Bayesian methods in health economics

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Seminar Series of the Master in Advanced Artificial Intelligence
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• Health economic evaluation
  – What is health economics?
  – What does health economics do?
Outline

- **Health economic evaluation**
  - What is health economics?
  - What does health economics do?

- **Statistical modelling**
  - Models for individual-level data
  - Models for aggregated data
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- Economic modelling & Decision analysis
  - Cost-effectiveness/cost-utility analysis
  - Criteria for decision-making in health economics
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- **Uncertainty analysis**
  - Rationale
  - Main ideas
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  - Rationale
  - Main ideas
- **Conclusions**
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
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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.
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  - $c =$ suitable costs associated with an intervention

• 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 $\Rightarrow$ 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!
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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 (and statistical approach!)

Statistical model

- Combines the parameters to obtain a population average measure for costs and clinical benefits
- Varies with the type of available data and statistical model used
- Summarises the economic model by computing suitable measures of "cost-effectiveness"
- Dictates the best course of actions, given current evidence
- Standardised process
- Assesses the impact of uncertainty (e.g., in parameters or model structure) on the economic results
- Fundamentally Bayesian!

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Bayesian methods in health economics
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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)
Models for individual-level data

- Observe vectors \((e, c)\) 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 \(\theta^t = (\theta_e^t, \theta_c^t)\)
  - 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 \(t\)
  \[\mu_e^t = \mathbb{E}[e \mid \theta^t]\quad \text{and} \quad \mu_c^t = \mathbb{E}[c \mid \theta^t]\]

- **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
Can factorise the joint distribution, for example as $p(e, c) = p(c)p(e \mid c)$
Models for individual-level data

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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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- $E[e_{it}] = \phi_{it}; \quad g(\phi_{it}) = \xi_t + \gamma_t(c_{it} - \mu_{ct}) \Rightarrow \mu_{et} = g^{-1}(\xi_t)$
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
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Example: influenza

Prophylactic NIs?

Yes $p_1$ Cost with NIs + cost influenza

No $(1 - p_1)$ Cost with NIs

Influenza?

Yes $(p_0)$ Cost influenza

No $(1 - p_0)$ Cost with no NIs
Decision-analytic models

\[
\begin{align*}
p_1 & \quad p_0 \\
p_0 & \quad \rho \\
\mu_\gamma & \quad \sigma^2_\gamma \\
\gamma_h & \quad \beta_h \\
m_h & \quad x_h \\
h = 1, \ldots, H \\
\end{align*}
\]

\[
\begin{align*}
\mu_\delta & \quad \sigma^2_\delta \\
\delta_s & \quad \pi_s^{(1)} \\
\pi_s^{(0)} & \quad \alpha_s \\
n_s^{(1)} & \quad n_s^{(0)} \\
r_s^{(1)} & \quad r_s^{(0)} \\
s = 1, \ldots, S \\
\end{align*}
\]
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**

\[ \Delta_e = E[e | \theta^1] - E[e | \theta^0] \]

\[ \mu_e^1 - \mu_e^0 \]

- The **increment in mean costs**:

\[ \Delta_c = E[c | \theta^1] - E[c | \theta^0] \]

\[ \mu_c^1 - \mu_c^0 \]

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

- When using individual-level data, estimation typically directly available from the statistical model; for decision-analytic models, it may be necessary to combine the parameters to obtain these
In order to compare the two interventions \((t = 0, 1)\), we define suitable health economic indicators:

- **The population average increment in benefits**
  
  \[
  E[\Delta e] = \bar{e}_1 - \bar{e}_0 = E[\mu_1^e] - E[\mu_0^e]
  \]

- **The population average increment in costs**:
  
  \[
  E[\Delta c] = \bar{c}_1 - \bar{c}_0 = E[\mu_1^c] - E[\mu_0^c]
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3. Decision analysis

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- **The population average increment in costs**:

  \[
  E[\Delta_c] = \bar{c}_1 - \bar{c}_0 = E[\mu_1^c] - E[\mu_0^c]
  \]

