Online Advanced Methods for Cost-Effectiveness Analysis

Presentation 3: Populating models - effectiveness
3.9: Incorporating effectiveness evidence in decision models

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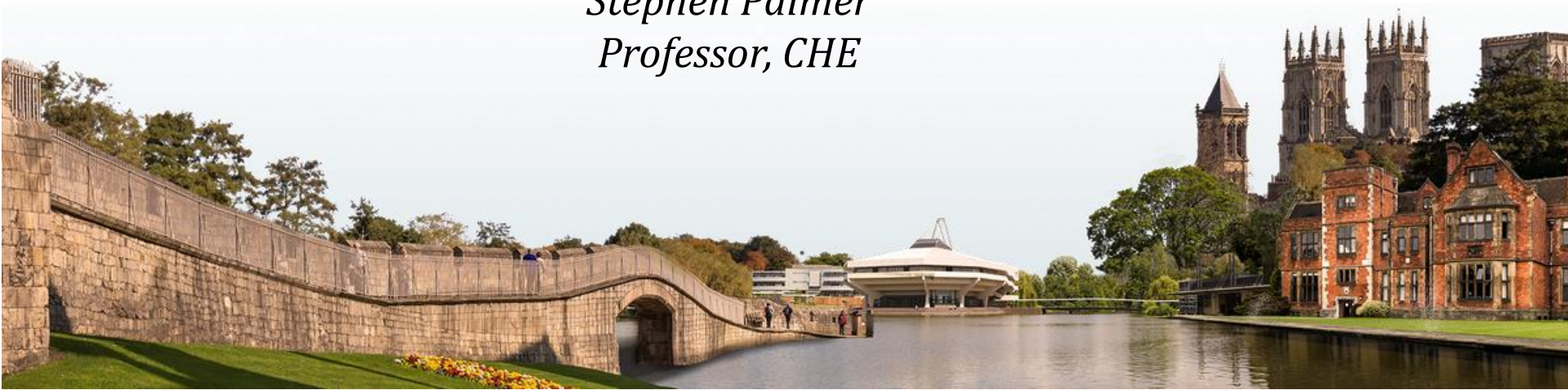


Objectives

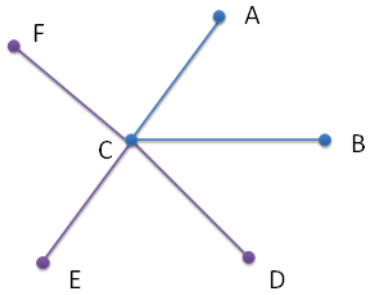
- Understand the general principles of applying (network) meta-analysis in decision models
- Identify appropriate methods to translate relative effects to absolute estimates of outcomes
- Understand how (network) meta-analysis results can be incorporated into different model structures
- Explore the role of synthesis for other types of input parameters

General principles of using (network) meta-analysis within models

- (Network) meta-analysis provides estimates of relative treatment effects compared to a reference treatment
  - e.g. standard of care, placebo, an active treatment
- Relative effect may be on a range of scales
  - e.g. risk difference (RD), relative risk (RR), odds ratio (OR), hazard ratio (HR)
- Models require absolute estimate of outcome
  - e.g. probability of death, probability of response

General principles of using (network) meta-analysis within models

- To translate NMA results from relative to absolute effects require absolute measure of outcome for one comparator
- Consider the following network



- A binary endpoint NMA on relative risk (RR) scale produces:

