Online Advanced Methods for Cost-Effectiveness Analysis

Presentation 5: Working with Individual Patient Data

5.2: Know your data and learn how to analyse them

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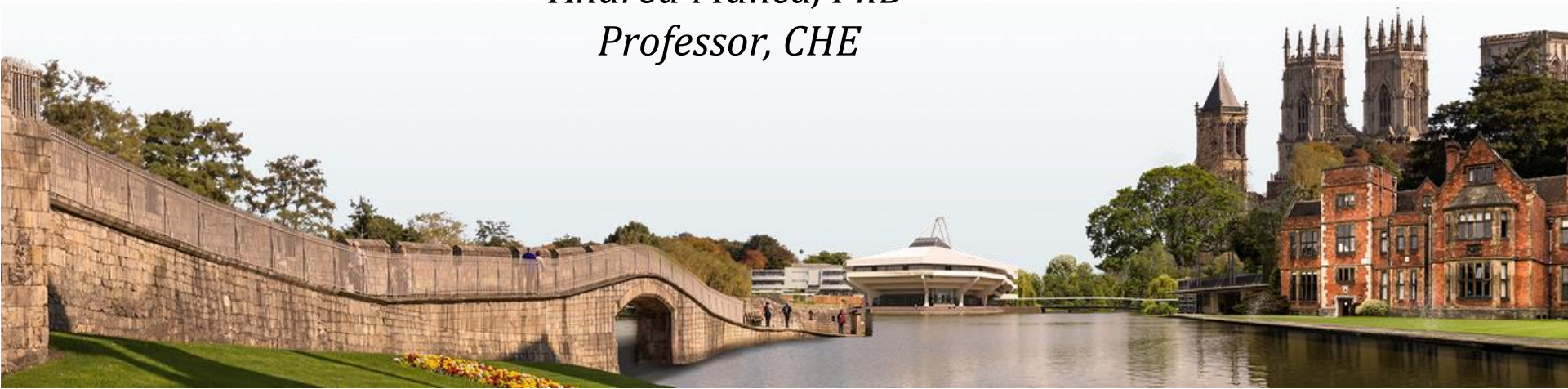


Objectives

- Learn (how) to
  - recognise the idiosyncrasies of the key outcomes in CEA and why we can't just use statistical methods based on the Normal distribution assumption
  - analyse individual patient level costs and QALYs data (in a very simple way)

