Online Advanced Methods for Cost-Effectiveness Analysis

Presentation 2: Planning and Conceptualising an Economic Evaluation
2.4: Conceptualisation

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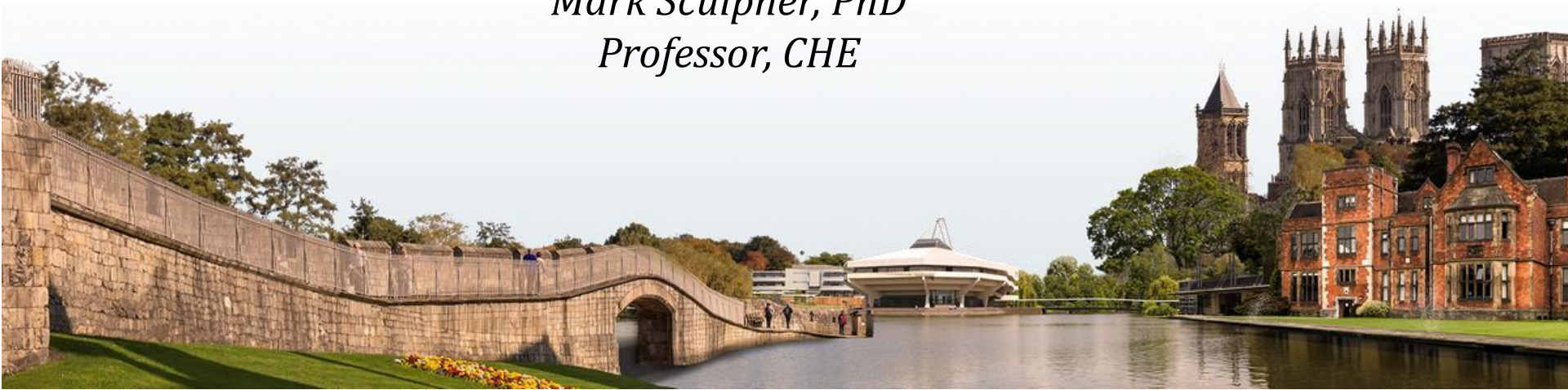


Objectives

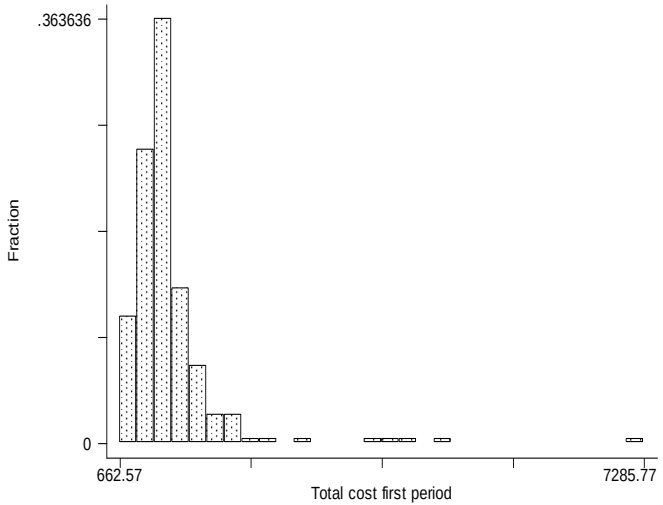
- Understand models and trials as vehicles for analysis
- Appreciate the importance of models
- Consider key concepts in conceptualisation
- Gain insights on conceptualisation with a case study

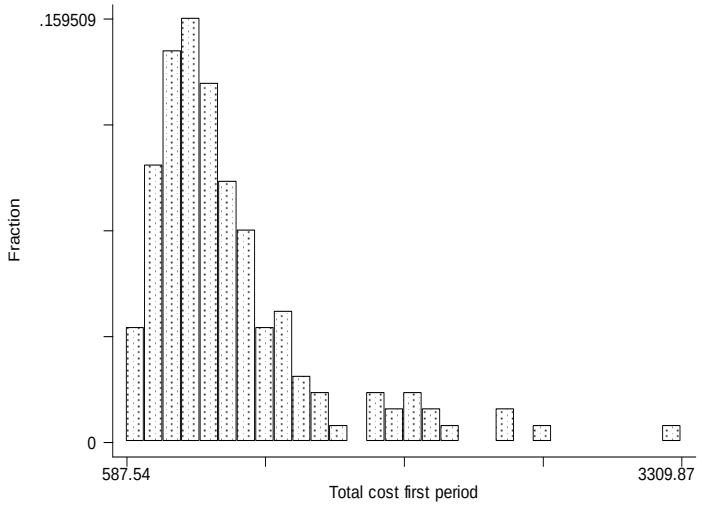
Vehicles for economic evaluation

- Trial-based
- Model-based

Trial-based economic evaluation: EVALUATE trial - costs

	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)





Sculpher *et al. BMJ* 2004; 328: 134.

