4. Introduction to health economic evaluation

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STAT0019 - Bayesian Methods in Health Economics, UCL

UCL Statistical Science

Summary

- Health economic evaluation
  - What is and why do we need health economics?
- A framework for health economic evaluation
  - Statistical modelling
  - Economic modelling
  - Decision analysis
  - Uncertainty analysis
- Standard vs Bayesian HTA
  - Two-stage vs integrated approach
- Decision-making
  - Cost-effectiveness plane; ICER; EIB

References

Bayesian Methods in Health Economics, chapters 1, 3 Library Book website (CRC) Book website Code

Bayesian Cost-Effectiveness Analysis with the R package BCEA Book website (Springer) Book website

Evidence Synthesis for Decision Making in Healthcare Library Book website

Objective

- Combine costs and benefits of a given intervention into a rational scheme for allocating resources

> *Health technology assessment (HTA) is a method of evidence synthesis that considers evidence regarding clinical effectiveness, safety, cost-effectiveness and, when broadly applied, includes social, ethical, and legal aspects of the use of health technologies. The precise balance of these inputs depends on the purpose of each individual HTA. A major use of HTAs is in informing reimbursement and coverage decisions, in which case HTAs should include benefit-harm assessment and economic evaluation.*
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> Luce et al, 2010

(Quote stolen from a brilliant presentation by Cynthia Iglesias)

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A relatively new discipline

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- Arguably, a **historical accident**...
  - Economists take the lead in developing the main theory $\Rightarrow$ *Health Economics*
  - But there's so much more to it (more on this later...)

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(Truly...) World-beating Britain

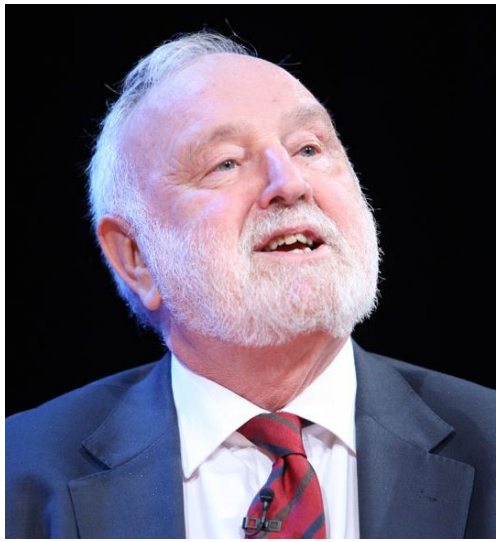
- Since its establishment, the **National Institute for Health and Care Excellence** (originally: National Institute for Clinical Excellence, **NICE**), has gained prominence as the global powerhouse for HTA

NICE

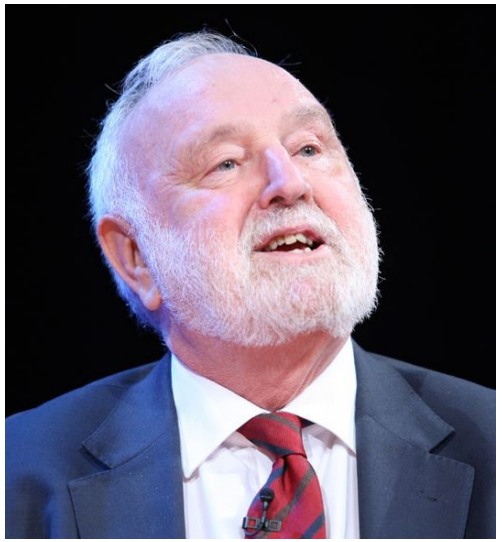
- Established in 1999, during the first New Labour government
- Health Secretary Frank Dobson on whether it will work:

> *Probably not, but it's worth a bloody try!*

Rawlins, 2009



NICE



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- Main driver: tackle the inequalities and inefficiencies generated by the "**postcode lottery**"
  - Decisions about which drugs to fund through the NHS had historically been taken at a local level
  - Concerns over the fact that patients in some areas of the country could access treatments that people elsewhere, sometimes in neighbouring streets, could not $\Rightarrow$ large inequalities in access to resources!

- Ancillary objectives
  - Set quality standard *nationally* (although NICE is technically responsible for England & Wales only...)
  - De-politicise reimbursement/coverage decisions
  - Align with growing body of literature and experience in other countries (PBAC in Australia, CADTH in Canada, NZHTA in New Zealand,...)

NICE – *influenzing* the outcomes...

20 years of NICE

- The first drug appraisal was for the antiviral treatment for influenza, Relenza
- Specifically, NICE said that

> *there was insufficient evidence to show Relenza reduced the severity of the illness for those most at risk, the elderly and people with asthma*

and so concluded that it

> *was not cost effective and should not be provided on the NHS*

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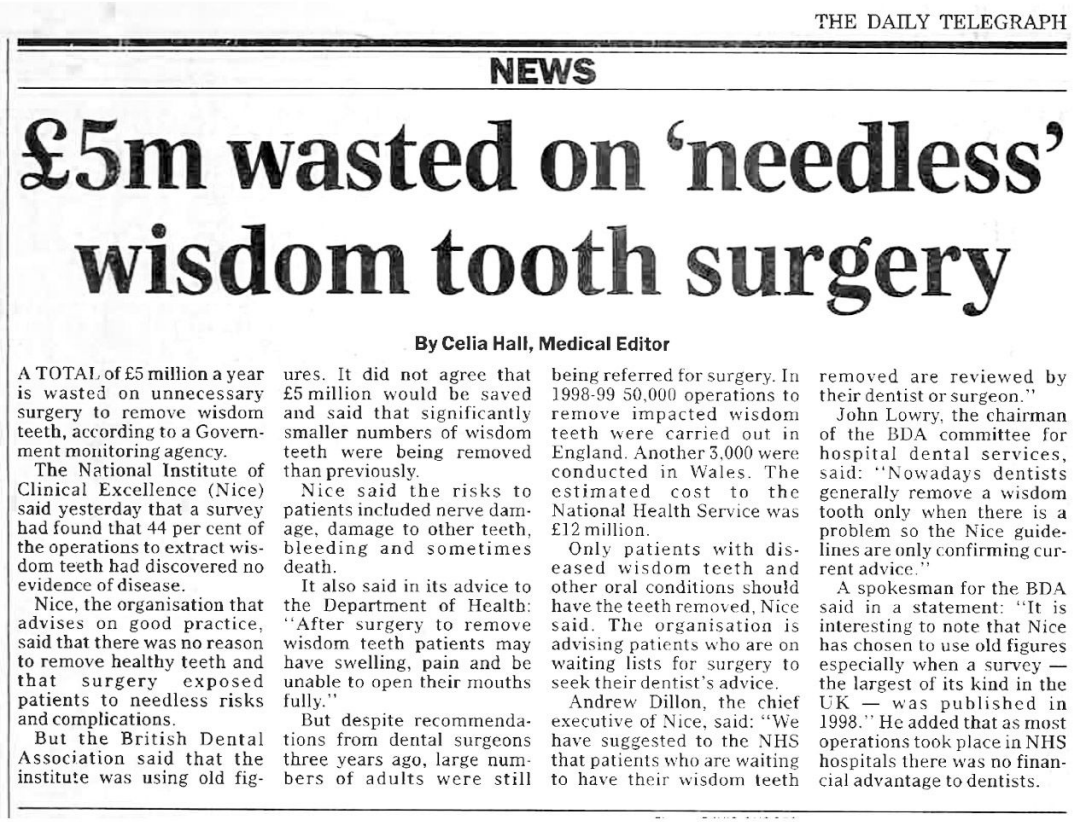
- This didn't go down very well with the manufacturer, with the then CEO Sir Richard Sykes reportedly threatening that

> *if the decision is not reversed, Glaxo Wellcome would consider leaving the UK*

- Eventually, Relenza *was* made available on the NHS, but only with a limited basis (restricted population)

NICE – *teething problems*



THE DAILY TELEGRAPH

NEWS

£5m wasted on 'needless' wisdom tooth surgery

By Celia Hall, Medical Editor

A TOTAL of £5 million a year is wasted on unnecessary surgery to remove wisdom teeth, according to a Government monitoring agency.

The National Institute of Clinical Excellence (Nice) said yesterday that a survey had found that 44 per cent of the operations to extract wisdom teeth had discovered no evidence of disease.

Nice, the organisation that advises on good practice, said that there was no reason to remove healthy teeth and that surgery exposed patients to needless risks and complications.

But the British Dental Association said that the institute was using old figures. It did not agree that £5 million would be saved and said that significantly smaller numbers of wisdom teeth were being removed than previously.

Nice said the risks to patients included nerve damage, damage to other teeth, bleeding and sometimes death.

It also said in its advice to the Department of Health: "After surgery to remove wisdom teeth patients may have swelling, pain and be unable to open their mouths fully."

But despite recommendations from dental surgeons three years ago, large numbers of adults were still being referred for surgery. In 1998-99 50,000 operations to remove impacted wisdom teeth were carried out in England. Another 3,000 were conducted in Wales. The estimated cost to the National Health Service was £12 million.

Only patients with diseased wisdom teeth and other oral conditions should have the teeth removed, Nice said. The organisation is advising patients who are on waiting lists for surgery to seek their dentist's advice.

Andrew Dillon, the chief executive of Nice, said: "We have suggested to the NHS that patients who are waiting to have their wisdom teeth removed are reviewed by their dentist or surgeon."

John Lowry, the chairman of the BDA committee for hospital dental services, said: "Nowadays dentists generally remove a wisdom tooth only when there is a problem so the Nice guidelines are only confirming current advice."

A spokesman for the BDA said in a statement: "It is interesting to note that Nice has chosen to use old figures especially when a survey — the largest of its kind in the UK — was published in 1998." He added that as most operations took place in NHS hospitals there was no financial advantage to dentists.

20 years of NICE

- The first full technology appraisal recommended that

> *healthy wisdom teeth should not be removed as a precaution which was estimated might save the NHS £5m a year*

- Very quickly got traction in the media as decisions would be (politically) sensitive – one way or the other...

NICE – Courting controversy

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'They don't care that time is ticking for my son': Mother's anger after NHS refuses to approve drug that could keep her six-year-old out of a wheelchair

- Kirath Mann, 6, has muscle-wasting Duchenne Muscular Dystrophy
- Disorder leaves many in a wheelchair by age 10 and most don't live past 30
- NICE refuses to approve breakthrough treatment called Translarna as it says there is not enough evidence that it provides value for money
- Kirath's mother, Jaspal, 39, is campaigning for drug to be made available

By MADLEN DAVIES FOR MAILONLINE
PUBLISHED: 18:01 BST, 19 October 2015 | **UPDATED:** 20:22 BST, 19 October 2015

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A devastated mother says 'time is ticking' for her son after health bosses refused to

- The Evaluation consultation document says

> *There were no statistically significant differences in quality of life between the ataluren and placebo groups. The company stated there was a positive trend towards improved quality of life with ataluren 40 mg/kg daily in the physical functioning subscale. The company submission also described a positive effect on school functioning and a negative trend in emotional and social subscales*

- Estimated total cost per person per year of treatment with ataluren of £220,256
- This is hugely affected by the uncertainty in the evidence and assumptions enconded in the model presented for assessment!

