Health economic evaluation: a very Bayesian thing

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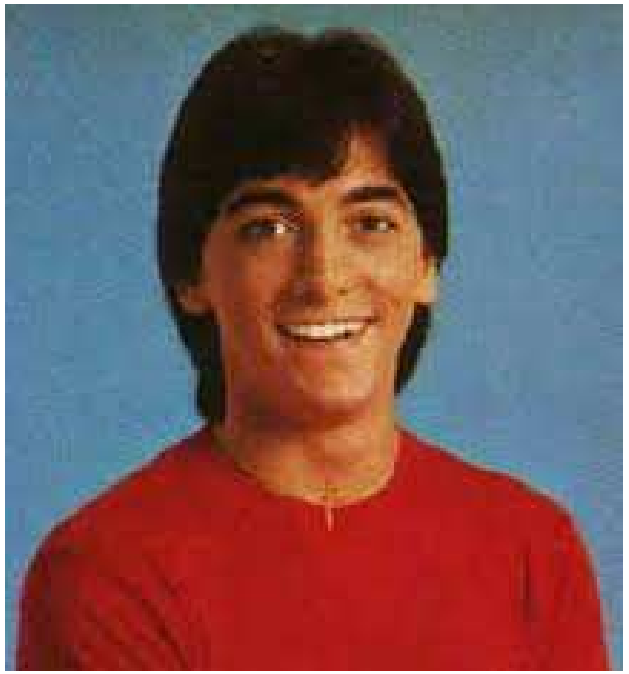
That's us (or is it?)...

Nixon

Jackson



Baio

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

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  - 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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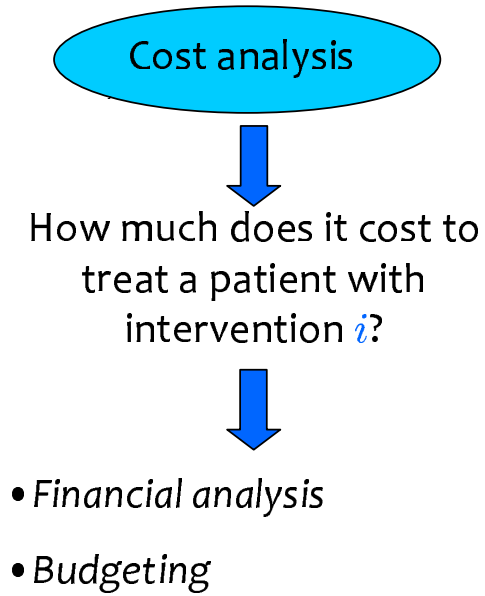
  - Main ideas
- *Conclusions*

What is health economics?

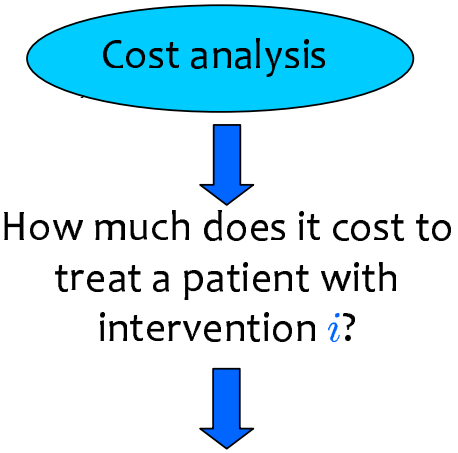


What is health economics?

Cardiovascular system (C)	*Expenditure*[1]	*%**	*DDD*[2]	*%**
Bosentan	37.0	47.9	0.3	0.2
Cardiac stimulants	8.8	11.4	3.5	2.1
Statins	5.5	7.2	15.9	9.9
Calcium Antagonists (diidro.)	4.5	5.8	20.1	12.4
Nitrates	3.7	4.8	21.0	13.0
Diuretics	2.2	2.8	18.8	11.6
Ace Inhibitors	2.1	2.8	24.0	14.8
Beta Blockers	1.7	2.2	17.2	10.7
Alfa Blockers	1.0	1.3	3.2	2.0
Angiotensin II Antagonists	0.9	1.1	3.5	2.2
…				

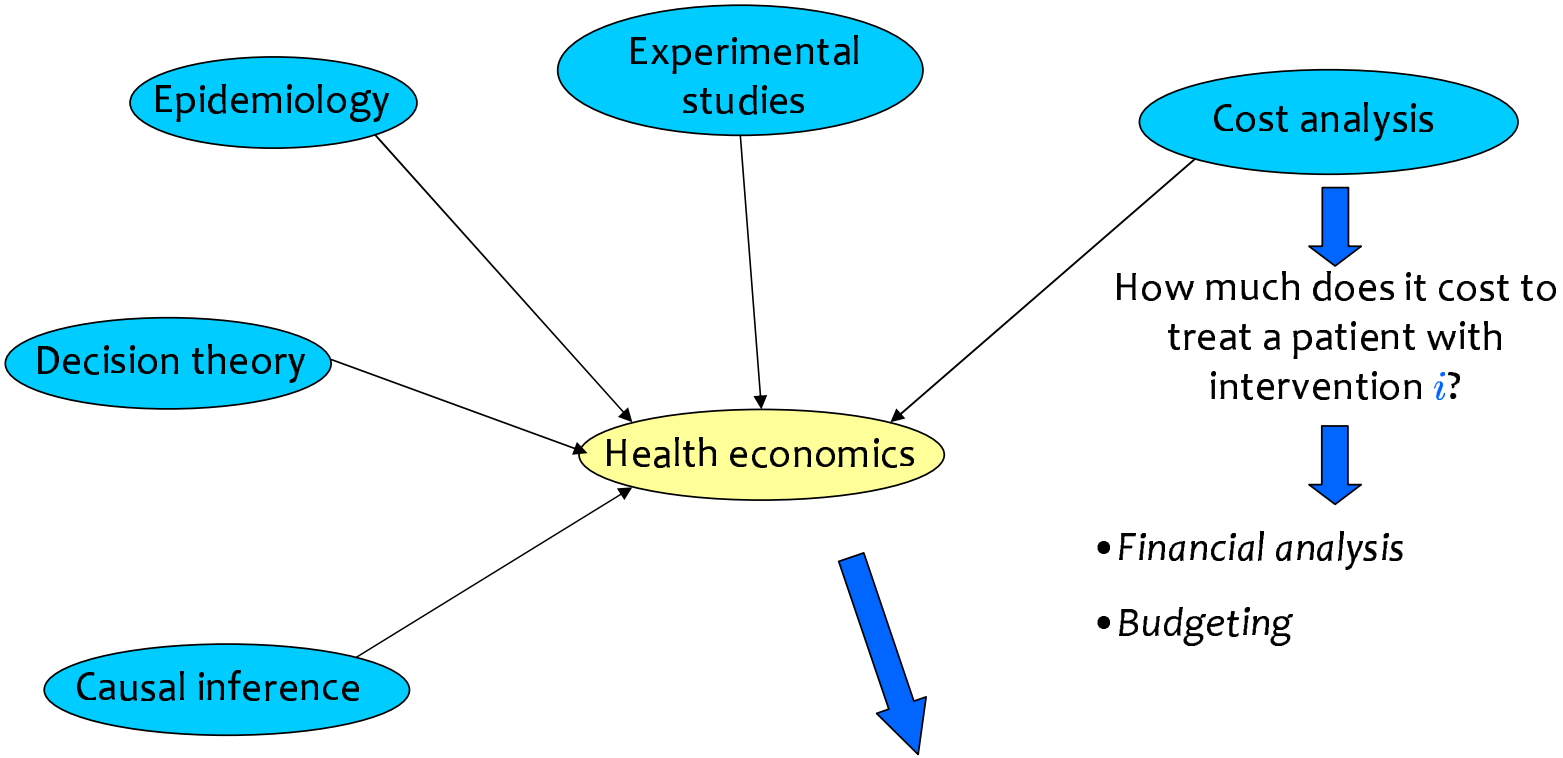
[1] Millions €
[2] Millions days of therapy
*Percentages are calculated over the total of the ATC category

Source: Osmed (2007)



- *Financial analysis*
- *Budgeting*

What is health economics?