Trial-based economic evaluation: EVALUATE Trial - QALYs

	Lap-assisted		Standard
Mean weights			
baseline	0.746		0.758
6 weeks	0.875		0.852
4 months	0.911		0.918
12 months	0.920		0.917
Mean QALYs over 1 year	0.899		0.897
Difference in QALYs*		0.0015	
(95% confidence interval)		(-0.015,0.018)	

* (Lap - standard)

Sculpher *et al. BMJ* 2004; 328: 134.

Trials, decisions and decision analysis

Needs of decisions	Decision modelling	Focus of clinical trials
Absolute change in net health benefit	Surrogacy	Relative effects in clinical outcomes
Consider full range of options	Synthesis	Subset of options (focus on the new)
Over relevant time-horizon	Extrapolation	Time until a clinically-relevant effect
Sub-groups with net health benefit	Heterogeneity	Positive average effect

Trials versus models

- To support decisions, models are generally necessary
- Trials remain key source of evidence for models
- Trial-based studies may be suitable:
  - Time horizon and follow-up the same
  - All options included
  - Trial and decision population the same
- Some jurisdictions support RCT-based studies
- Methods RCT-based analysis

What is conceptualization?

- Sometimes called ‘model conceptualization’ or developing a ‘conceptual model’
- Precedes decisions about type or structure of model (e.g. Markov, decision tree)
- How do we understand the impact of a disease on patients’ health and costs?
  - Over time
  - Using no intervention or standard of care (‘natural history’)
  - How does this vary between patients?
- How do we understand the effects of different options on that disease
  - Over time
  - Based on partial evidence
  - How does this vary between patients?
  - Intended and unintended effects

Common issues with conceptualization

Characterizing disease - events

- Distinct and rapid changes in clinical status
- Examples: stroke, exacerbations, death
- Can impact current health (QoL)
- Can impact costs
- Can impact future health (prognostic)
- Event likelihoods expressed as rates (which determine probabilities)
- Interventions can change event rates (treatment, prevention)

