Online Advanced Methods for Cost-Effectiveness Analysis

Presentation 2: Planning and Conceptualising an Economic Evaluation
2.2: Planning an analysis

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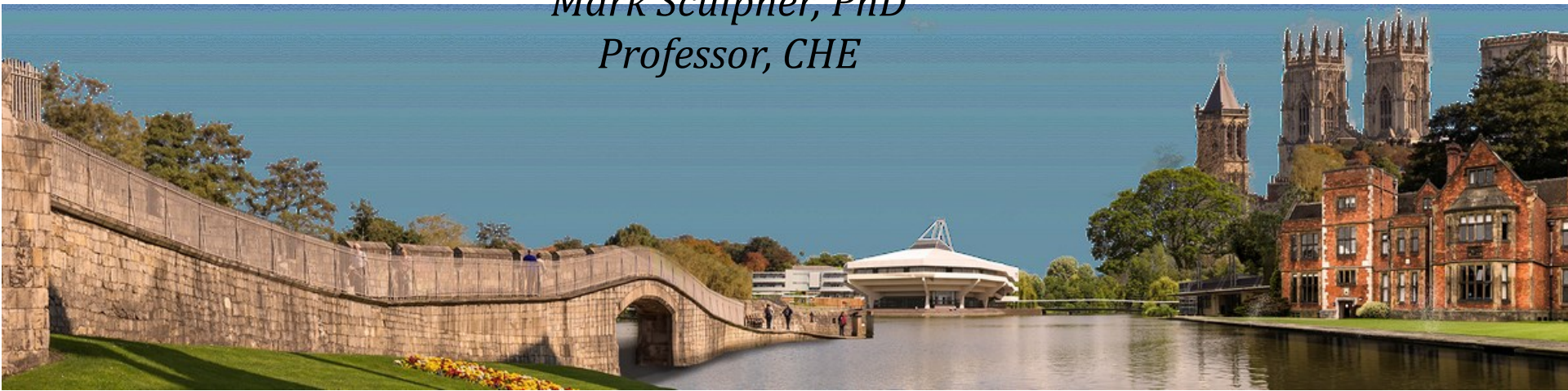


Objectives

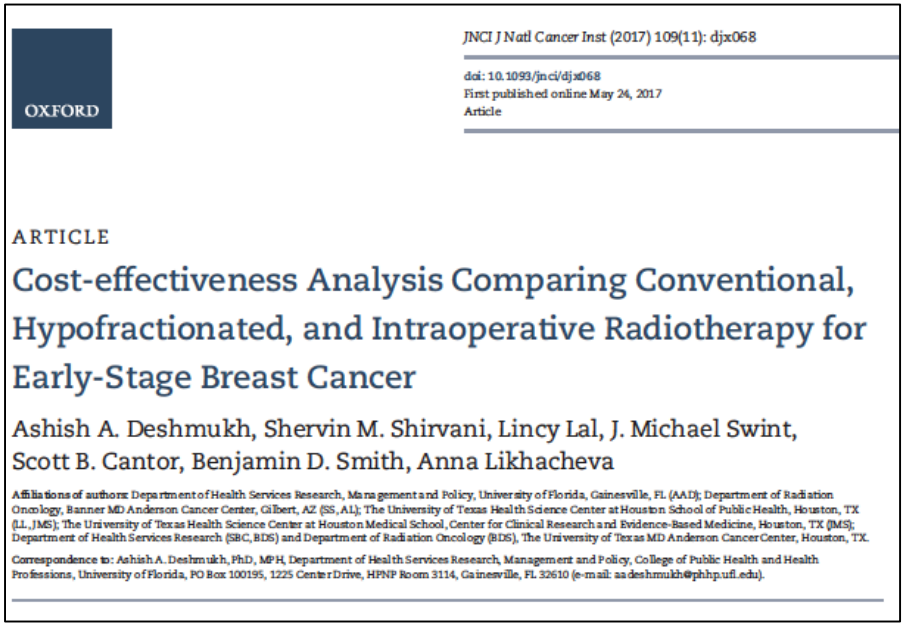
- Understand the key elements of a decision problem
- Appreciate the principles associated with selecting a study population
- Understand the challenges of defining sub-populations/sub-groups
- Determine the ways of identifying relevant options for comparison