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

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.*

Health economic outcome

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  - e = suitable measure of clinical benefit of an intervention
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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
    - Negative correlation — more effective treatments may reduce total care pathway costs e.g. by reducing hospitalisations, side effects, etc.
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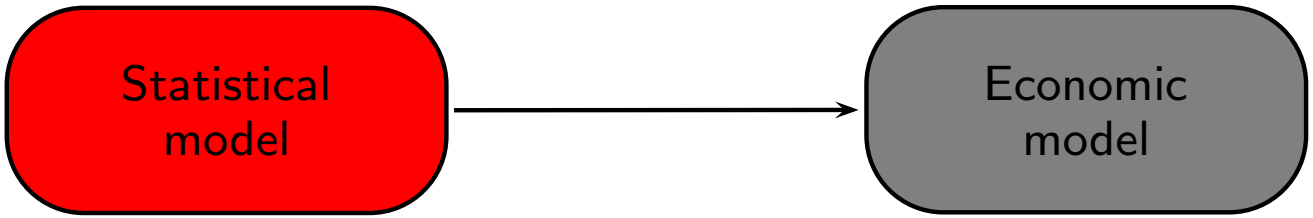
- There are different ways in which we can define (e, c) for a specific problem
  - Direct vs indirect vs intangible costs
  - "Hard-" vs utility-based clinical outcomes
  - Public (*e.g.* NHS) vs private (*e.g.* insurance) perspective

Health economic evaluations

Statistical model

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

Health economic evaluations



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

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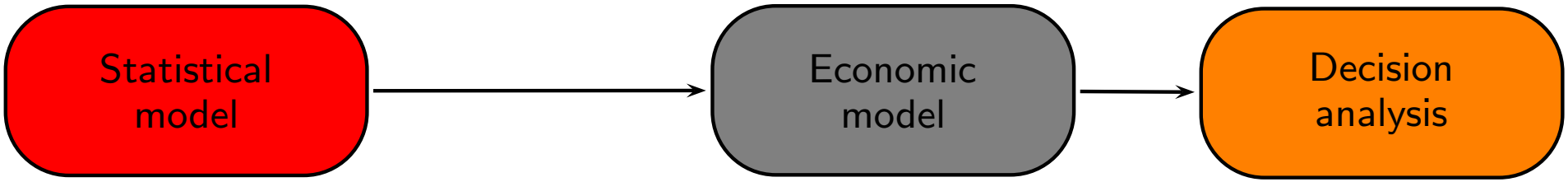

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- Dictates the best course of actions, given current evidence
- Standardised process

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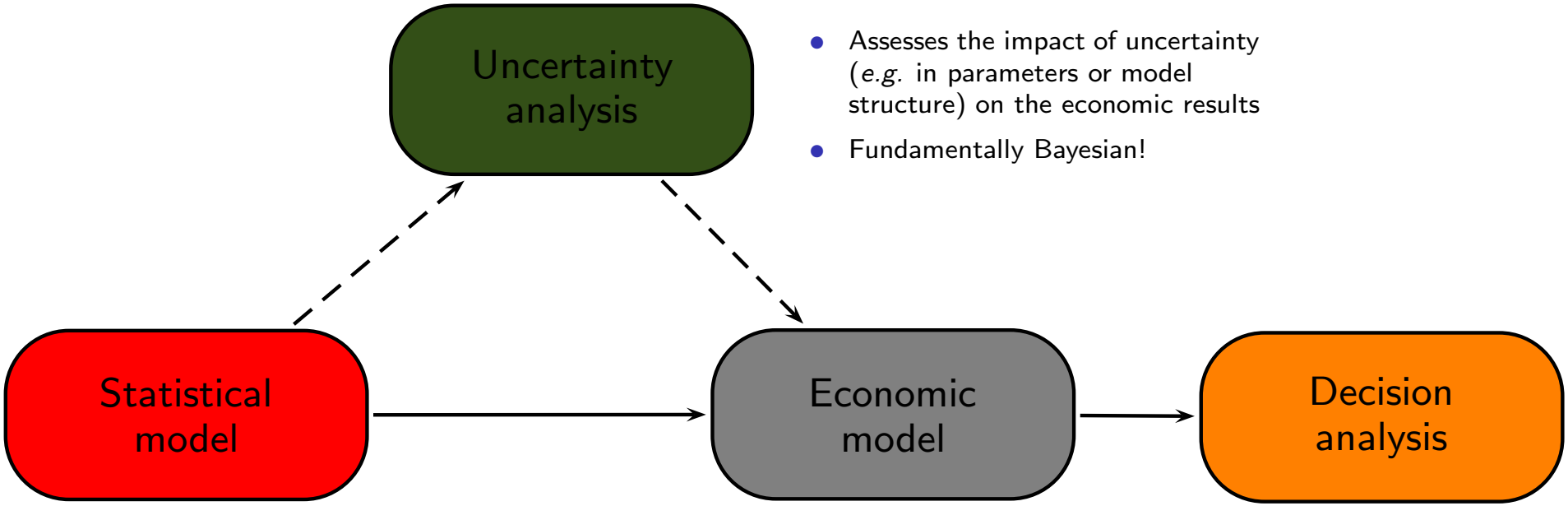

- Assesses the impact of uncertainty (*e.g.* in parameters or model structure) on the economic results
- Fundamentally Bayesian!

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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

1. Statistical modelling

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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
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  - Poor external validity
- 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

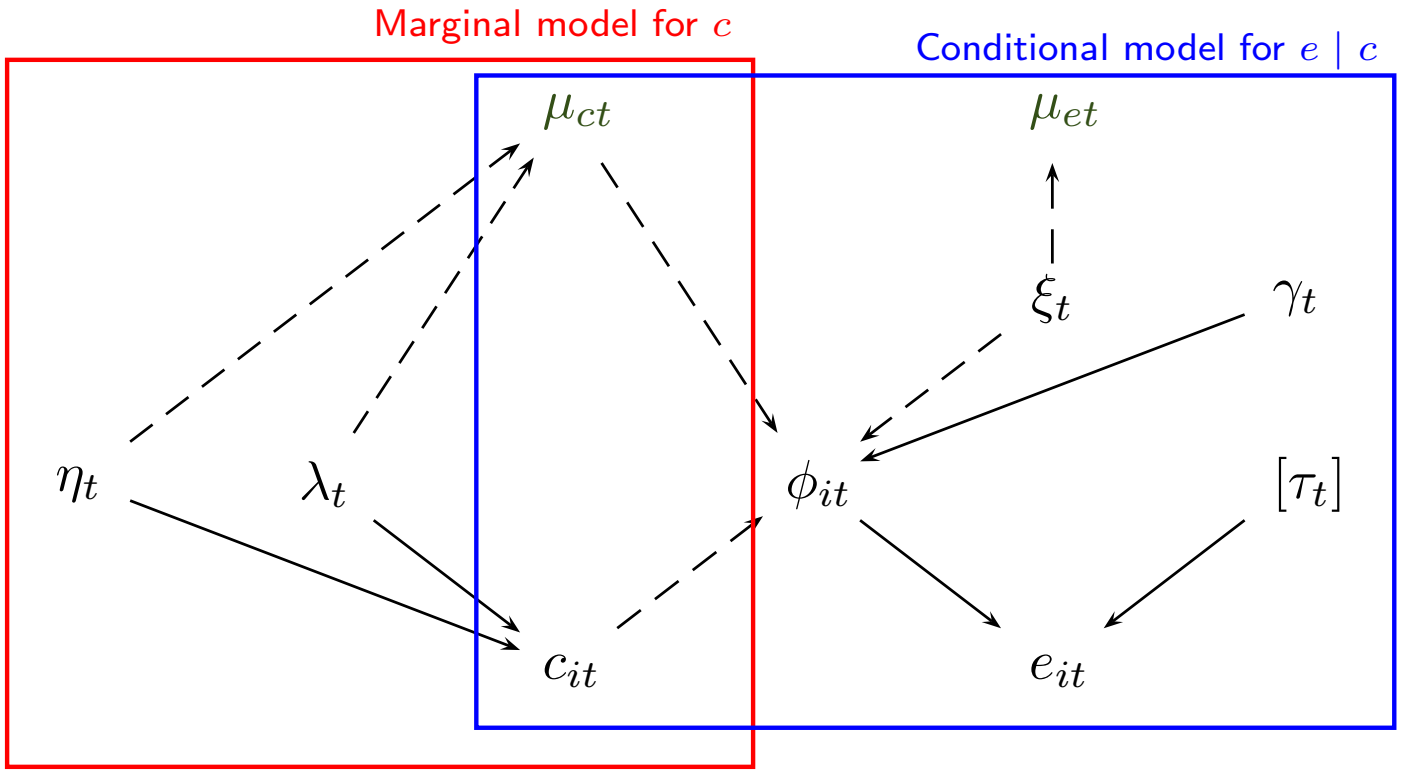
- Observe a vector (e_i, c_i) under each intervention being compared
  - May also observe other variables (covariates) — *e.g.* individual values for age, sex, co-morbidities, etc
- Use observed data to estimate the relevant population parameters $\boldsymbol{\theta}^t = (\boldsymbol{\theta}^t_e, \boldsymbol{\theta}^t_c)$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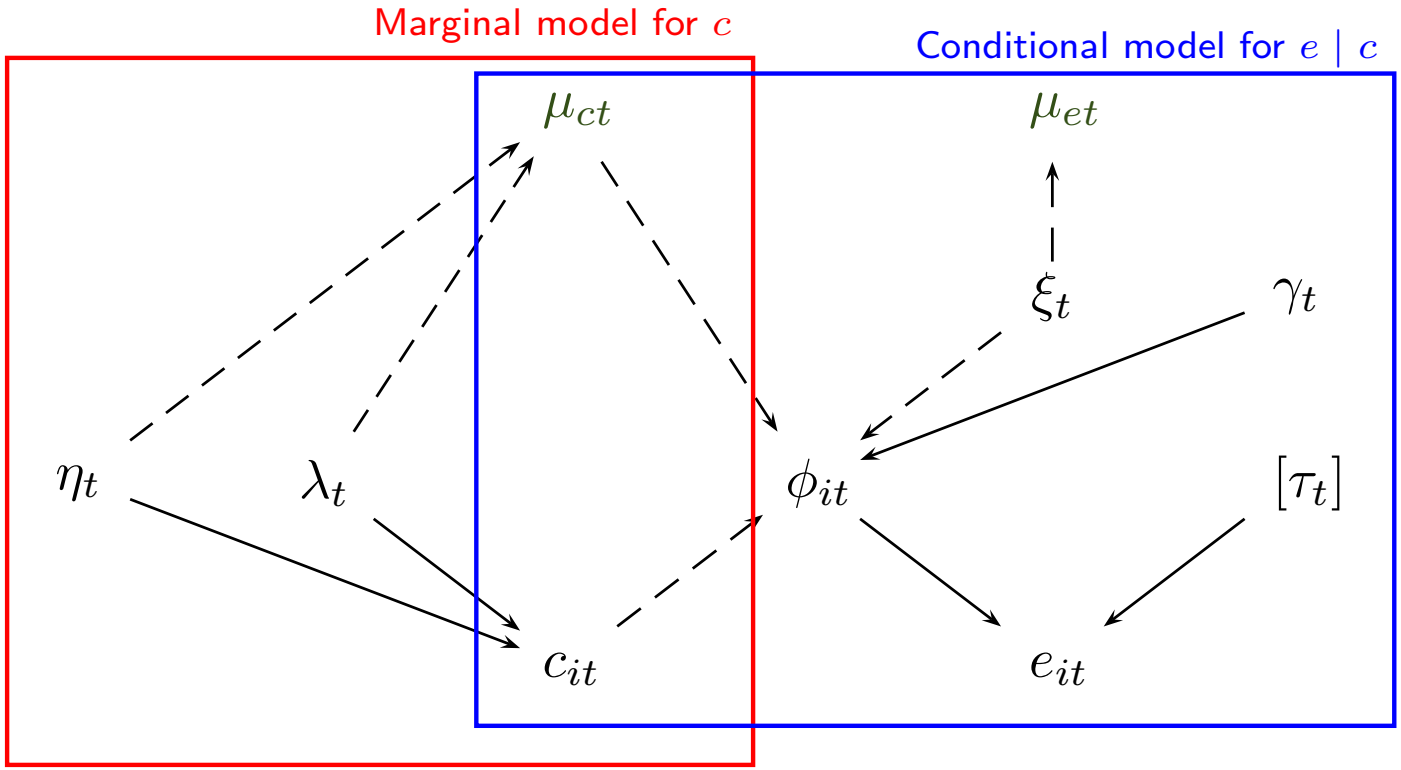