  RR_{AC}, RR_{BC}, RR_{DC}, RR_{EC}, RR_{FC}

  If p_C is the probability of the event for intervention C

  $p_A = RR_{AC} * p_C$

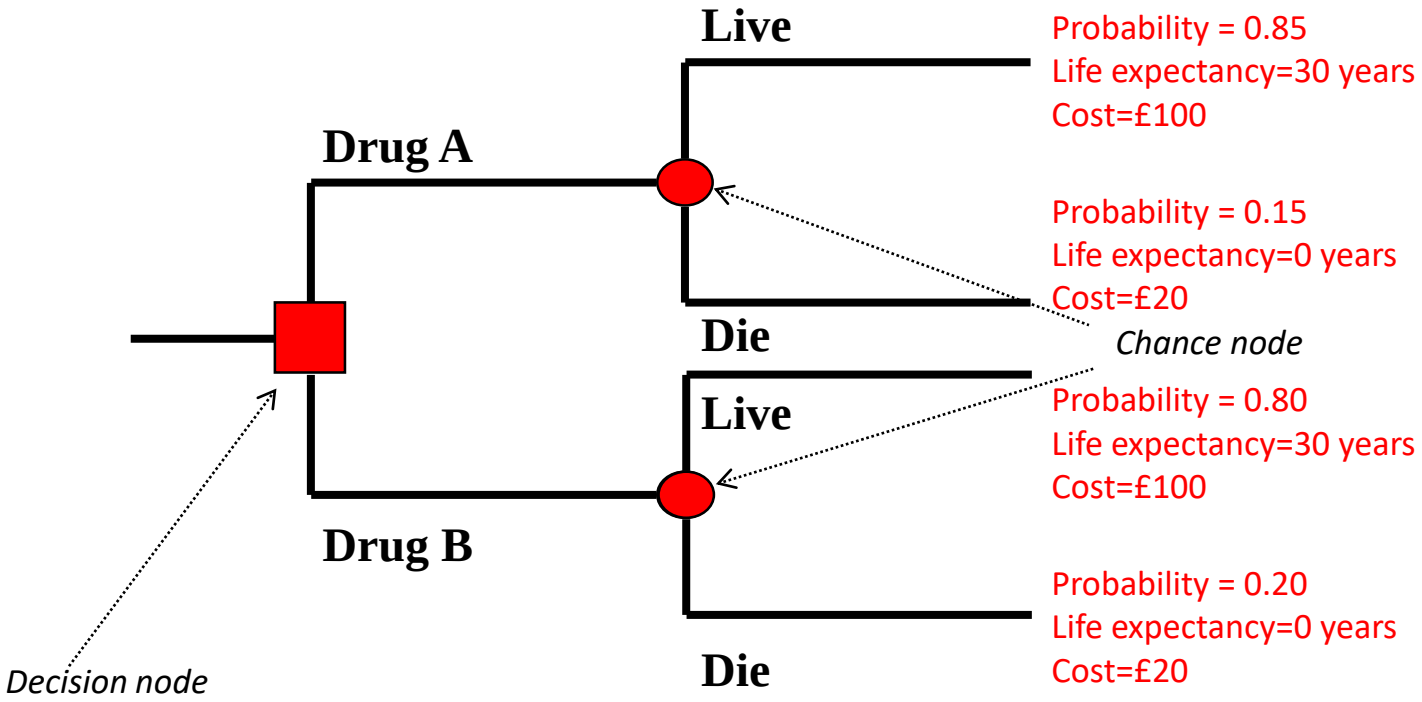
  $p_B = RR_{BC} * p_C$ etc.

Methods for translating from relative effects to absolute scale

Binary endpoint	
Risk difference	$p_A = p_C + d_{AC}$
Relative risk	$p_A = p_C \cdot d_{AC}$
Odds ratio	$odds_C = p_C/(1-p_C)$ $odds_A = odds_C \cdot d_{AC}$ $p_A = odds_A / (odds_A + 1)$
Continuous data	$\mu(t)_A = \mu(t)_C + d_{AC}$
Time to event data	$h(t)_A = h(t)_C \cdot d_{AC}$ A set of formulae exist to convert from hazards to survival curves or transition probabilities

Where p represents a probability, $\mu(t)$ the mean outcome at time t, and $h(t)$ the hazard at time t

