Bayesian methods in health economics

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Seminar Series of the Master in Advanced Artificial Intelligence

Madrid, Universidad Nacional De Educación a Distancia

Thursday 11 June 2015

Outline

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

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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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  - 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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  - 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
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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

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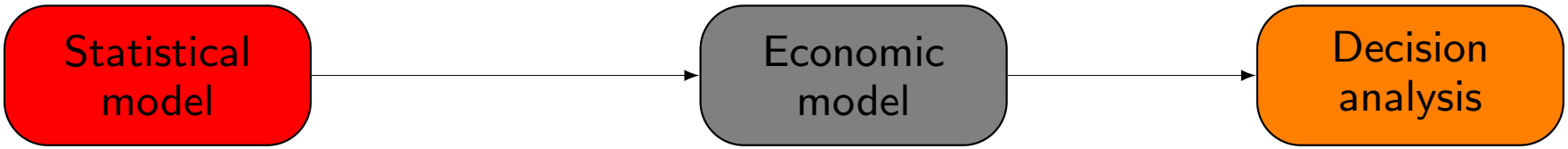

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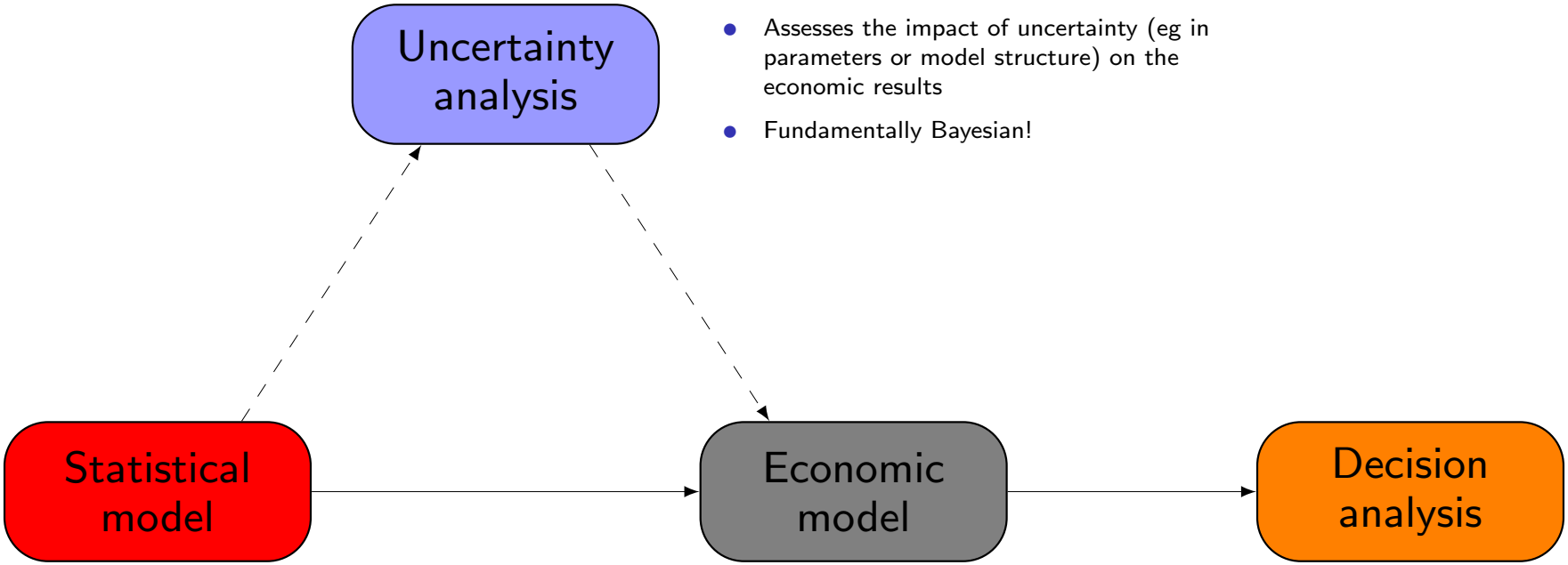
- Dictates the best course of actions, given current evidence
- Standardised process

Health economic evaluations



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

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- Sampling variability for the health economic outcomes is described by a distribution $p(e, c \mid \boldsymbol{\theta}^t)$, which depends on a set of population parameters $\boldsymbol{\theta}^t$
  - 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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- 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

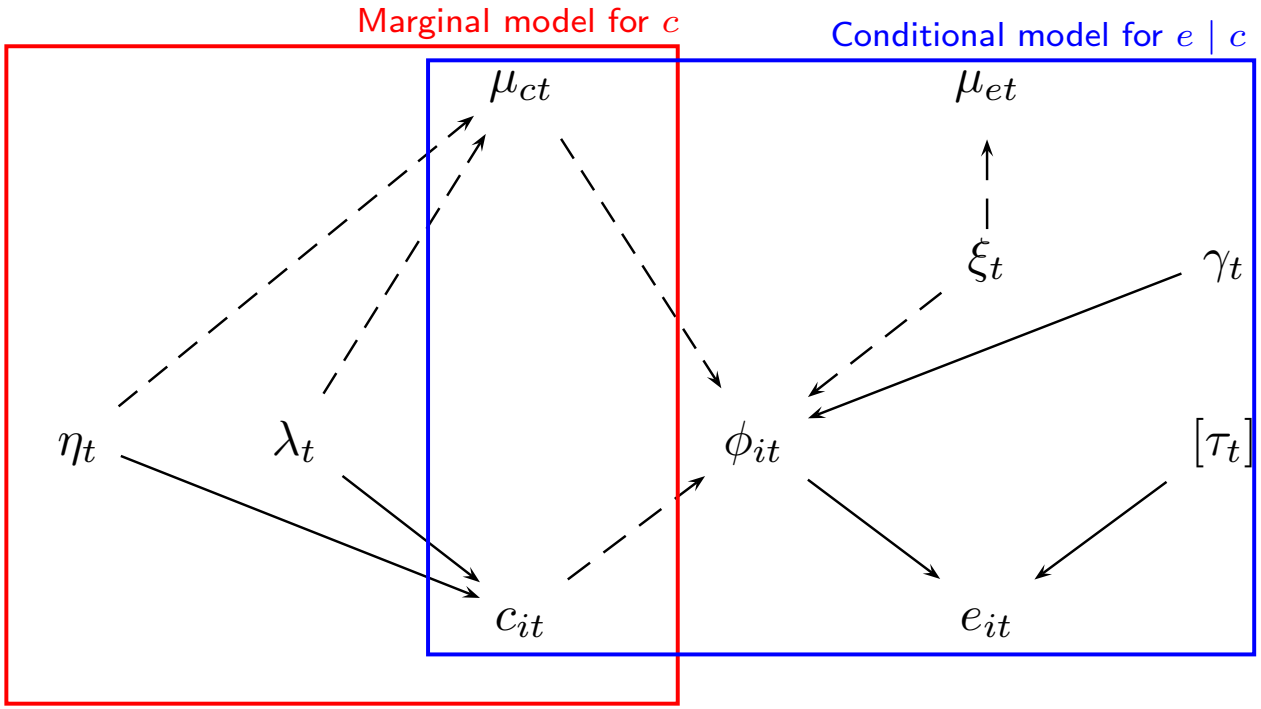
- Observe vectors (e, c) under each intervention being compared
  - May also observe other variables (covariates) — *e.g.* individual values for age, sex, co-morbidities, etc
- Use observed data to estimate the relevant population parameters $\boldsymbol{\theta}^t = (\boldsymbol{\theta}^t_e, \boldsymbol{\theta}^t_c)$
  - 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

$$\mu^t_e = \mathsf{E}[e \mid \boldsymbol{\theta}^t] \qquad \text{and} \qquad \mu^t_c = \mathsf{E}[c \mid \boldsymbol{\theta}^t]$$