Context

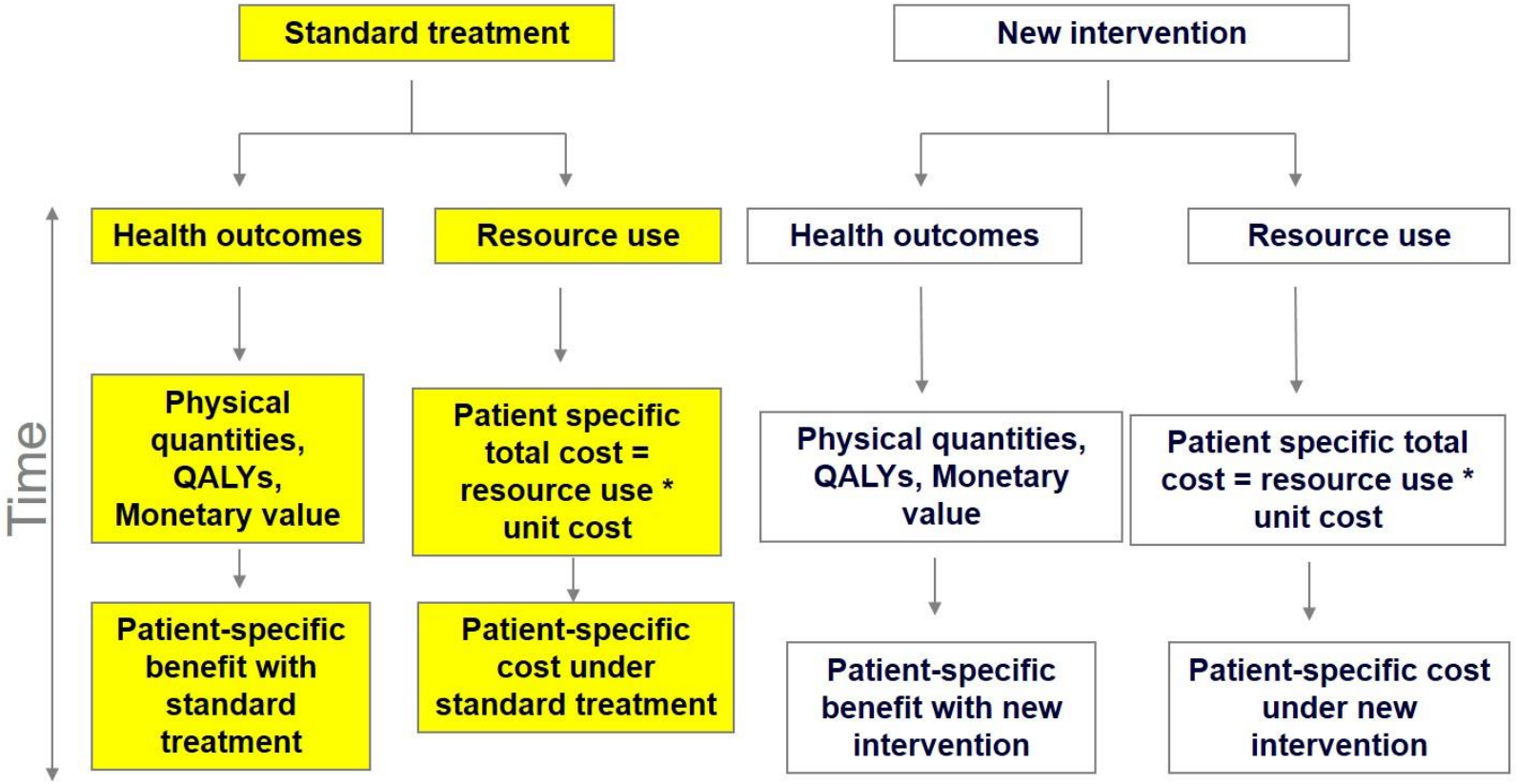
- Increasing need evidence synthesis and decision analysis
  - RCTs continue to be a key a key source of evidence
  - Decisions occasionally made on the basis of evidence from a single RCT

- We have looked at the role of models in HTA decision making in lecture 1.4

- A few jurisdictions continue to prefer economic evidence derived from RCT studies