- Generally, economic summaries are computed in the form of “cost per outcome” ratios

  \[
  \text{ICER} = \frac{E[\Delta_c]}{E[\Delta_e]} = \text{Additional cost to gain 1 unit of benefit}
  \]
3. Decision analysis (cont’d)

Cost-effectiveness plane

\[ \Delta_e \]

\[ \Delta_c \]

Cost differential

Effectiveness differential
3. Decision analysis (cont’d)

Cost-effectiveness plane

\[ \text{ICER} = \frac{\mathbb{E}[\Delta_c]}{\mathbb{E}[\Delta_e]} = \text{Cost per QALY} \]

Cost differential

Effectiveness differential
3. Decision analysis (cont’d)

- When considering only two interventions $t = 0, 1$, can equivalently represent the problem using the *Expected Incremental Benefit*

\[
EIB = k \cdot E[\Delta_e] - E[\Delta_c]
\]

where $k$ is the **willingness to pay**

- Puts costs and benefits on the same scale
- Represents the amount of the decision-maker is willing to invest to increment the benefits by 1 unit
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- One-to-one relationship between ICER and EIB

  $$\text{EIB} > 0 \iff k > \frac{E[\Delta_c]}{E[\Delta_e]} = \text{ICER}$$
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- One-to-one relationship between ICER and EIB

\[
EIB > 0 \Rightarrow k > \frac{E[\Delta_c]}{E[\Delta_e]} = ICER
\]

- The EIB is also more directly linked to a (Bayesian) decision-theoretic approach
  - Define a utility function to quantify the “value” of an intervention
  - Compute the expected utility (wrt to both individual & population variations)
  - Choose the intervention with the highest expected utility
Cost-effectiveness plane vs EIB vs ICER

Cost effectiveness plane
New Chemotherapy vs Old Chemotherapy

Effectiveness differential
Cost differential

\[ \text{ICER} = 6497.10 \]

\[ k = 1000 \]
Cost-effectiveness plane vs EIB vs ICER

**Cost effectiveness plane**

New Chemotherapy vs Old Chemotherapy

Effectiveness differential

Cost differential

\[ -200 \quad -100 \quad 0 \quad 100 \quad 200 \]

\[ -200000 \quad 0 \quad 200000 \quad 600000 \]

\[ \text{ICER}=6497.10 \quad \text{k} = 25000 \]

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Bayesian methods in health economics

Seminar UNED, 11 Jun 2015
Cost-effectiveness plane vs EIB vs ICER

Expected Incremental Benefit

Willingness to pay vs EIB

k* = 6700
4. Uncertainty analysis

So: problem solved?

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

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1. Estimation (base-case)

\[ \hat{\theta} = f(Y) \]

\[ p(y | \theta) \]

2. PSA

\[ p(\theta) \sim g(\hat{\theta}) \]

Economic model

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Uncertainty analysis — Frequentist vs Bayesian approach

1. Estimation (base-case)

\[ \hat{\theta} = f(Y) \]

\[ p(y \mid \theta) \]

2. PSA

\[ p(\theta) \leftrightarrow g(\hat{\theta}) \]

Economic model

Estimation & PSA (one stage)

\[ p(\theta) \]

\[ p(\theta \mid y) \]

Economic model

\[ p(y \mid \theta) \]

\[ y \]
PSA to parameter uncertainty

### Parameters

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

### Model structure

#### $t = 0$: Old chemotherapy

- $A_0$
- Ambulatory care ($\gamma$)
- Blood-related side effects ($\pi_0$)
- Hospital admission ($1 - \gamma$)

#### $t = 1$: New chemotherapy

- $A_0$
- Ambulatory care ($\gamma$)
- Blood-related side effects ($\pi_1 = \pi_0 \rho$)
- Hospital admission ($1 - \gamma$)

### Decision analysis

<table>
<thead>
<tr>
<th>Old chemotherapy</th>
<th>Benefits</th>
<th>Costs</th>
</tr>
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<tbody>
<tr>
<td>$N - SE_0$ No side effects ($1 - \pi_0$)</td>
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### ICER