For instance, can model

- $c_{it} \sim \text{Gamma}(\eta_t, \lambda_t)$ [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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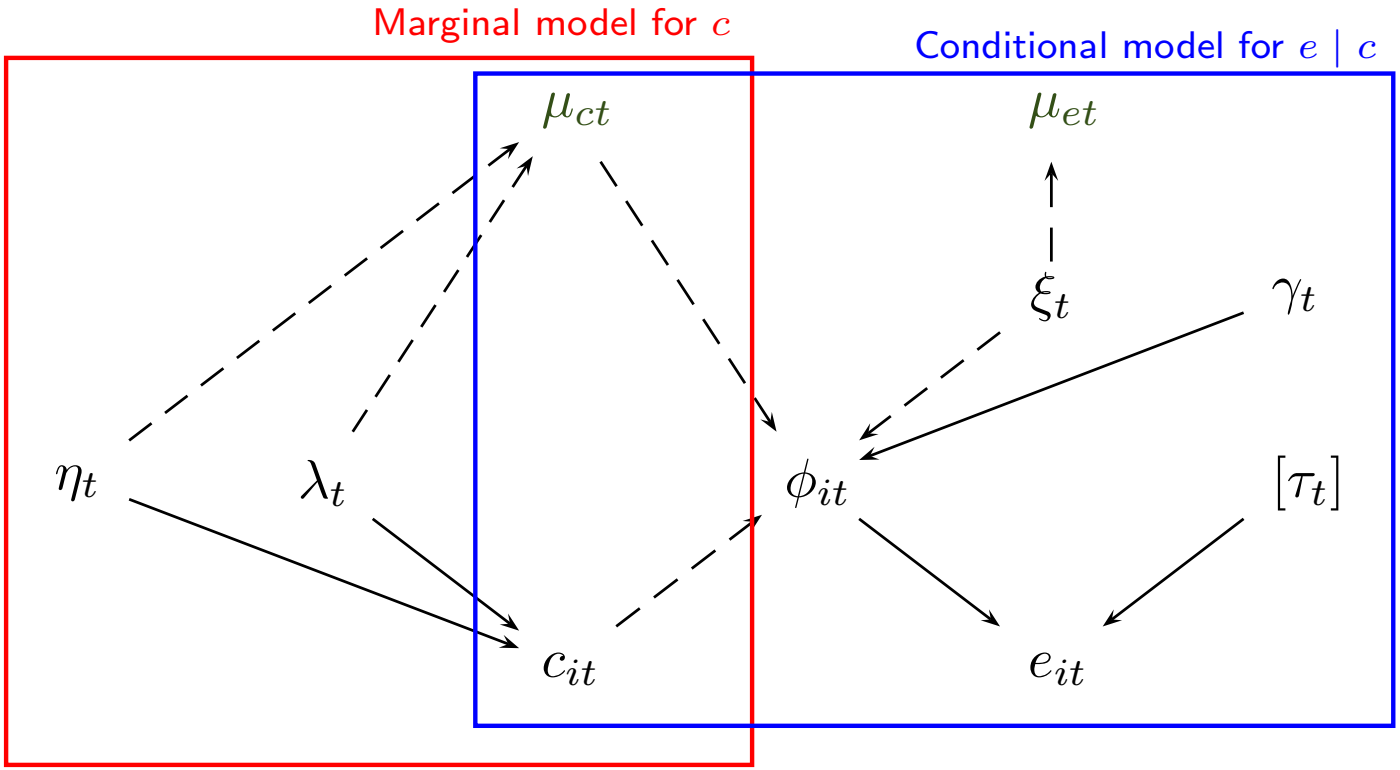

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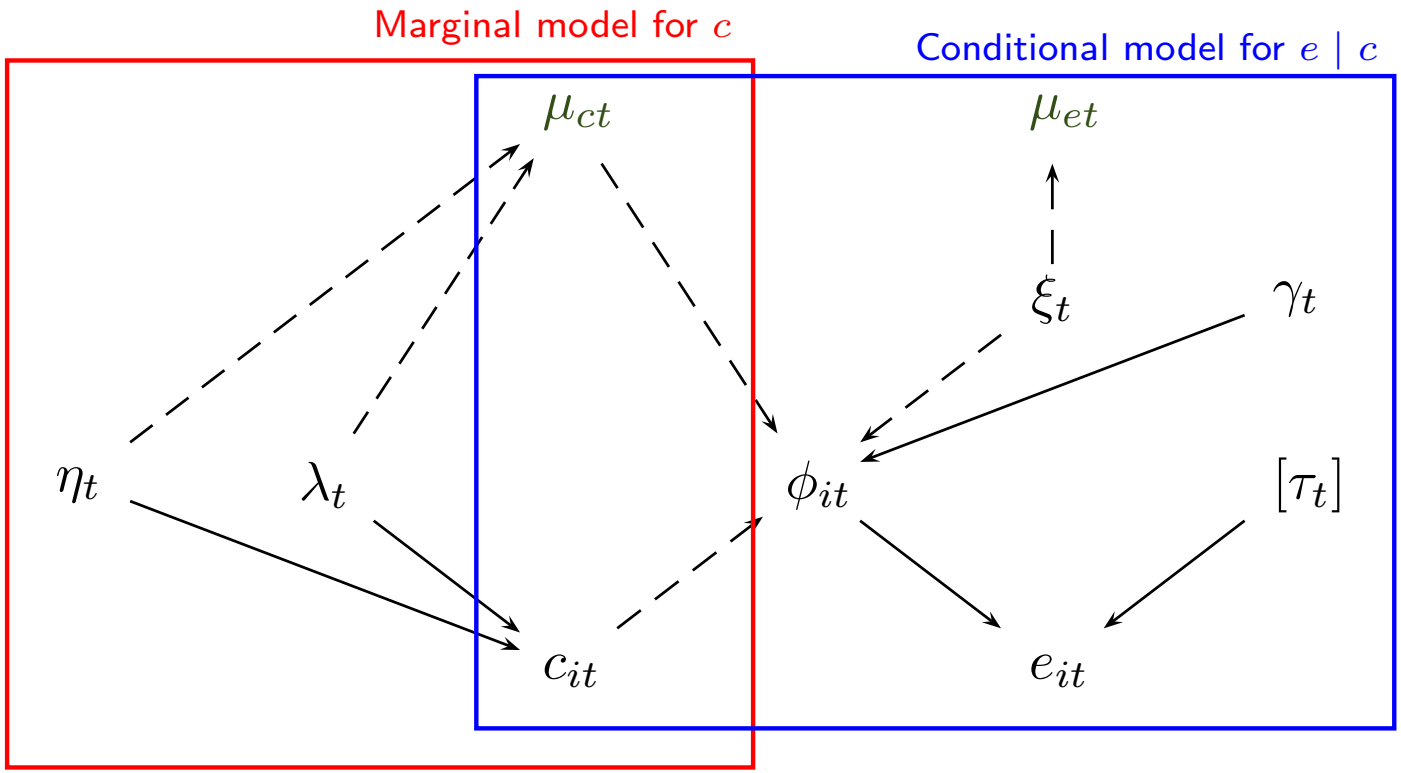