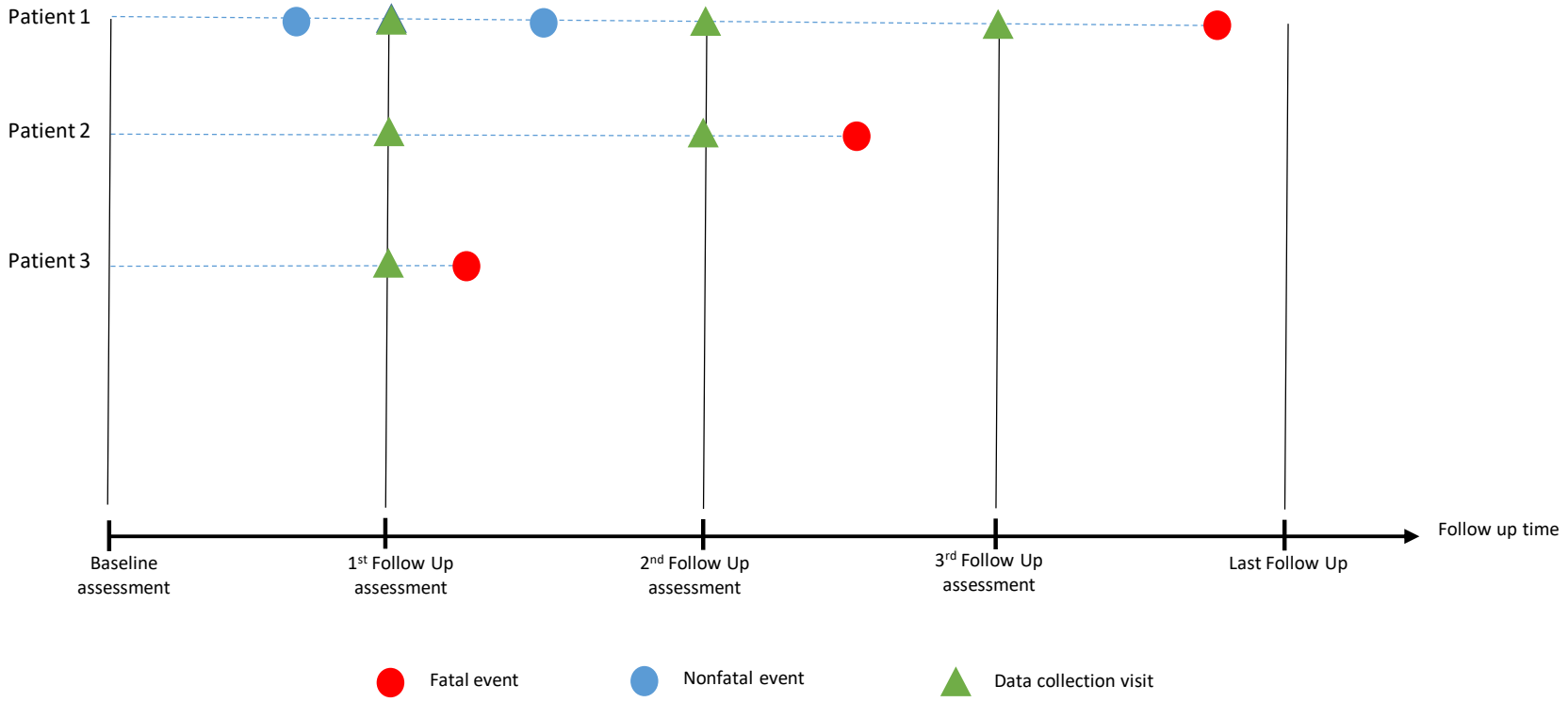
- Important to ensure appropriate analysis of RCT-based economic data, even if such data need to be synthesised with other evidence

Structure of a RCT-based CEA



Patient's history and data accrual

(simple case with no censoring)



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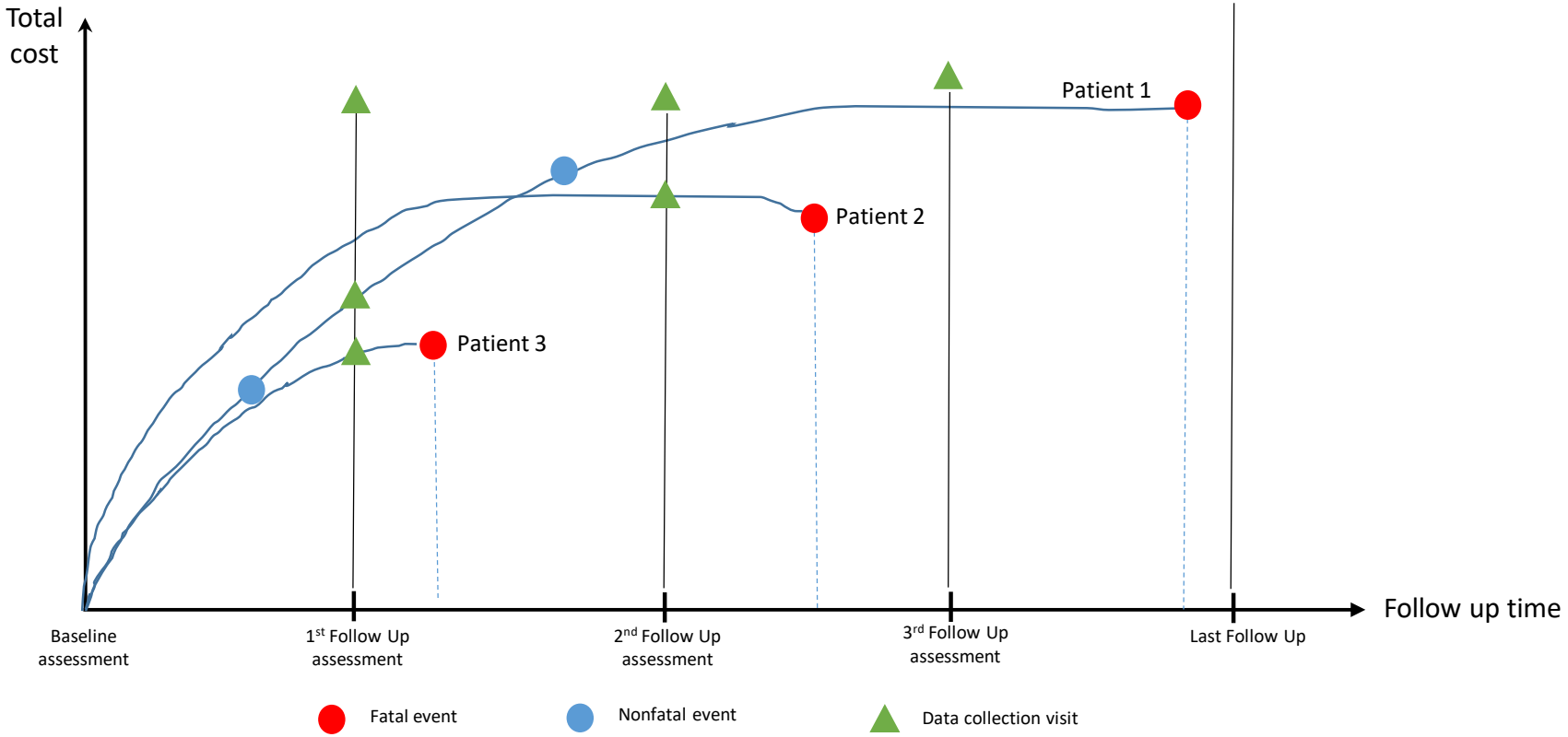