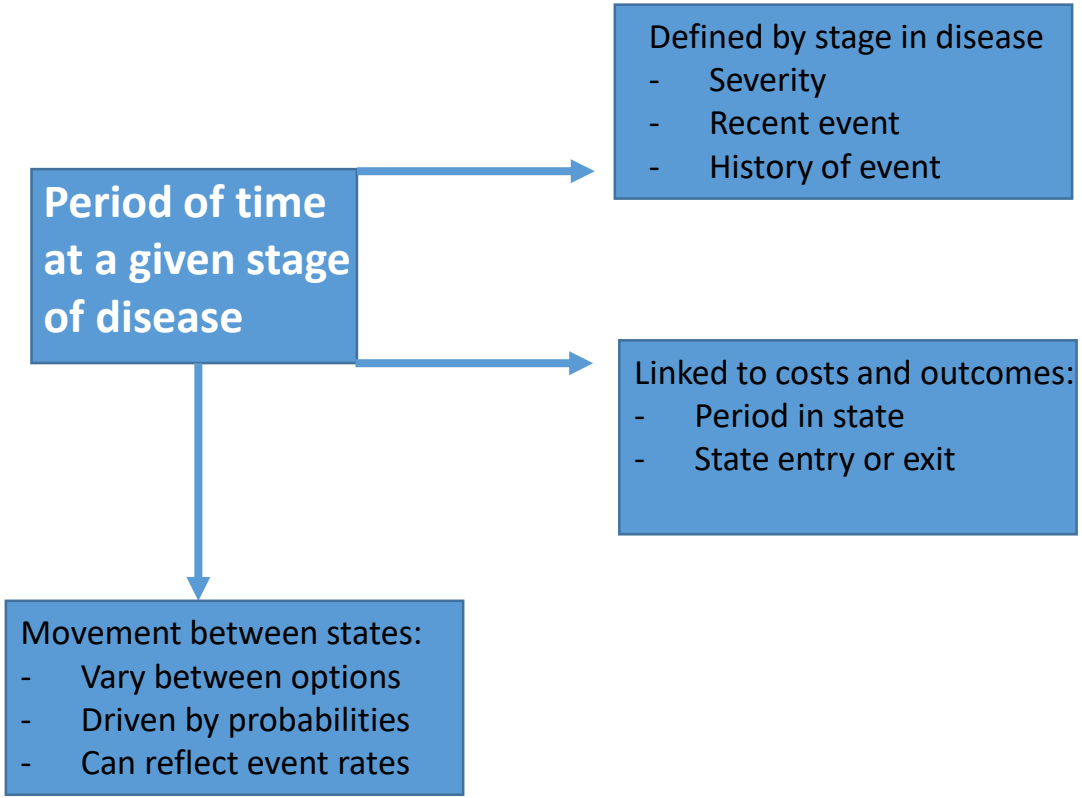
Common issues with conceptualization

Characterizing disease – continuous measures

- Clinical status reflected on a scale
- Examples:
  - Expanded Disability Status Scale (EDSS) in multiple sclerosis
  - Psoriasis Area and Severity Index (PASI)
- Change in measure can affect costs, health and prognosis
- Interventions can change level measure