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- $\text{E}[e_{it}] = \phi_{it}$; $g(\phi_{it}) = \xi_t + \gamma_t(c_{it} - \mu_{ct}) \Rightarrow \mu_{et} = g^{-1}(\xi_t)$

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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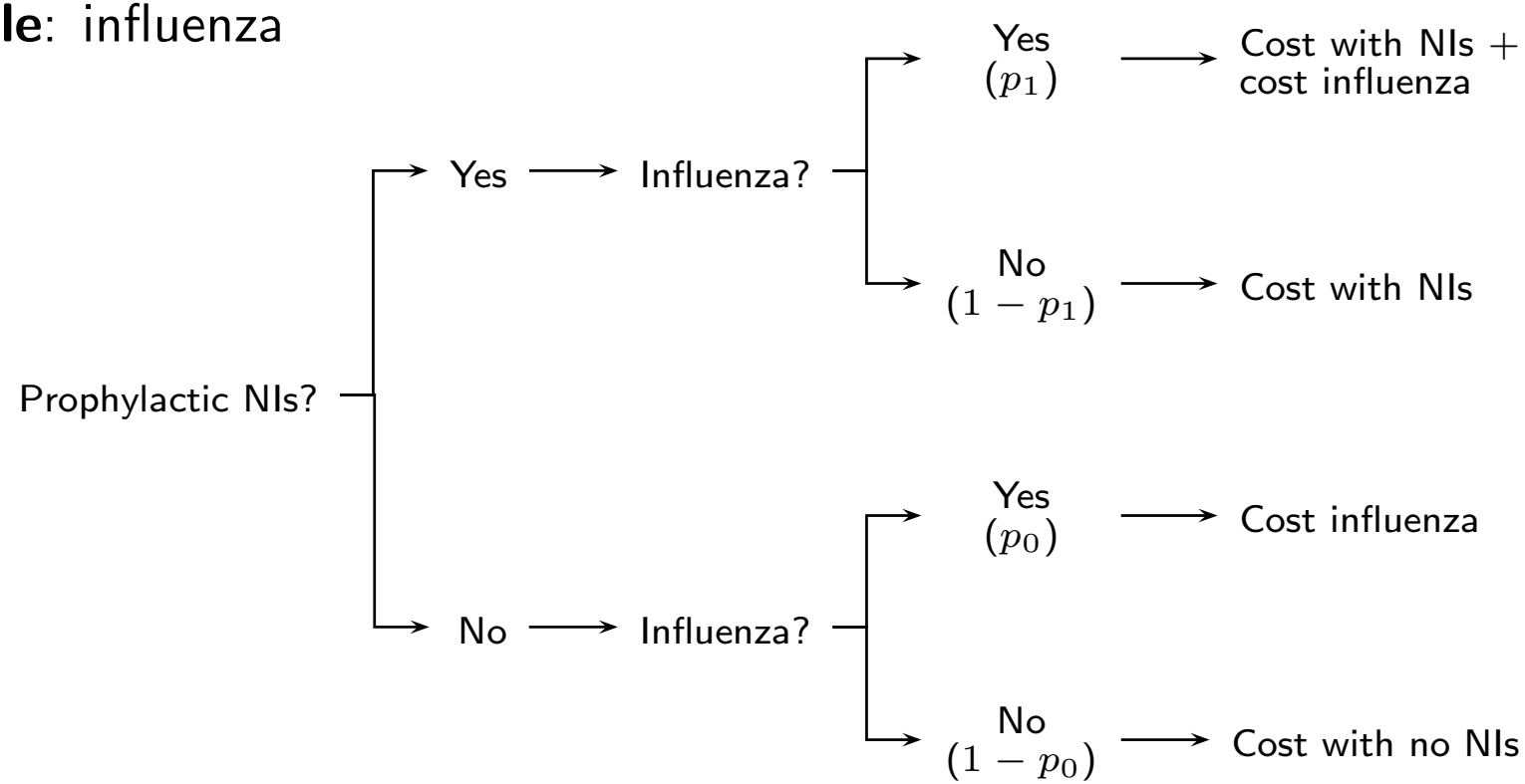
Example: influenza



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- Data sources for a decision-analytic model include
  - Published literature (*e.g.* probability of influenza in the range $[0.2 - 0.4]$)
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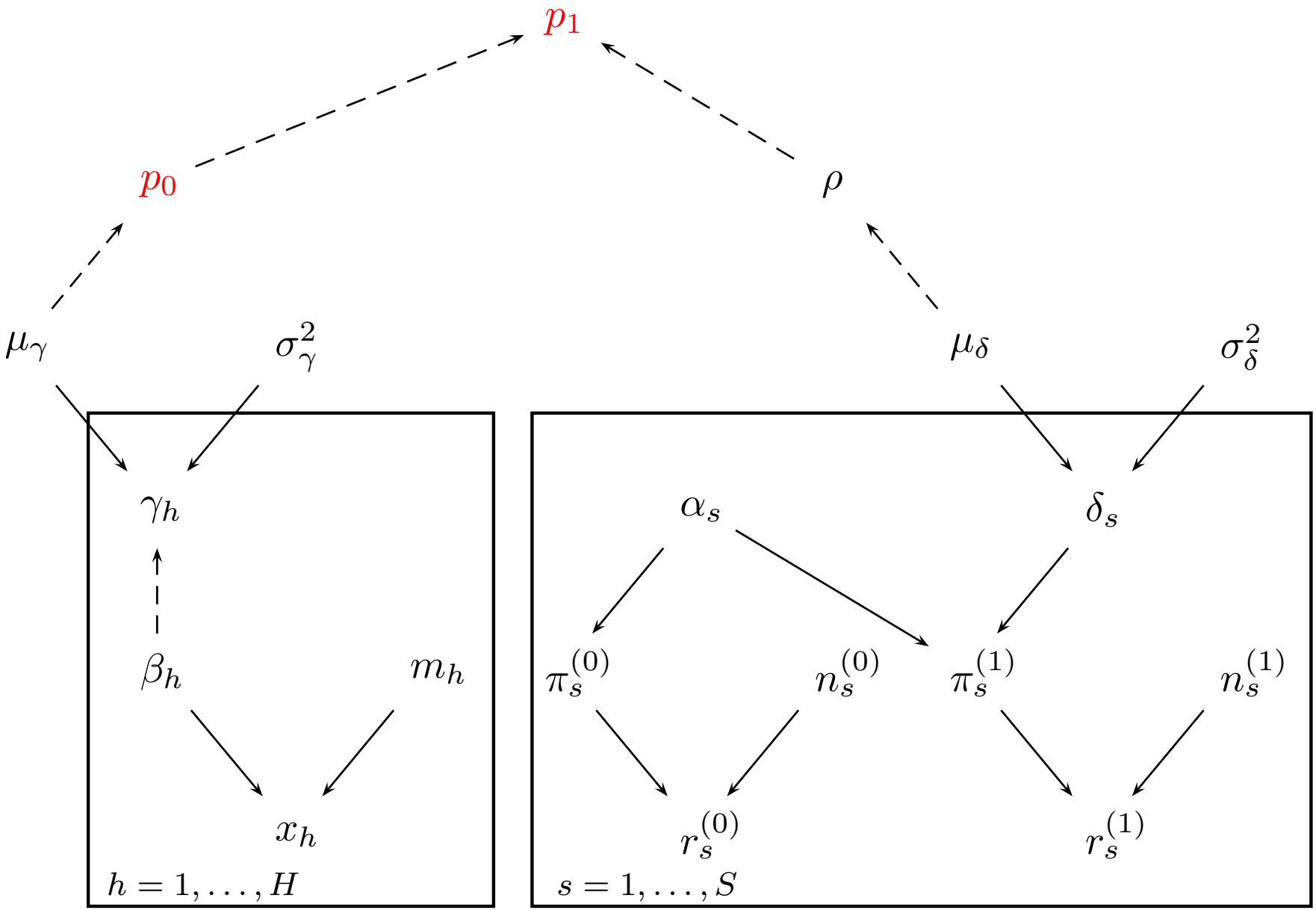
- We need to combine the parameters of the population model to derive suitable measures of costs and benefits
  - $c_0 = (1 - p_t)c^{\text{GP}} + p_t \left(c^{\text{GP}} + c^{\text{Inf}}\right) \Rightarrow$ avg cost for $t = 0$
  - $c_1 = (1 - p_t) \left(c^{\text{GP}} + c^{\text{NI}}\right) + p_t \left(c^{\text{GP}} + c^{\text{NI}} + c^{\text{Inf}}\right) \Rightarrow$ avg cost for $t = 1$
  - $e_t = lp_t \Rightarrow$ 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