- **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

Models for individual-level data

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



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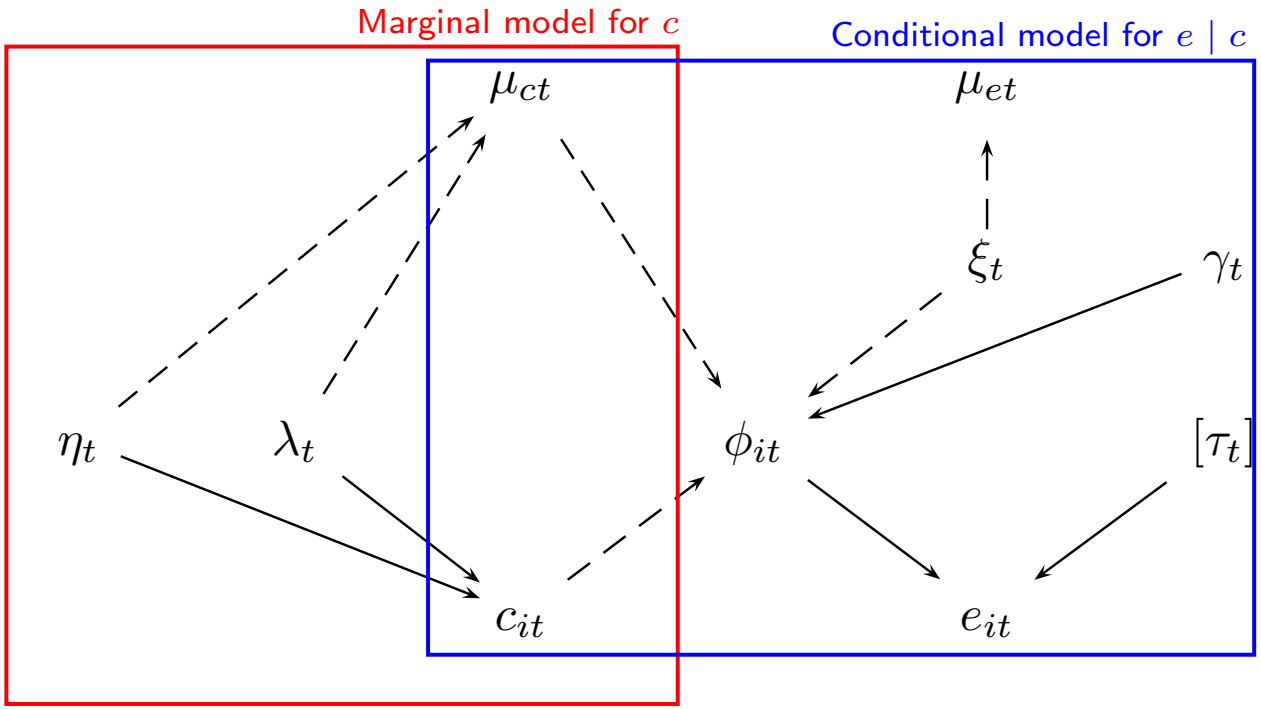

For instance, can model

- $c_{it} \sim \text{Gamma}(\eta_t, \lambda_t)$ [rate & shape] $\Rightarrow \mu_{ct} = \eta_t/\lambda_t$

  $c_{it} \sim \text{logNormal}(\eta_t, \lambda_t)$ [log mean & log sd] $\Rightarrow \mu_{ct} = \exp\left(\eta_t + \lambda_t^2/2\right)$

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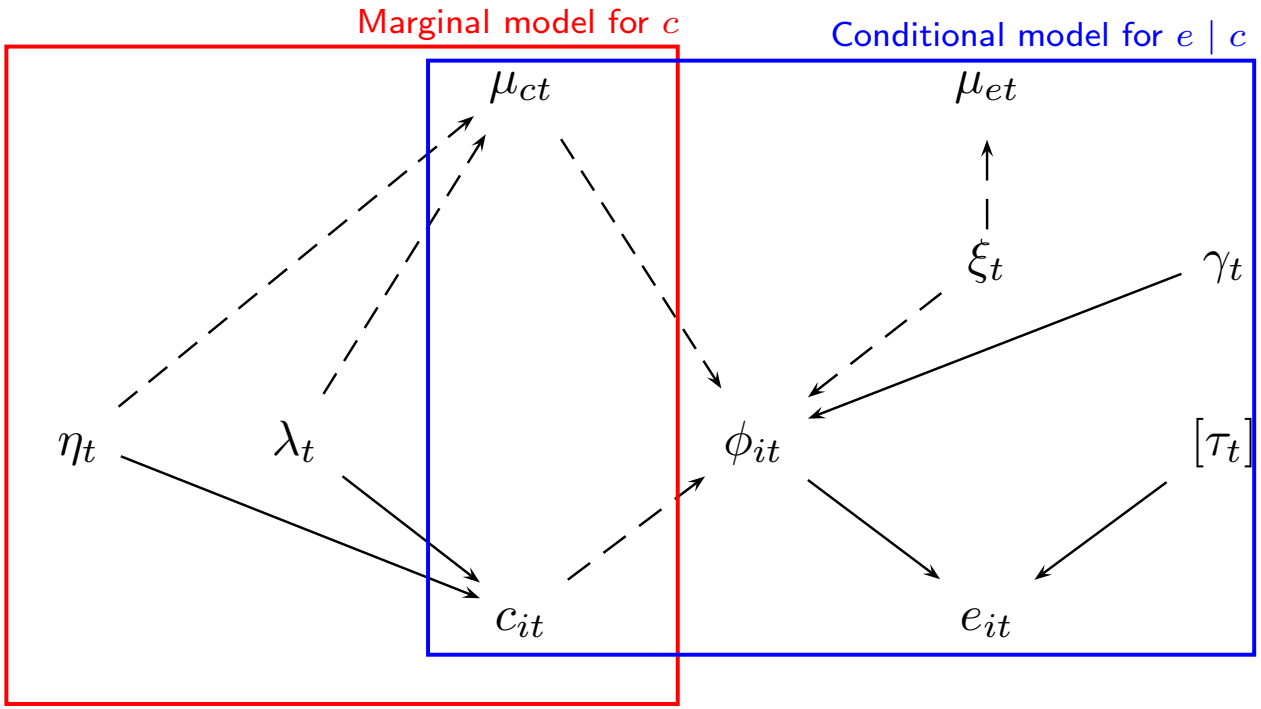

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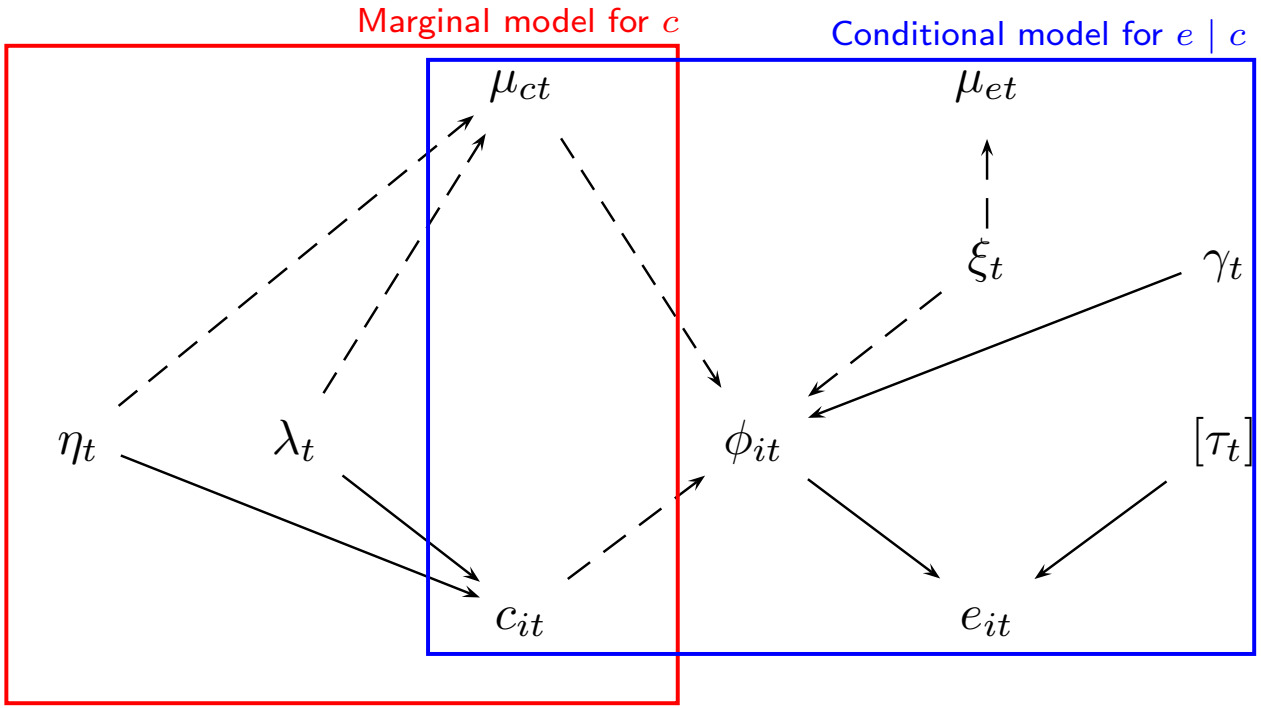

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- $\text{E}[e_{it}] = \phi_{it}$; $g(\phi_{it}) = \xi_t + \gamma_t(c_{it} - \mu_{ct}) \Rightarrow \mu_{et} = g^{-1}(\xi_t)$