Defining the decision problem

- Population and sub-populations
- The intervention of interest
- Comparators

} Options under comparison

Defining the relevant population



OXFORD

JNCI J Natl Cancer Inst (2017) 109(11): djx068

doi: 10.1093/jnci/djx068
First published online May 24, 2017
Article

ARTICLE

Cost-effectiveness Analysis Comparing Conventional, Hypofractionated, and Intraoperative Radiotherapy for Early-Stage Breast Cancer

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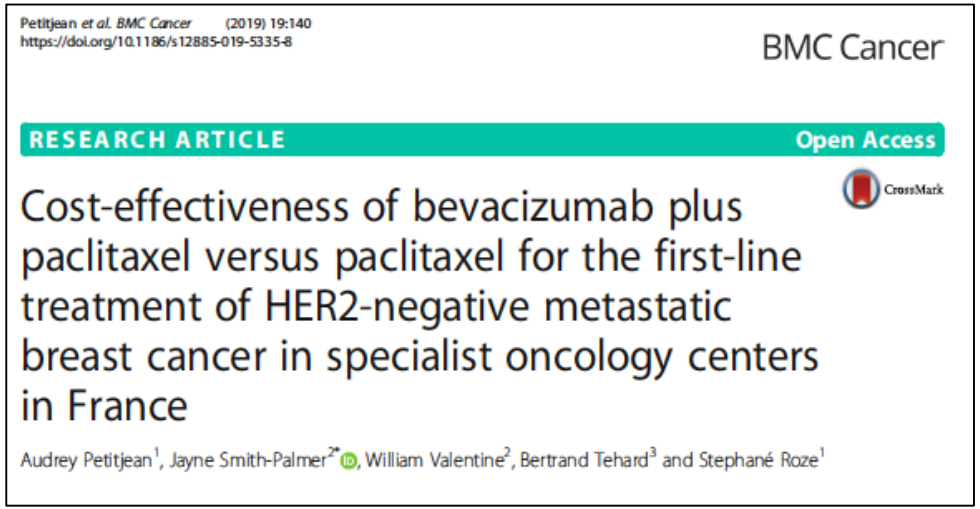

Petitjean et al. BMC Cancer (2019) 19:140
https://doi.org/10.1186/s12885-019-5335-8

BMC Cancer

RESEARCH ARTICLE Open Access

Cost-effectiveness of bevacizumab plus paclitaxel versus paclitaxel for the first-line treatment of HER2-negative metastatic breast cancer in specialist oncology centers in France

Audrey Petitjean[1], Jayne Smith-Palmer[2*], William Valentine[2], Bertrand Tehard[3] and Stephané Roze[1]

Defining the relevant sub-populations (sub-groups) (1)

EUROPEAN JOURNAL OF CANCER 47 (2011) 2517–2530

available at www.sciencedirect.com

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journal homepage: www.ejconline.com

The cost-effectiveness of adjuvant chemotherapy for early breast cancer: A comparison of no chemotherapy and first, second, and third generation regimens for patients with differing prognoses ☆

H.E. Campbell [a,*], D. Epstein [b], D. Bloomfield [c], S. Griffin [b], A. Manca [b], J. Yarnold [d], J. Bliss [e], L. Johnson [e], H. Earl [f], C. Poole [g], L. Hiller [h], J. Dunn [h], P. Hopwood [e], P. Barrett-Lee [i], P. Ellis [j], D. Cameron [k], A.L. Harris [l], A.M. Gray [a], M.J. Sculpher [b]

Defining the relevant sub-populations (sub-groups) (2)