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**:

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

- **NB**: In a Bayesian context, these are functions of $\boldsymbol{\theta}$ 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 $p(e, c, \boldsymbol{\theta}^t) = p(e, c \mid \boldsymbol{\theta}^t)p(\boldsymbol{\theta}^t)$
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 $\mathcal{U}^t = \mathsf{E}[u(e, c; t)]$
4. Choose the intervention that maximises the expected utility
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NB: When only two interventions are being compared, this is equivalent to assessing whether

$$\mathsf{EIB} = \mathcal{U}^1 - \mathcal{U}^0 > 0$$

So, if $\mathsf{EIB} > 0$ then $t = 1$ is more cost-effective than $t = 0$

EIB vs ICER

- Alternative criterion for making decisions

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

  - $\Delta_e = \underbrace{\mathsf{E}[e \mid \theta^1]}_{\mu_1^e} - \underbrace{\mathsf{E}[e \mid \theta^0]}_{\mu_0^e}$ = increment in mean benefits
  - $\Delta_c = \underbrace{\mathsf{E}[c \mid \theta^1]}_{\mu_1^c} - \underbrace{\mathsf{E}[c \mid \theta^0]}_{\mu_0^c}$ = increment in mean costs

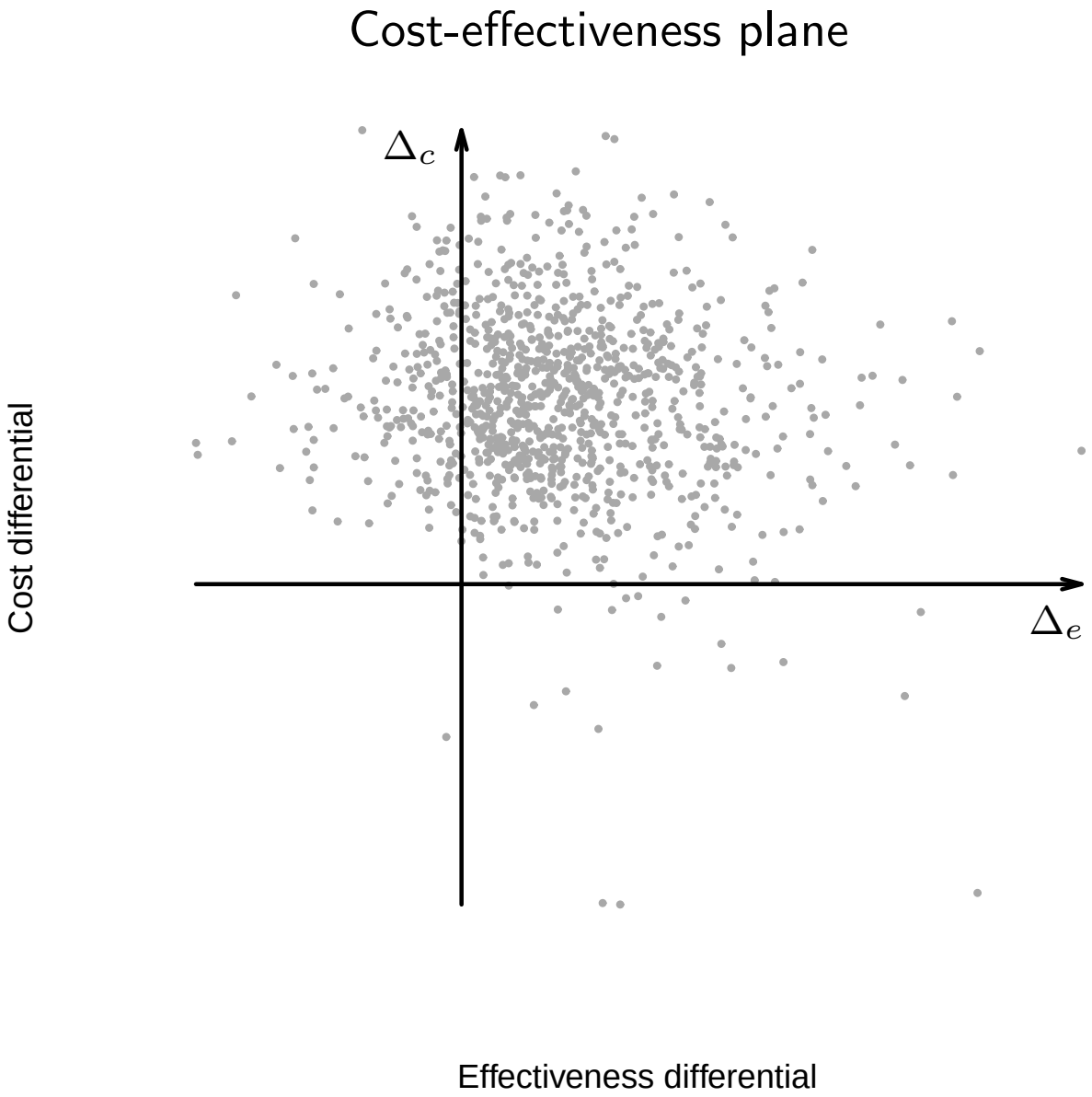
- When the MNB is used as utility function and $\mathcal{T} = (0, 1)$

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

and thus

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

Cost-effectiveness plane vs ICER



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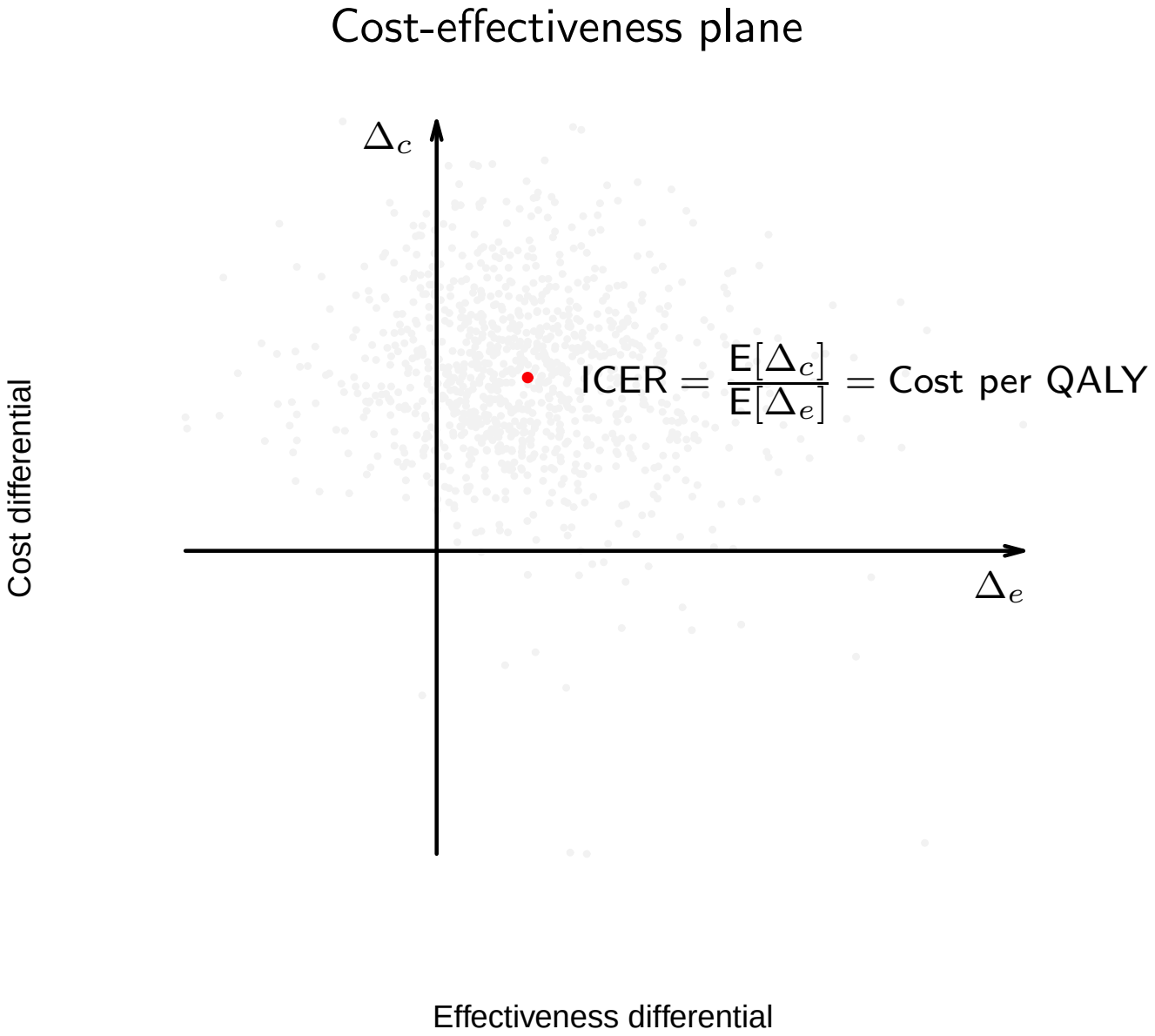