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

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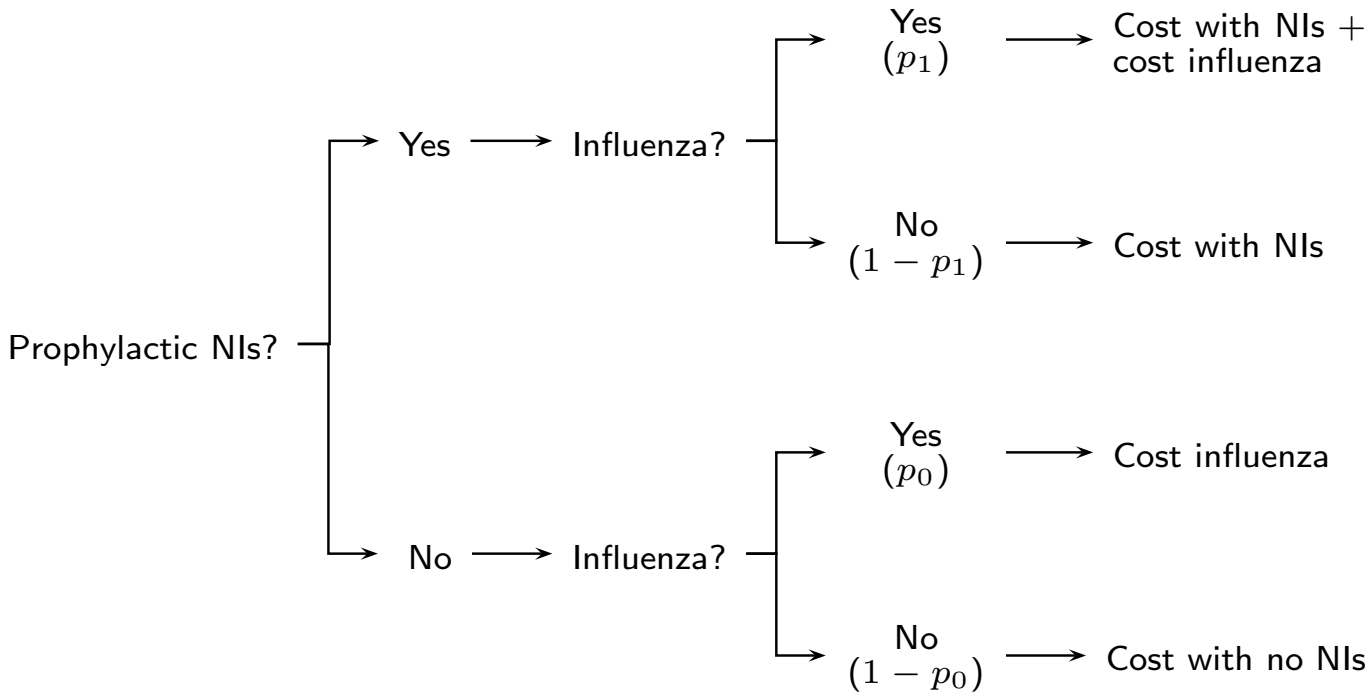
Example: influenza



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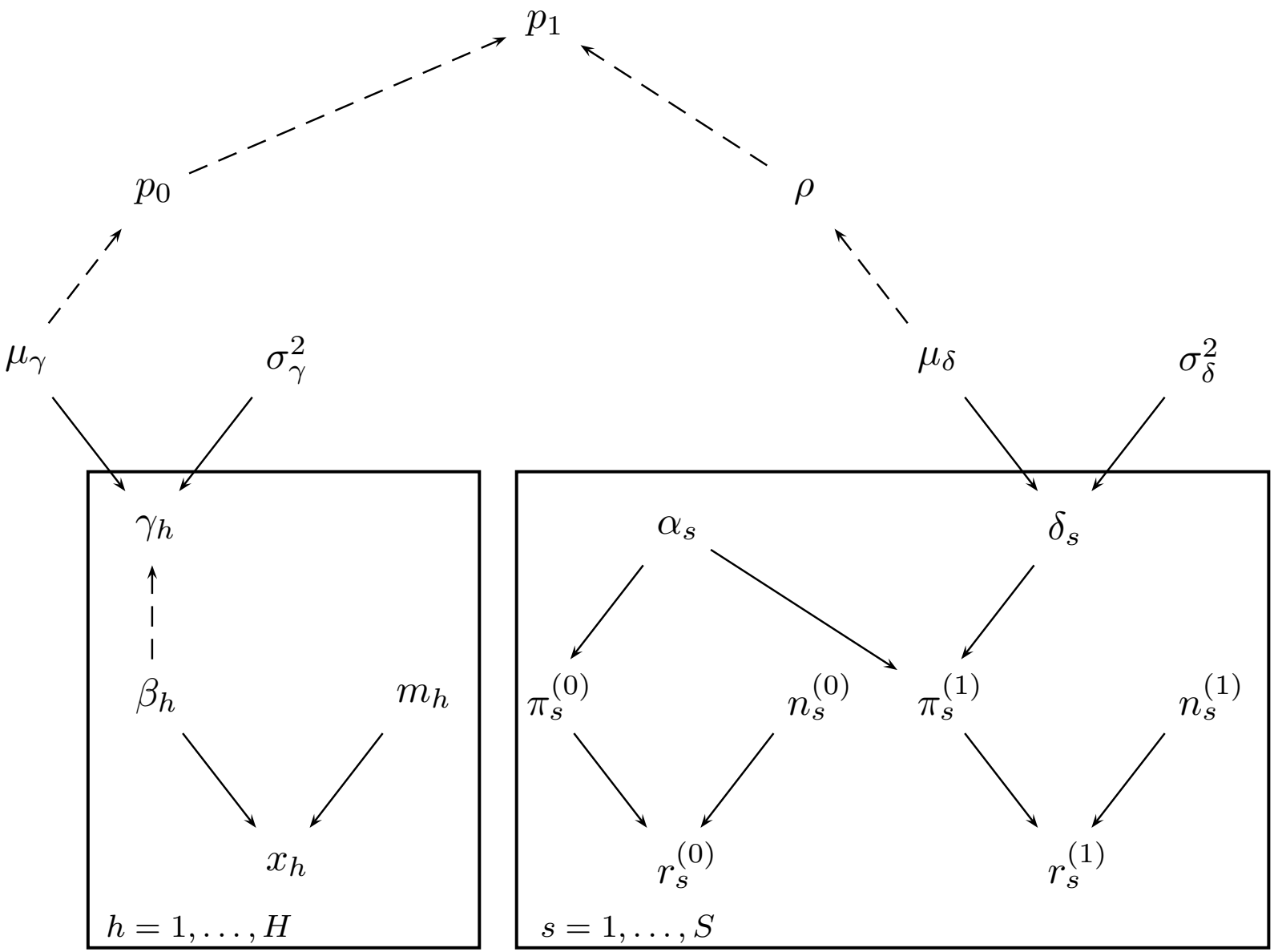

2. Economic modelling (types of evaluations)

- 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

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- **Cost-effectiveness analysis** (CEA)
  - Evaluates cost-per-outcome gained
  - Outcomes are usually "hard" measurements (eg death) $\Rightarrow$ 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!)

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**

$$\Delta_e = \underbrace{\mathsf{E}[e \mid \theta^1]}_{\mu_1^e} - \underbrace{\mathsf{E}[e \mid \theta^0]}_{\mu_0^e}$$

- The **increment in mean costs**:

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- **NB**: In a Bayesian context, these are functions of $\boldsymbol{\theta}$ 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**

$$\mathsf{E}[\Delta_e] = \bar{e}_1 - \bar{e}_0 = \mathsf{E}[\mu_1^e] - \mathsf{E}[\mu_0^e]$$

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

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3. Decision analysis

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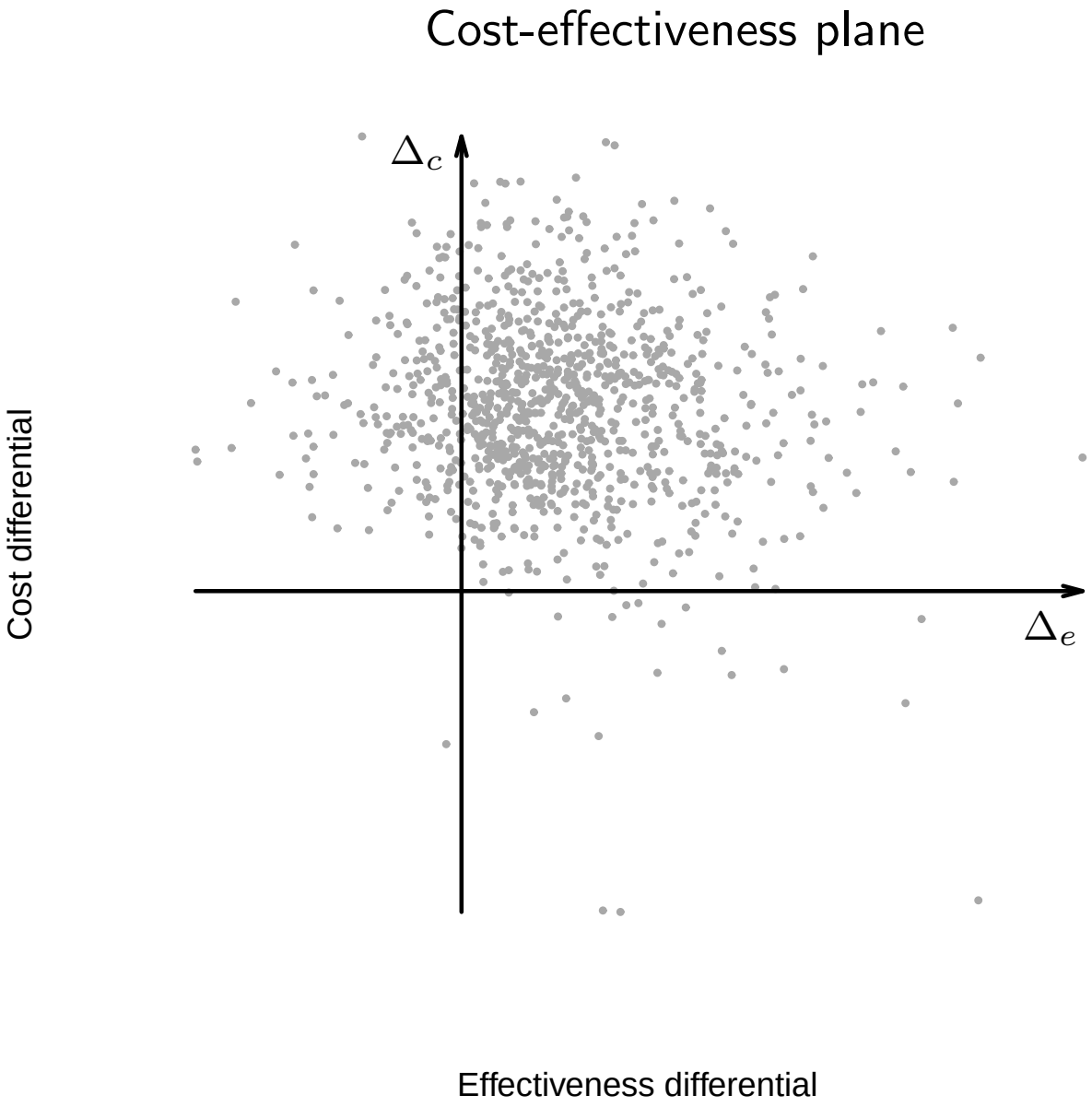
- Generally, economic summaries are computed in the form of "cost per outcome" ratios