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Objective: Combine costs and benefits of a given intervention into a rational scheme for allocating resources

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$$\dots$$

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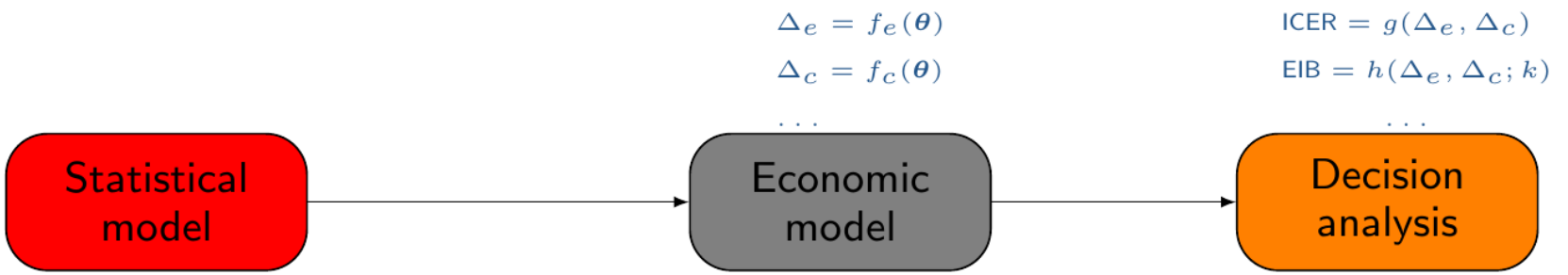

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- Standardised process

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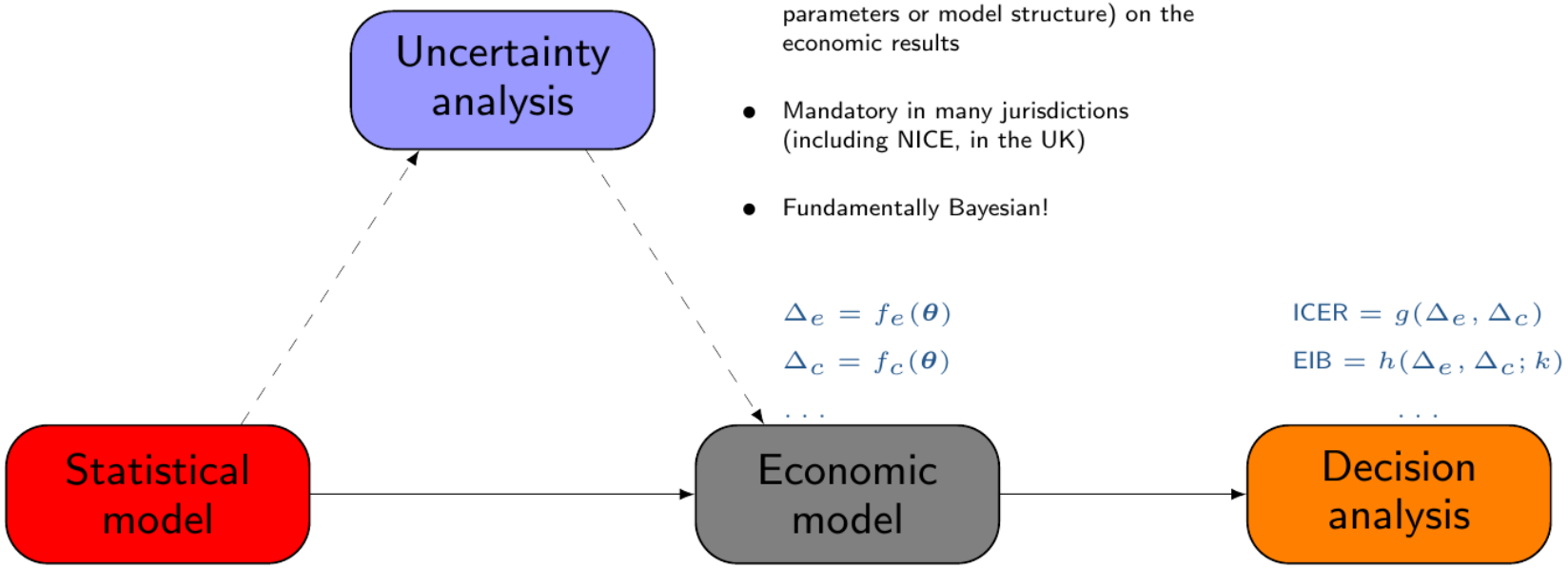

- Assesses the impact of uncertainty (eg in parameters or model structure) on the economic results
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- Fundamentally Bayesian!

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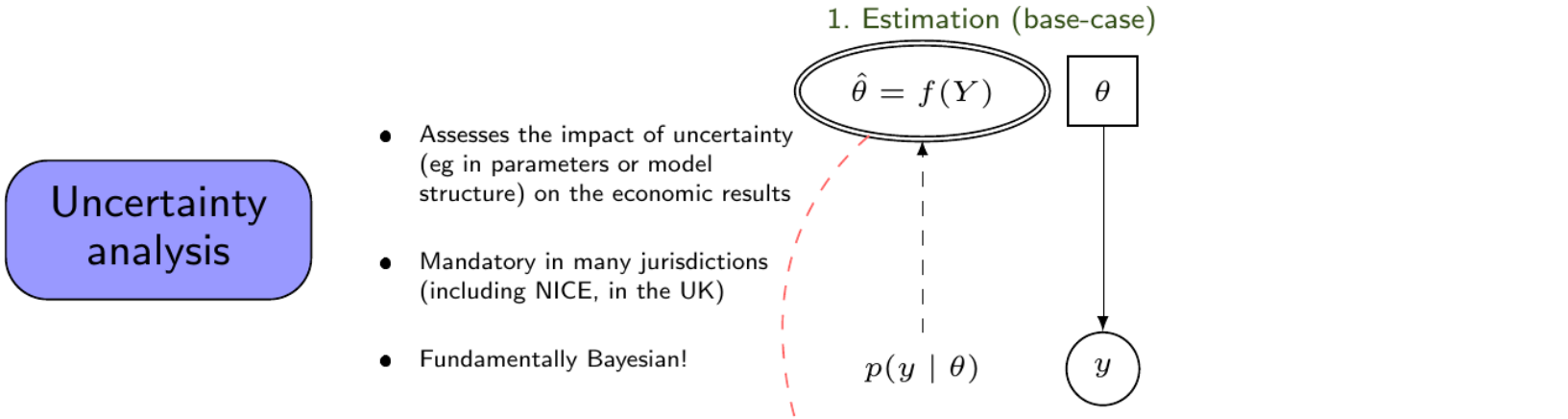
Two-stage



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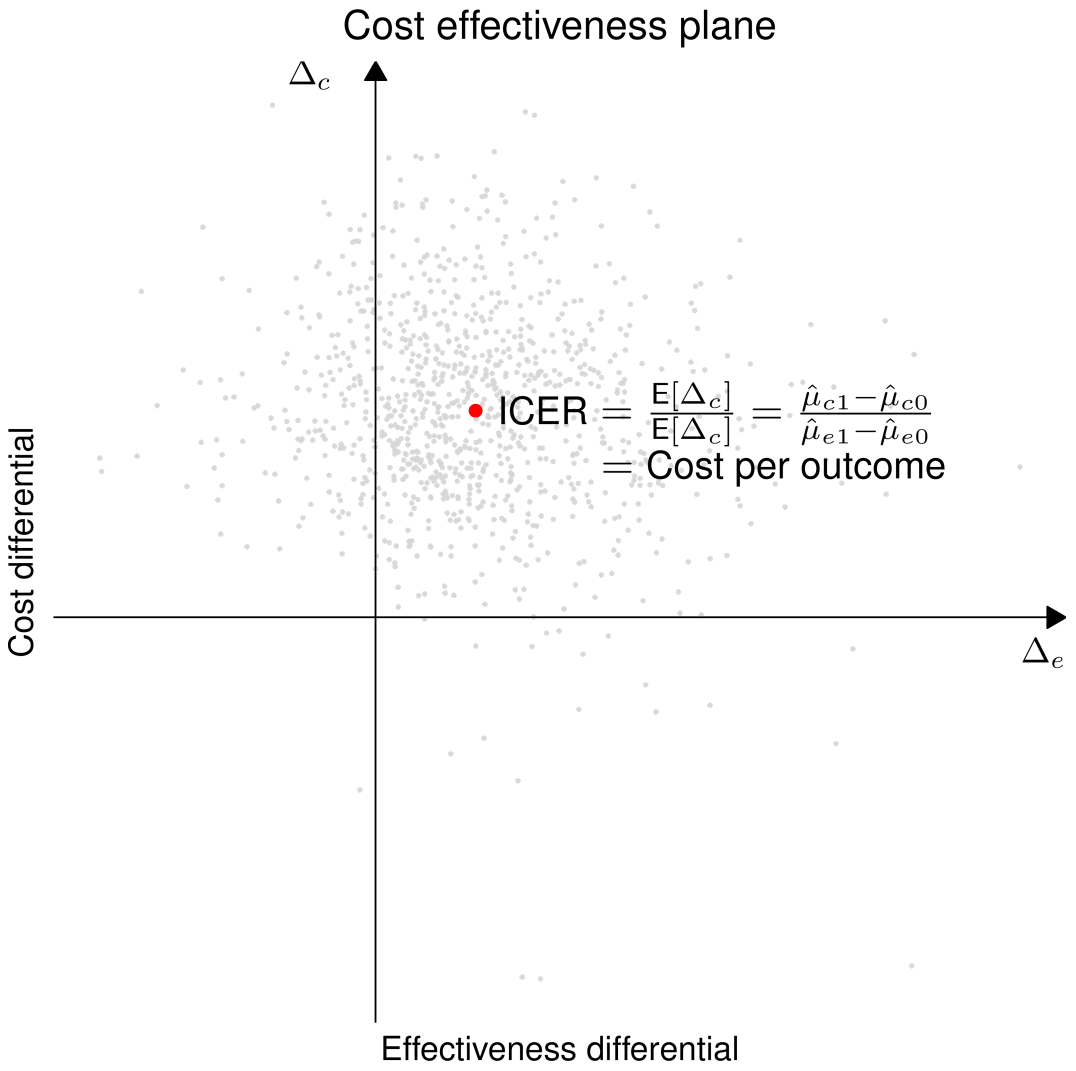
Base-case scenario



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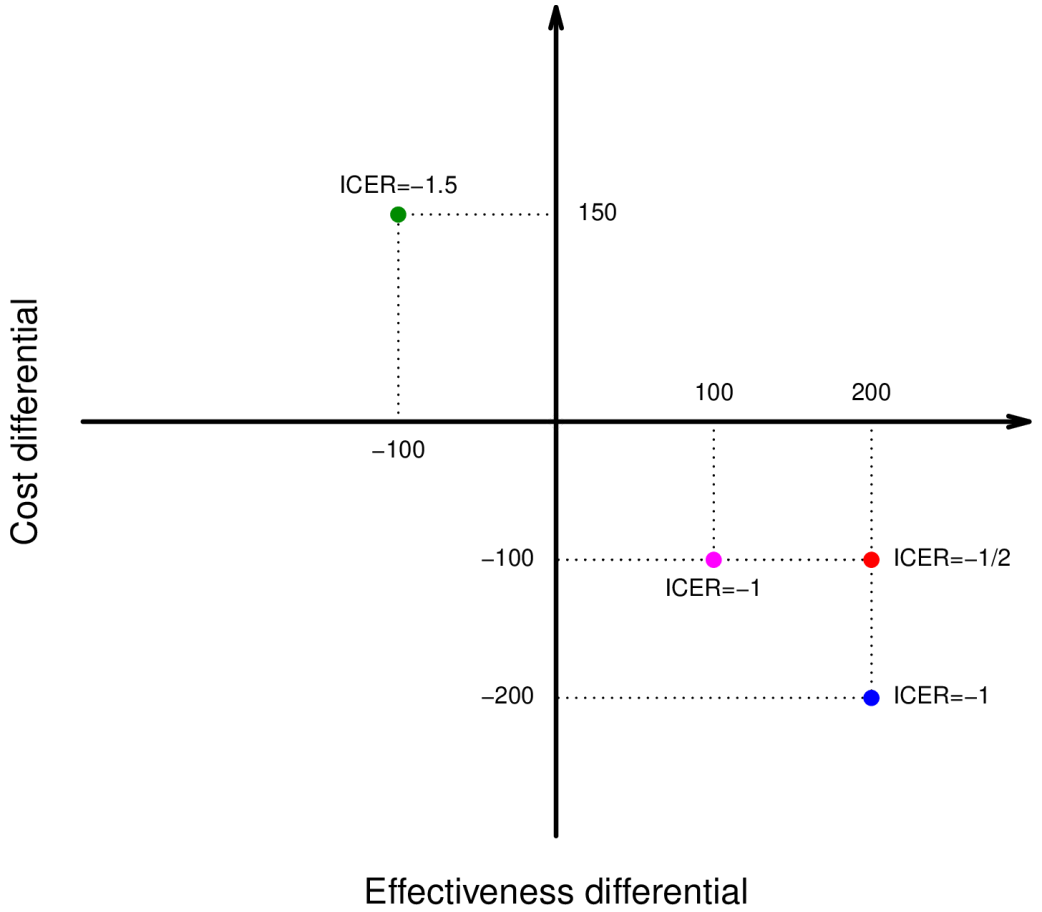
Limitations of ICER