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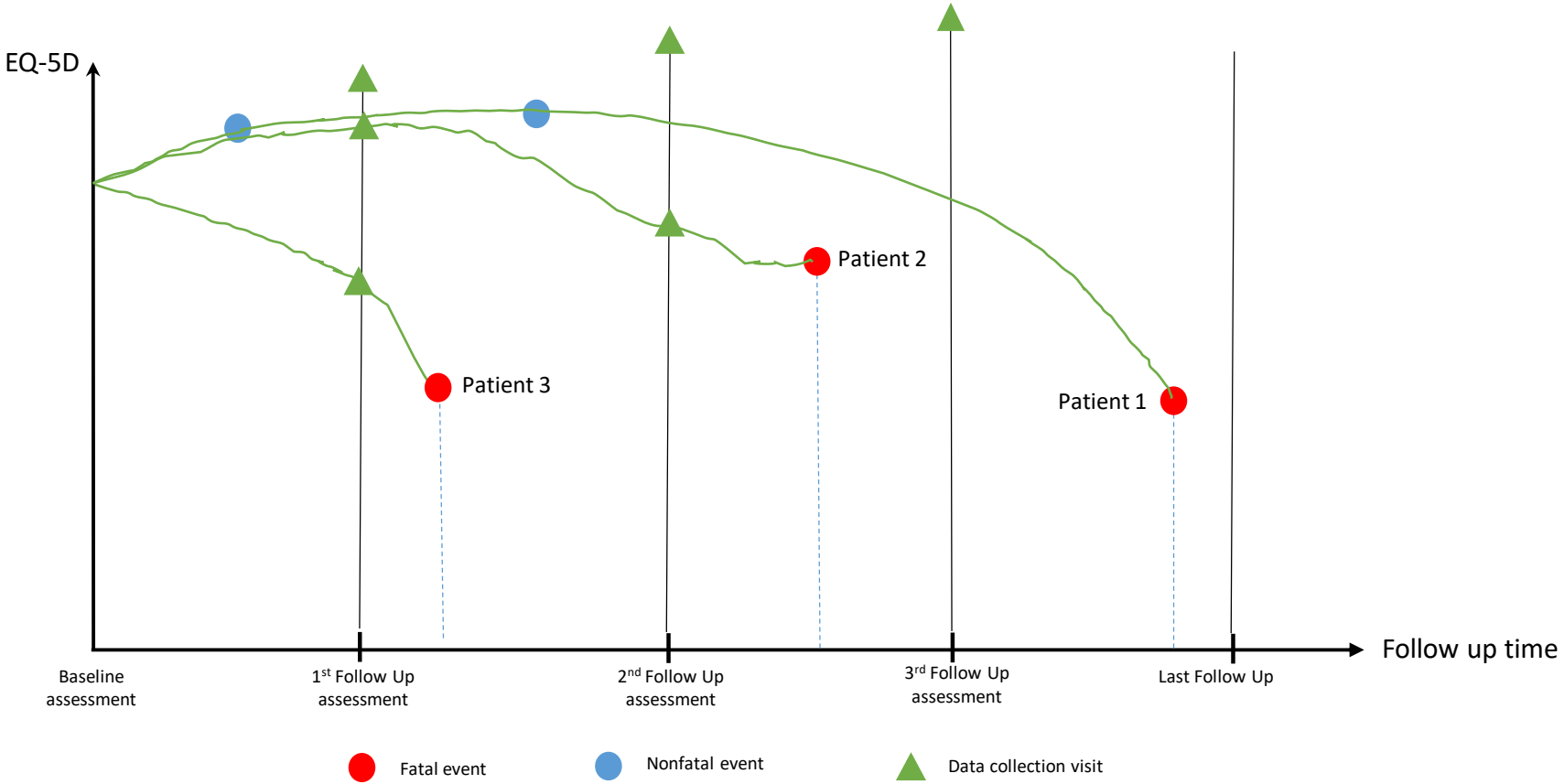