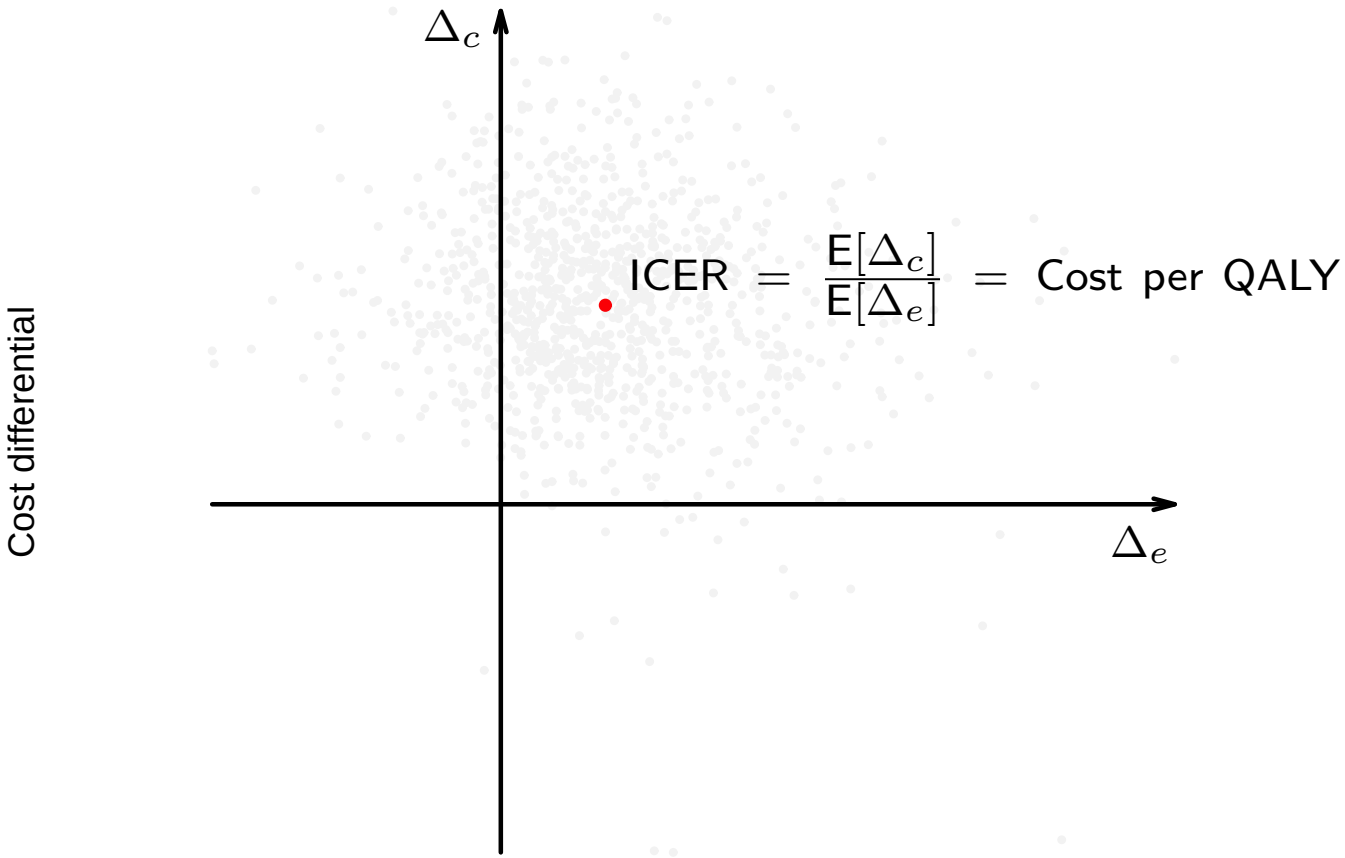
$$\text{ICER} = \frac{\mathsf{E}[\Delta_c]}{\mathsf{E}[\Delta_e]} = \text{Additional cost to gain 1 unit of benefit}$$

3. Decision analysis (cont'd)



3. Decision analysis (cont'd)

Cost-effectiveness plane



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

$$\text{EIB} = k\text{E}[\Delta_e] - \text{E}[\Delta_c]$$

where k is the willingness to pay

  - Puts costs and benefits on the same scale
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- One-to-one relationship between ICER and EIB

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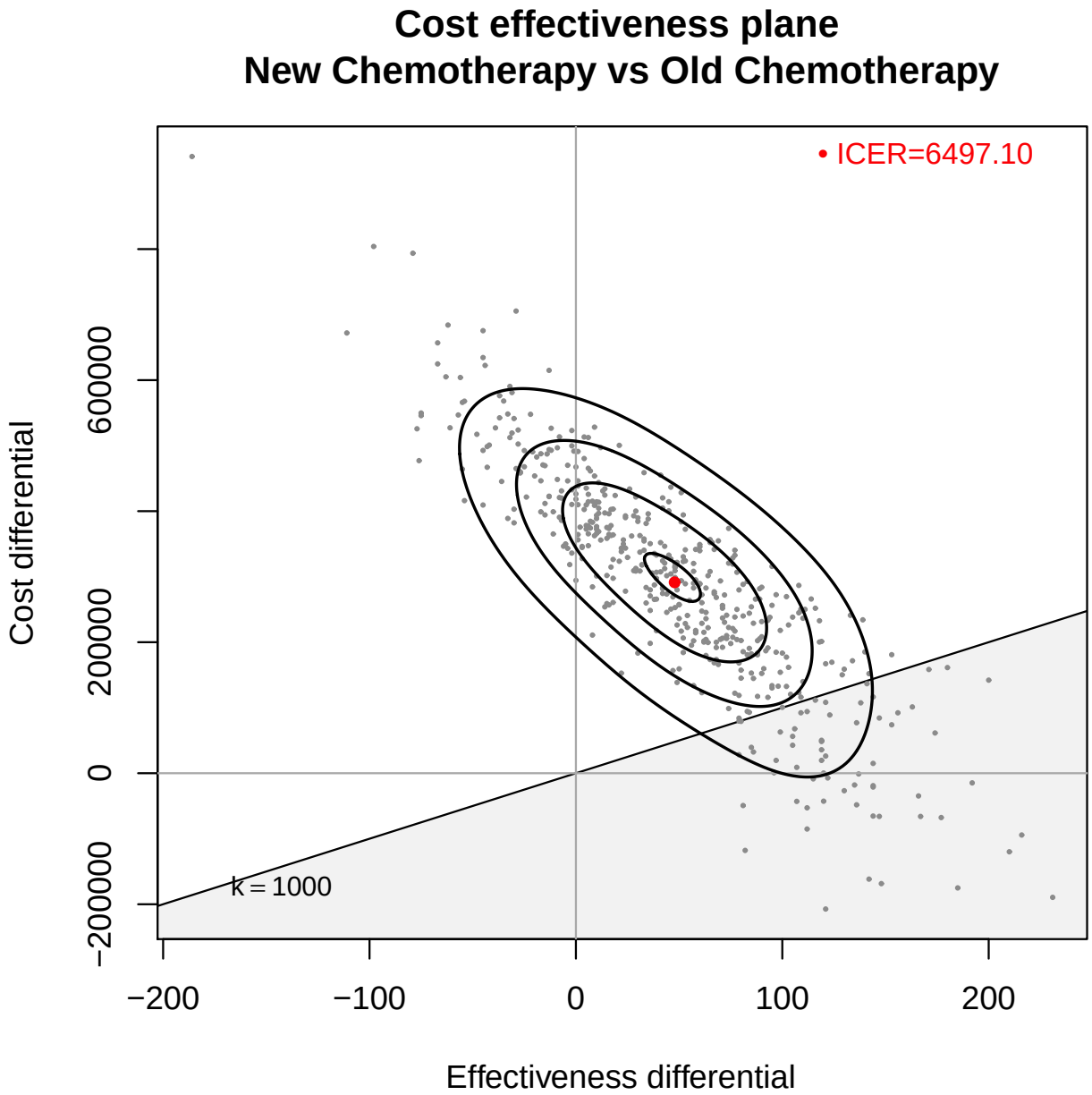
$$\text{EIB} > 0 \Rightarrow k > \frac{\text{E}[\Delta_c]}{\text{E}[\Delta_e]} = \text{ICER}$$