The ICER is **not** an *ordered* statistic

- –200/200 better than –100/200 better than –100/100 in terms of decision, but ratios are -1, $-1/2$, -1
- ICERs in the NW quadrant indicate an intervention that is **dominated** ($+$ costs / $-$ effectiveness)



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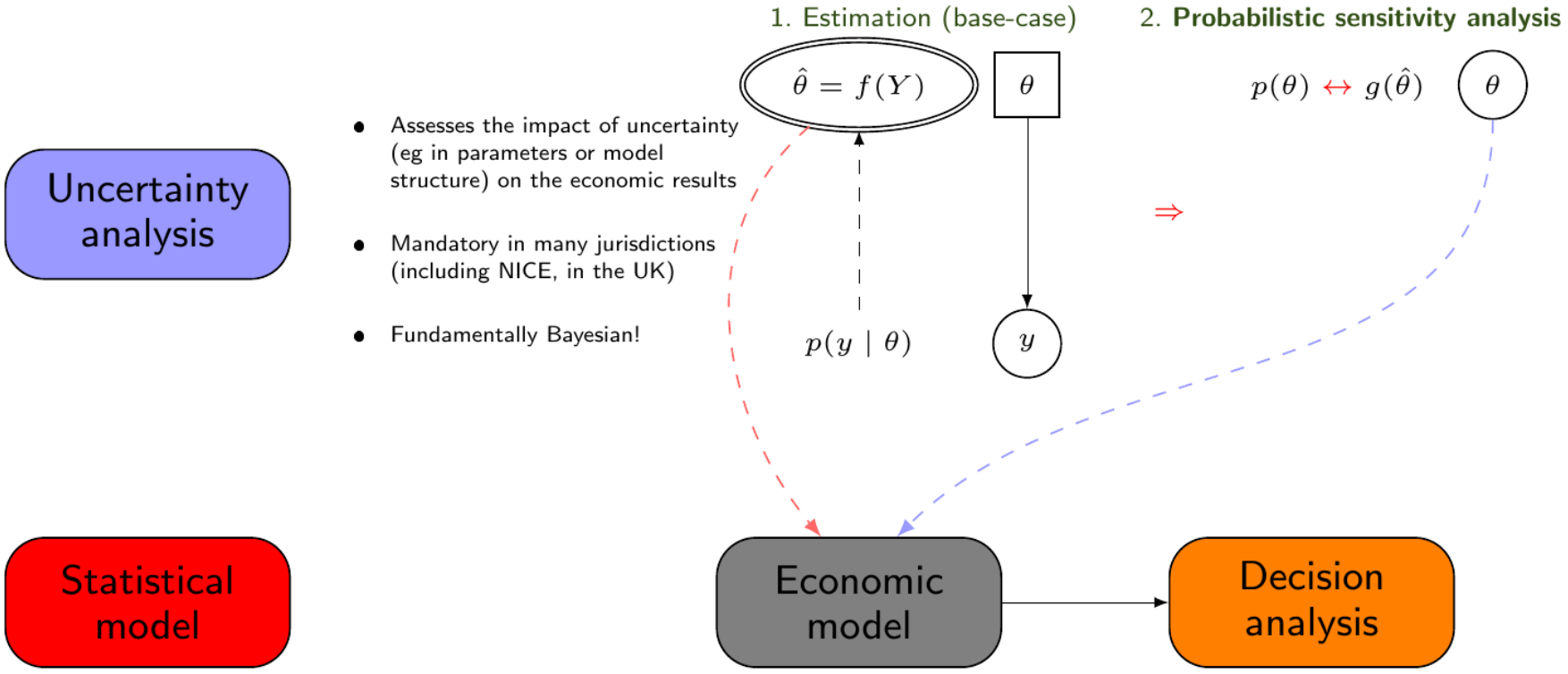

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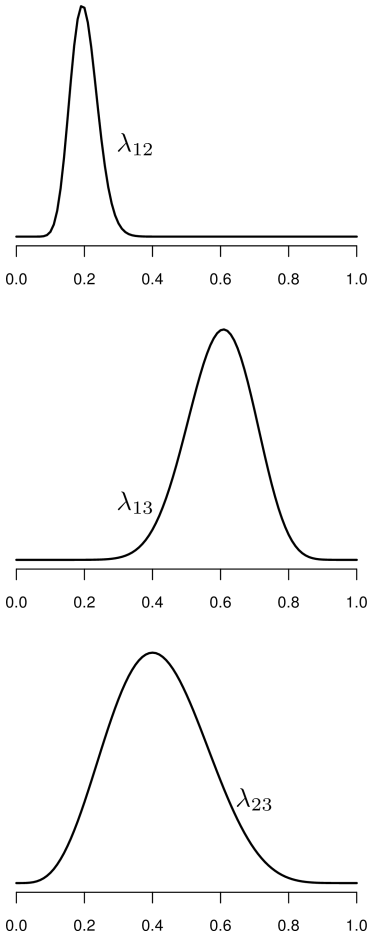
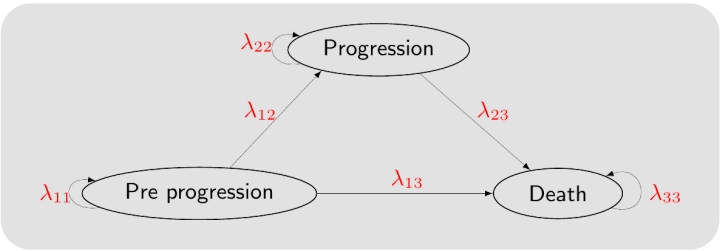
⚠ Uncertainty induced by $g(\hat{\boldsymbol{\theta}}_0), g(\hat{\boldsymbol{\theta}}_1)$ – typically **independent** simulations

Statistical model

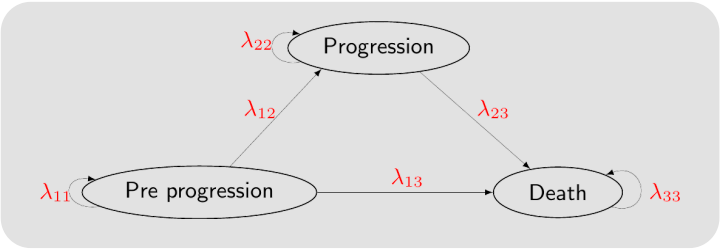


Economic model

Status quo



New drug



Decision analysis

Status quo	
Benefits	Costs

New drug	
Benefits	Costs

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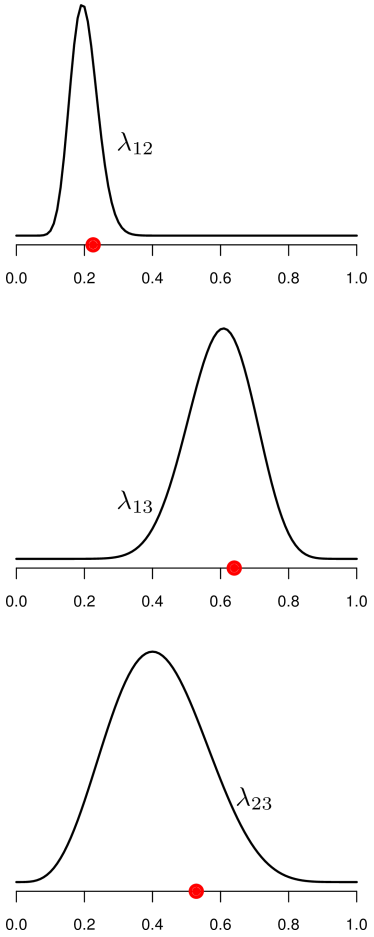
Statistical model → Economic model → Decision analysis



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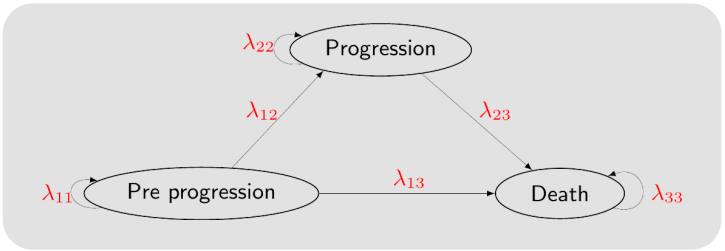

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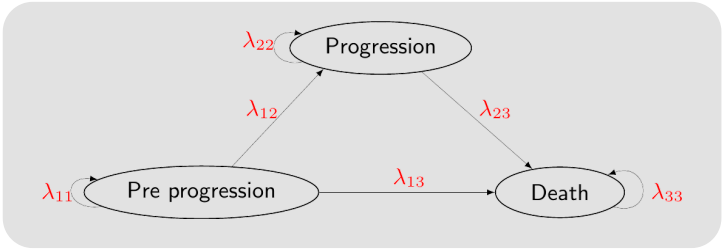

Status quo

Benefits	Costs
741	670382.1

New drug

Benefits	Costs
732	1131978

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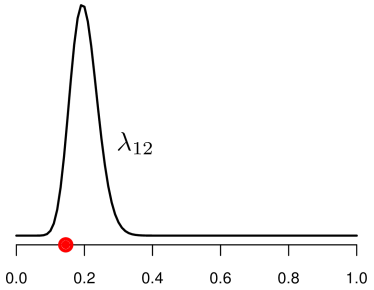

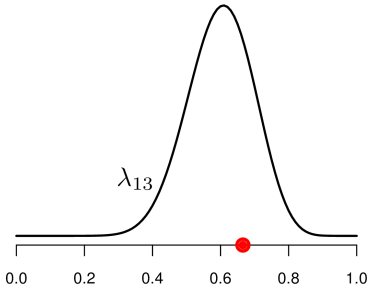

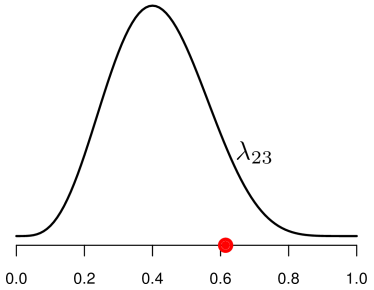

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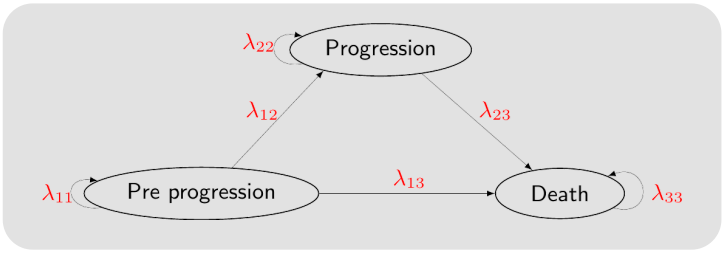

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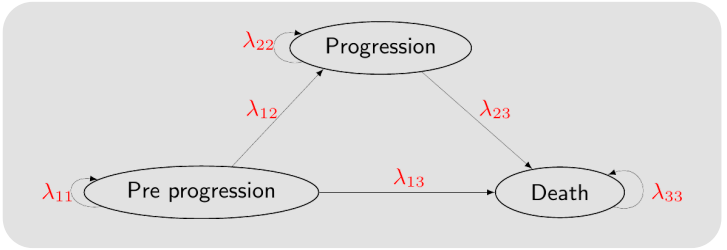