EIB vs ICER

- Another criterion for making decisions is based on

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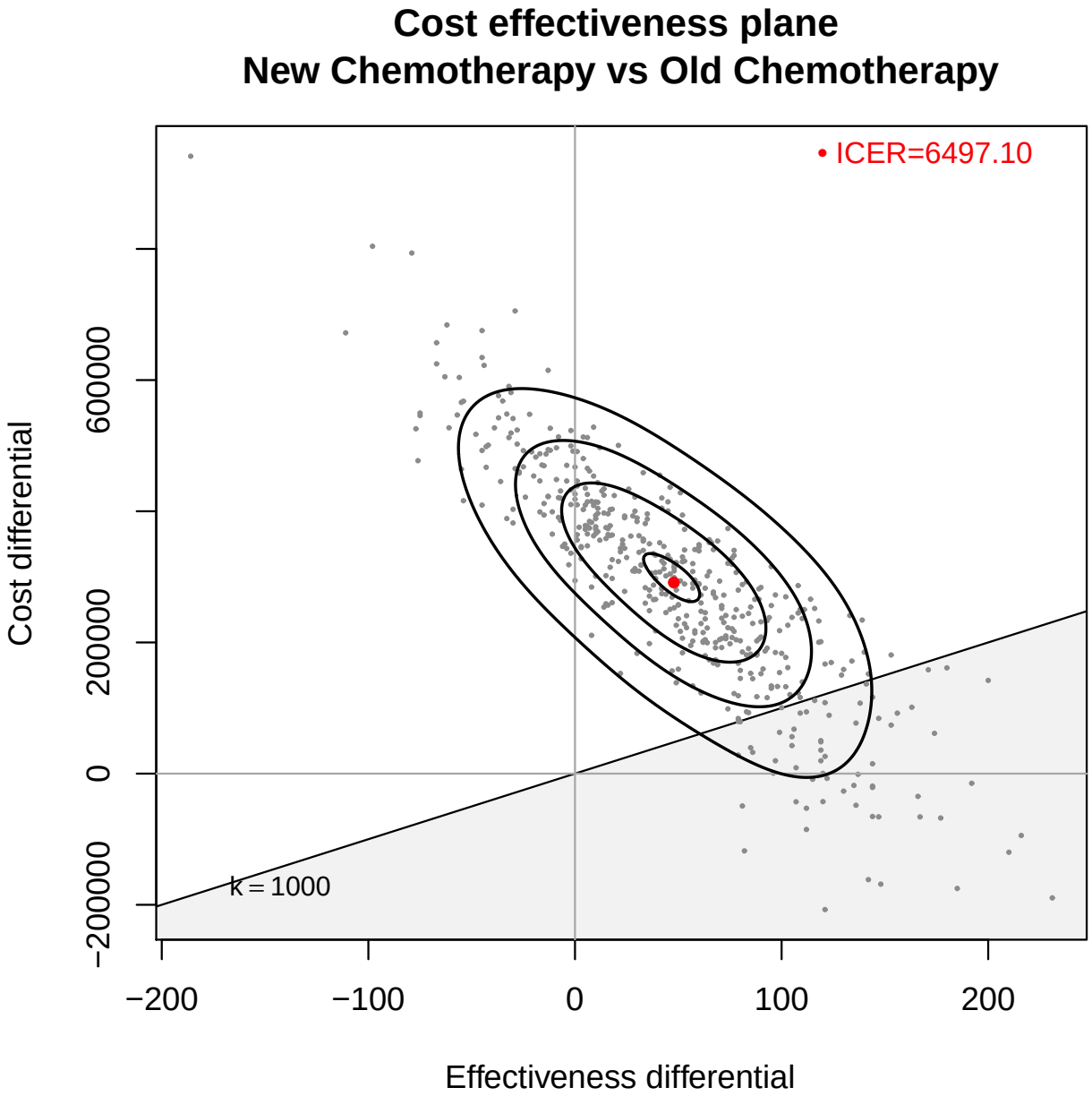
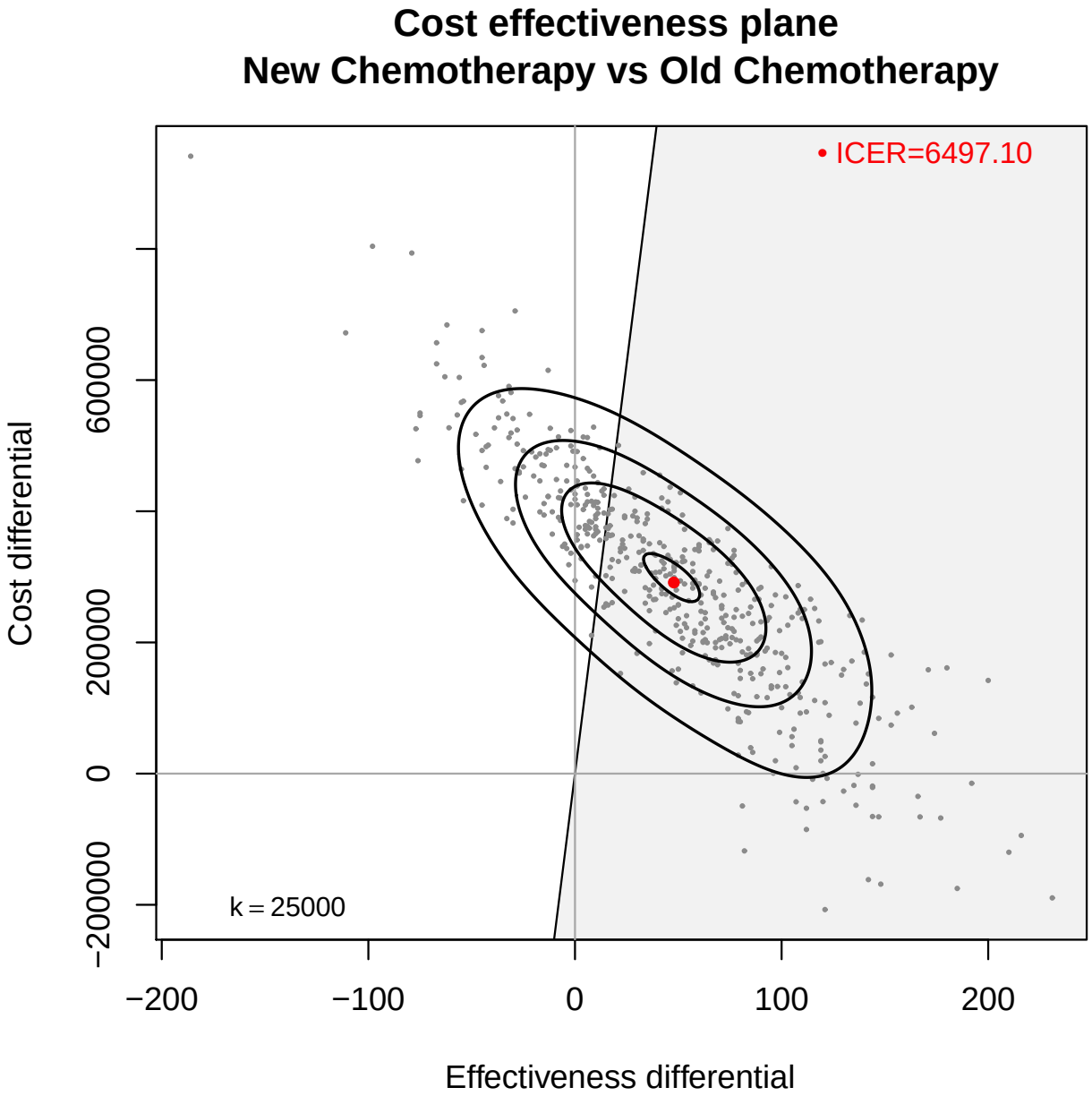
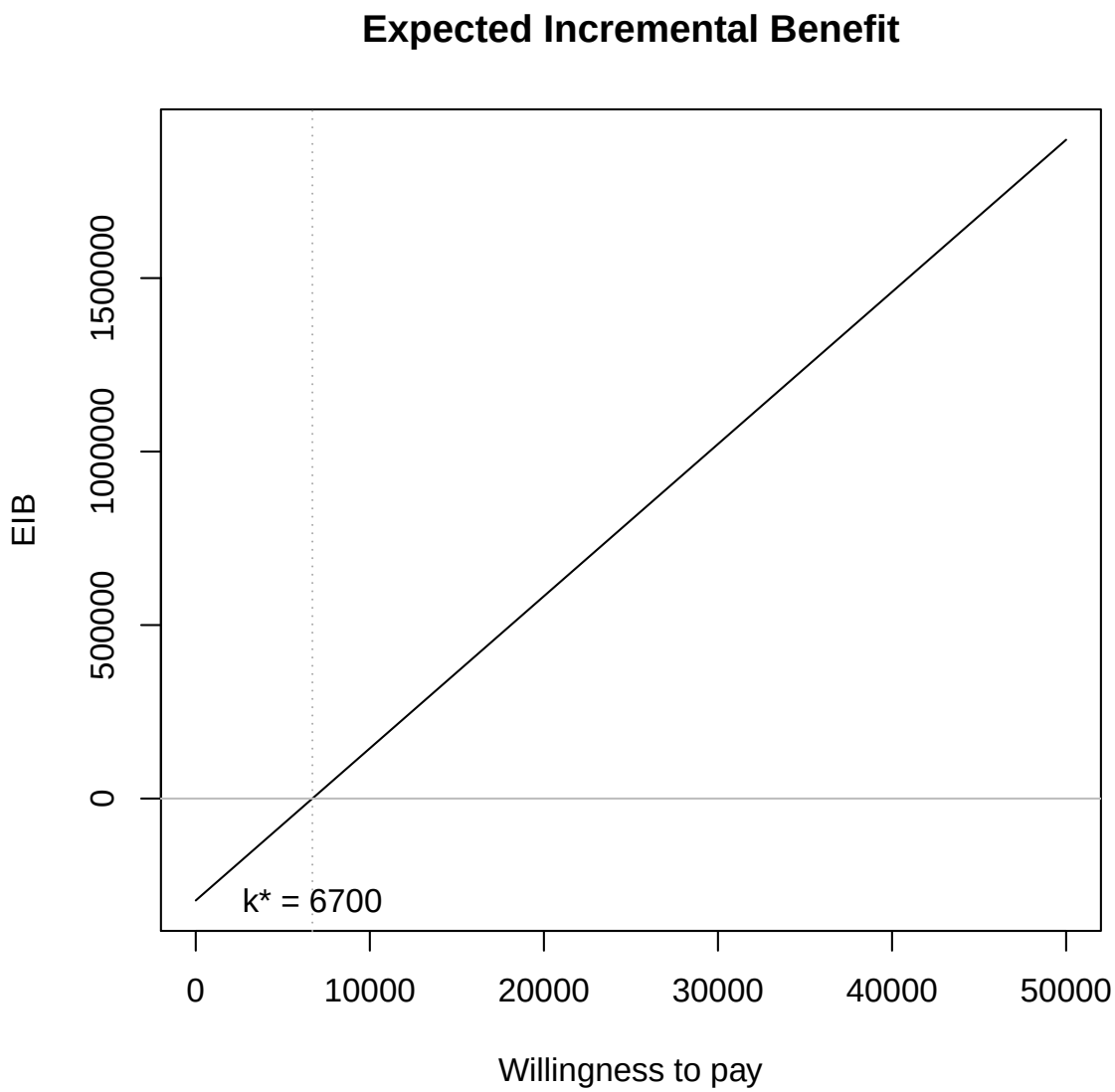