- 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



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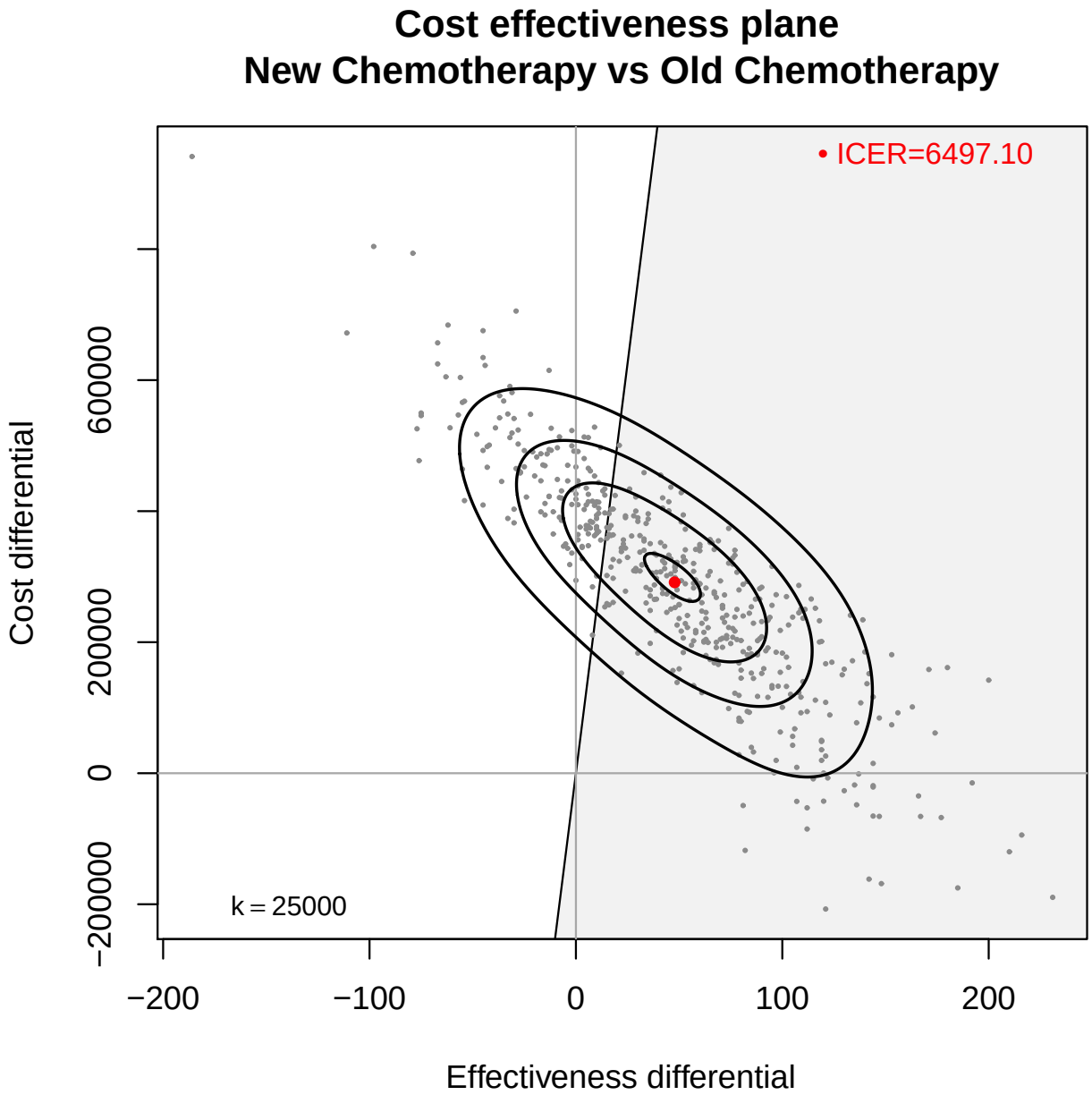

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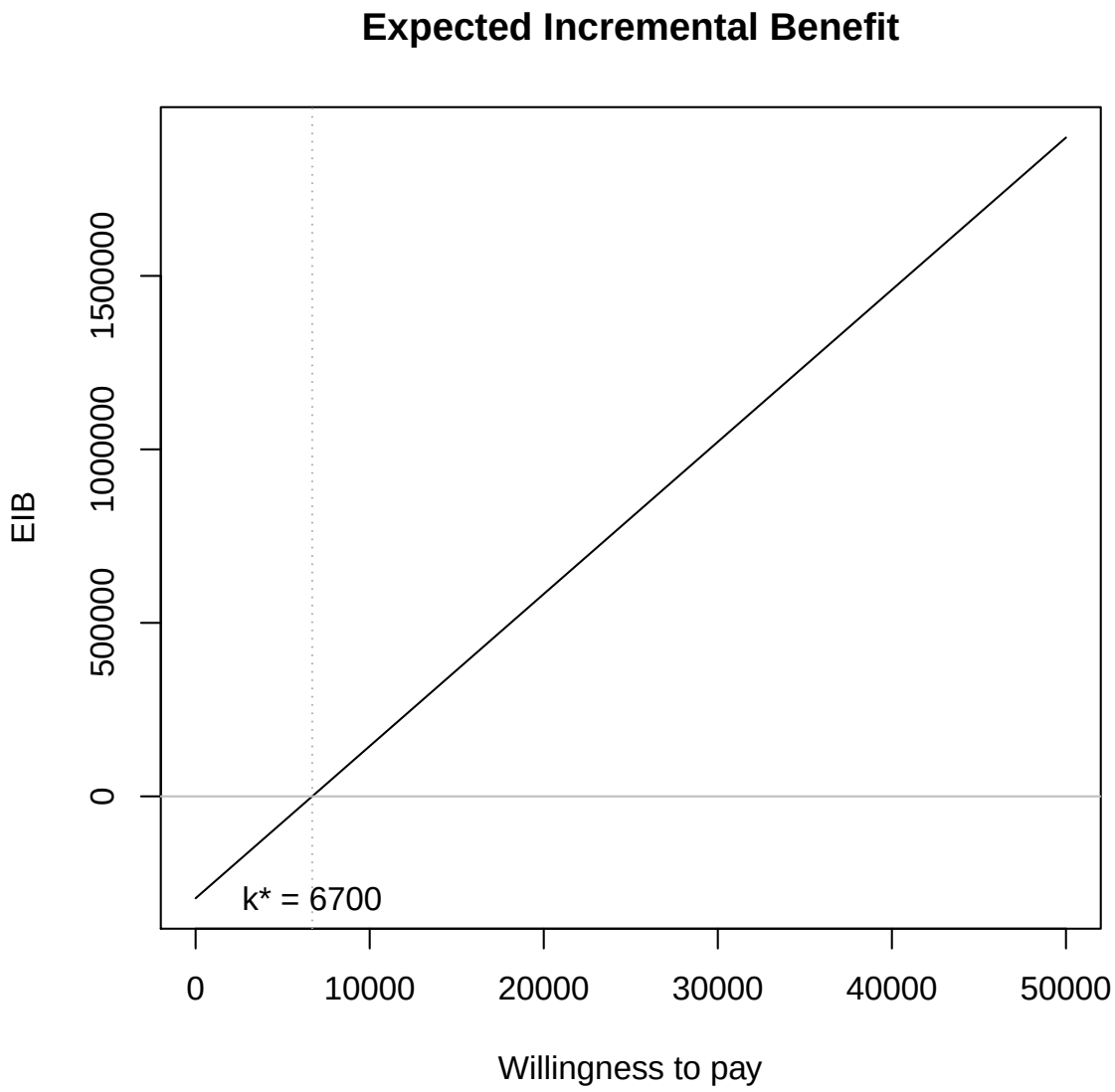

So: problem solved?