	ICER (Probability that strategy is cost-effective at £20,000 per QALY[a])			
	No chemotherapy	CMF chemotherapy	E-CMF/FEC60 chemotherapy	FEC-D chemotherapy
Reference-case results				
Average risk woman aged 40 years and ER negative[b]	–(0)	Dom (0)	£603 (0.28)	£13,704 (0.72)
Sub-group analyses				
Average risk altering age and ER status				
Average risk woman aged 60 years and ER negative[b]	–(0)	Dom (0)	£4,172 (0.46)	£18,550 (0.54)
Average risk woman aged 40 years and ER positive[b]	–(0)	Dom (0)	£1,730 (0.66)	£24,107 (0.34)
Average risk woman aged 60 years and ER positive[b]	–(0.23)	Dom (0)	£14,324 (0.74)	£45,918 (0.03)
High risk altering age				
High risk woman aged 40 years and ER negative[c]	–(0)	Dom (0)	£249 (0.12)	£8,770 (0.88)
High risk woman aged 60 years and ER negative[c]	–(0)	Dom (0)	£2,317 (0.21)	£11,195 (0.79)
Low risk altering age				
Low risk woman aged 40 years and ER positive[d]	–(0.01)	Dom (0.02)	£7,151 (0.97)	£70,116 (0)
Low risk woman aged 60 years and ER positive[d]	(1)	Dom (0)	Dom (0)	£539,470 (0)

Campbell *et al, European Journal of Cancer*, 2011; 47: 2517-30

Selecting populations

- Select based on the nature of the decision
- “What is the best way of treating patients with disease X?”
  - Relevant to many guideline decisions
- “Is intervention Y worth funding?”
  - Many ‘HTA’/reimbursement decisions
  - How is the population defined?
- Relevant populations defined by product licences
  - Drives many decisions
  - Focus may be a sub-group
- How is an intervention used/expected to be used in practice?
  - Some drug licenses very broad (e.g. antibiotics)
  - Some technologies can be used in many different ways (e.g. diagnostics)
- Some interventions relate to broad and heterogenous populations
  - Public health
  - Health system changes

Population driven by the product licences

Rheumatology 2007;46:1729–1735 doi:10.1093/rheumatology/kem221

The cost-effectiveness of etanercept and infliximab for the treatment of patients with psoriatic arthritis

Y. Bravo Vergel, N. S. Hawkins, K. Claxton, C. Asseburg, S. Palmer, N. Woolacott[1], I. N. Bruce[2] and M. J. Sculpher

Objective. Tumour necrosis factor (TNF) antagonists have been shown to improve the outcomes in patients with rheumatoid arthritis (RA) and psoriatic arthritis (PsA). We assess the cost-effectiveness of two TNF antagonists and so-called 'palliative care' for the treatment of active PsA from the perspective of the UK National Health Service (NHS).

Methods. Bayesian statistical methods were used to synthesize evidence from three Phase III trials, identified through a systematic review, and estimate the relative efficacy of etanercept, infliximab and palliative care. A probabilistic decision analytic model was then used to compare these treatments after the failure of at least two conventional disease-modifying anti-rheumatic drugs (DMARDs), following the British Society for Rheumatology (BSR) guidelines for use. The primary outcome measure, quality-adjusted life years (QALYs), was derived from utility values estimated as a function of disability measured by the Health Assessment Questionnaire (HAQ). The deterioration experienced in HAQ at treatment withdrawal (rebound) was incorporated using alternative scenarios to represent best- and worst-case assumptions. The model was extended beyond the trial duration to a 10-yr and lifetime horizon, using available evidence and expert opinion-based assumptions on disease progression. Resource utilization was based on literature, national databases and expert opinion. Prices were obtained from routine NHS sources and published literature.

Results. At a 10-yr time horizon, the incremental cost-effectiveness ratio (ICER) for etanercept compared with palliative care was £26 361 per QALY gained for the best-case rebound scenario, which increased to £30 628 for the worst-case. The ICERs for infliximab compared with etanercept were £165 363 and £205 345 per QALY, respectively. These findings are mainly explained by the fact that infliximab has higher acquisition and administration costs without substantially superior effectiveness compared with etanercept. Results were sensitive to estimates of rebound assumptions at withdrawal and the time horizon.

Conclusions. Only results for etanercept remained within the range of cost-effectiveness estimates considered to represent value for money in the NHS by the National Institute for Health and Clinical Excellence. Further research appears most valuable in relation to the short-term effectiveness, utility parameters and assumptions regarding the effect of rebound.

