Online Advanced Methods for Cost-Effectiveness Analysis

Presentation 3: Populating models - effectiveness
3.10: Reflecting heterogeneity in decision models

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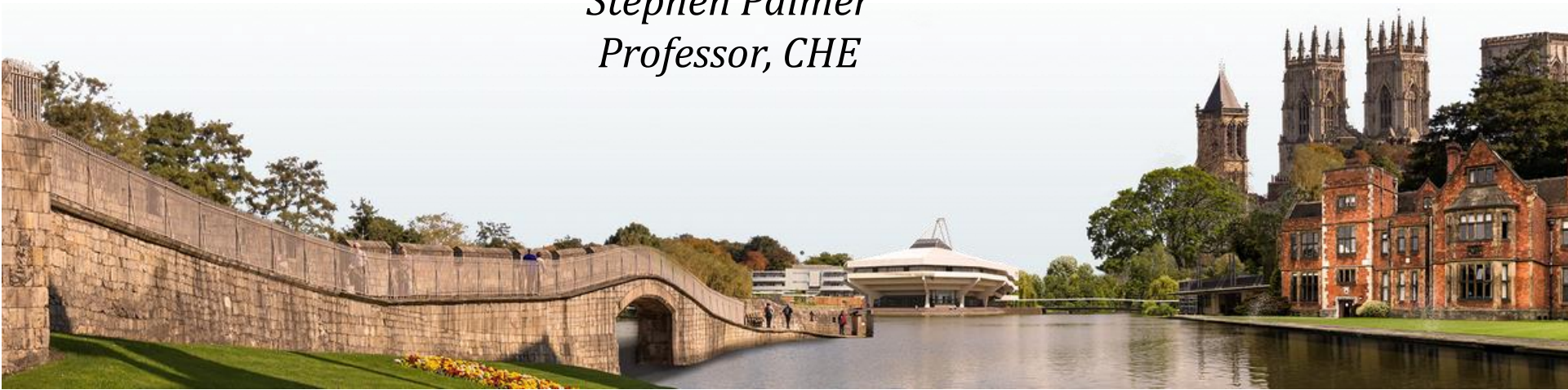

Objectives

- Understand the importance of heterogeneity for policy decisions
- Identify different sources of heterogeneity for cost-effectiveness analysis
- Understand the importance of subgroup analysis and principles for cost-effectiveness analysis

Importance of heterogeneity: Policy context

- Growing demands to maximise value from limited health care budgets
- Political pressure to find a middle ground between refusal to reimburse and reimbursement as per license
- Restricted use: give to the sub-groups in which therapy cost-effective
- Traditional caution of trialists and EBM towards sub-group analysis

Subgroups and relative effectiveness

- Commonly used to explore difference in treatment effects between subgroups
  - “subgroup effect”, “effect modification”, or “interaction between a subgroup variable and treatment”
- Range of principles proposed for analysing and interpreting subgroup effects in clinical literature
  - Emphasis on relative effects
  - Use of baseline rather than post-randomisation characteristics
  - A priori specification (including direction)
  - Relatively few
  - Statistical significance
  - Biological rationale

Heterogeneity in cost-effectiveness analysis

- Individual patients vary in terms of different disease-related parameters
  - Underling risk of events (“baseline risk”)
  - Cost of an event
  - Utility of an event
- Individual patients vary in terms of treatment-related parameters
  - Relative risk for response to treatment (“treatment effects”)
  - Experience of adverse events
- Some of this variability can be explained by patient characteristics known at treatment initiation.
  - Age
  - Gender
  - Clinical characteristics

Importance of subgroups in cost-effectiveness

Heterogeneity in baseline risks and treatment effects

Example from RITA-3 economic analysis

	First quartile*	Second quartile*	Third quartile*	Fourth lower quartile*	Fourth upper quartile*
Age	45	52	52	61	66
Diabetes	0	0	0	0	1
Previous myocardial infarction	0	0	1	1	1
Smoker	0	1	0	1	0
Pulse	8	10	10	11	13
ST depression	0	0	1	1	1
Angina	1	0	1	0	0
Male	0	1	1	1	1
Left bundle branch block	0	0	0	0	0
ICER (no interaction)	49,754	22,145	20,765	11,682	12,490
ICER (interaction)	783,283	42,877	27,626	11,702	10,190

Henriksson *et al (2008)*. The cost-effectiveness of an early interventional strategy in non-ST-elevation acute coronary syndrome based on the RITA 3 trial. *Heart*; 94:717-23.

Ignoring heterogeneity - implications for population health

Subgroup (% patients)	QALYs	Costs	QALYs displaced (λ=£20,000/ QALY)	NHB in QALYs (λ=£20,000/ QALY)
Subgroup A (50%)	0.60	£10,000	⇨ 0.5	0.10
Subgroup B (50%)	0.30	£10,000	⇨ 0.5	-0.20
Average patient	0.45	£10,000	⇨ 0.5	-0.05

- Reimbursement as per license results in a <u>negative</u> population health gain per treated patient
- Restricting reimbursement to Subgroup A results in 0.10 QALY population health gain per treated patient
- Restricted decisions can improve population health

Principles of subgroup analyses for cost-effectivenes

- Relevant subgroups identified in terms of contribution to absolute treatment effect (baseline and relative effect)
- Pre-specification prior to data analysis based on clinical and economic plausibility
- Appropriate quantification of uncertainty rather than statistical significance
- Magnitude of population health gains (losses)
- Implementation issues in routine practice
  - Feasibility, costs, constraints

Summary

- Heterogeneity is an important issue for reimbursement and policy
- Heterogeneity manifests in different disease and treatment related parameters
- Important to establish principles of subgroups for cost-effectiveness
- Ignoring heterogeneity has implications for population health