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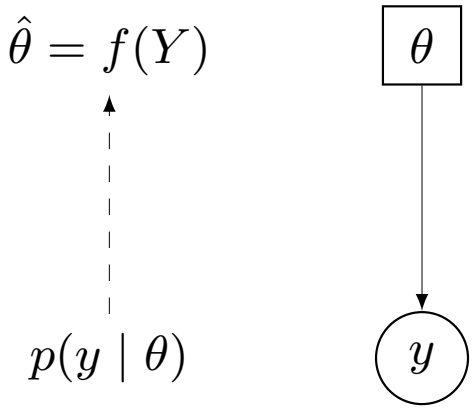
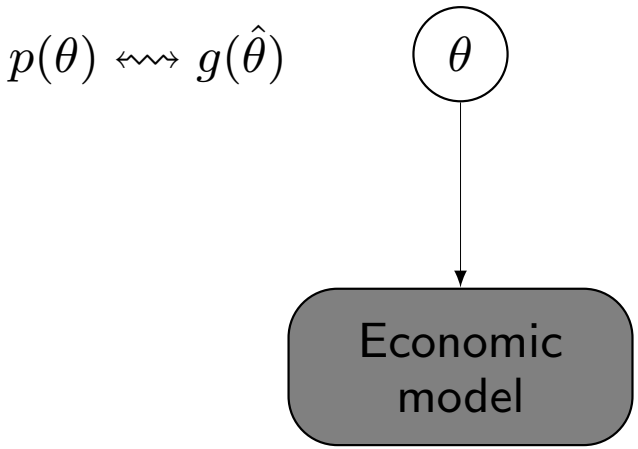
- This leads to the necessity of performing *(probabilistic) sensitivity analysis* **(PSA)**
  - Formal quantification of the impact of uncertainty in the parameters on the results of the economic model
  - Standard requirement in many health systems (e.g. for NICE in the UK), but still not universally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

1. Estimation (base-case)



$\Rightarrow$

2. PSA



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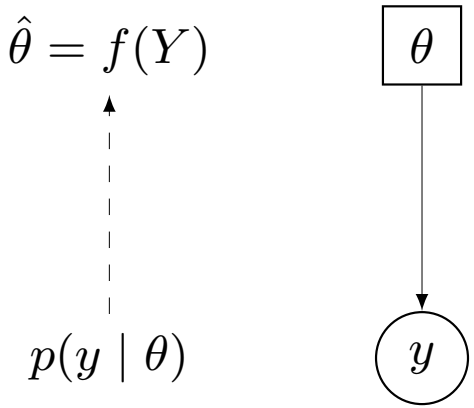

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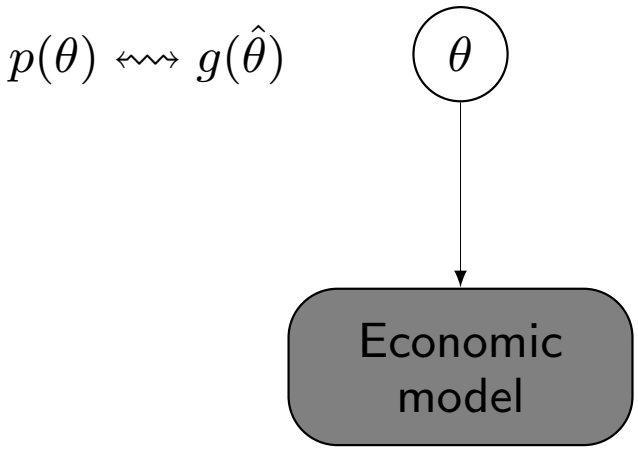
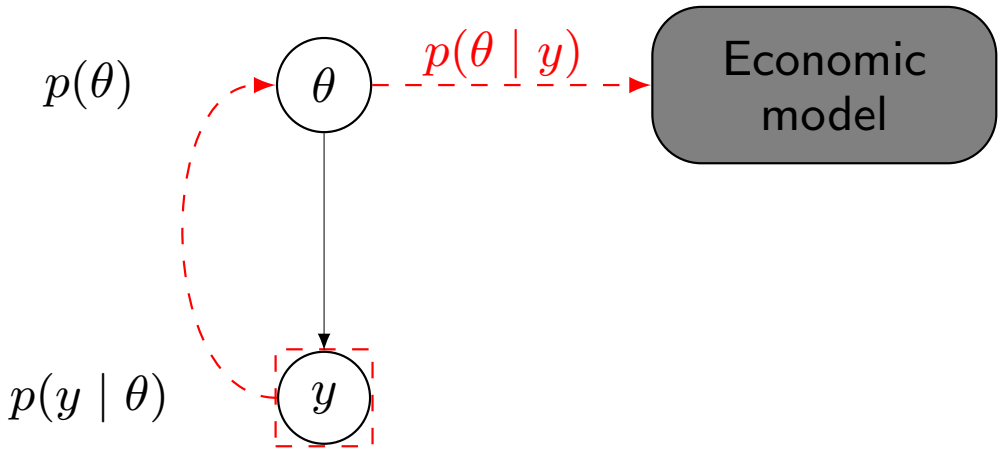
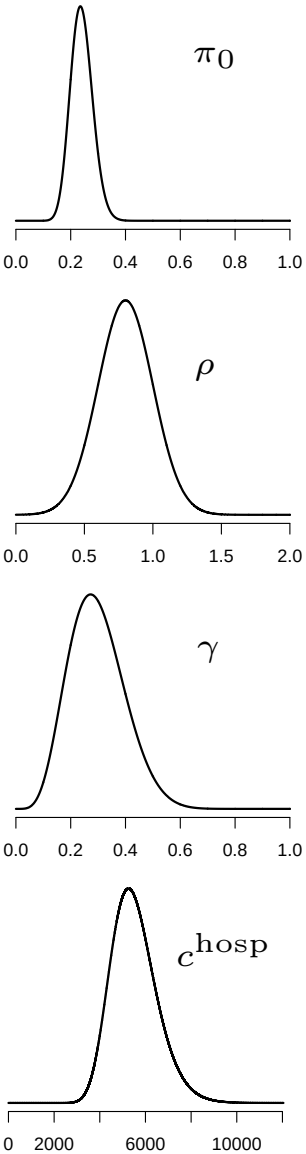


Estimation & PSA (one stage)

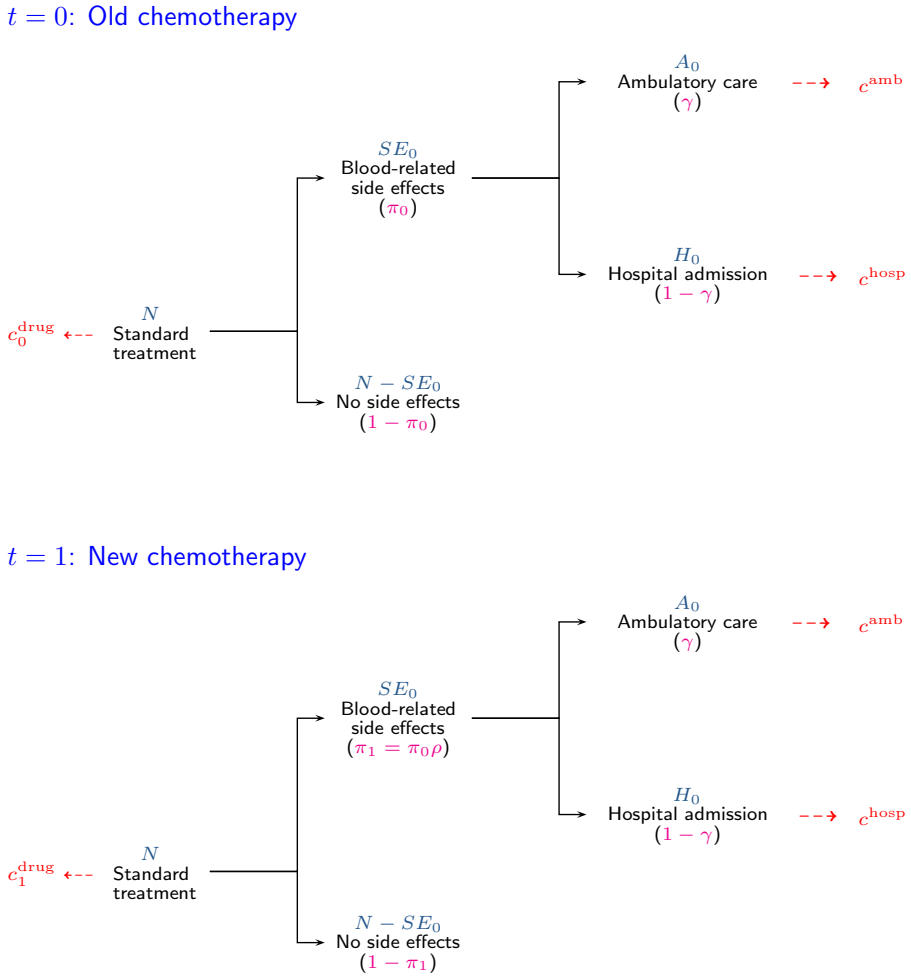


PSA to **parameter** uncertainty

Parameters



Model structure



Decision analysis

Old chemotherapy	
Benefits	Costs

New chemotherapy	
Benefits	Costs

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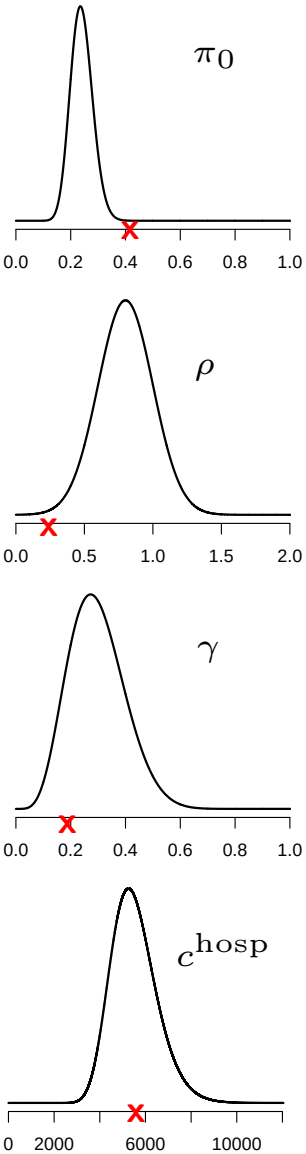

