clinical and economic outcomes
  - Although it is possible to answer some unresolved questions after market authorisation, relevant decisions such as that on reimbursement (which determines the overall access to the new treatment) have already been taken
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  - Although it is possible to answer some unresolved questions after market authorisation, relevant decisions such as that on reimbursement (which determines the overall access to the new treatment) have already been taken

- This leads to the necessity of performing (probabilistic) sensitivity analysis (PSA)
  - Formal quantification of the impact of uncertainty in the parameters on the results of the economic model
  - Standard requirement in many health systems (e.g. for NICE in the UK), but still not universally applied
  - Often limited to parametric uncertainty, but should be extended to structural uncertainty too (more on these in the next talks!)
PSA to parameter uncertainty

**Parameters**
- $\pi(0)$
- $\rho$
- $\gamma$
- $c_{\text{hosp}}$

**Model structure**

**Old chemotherapy**
- $\pi(0)$
- Standard treatment $c_{\text{amb}}$ (New to $\pi_{\text{amb}}$)
- Hospital admission $H_0$ (New to $\pi_{\text{hosp}}$)
- $N - SE_0$ (New to $\pi_{\text{amb}}$)
- $H_0$ (New to $\pi_{\text{hosp}}$)

**New chemotherapy**
- $\pi(1)$
- Blood-related side effects $SE_1$ (New to $\pi_{\text{hosp}}$
- $N - SE_1$ (New to $\pi_{\text{amb}}$
- $H_0$ (New to $\pi_{\text{hosp}}$

**Decision analysis**

**Old chemotherapy**
- Benefits
- Costs

**New chemotherapy**
- Benefits
- Costs

**Benefits and Costs**

Old chemotherapy
- $\pi_0$
- $\rho$
- $\gamma$
- $c_{\text{hosp}}$

New chemotherapy
- $\pi_1$
- $\rho$
- $\gamma$
- $c_{\text{hosp}}$

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### Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Distribution</th>
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</thead>
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<td>( \pi(0) )</td>
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<tr>
<td>( \rho )</td>
<td>Normal</td>
</tr>
<tr>
<td>( \gamma )</td>
<td>Normal</td>
</tr>
<tr>
<td>( c_{\text{hosp}} )</td>
<td>Normal</td>
</tr>
</tbody>
</table>

### Model structure

#### Old chemotherapy

- **Ambulatory care**
  - \( A_0 \)
- **Hospital admission**
  - \( H_0 \)
- **Blood-related side effects**
  - \( SE_0 \)
- **No side effects**
  - \( N - SE_0 \)

#### New chemotherapy

- **Ambulatory care**
  - \( A_1 \)
- **Hospital admission**
  - \( H_1 \)
- **Blood-related side effects**
  - \( SE_1 \)
- **No side effects**
  - \( N - SE_1 \)

### Decision analysis

<table>
<thead>
<tr>
<th>Old chemotherapy</th>
<th>Benefits</th>
<th>Costs</th>
</tr>
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<td></td>
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<td>670382.1</td>
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</table>

<table>
<thead>
<tr>
<th>New chemotherapy</th>
<th>Benefits</th>
<th>Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>732</td>
<td>1131978</td>
</tr>
</tbody>
</table>

\[ \text{ICER} = 20,000 \] 1QALY

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**Parameters**

- \( \pi(0) \)
- \( \rho \)
- \( \gamma \)
- \( c_{\text{hosp}} \)

**Model structure**

**Old chemotherapy**

- Ambulatory care \( A_0 \) → \( \rho_{\text{amb}} \)
- Blood-related side effects \( SE_0 \)
- Hospital admission \( H_0 \) \( (1 - \gamma) \)
- No side effects \( N - SE_0 \) \( (1 - \gamma) \)

**New chemotherapy**

- Ambulatory care \( A_1 \) → \( \rho_{\text{amb}} \)
- Blood-related side effects \( SE_1 \)
- Hospital admission \( H_1 \) \( (1 - \gamma) \)
- No side effects \( N - SE_1 \) \( (1 - \gamma) \)

**Decision analysis**

<table>
<thead>
<tr>
<th>Old chemotherapy</th>
<th>Benefits</th>
<th>Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>741</td>
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<td>871273.3</td>
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</tr>
</tbody>
</table>
PSA to parameter uncertainty

Parameters

- $\pi(0)$
- $\rho$
- $\gamma$
- $c_{\text{hosp}}$

Model structure

Old chemotherapy

New chemotherapy

Decision analysis

Old chemotherapy

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<tr>
<td>726</td>
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| Total    | 743.1     | 656644.6 |

New chemotherapy

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</tr>
<tr>
<td>811</td>
<td>766411.4</td>
</tr>
</tbody>
</table>

| Total    | 794.6     | 991804.0 |

$\text{ICER} = \frac{794.6 - 743.1}{51.6} = 6497.1$
Conclusions

- Bayesian modelling particularly effective in health economic evaluations
- Allows the incorporation of external, additional information to the current analysis
  - Previous studies
  - Elicitation of expert opinions
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  - This is particularly effective in decision-models, where information from different sources may be combined into a single framework
  - Useful in the case of individual-level data (e.g., from Phase III RCT)
- Using MCMC methods, it is possible to produce the results in terms of simulations from the posterior distributions
  - These can be used to build suitable variables of cost and benefit
  - Particularly effective for running “probabilistic sensitivity analysis”
Thank you!