$\text{ICER} = 20,000 / 1\text{QALY}$
PSA to parameter uncertainty

### Parameters

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

### Model structure

**t = 0: Old chemotherapy**

- $A_0$
- $H_0$
- $SE_0$
- $SE_1$

**Benefits Costs**

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<td>670 382.1</td>
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\[ \text{ICER} = 20000 \text{ per QALY} \]

**New chemotherapy**

- $A_0$
- $H_0$
- $SE_0$
- $SE_1$

**Benefits Costs**

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**Decision analysis**

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Parameters

$\pi_0$

$\rho$

$\gamma$

$c_{\text{hosp}}$

Model structure

$t = 0$: Old chemotherapy

$A_0$

Ambulatory care ($\gamma$) \rightarrow $c_{\text{amb}}$

$SE_0$

Blood-related side effects ($\pi_0$)

$H_0$

Hospital admission ($1 - \gamma$) \rightarrow $c_{\text{hosp}}$

$N - SE_0$

No side effects ($1 - \pi_0$)

$t = 1$: New chemotherapy

$A_0$

Ambulatory care ($\gamma$) \rightarrow $c_{\text{amb}}$

$SE_0$

Blood-related side effects ($\pi_1 = \rho \pi_0$)

$H_0$

Hospital admission ($1 - \gamma$) \rightarrow $c_{\text{hosp}}$

$N - SE_0$

No side effects ($1 - \pi_1$)

Decision analysis

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PSA to parameter uncertainty

Parameters

$t = 0$: Old chemotherapy

$t = 1$: New chemotherapy

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<td>726</td>
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<th>Benefits</th>
<th>Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>New chemotherapy</td>
<td></td>
</tr>
<tr>
<td>732</td>
<td>1 131 978</td>
</tr>
<tr>
<td>664</td>
<td>1 325 654</td>
</tr>
<tr>
<td>\ldots</td>
<td>\ldots</td>
</tr>
<tr>
<td>811</td>
<td>766 411.4</td>
</tr>
<tr>
<td>\textbf{774.5}</td>
<td>\textbf{1 066 849.8}</td>
</tr>
</tbody>
</table>

\[ \text{ICER} = \frac{276 468.6}{58.3} = 6 497.1 \]
Cost Effectiveness Acceptability Curve

Probability of cost effectiveness

Willingness to pay
Is this *all* we need?

- The CEAC only deals with the *probability* of making the “right decision”
- But it does not account for the *payoff/penalty* associated with making the “wrong” one!

*Example 1:* Intervention $t=1$ is the most cost-effective, given current evidence – $\Pr(t=1 \text{ is cost-effective}) = 0.51$.
- If we get it wrong: Increase in costs = £3
- If we get it wrong: Decrease in effectiveness = 0.000001 QALYs

*Example 2:* Intervention $t=1$ is the most cost-effective, given current evidence – $\Pr(t=1 \text{ is cost-effective}) = 0.999$.
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• Usually, it is impossible to buy information on all the model parameters
  – Some parameters are not even *that* interesting — e.g. fixed costs, “things” we cannot change, …
  – Some other though, are interesting, because we can conduct a study to learn more and thus potentially change the optimal decision
  – Can consider the **Expected Value of Partial Perfect Information**
Expected Value of Partial Information

- Suppose the parameters of your model are collected in a vector $\theta$
- And that you can split them into two subsets
  - The “important” parameters $\phi$ and the “unimportant” parameters $\psi$
- We are interested in quantifying the value of gaining more information on $\phi$, while leaving the current level of uncertainty on $\psi$ unchanged

Technical issue: because $\phi$ and $\psi$ are typically correlated, we cannot make easy computations for the EVPPI (certainly not in Excel!)
- Nested Monte Carlo simulations
  1. Simulate a large number of values for $\phi$
  2. For each of the simulated values of $\phi$, simulate a large values of $\psi$
  3. This means we may need to run a PSA with 10,000s × 10,000s iterations — too big!
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  - Can use a standard run of 1,000 PSA simulations and can approximate the true value of the EVPPI very accurately!
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Gianluca Baio (UCL)
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Thank you!
Some references