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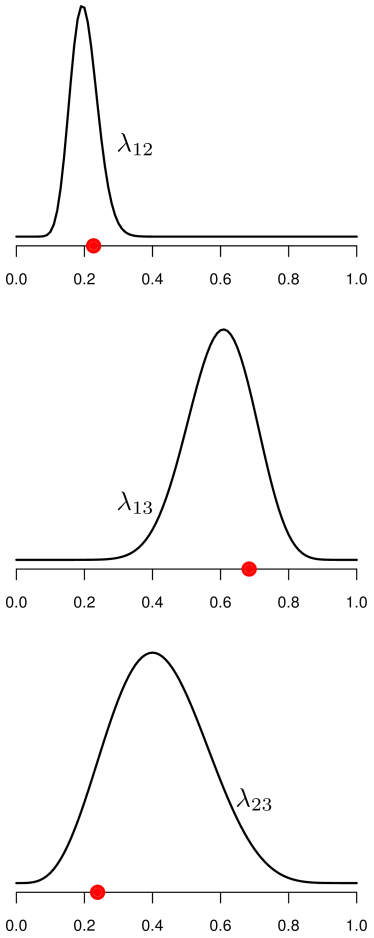

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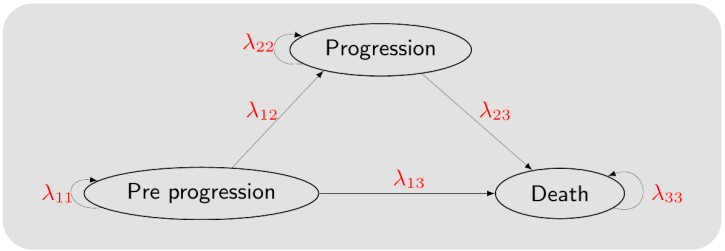

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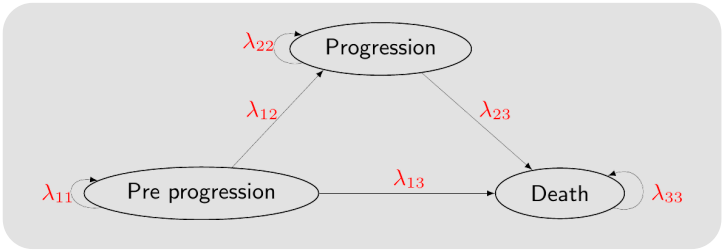

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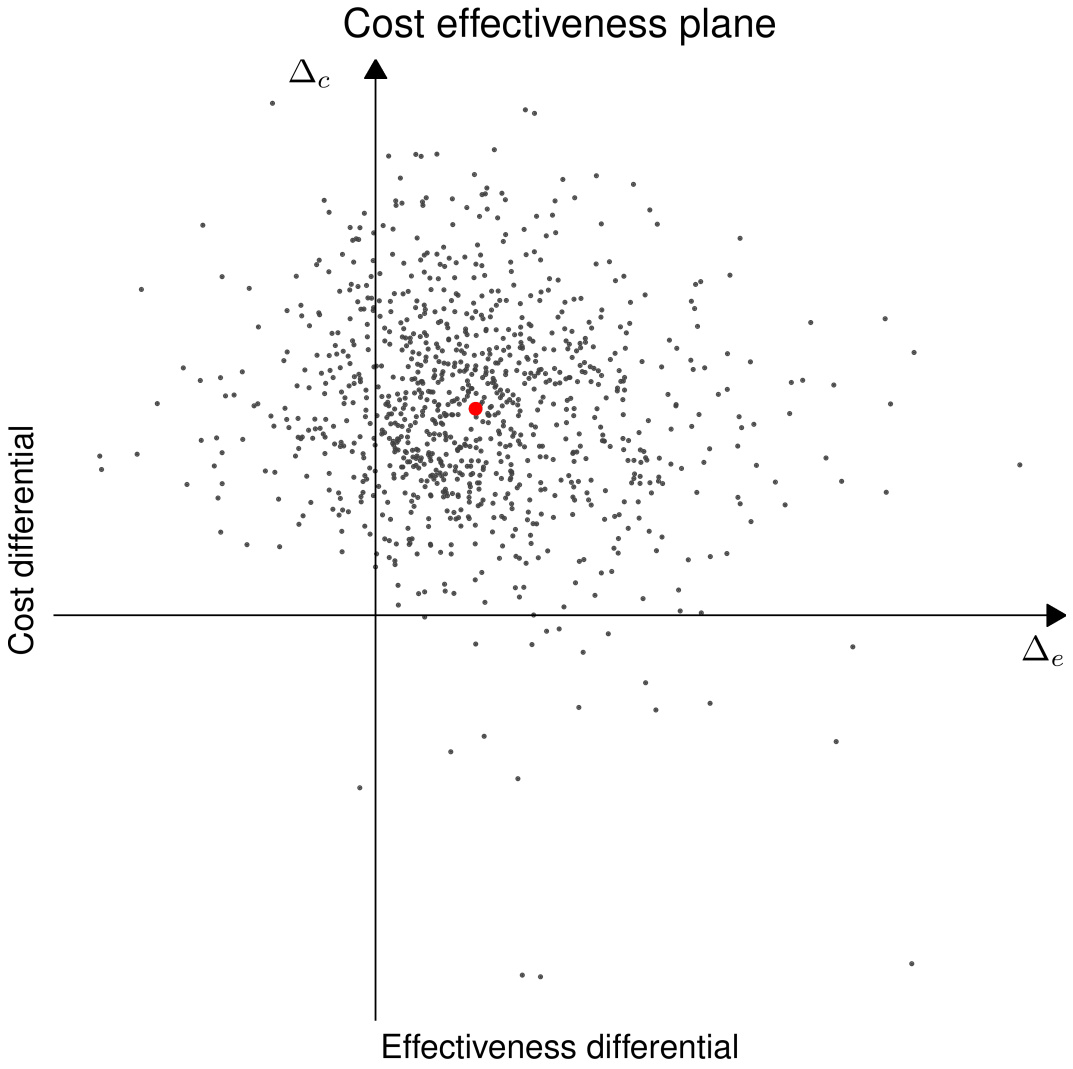
Benefits	Costs
741	670382.1
699	871273.3
...	...
726	425822.2
716.2	**790381.2**

New drug

Benefits	Costs
732	1131978
664	1325654
...	...
811	766411.4
774.5	**1066849.8**

$$\text{ICER} = \frac{276468.6}{58.3} = 6497.1$$



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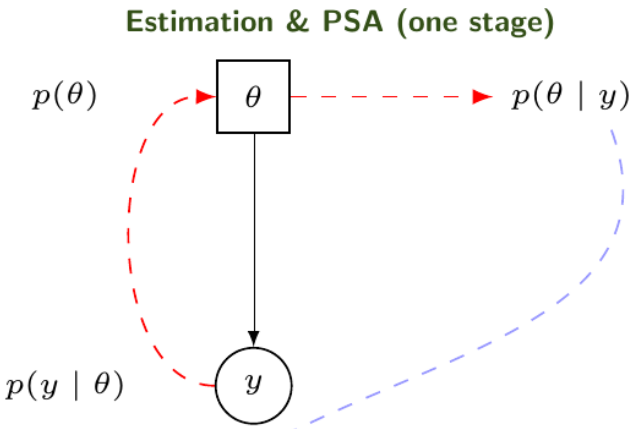
Integrated



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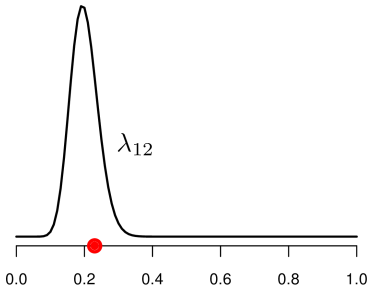
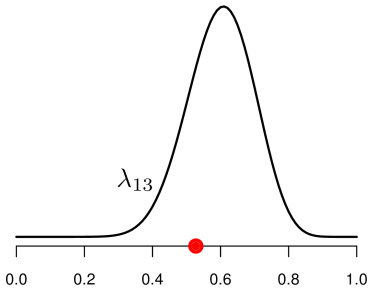
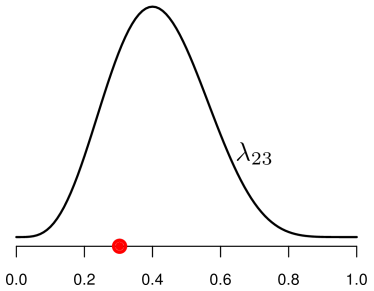
⚠ Uncertainty induced by $p(\boldsymbol{\theta} \mid \text{data})$ – uses the **joint** posterior of all the parameters!

Statistical model → Economic model → Decision analysis







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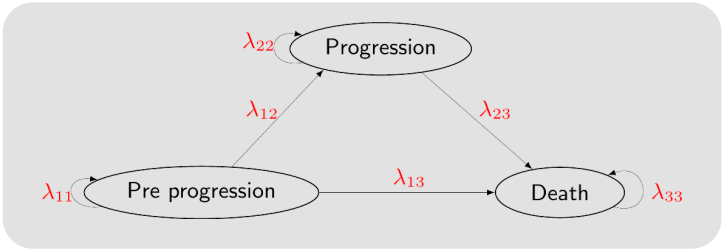

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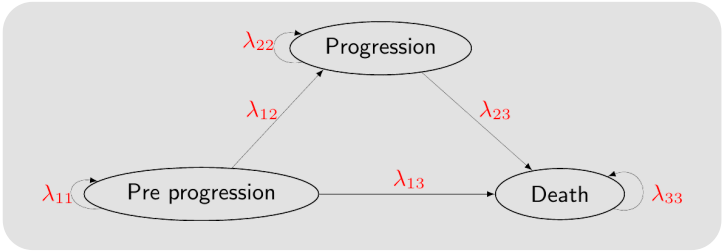