Sample dataset

id	group	Follow up visit	EQ-5D	GP visits	Out-patient visits	In-patient LOS (days)	Medication use (mg)	Dead
1	0	0	0.80	NA	NA	NA	NA	0
1	0	1	0.85	2	1	0	180	0
1	0	2	0.87	3	1	2	180	0
1	0	3	0.54	0	3	20	340	0
1	0	4	-	-	-	-	-	1
2	1	0	0.80	NA	NA	NA	NA	0
2	1	1	0.83	2	1	3	160	0
2	1	2	0.60	4	1	15	180	0
2	1	3	-	-	-	-	-	1
2	0	4	-	-	-	-	-	1

Can you try and add the rows for patient 3?

Data structure

Two independent groups

Control

Patient	(Cost, Effect)
1	C_c^1, E_c^1
2	C_c^2, E_c^2
3	C_c^3, E_c^3
.	
.	
n_c	C_c^n, E_c^n

Intervention

Patient	(Cost, Effect)
1	C_n^1, E_n^1
2	C_n^2, E_n^2
3	C_n^3, E_n^3
.	
.	
n_n	C_n^n, E_n^n

Focus of the analysis

- The interest rests on appropriate quantification
  - mean costs and effects
  - measures of sample uncertainty

- Mean costs are of direct relevance to decision makers for policy making
  - (Mean cost x Number of individuals to be treated) = Total Cost

- Other measures of central tendency are unhelpful
  - Because costs are right skewed the median can be misleading
  - ➔ median < arithmetic mean ➔
    (Median cost x Number of individuals to be treated) < Total Cost
  - Same applies to health outcomes (EQ-5D and QALYs usually left skewed)

Idiosyncrasies of cost data

(issues apply also to QALYs)

- Problems with standard statistical methods of estimation
  - many statistical estimation methods rely on normality
  - problematic to work directly on costs scale
- Reasons why cost data are right skewed
    - large proportion of patients with similar resource use
    - few patients with large resource use
    - presence of zero costs
- Some suggested solutions for statistical inference
  - non parametric tests
  - log transformed cost data and use of back-transformation
  - use non-parametric bootstrap
  - recent return to parametric methods (needed for extrapolation)

Source: Briggs A and Gray A (1999)