Cost-effectiveness plane vs EIB vs ICER



Health economic evaluation based on EIB



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4. Uncertainty analysis

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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

4. Uncertainty analysis

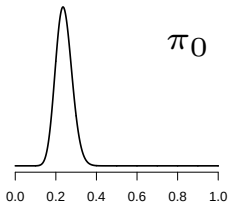
So: problem solved?**... Well, not really!**

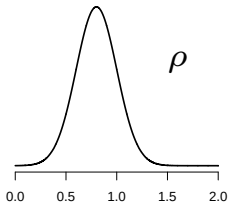
- The quality of the current evidence is often limited
  - During the pre-market authorisation phase, the regulator should decide whether to grant reimbursement to a new product — and in some countries also set the price — on the basis of uncertain evidence, regarding both clinical and economic outcomes
  - 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

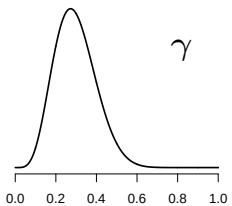
- This leads to the necessity of performing *(probabilistic) sensitivity analysis* **(PSA)**
  - Formal quantification of the impact of uncertainty in the parameters on the results of the economic model
  - Standard requirement in many health systems (e.g. for NICE in the UK), but still not universally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

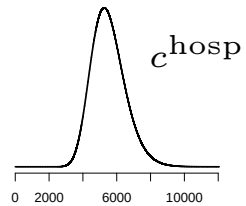
PSA to **parameter** uncertainty

Parameters



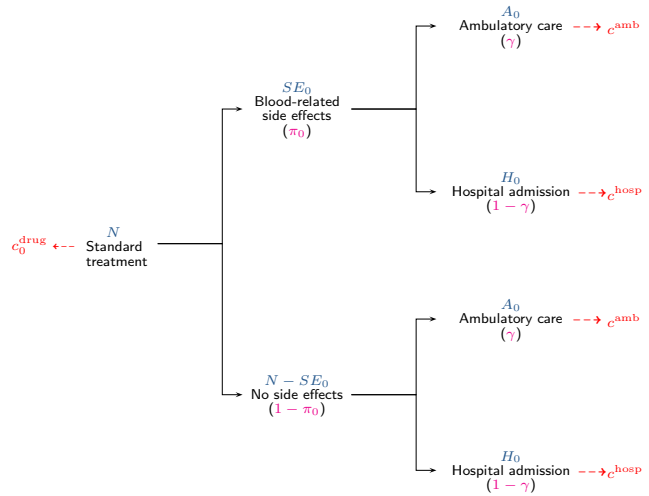




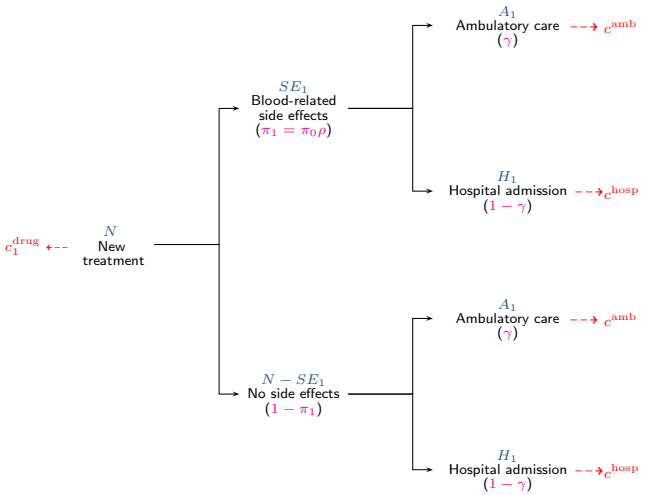


Model structure

Old chemotherapy



New chemotherapy



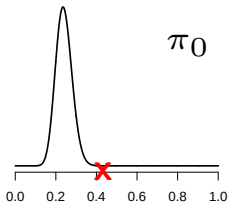
Decision analysis

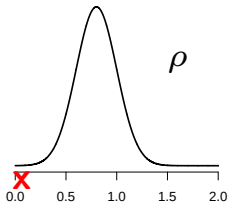
Old chemotherapy	
Benefits	Costs

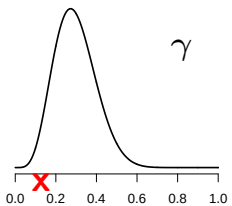
New chemotherapy	
Benefits	Costs

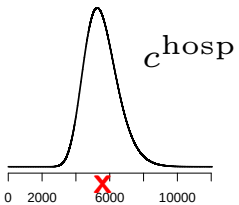
PSA to **parameter** uncertainty

Parameters





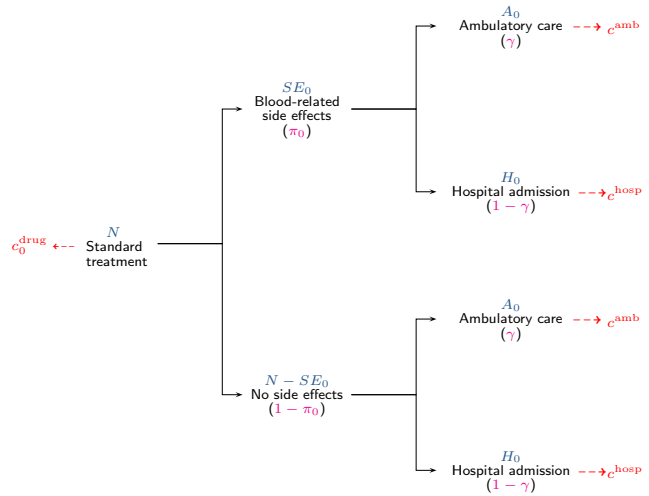