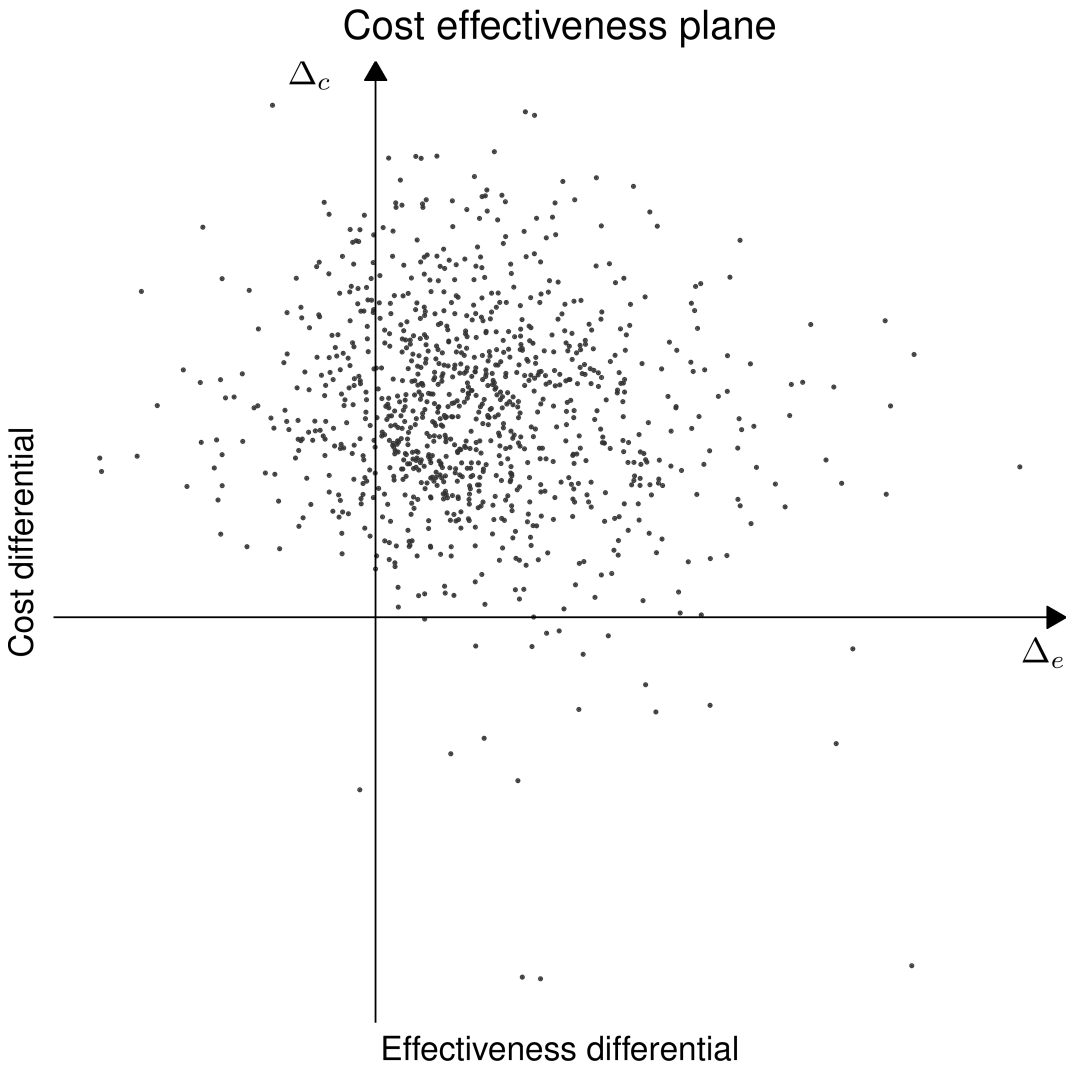
Status quo

Benefits	Costs
741	670382.1
699	871273.3
...	...
726	425822.2
716.2	**790381.2**

New drug

Benefits	Costs
732	1131978
664	1325654
...	...
811	766411.4
774.5	**1066849.8**

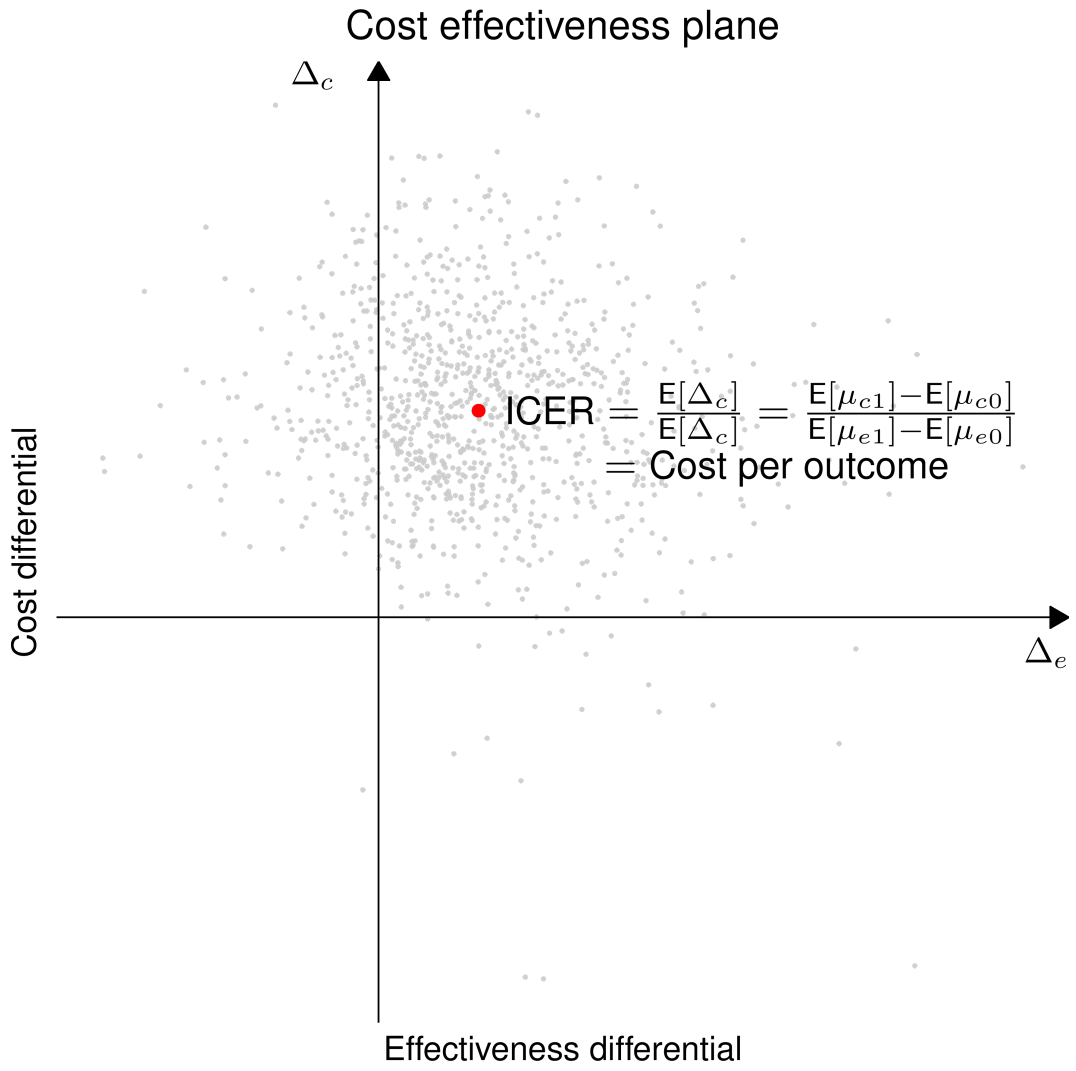
$$\text{ICER} = \frac{276468.6}{58.3} = 6497.1$$



$$\Delta_e = \underbrace{\mathsf{E}[e \mid \boldsymbol{\theta}_1]}_{\mu_{e1}} - \underbrace{\mathsf{E}[e \mid \boldsymbol{\theta}_0]}_{\mu_{e0}}$$

$$\Delta_c = \underbrace{\mathsf{E}[c \mid \boldsymbol{\theta}_1]}_{\mu_{c1}} - \underbrace{\mathsf{E}[c \mid \boldsymbol{\theta}_0]}_{\mu_{c0}}$$

*Induced by $p(\boldsymbol{\theta} \mid \text{data})$



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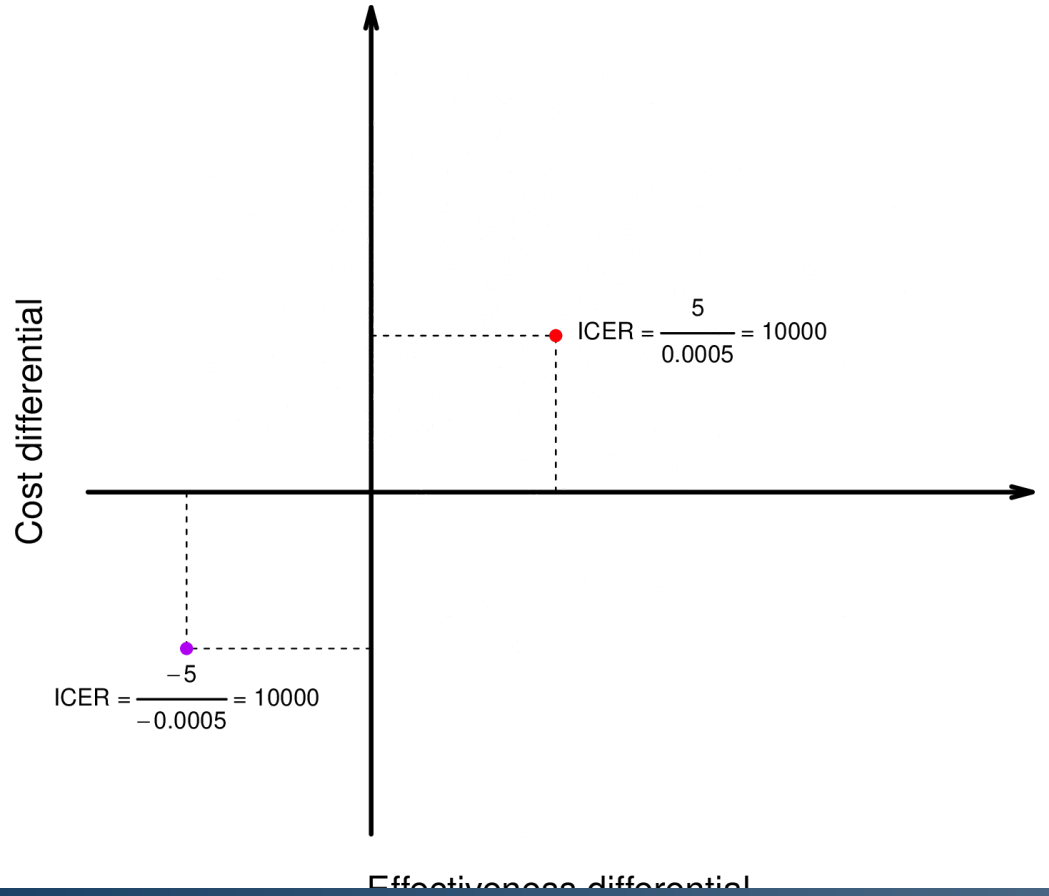
$$\Delta_c = \underbrace{\mathsf{E}[c \mid \boldsymbol{\theta}_1]}_{\mu_{c1}} - \underbrace{\mathsf{E}[c \mid \boldsymbol{\theta}_0]}_{\mu_{c0}}$$

Limitations of ICER (continued...)

Equivalent ICERs can mean very different things!

- $(\mathrm{E}[\Delta_e], \mathrm{E}[\Delta_c]) = (0.0005, 5)$, indicates that the new treatment produces on average an increase in effectiveness of 0.0005 units at the cost of extra £10 000
- $(\mathrm{E}[\Delta_e], \mathrm{E}[\Delta_c]) = (-0.0005, -5)$] indicates that the new intervention is less effective, but cheaper
- In both cases, ICER = £10 000



Decision-theoretic approach to HTA

- Analytic framework for decision-making in the face of uncertainty
- Considers a set of **prescriptive** axioms to ensure rationality in decision-making
- Identifies the best course of action given:
  - **Model specification**
  - **Current evidence**

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- Identifies the best course of action given:
  - **Model specification**
  - **Current evidence**

Process of rational decision-making

1. Describe uncertainty on all unknown quantities by means of a (possibly subjective) probability distribution $p(\boldsymbol{\omega}) = p(e, c \mid \boldsymbol{\theta})p(\boldsymbol{\theta})$
2. For each intervention t, outcomes $o = (e, c)$ are valued by means of a pre-specified measure of utility $u(e, c; t)$
3. Select as the most "cost-effective" the intervention that is associated with the maximum expected utility $\mathcal{U}^t = \mathrm{E}_{\boldsymbol{\omega}}[u(e, c; t)]$

- Typical utility function in HTA: Monetary Net Benefit $u(e, c; t) = nb_t = ke_t - c_t$
  - k is the "willingness to pay", i.e. the *cost per extra unit of effectiveness gained*
  - Fixed, linear form, which simplifies computations
  - Assumes decision-maker is *risk neutral*. Not necessarily true!

Expected Incremental Benefit

- Under the MNB, the expected utility is

$$\begin{aligned}\mathcal{U}^t = \mathcal{NB}_t &= \mathsf{E}_{\boldsymbol{\omega}}[u(e,c;t)] \\ &= k\mathsf{E}_{\boldsymbol{\omega}}[e_t] - \mathsf{E}_{\boldsymbol{\omega}}[c_t] \\ &= k\mathsf{E}_{\boldsymbol{\theta}}[e \mid \boldsymbol{\theta}_t] - \mathsf{E}_{\boldsymbol{\theta}}[c \mid \boldsymbol{\theta}_t] = k\mathsf{E}[\mu_{et}] - \mathsf{E}[\mu_{ct}]\end{aligned}$$

NB: The expectation is taken with respect to $p(\boldsymbol{\omega})$ so $\mathcal{NB}_t$ is a pure number!

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  NB: The expectation is taken with respect to $p(\boldsymbol{\omega})$ so $\mathcal{NB}_t$ is a pure number!