Case Study

EVALUATE Trial

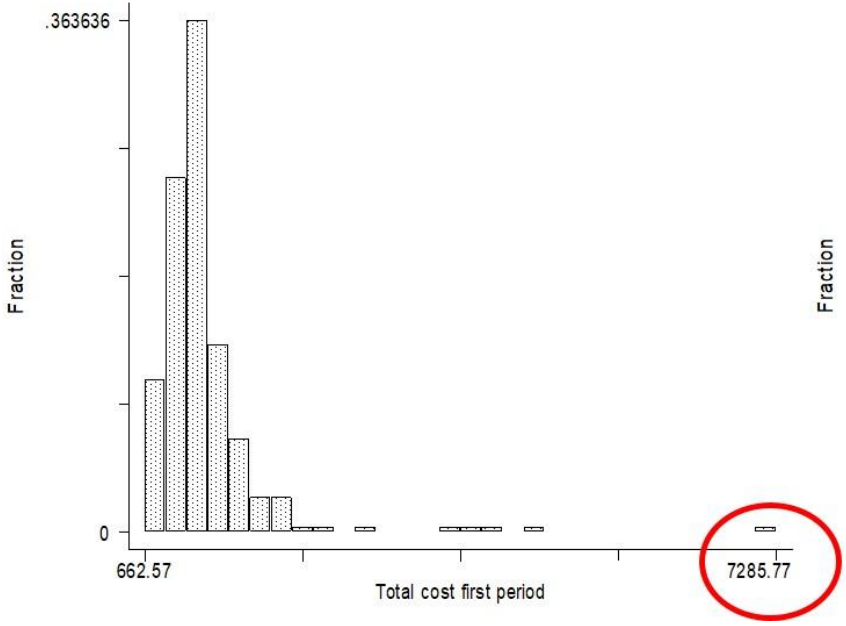
- Multi centre RCT comparing laparoscopic-assisted *versus* standard (abdominal or vaginal) hysterectomy
- Total of 859 patients in 30 centres (25 from England)
- Median follow-up: 12 months
- Follow up: baseline, 6-week, 4 and 12 months
- CEA from UK NHS perspective
- Health outcomes in terms of QALYs

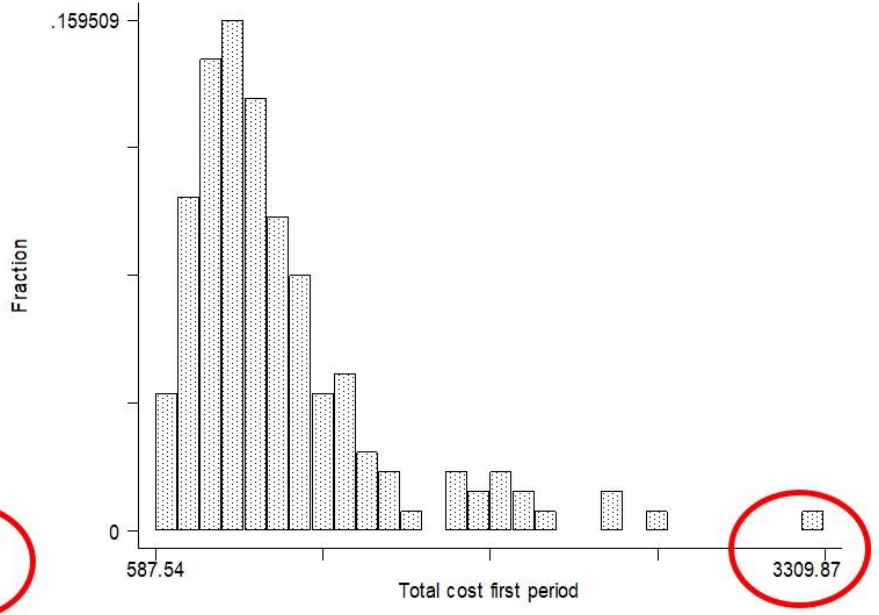
Source: Sculpher MJ, Manca A, *et al.* (2004)

Analysis of cost data

EVALUATE trial

	Abdominal	Laparoscopic
Cost (6 weeks)		
mean (SD)	1,286 (611)	1,561 (1,107)
median	1,167	1,290
range	(662 – 7,286)	(587 – 3,309)