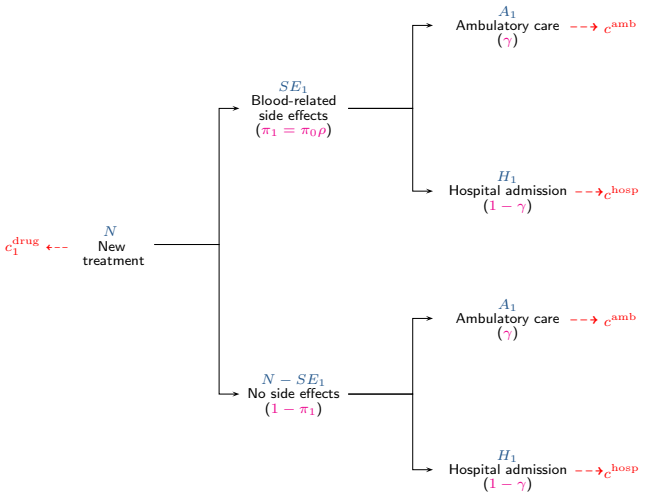
$\Rightarrow$

Model structure

Old chemotherapy



New chemotherapy



$\Rightarrow$

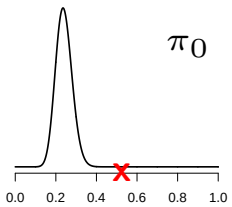
Decision analysis

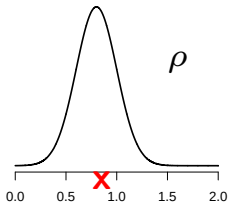
Old chemotherapy	
Benefits	Costs
741	670 382.1

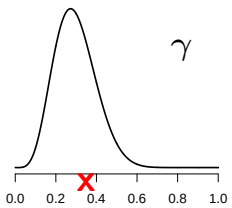
New chemotherapy	
Benefits	Costs
732	1 131 978

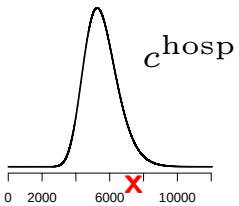
PSA to **parameter** uncertainty

Parameters





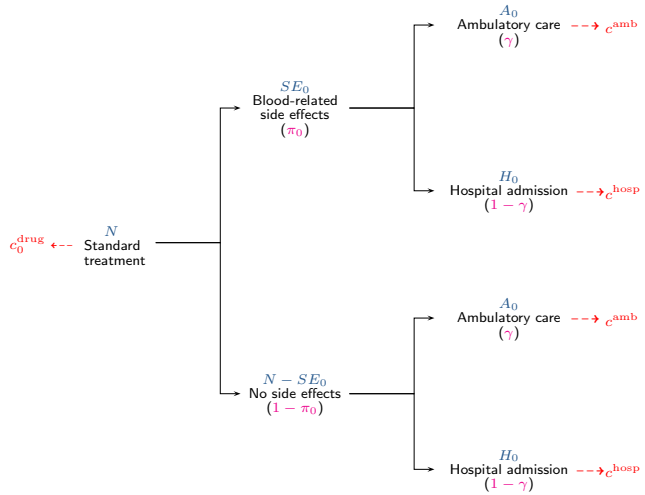




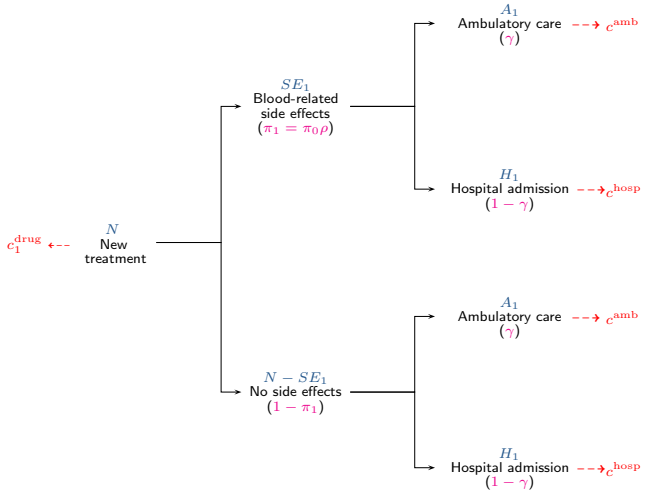
$\Rightarrow$

Model structure

Old chemotherapy



New chemotherapy



$\Rightarrow$

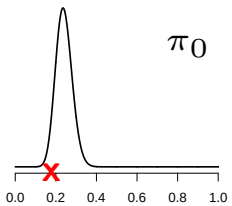
Decision analysis

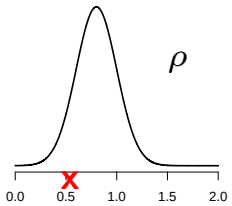
Old chemotherapy	
Benefits	Costs
741	670 382.1
699	871 273.3

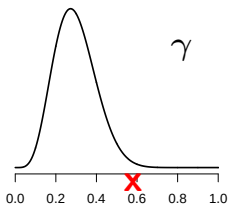
New chemotherapy	
Benefits	Costs
732	1 131 978
664	1 325 654

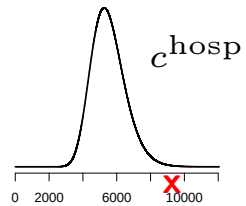
PSA to **parameter** uncertainty

Parameters





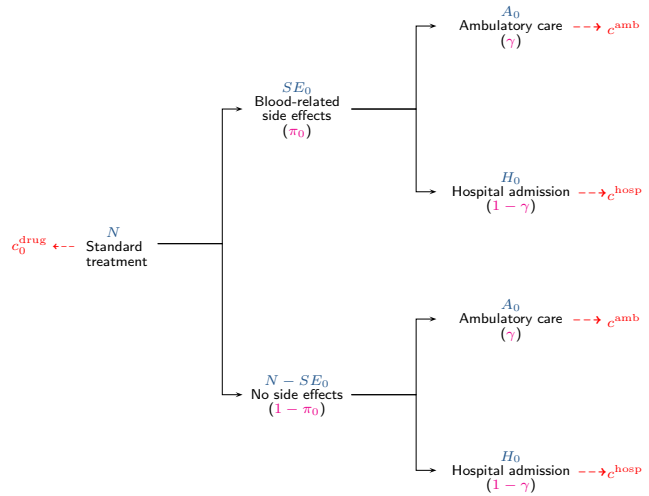




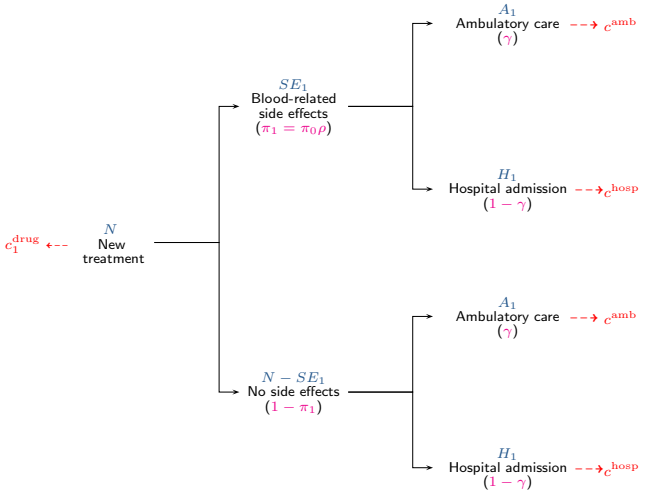
$\Rightarrow$

Model structure

Old chemotherapy



New chemotherapy



$\Rightarrow$

Decision analysis

Old chemotherapy	
Benefits	Costs
741	670 382.1
699	871 273.3
...	...
726	425 822.2
743.1	**656 644.6**

New chemotherapy	
Benefits	Costs
732	1 131 978
664	1 325 654
...	...
811	766 411.4
794.6	**991 804.0**

$$\text{ICER} = \frac{335\,159.4}{51.6} = 6\,497.1$$

Conclusions

- Bayesian modelling particularly effective in health economic evaluations
- Allows the incorporation of external, additional information to the current analysis
  - Previous studies
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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!