- Assuming we are considering only two interventions $t = (0, 1)$, decision-making can be effected by looking at the Expected Incremental Benefit

$$\begin{aligned}\mathsf{EIB} &= \mathcal{NB}_1 - \mathcal{NB}_0 \\ &= (k\mathsf{E}[\mu_{e1}] - \mathsf{E}[\mu_{c1}]) - (k\mathsf{E}[\mu_{e0}] - \mathsf{E}[\mu_{c0}]) \\ &= k\mathsf{E}[\Delta_e] - \mathsf{E}[\Delta_c]\end{aligned}$$

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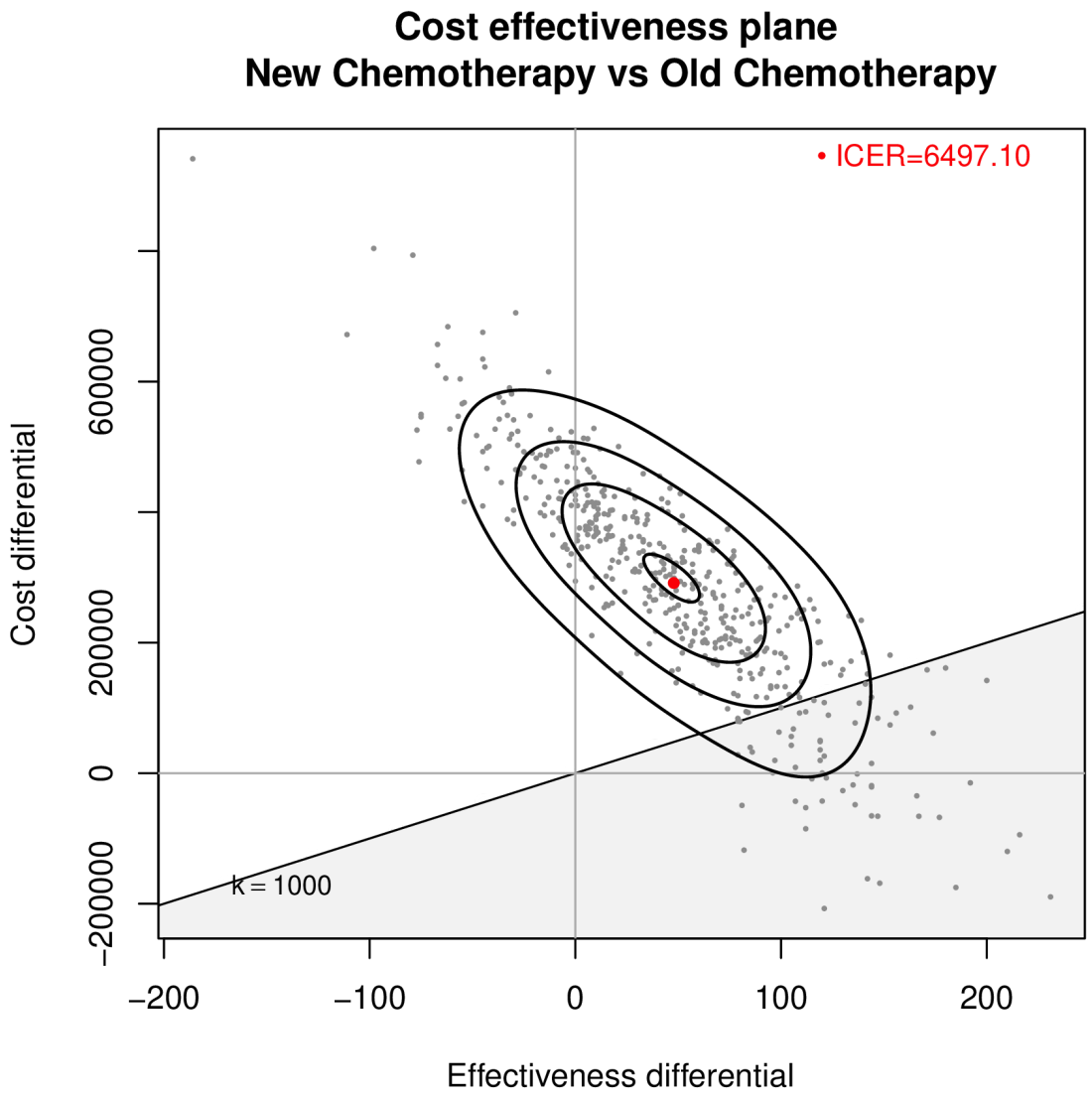
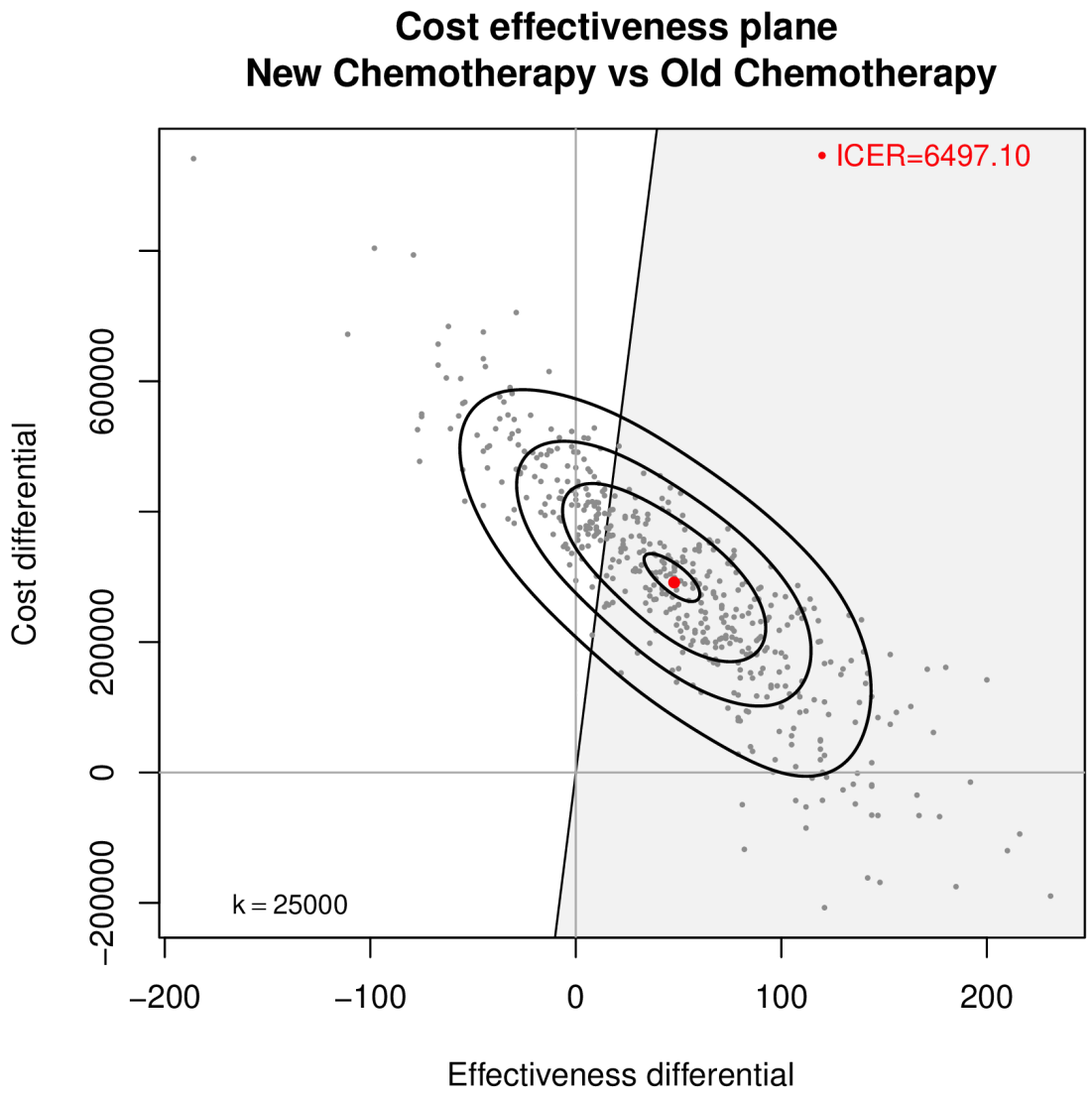
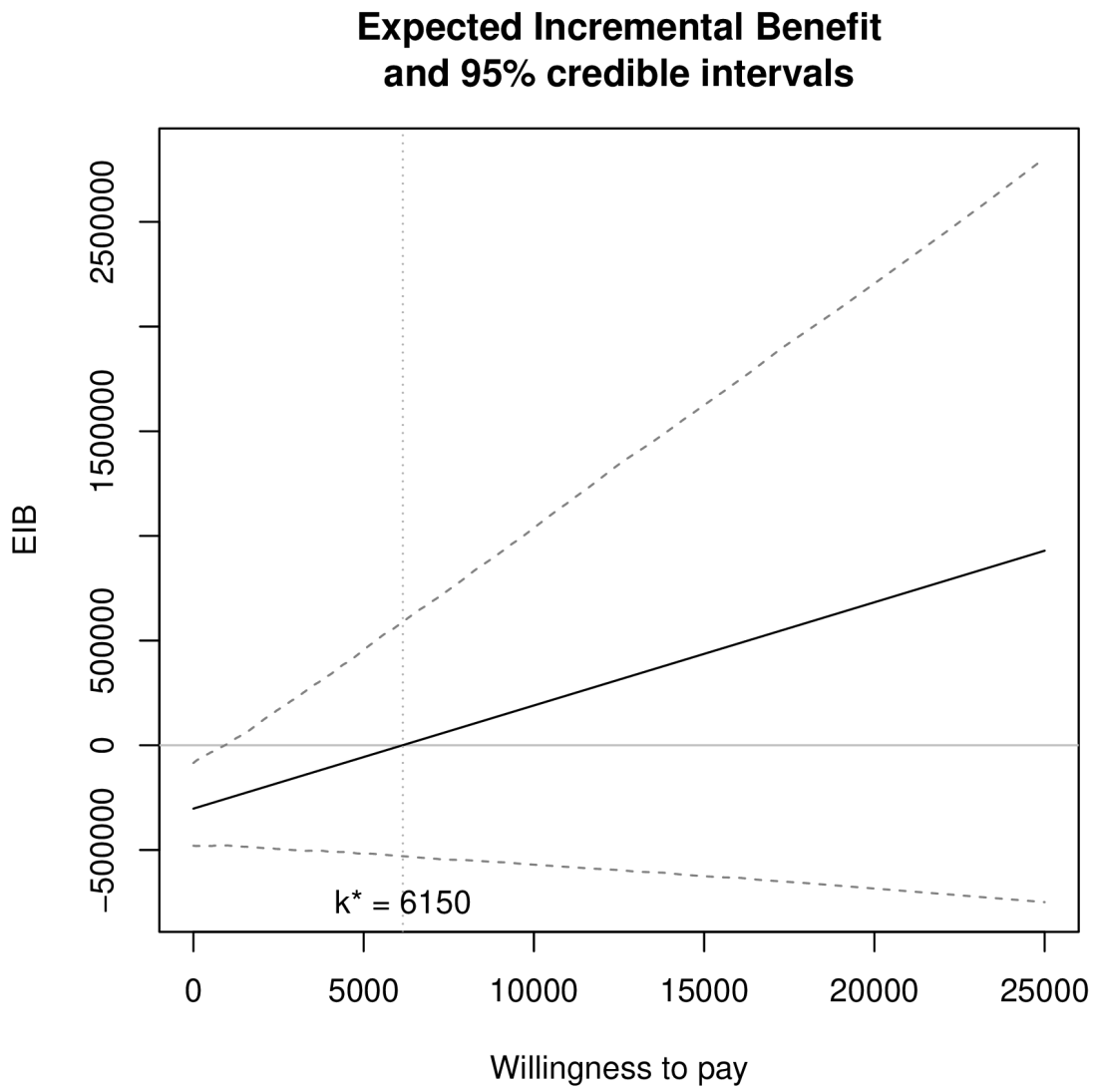
- The reference treatment $t = 1$ is more cost-effective than the comparator $t = 0$ if

$$\mathsf{EIB} > 0 \Rightarrow k > (<)\frac{\mathsf{E}[\Delta_c]}{\mathsf{E}[\Delta_e]} = \mathsf{ICER} \quad \text{if } \mathsf{E}[\Delta_e] > (<)0$$