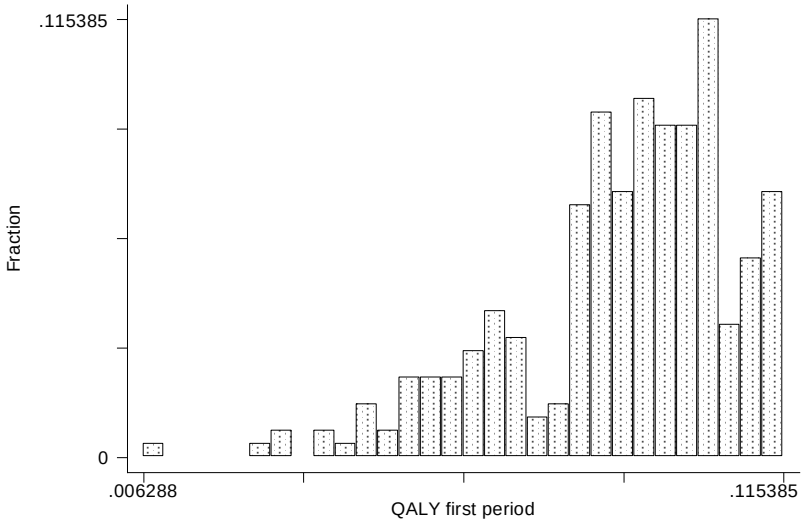


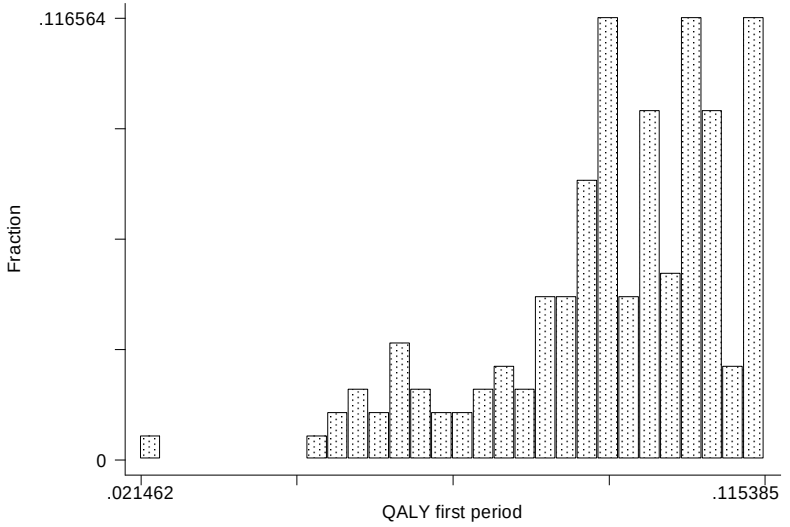


Analysis of effectiveness data

EVALUATE trial

	Abdominal	Laparoscopic
QALYs (6 weeks)		
mean (SD)	0.088 (0.019)	0.090 (0.020)
median	0.09	0.09
range	(0.006 - 0.115)	(0.02 - 0.115)





Quantities of interest

- The analysis of IPD is inherently stochastic; we need to estimate
  - Difference in mean costs: $\overline{\Delta C}$ = ($\overline{C_i}$ - $\overline{C_c}$)
  - Difference in mean QALYs: $\overline{\Delta E}$ = ($\overline{E_i}$ - $\overline{E_c}$)
  - Standard error of the mean costs: $\mathrm{SE}(\overline{\Delta C})$
  - Standard error of the mean costs: $\mathrm{SE}(\overline{\Delta E})$
  - Correlation coefficient between $\overline{\Delta C}$ and $\overline{\Delta E}$

- From which we can derive
  - Mean ICER, mean net benefits
  - 95% confidence intervals for these above quantities

Sampling uncertainty around the ICER

- The ICER is a random variable, just like costs and effects
- Its distribution is unknown, as it is the result of a non-linear combination non-Normal random variables.
- How do we estimate confidence intervals around the ICER?
- Several methods have been proposed

Summary

- Individual patient level data from RCTs can also include costs, quality of life and other outcomes relevant to economic evaluation for HTA

- These data can be analysed using statistical methods that take into consideration the features of these data, to quantify the key parameters that inform HTA decisions

- These parameters are derived from a sample and it is important to quantify both their mean value and sample uncertainty values