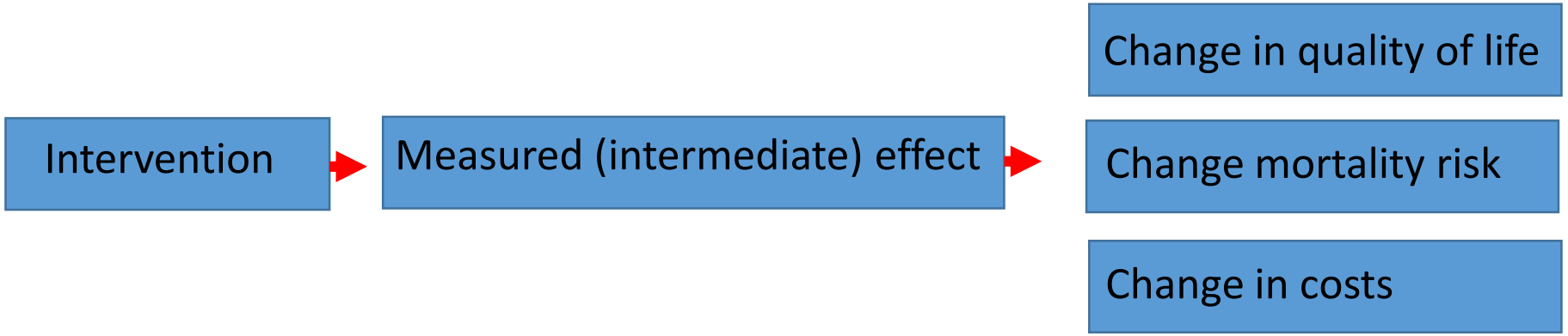
Common issues with conceptualization

Characterizing disease - disease states



Common issues with conceptualization

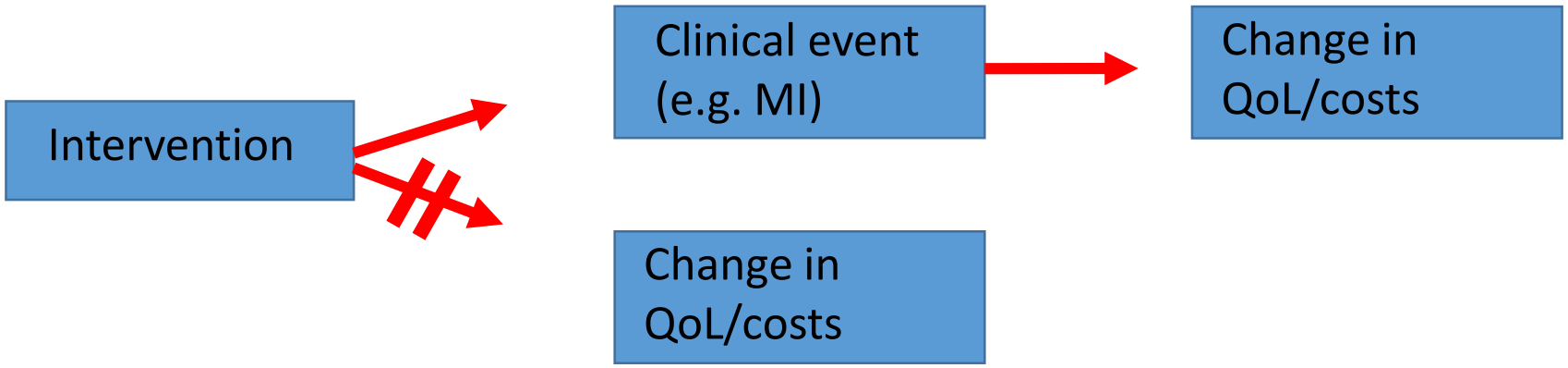
Intermediate effects



- Surrogate = a good intermediate effect
- Examples:
  - FEV1 in asthma
  - Cancer recurrence

Common issues with conceptualization

Conditional independence



Conceptualisation– case study

Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study

*Karl Swedberg, Michel Komajda, Michael Böhm, Jeffrey S Borer, Ian Ford, Ariane Dubost-Brama, Guy Lerebours, Luigi Tavazzi, on behalf of the SHIFT Investigators**

Summary

Background Chronic heart failure is associated with high mortality and morbidity. Raised resting heart rate is a risk factor for adverse outcomes. We aimed to assess the effect of heart-rate reduction by the selective sinus-node inhibitor ivabradine on outcomes in heart failure.

Methods Patients were eligible for participation in this randomised, double-blind, placebo-controlled, parallel-group study if they had symptomatic heart failure and a left-ventricular ejection fraction of 35% or lower, were in sinus rhythm with heart rate 70 beats per min or higher, had been admitted to hospital for heart failure within the previous year, and were on stable background treatment including a β blocker if tolerated. Patients were randomly assigned by computer-generated allocation schedule to ivabradine titrated to a maximum of 7·5 mg twice daily or matching placebo. Patients and investigators were masked to treatment allocation. The primary endpoint was the composite of cardiovascular death or hospital admission for worsening heart failure. Analysis was by intention to treat. This trial is registered, number ISRCTN70429960.

Findings 6558 patients were randomly assigned to treatment groups (3268 ivabradine, 3290 placebo). Data were available for analysis for 3241 patients in the ivabradine group and 3264 patients allocated placebo. Median follow-up was 22·9 (IQR 18–28) months. 793 (24%) patients in the ivabradine group and 937 (29%) of those taking placebo had a primary endpoint event (HR 0·82, 95% CI 0·75–0·90, p<0·0001). The effects were driven mainly by hospital admissions for worsening heart failure (672 [21%] placebo *vs* 514 [16%] ivabradine; HR 0·74, 0·66–0·83; p<0·0001) and deaths due to heart failure (151 [5%] *vs* 113 [3%]; HR 0·74, 0·58–0·94, p=0·014). Fewer serious adverse events occurred in the ivabradine group (3388 events) than in the placebo group (3847; p=0·025). 150 (5%) of ivabradine patients had symptomatic bradycardia compared with 32 (1%) of the placebo group (p<0·0001). Visual side-effects (phosphenes) were reported by 89 (3%) of patients on ivabradine and 17 (1%) on placebo (p<0·0001).

Interpretation Our results support the importance of heart-rate reduction with ivabradine for improvement of clinical outcomes in heart failure and confirm the important role of heart rate in the pathophysiology of this disorder.

Funding Servier, France.

Published Online August 29, 2010 DOI:10.1016/S0140-6736(10)61198-1

See Online/Article DOI:10.1016/S0140-6736(10)61259-7

See Online/Comment DOI:10.1016/S0140-6736(10)61314-1

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Ivabradine – key conceptual considerations

Intervention for chronic disease	→	Duration of treatment effect Long-term time horizon
Cardiovascular	→	Possible heterogeneity in baseline risk
Outcomes trial measuring events	→	Unlikely need for surrogates Event driven costs and QoL effects
New therapy on top of ‘standard practice’	→	Limited scope for other comparators
Potential mortality effect	→	Long-term extrapolation
Composite endpoint	→	Likely need to separate out effects

Summary

- RCTs (or other primary studies) can be appropriate vehicles for economic evaluation
- But decision models are more often appropriate to reflect the needs of decision making
- Conceptualisation is a key stage before selecting model type or structure
- Relates to how disease is characterized; key role for:
  - Events, scales and states
  - Considering changes over time