Cost effectiveness plane
New Chemotherapy vs Old Chemotherapy
• ICER=6497.10
k = 1000
Cost differential
Effectiveness differential
600000
200000
0
−200000
−200
−100
0
100
200


Cost effectiveness plane
New Chemotherapy vs Old Chemotherapy
• ICER=6497.10
k = 25000
Cost differential
Effectiveness differential
600000
200000
0
−200000
−200
−100
0
100
200


Expected Incremental Benefit
and 95% credible intervals
EIB
2500000
1500000
500000
0
−500000
k* = 6150
0
5000
10000
15000
20000
25000
Willingness to pay

Summarising PSA

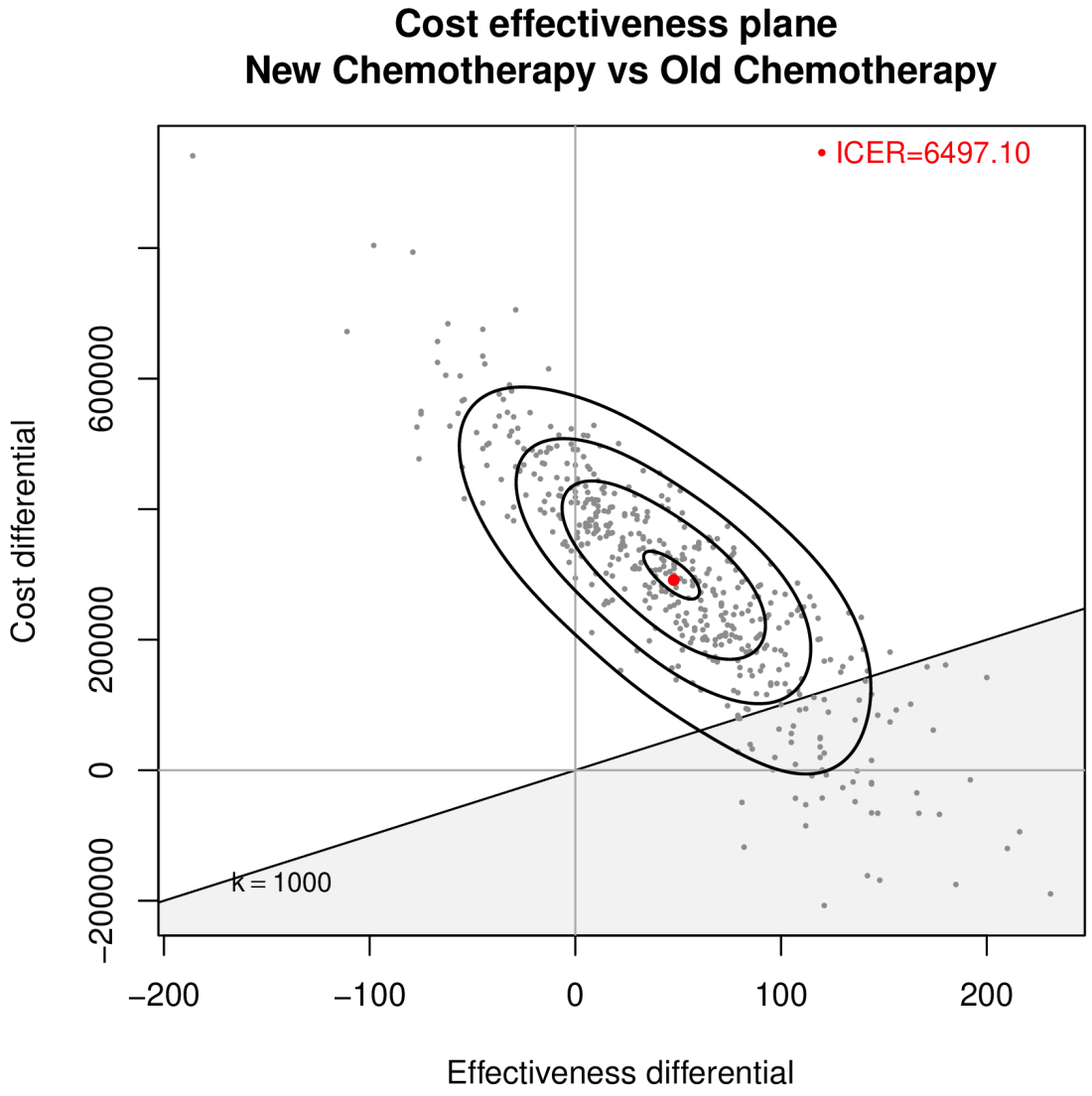
	Parameter simulations				Expected utility		
Iteration	λ_1	λ_2	λ_3	...	$\text{NB}_0(\boldsymbol{\theta})$	$\text{NB}_1(\boldsymbol{\theta})$	$\text{IB}(\boldsymbol{\theta})$
1	0.585	0.3814	0.4194	...	*77480*	67795	-9685
2	0.515	0.0166	0.0768	...	87165	*106535*	19370
3	0.611	0.1373	0.0592	...	*58110*	38740	-19370
4	0.195	0.7282	0.7314	...	77480	*87165*	9685
...	...	...	...	...	...	...	...
1000	0.0305	0.204	0.558	...	48425	*87165*	38740
				Average	$\mathcal{NB}_0$ =72365.35	$\mathcal{NB}_1$ =*77403.49*	EIB =5038.14

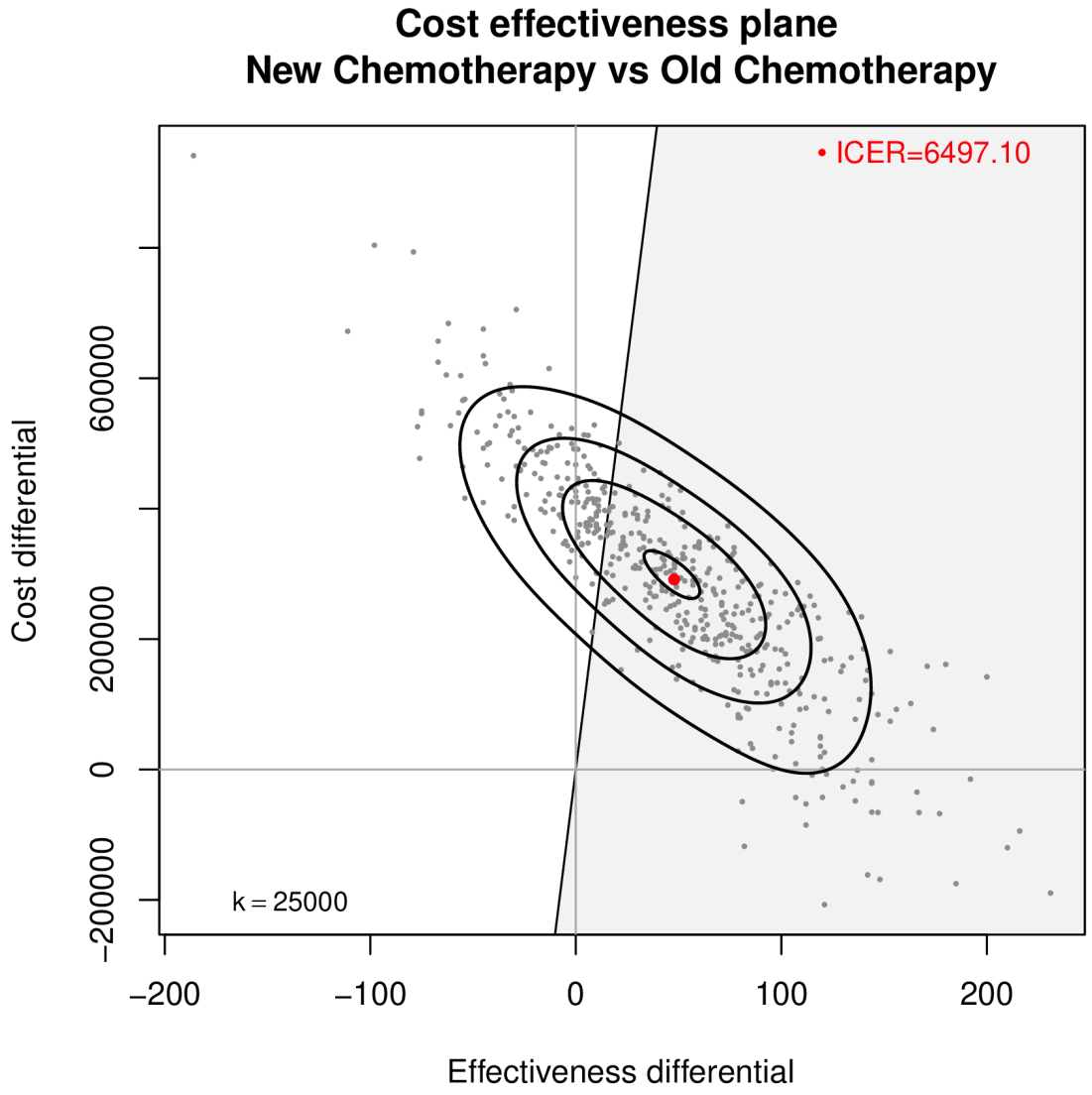
- $\text{NB}_t(\boldsymbol{\theta}) = k\mu_{et} - \mu_{ct}$ is the "known distribution" utility
- $\text{IB}(\boldsymbol{\theta}) = \text{NB}_1(\boldsymbol{\theta}) - \text{NB}_0(\boldsymbol{\theta})$ is the incremental benefit (as a function of $\boldsymbol{\theta}$)
- Can summarise uncertainty in the decision-making process using the **cost-effectiveness acceptability curve**