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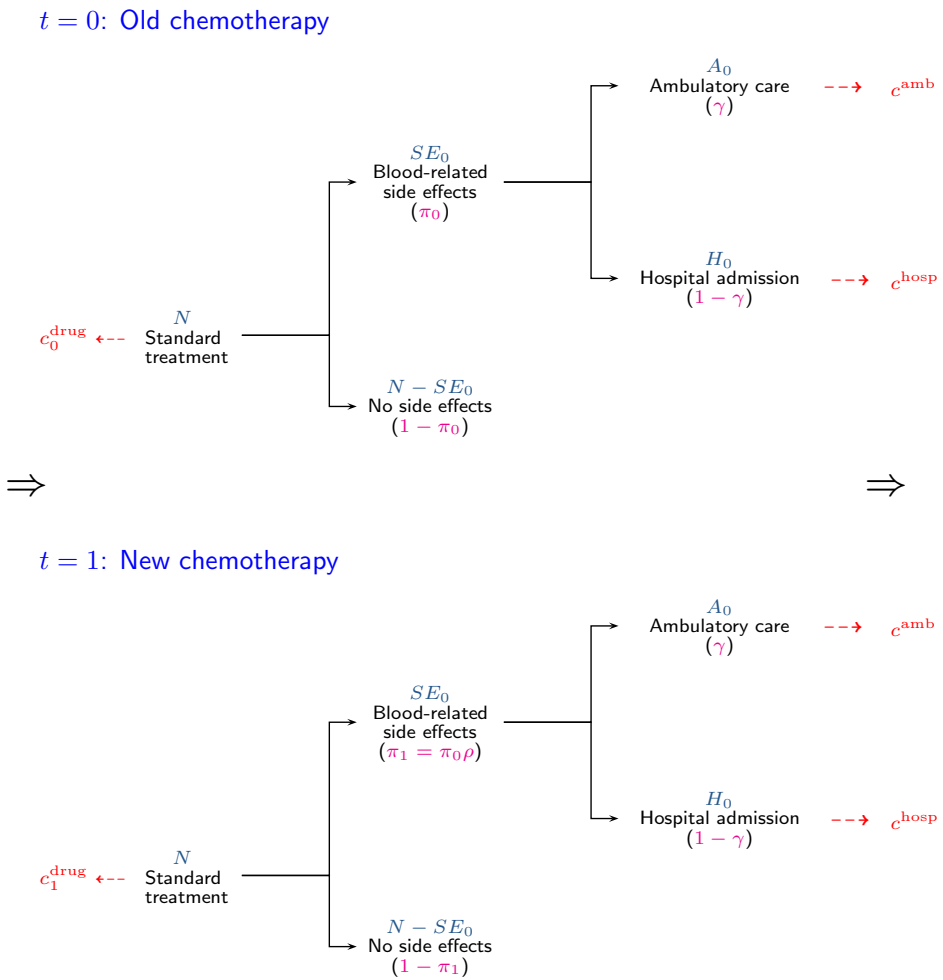

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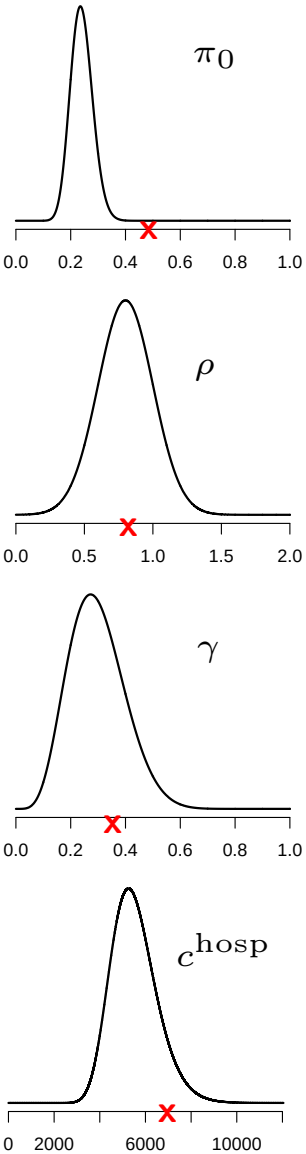
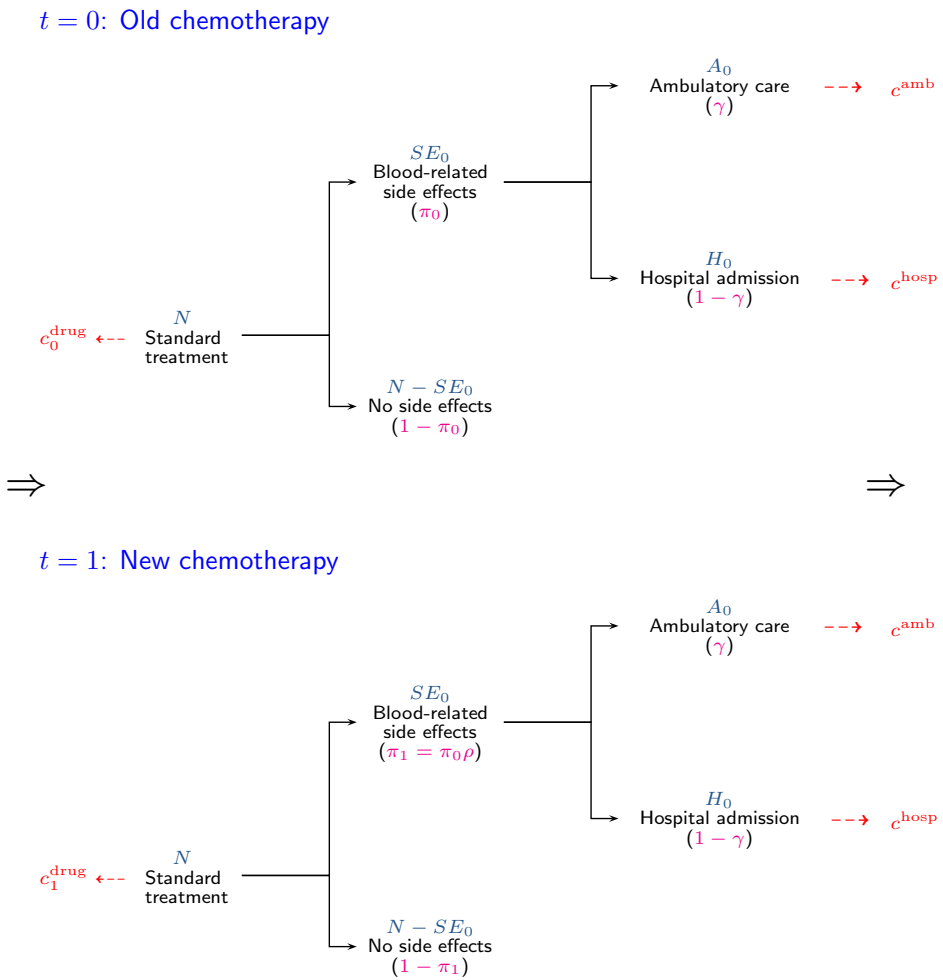