Key words: Cost-effectiveness, Etanercept, Infliximab, Psoriatic arthritis, Bayesian evidence synthesis

Selecting sub-populations (sub-groups)

- Rationale: cost-effectiveness can vary by different types of patient
- Includes (but broader than) clinical sub-group analysis
- Ideally identified in advance of analysis (pre-specified)
- Post-hoc analyses cannot be ruled out to inform decisions

The ‘intervention’

Intervention(s)	Donepezil and galantamine
Population(s)	People with vascular (multi-infarct) dementia, dementia with Lewy bodies, including Parkinson’s dementia, or any other non-Alzheimer dementia for which there is robust clinical evidence of efficacy. People with mixed dementia whose predominant dementia is considered to be non-AD.
Current standard treatments (comparators)	• Pharmacological (e.g. aspirin or a hypertensive drug) • Management without donepezil or galantamine
Other considerations	Outcomes include: • Health-related quality of life of patients and carers (analyses should be carried out separately for patients alone, and for patients and carers combined) • Ability to remain independent • Likelihood of admission to residential/nursing care • Survival • Long-term management of patients with

National Institute for Clinical Excellence
Invitation to participate in the appraisal of
new pharmaceutical treatments for non-Alzheimer dementias
Issue date: January 2004

Page 2 of 3

- Defined by a reimbursement process
- Defined by research funder
- Defined by researcher

Selecting comparators (options)
The principles

All other mutually exclusive ways that the population group could be managed

- May include ‘do nothing’
- Could include strategies (e.g. combination of options)
- May add to complexity

Selecting comparators (options) (1)
Planning questions

Planning question	Issues	Guidance
Can we identify options from the available RCTs?	• RCTs may not include all interventions used in practice • RCTs may relate to other jurisdictions	Do not base comparator section on what's been compared in RCTs
What can the literature tell us about option selection?	• Good and recent overviews may be helpful to get a list of possible options	Literature is helpful but cannot be the sole basis of option selection
Can we use clinical/specialist opinion?	• Helpful if this is broad and representative of jurisdiction	Always use suitable expert opinion
What can be learned from licenses, guidelines and funding decisions?	• Licenses only relate to certain interventions and are only a guide • Guidelines may not be current and may not be mandatory? • Are funding decisions mandatory and do they cover all types of interventions?	Official documents and guidelines are a useful source of information

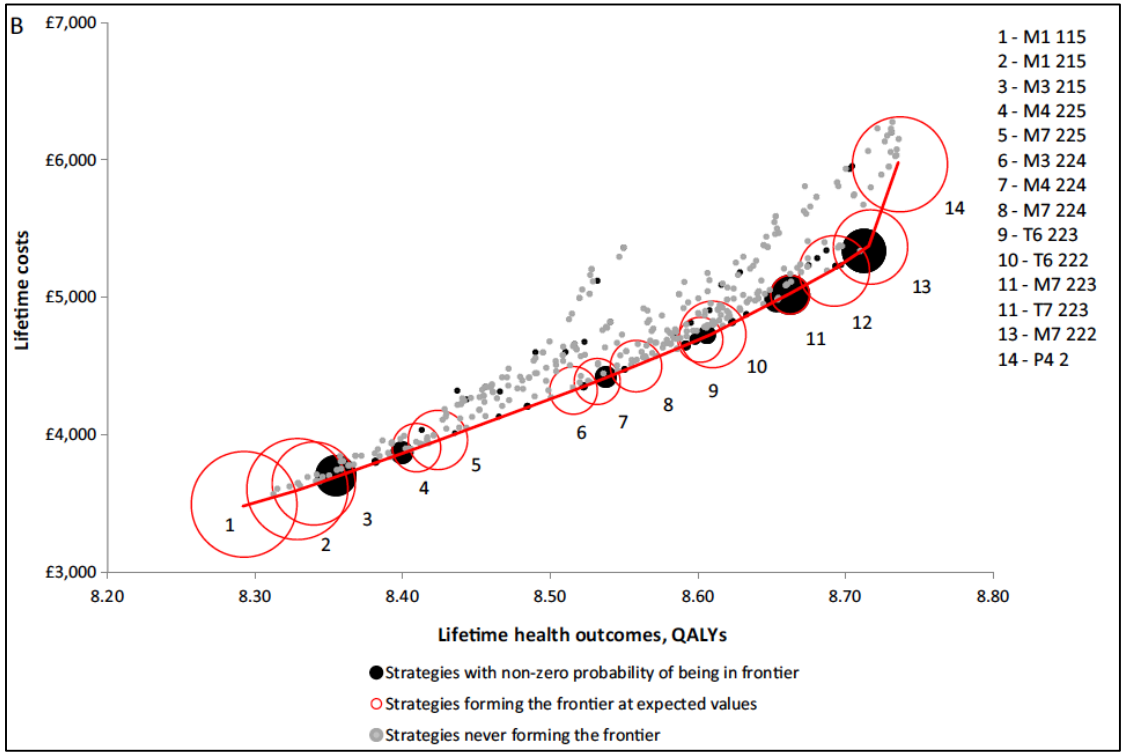
Selecting comparators (options) (2)
Planning questions