$$\text{CEAC} = \Pr(\text{IB}(\boldsymbol{\theta}) \mid \text{data}) > 0$$

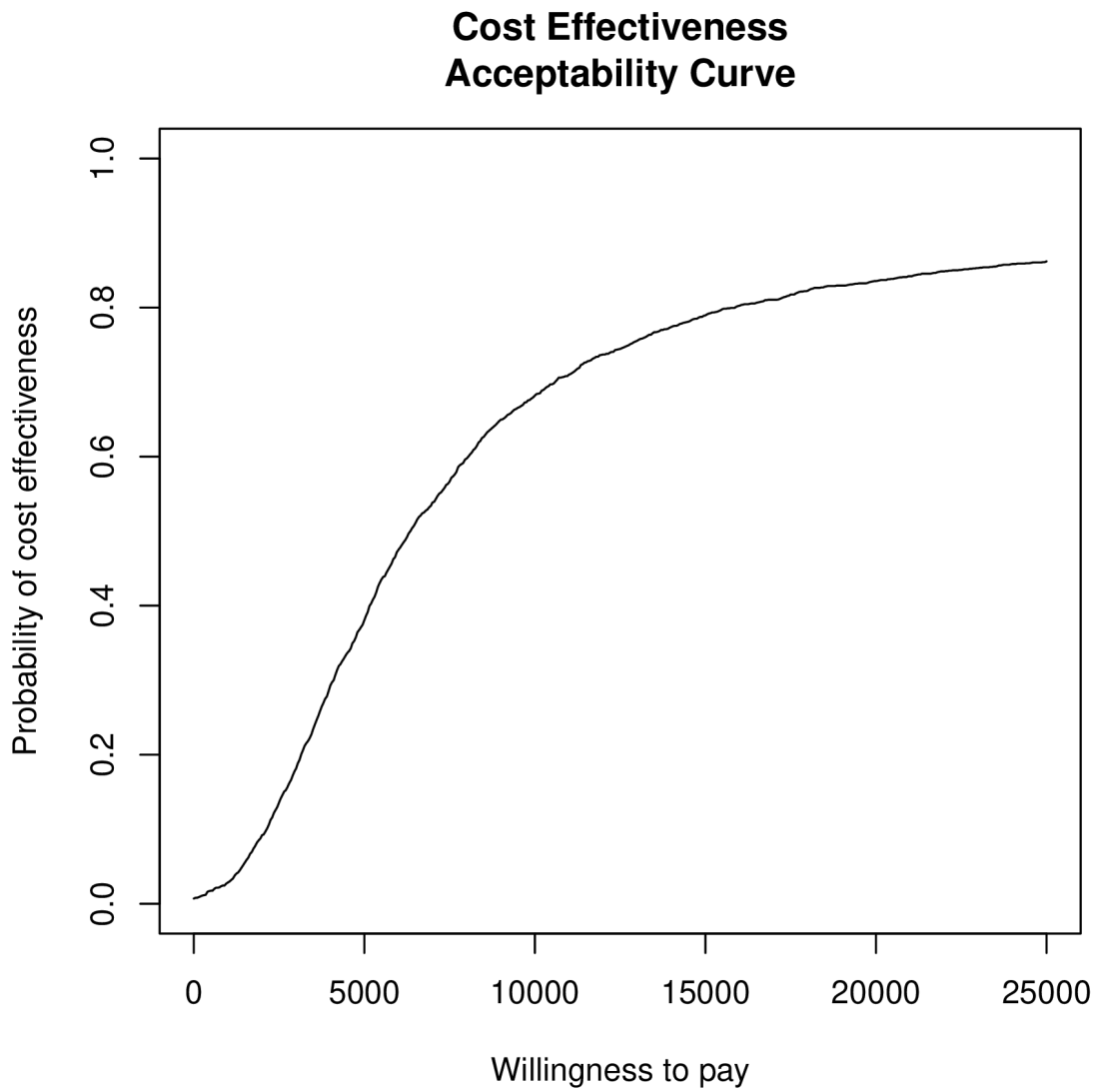
- Upon varying k, this is the **probability** that the optimal decision would not be reversed by reducing uncertainty

CE plane vs CEAC



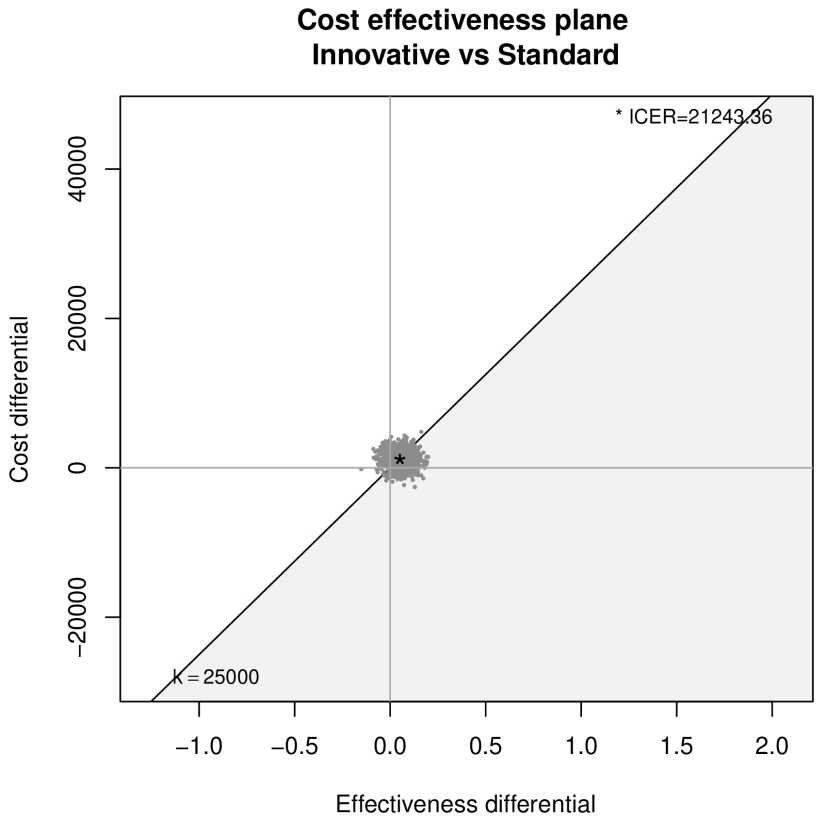


CE plane vs CEAC

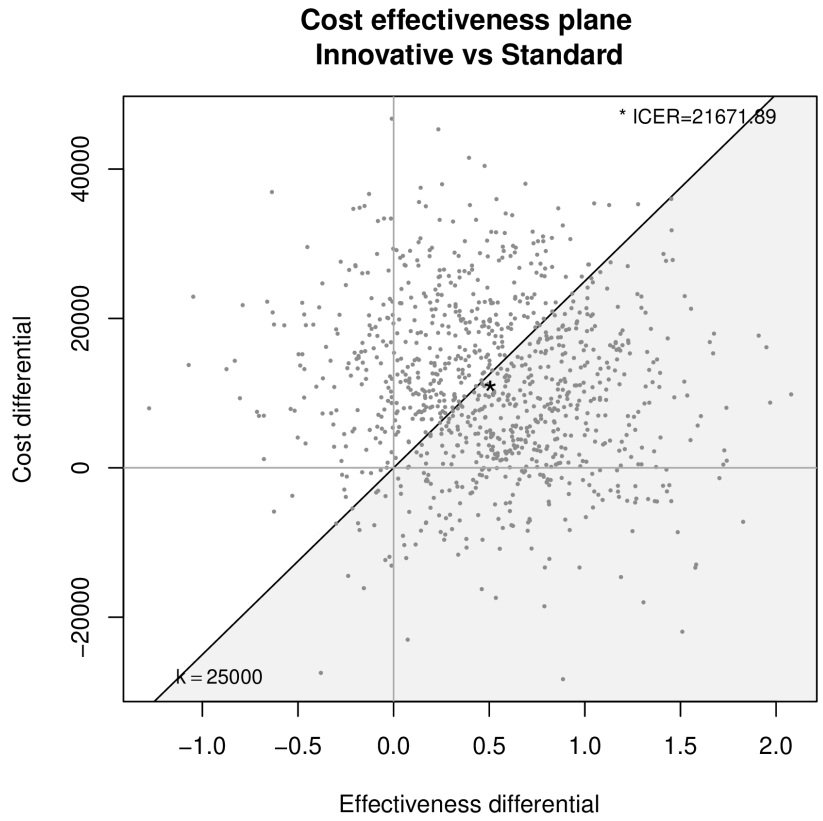


Limitations of CEACs

More on this in Lecture 11



- $\mathrm{E}[\Delta_c] =$ £1 100; $\mathrm{sd}(\Delta_c) =$ £1 100
- $\mathrm{E}[\Delta_e] = 0.05$; $\mathrm{sd}(\Delta_e) = 0.05$
- $\mathrm{Corr}(\Delta_e, \Delta_c) = 0$
- CEAC $= 0.53$ (for $k =$ £25 000)



- $\mathrm{E}[\Delta_c] =$ £11 100; $\mathrm{sd}(\Delta_c) =$ £11 100
- $\mathrm{E}[\Delta_e] = 0.5$; $\mathrm{sd}(\Delta_e) = 0.5$
- $\mathrm{Corr}(\Delta_e, \Delta_c) = 0$
- CEAC $= 0.53$ (for $k =$ £25 000)

A package for Bayesian health economics

What is BCEA not?

- BCEA is **not** a package to automatically run a Bayesian analysis
  - It cannot build the health economic model for you
  - It does not prepare the data to be used in the model
  - It does not automatically run the MCMC simulations
  - It does not choose the prior distributions for you

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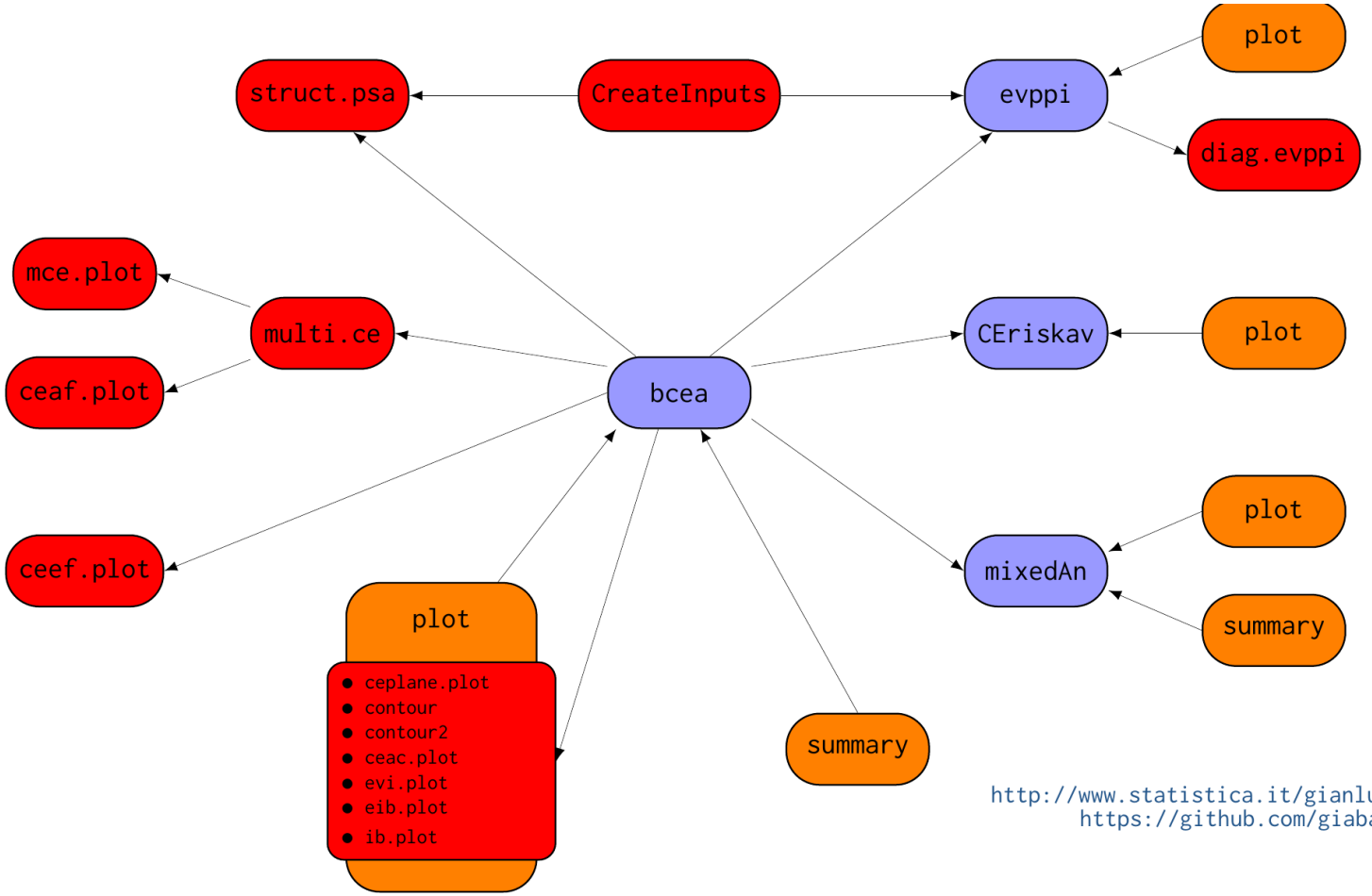
So what *is* it then?

- BCEA provides a set of specific functions to systematically post-process the output of a Bayesian health economic model
- Uses R http://cran.r-project.org/
  - Very good at interacting with standard MCMC software
  - BUGSwww.mrc-bsu.cam.ac.uk/bugs/winbugs/contents.shtml
  - JAGSwww.mcmc-jags.sourceforge.net/
  - **Free** and there is a very large community of contributors
  - Specifically designed for statistical analysis and has very good graphical capabilities

A package for Bayesian health economics



http://www.statistica.it/gianluca/BCEA
https://github.com/giabaio/BCEA

Next lecture