Model structure



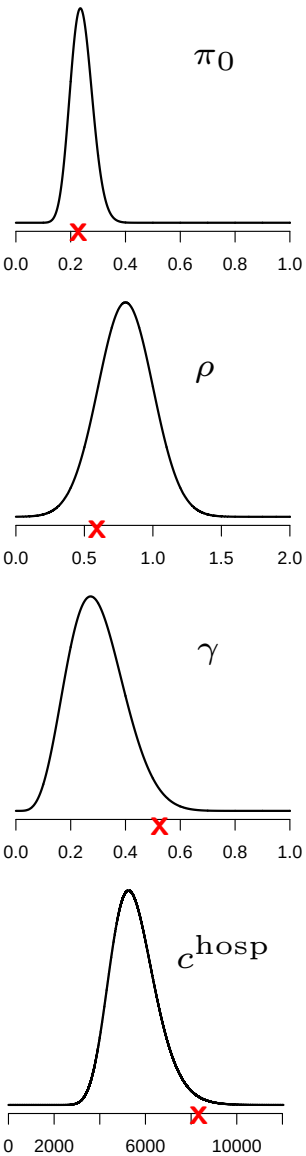
Decision analysis

Old chemotherapy	
Benefits	Costs
741	670 382.1
699	871 273.3

New chemotherapy	
Benefits	Costs
732	1 131 978
664	1 325 654

PSA to **parameter** uncertainty

Parameters



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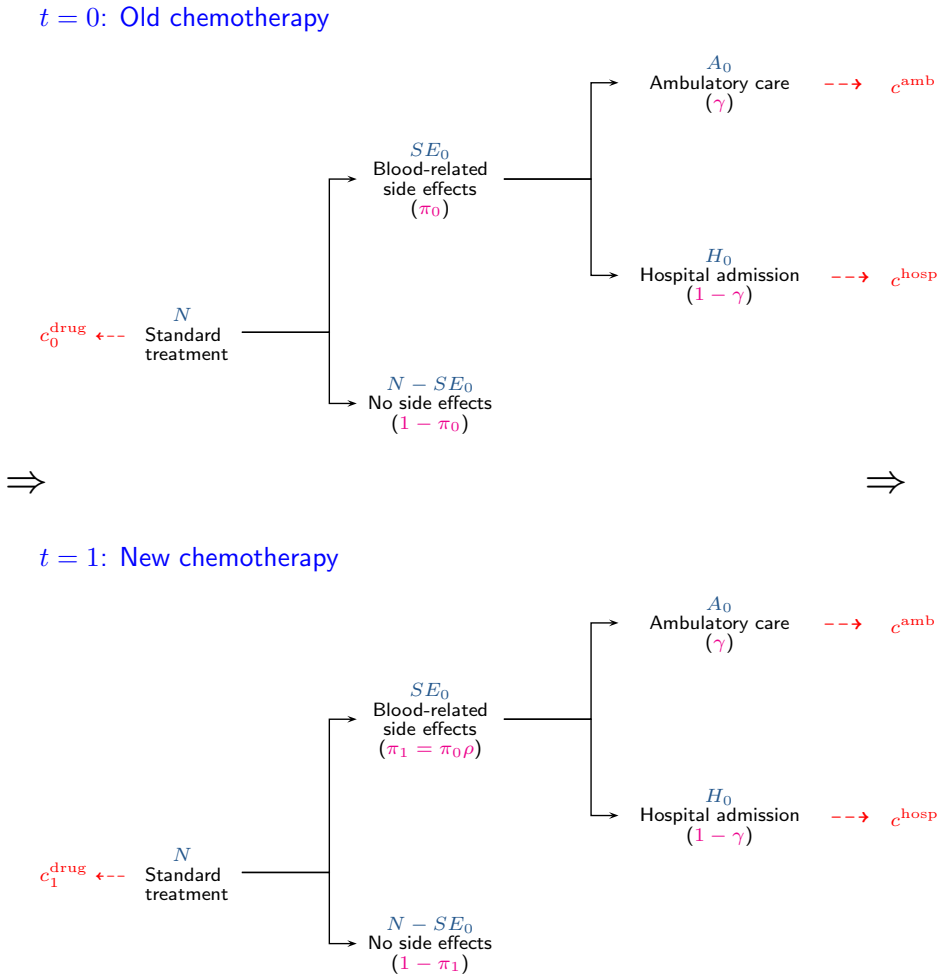

Decision analysis

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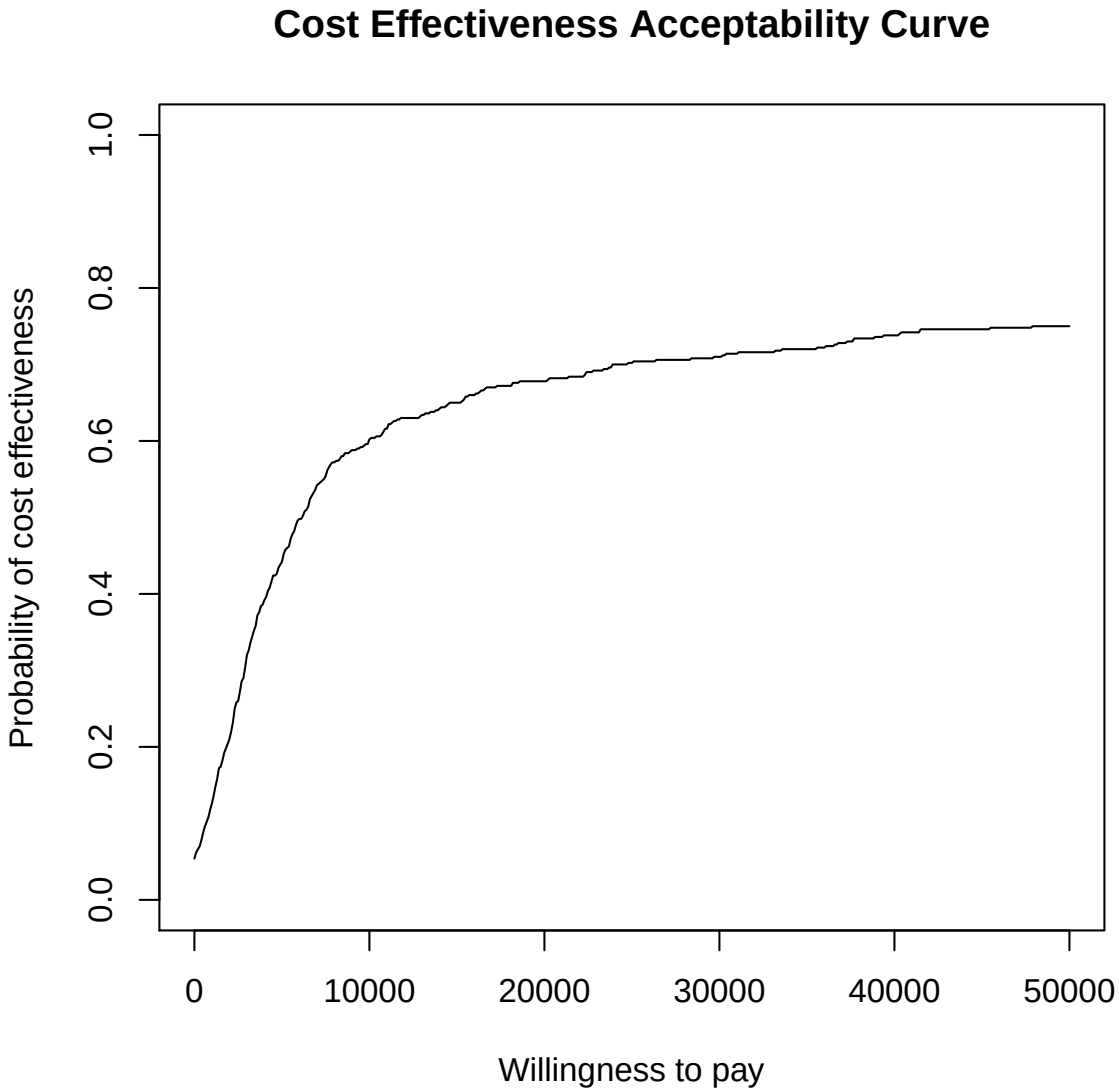
Benefits	Costs
741	670 382.1
699	871 273.3
...	...
726	425 822.2
716.2	**790 381.2**

New chemotherapy	
Benefits	Costs
732	1 131 978
664	1 325 654
...	...
811	766 411.4
774.5	**1 066 849.8**

$$\text{ICER} = \frac{276\,468.6}{58.3} = 6\,497.1$$

Summarising PSA — CEAC



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  - $\Pr(t = 1 \text{ is cost-effective}) = 0.999$
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- Comments:
  - "Perfect" information is just a hypothetical concept — that is why we consider the "expected value"
  - If the optimal treatment is not dominated at any point in the parameter space, the EVPI is equal to 0 and the uncertainty in the parameters has no impact on the decision process

Difficulties with the EVPI analysis

- Non-intuitive interpretation: when is the EVPI "low enough"?
  - Links with research prioritisation — compare the EVPI with the cost of buying information (e.g. a trial) and decide whether it is worth deferring the decision
  - Depends also on the size of the target population

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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 $\boldsymbol{\theta}$
- And that you can split them into two subsets
  - The "important" parameters $\boldsymbol{\phi}$ and the "unimportant" parameters $\boldsymbol{\psi}$
- We are interested in quantifying the value of gaining more information on $\boldsymbol{\phi}$, while leaving the current level of uncertainty on $\boldsymbol{\psi}$ unchanged

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- **Technical issue**: because $\boldsymbol{\phi}$ and $\boldsymbol{\psi}$ 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 $\boldsymbol{\phi}$
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  - New methods based on "non-parametric regression" (fancy stats)
    - 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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  - 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 (eg 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!

Some references


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