Planning question	Issues	Guidance
Is their scope for the analyst to include (as-yet) unused options?	• Different ways of using options may be revealed through analysis • These become additional options • Examples: stopping rules, repeat testing	Always need to consider different management strategies for a given set of 'core' options
How should treatment or test sequences be used?	• Each potential sequence is an option but may get complex	Sequence comparison is fundamental to some evaluations
How should comparisons of numerous options be handled?	• Sometimes options can get into the thousands + • Some may not be feasible • Can simplify by asking clinicians what would be used/are used • Need to beware of missing cost-effective options	Using clinical or other expert opinion to 'rule out' needs to be used cautiously Use flexible modelling and analysis Attempt to identify options with very low chance of being cost-effective

Managing complexity in options
Example of diagnostics and prostate cancer

Test	Strategies
MPMRI	
First test	M1–M7; N1–N7
Second test after TRUSB	T5–T9; P5–P9
TRUSB	
First test	T1–T9; P2–P9
Repeat TRUSB in men with no cancer detected	T2, T4
Repeat TRUSB in men with non-CS cancer detected	T3, T4
Second test after MPMRI: MRI-targeted TRUSB, in men with lesions visible at the MPMRI	M1–M7
Repeat MRI-targeted TRUSB in men with no previous cancer or non-CS cancer at first MRI-targeted TRUSB, but with lesions visible at MRI	M3–M7; T5–T9; N3–N7
TPMB	
First test	P1
Second test	P2–P4; N1–N4
Third test	P5–P9; N3–N7

MPMRI = multiparametric magnetic resonance imaging; TRUSB = transrectal ultrasound-guided biopsy; TPMB = template prostate mapping biopsy; CS = clinically significant. MRI-targeted TRUSB is a TRUSB informed by a prior MPMRI. All TRUSB post-MPMRI are assumed to be MRI-targeted TRUSB. Diagnostic strategies were labelled according to their test combination first (M1–M7, N1–N7, T1–T9, P1–P9), and then their biopsy TRUSB definition (1 or 2), MPMRI definition (1 or 2), and cut-off (2 to 5). T strategies start with TRUSB, M strategies start with MPMRI, P strategies are the same as T strategies, and N strategies are the same as M strategies but have TPMB as the last biopsy. For example, strategy M1 125 refers to test combination M1, in which all men were first assessed using MPMRI definition 2 and cut-off 5 and then followed up with biopsy definition 1 for those with a suspicion of CS cancer. See the Supplementary material, section 1, for full details on the test sequences for each diagnostic strategy.



Faria *et al*. *European Urology*, 2017; 73: 23-30

Summary

- Defining a decision problem focusses on the population, sub-populations and options
- Range of ways to determine the appropriate population
- Sub-populations (sub-group) ideally identified in advance of analysis
- The concept of a primary intervention and comparators is not always relevant: often simply comparing a set of options
- Identifying all relevant options can be challenging and may lead to complexity