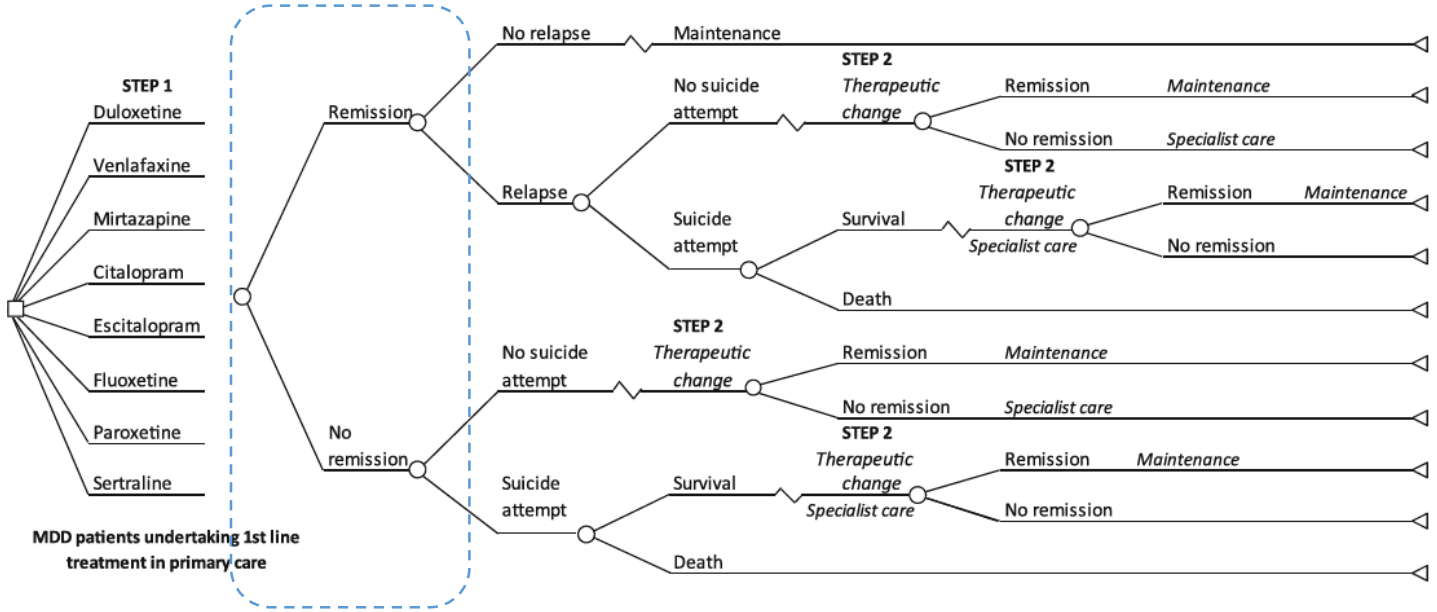
Incorporating NMA results in a decision tree



Life years A =
0.85*30+0.15*0=25.5
Cost A = 0.85*100+0.15*20=£88

Life years B =
0.80*30+0.20*0=24
Cost B = 0.80*100+0.20*20=£84

Example: pharmacological treatment for major depressive disorder



NMA informs probability of remission for each alternative

Annemans et al. Pharmacoeconomics 2014, DOI 10.1007/s40273-014-0138-x

Example: treatment for major depressive disorder

- Network meta-analysis of remission endpoint on odds ratio (OR) scale
  - Produced OR for each treatment vs fluoxetine
- Fluoxetine estimated to have remission probability of 40.21%
- Decision model requires probability of remission for each treatment

Example: treatment for major depressive disorder

- OR for venlafaxine vs. fluoxetine from NMA: 1.25 (95% CI 1.12, 1.39)
- What is the probability of remission for patients receiving venlafaxine?
  1. Odds of remission for fluoxetine = 0.4021/(1-0.4021) = 0.6725
  2. Odds of remission for pts. receiving venlafaxine = 0.6725*1.25 = 0.8407
  3. Probability of remission for pts. receiving venlafaxine = 0.8407/(1+0.8407)=0.4568

Clinical data	Data (%)	References
Remission rate in first therapeutic step		
SNRIs[a]		
Duloxetine	44.99	Wessling and Ramsberg (TLV) [1]
Venlafaxine	45.68	Wessling and Ramsberg (TLV) [1]
Mirtazapine	45.08	Wessling and Ramsberg (TLV) [1]
SSRIs		
Citalopram	40.50	Wessling and Ramsberg (TLV) [1]
Escitalopram	47.56	Wessling and Ramsberg (TLV) [1]
Fluoxetine	40.21	Wessling and Ramsberg (TLV) [1]
Paroxetine	42.70	Wessling and Ramsberg (TLV) [1]
Sertraline	43.02	Wessling and Ramsberg (TLV) [1]

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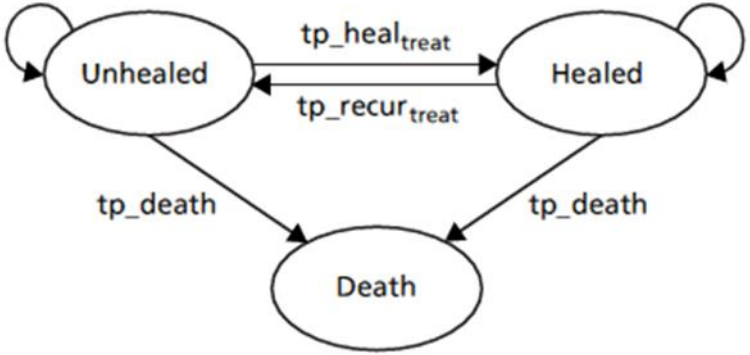
Incorporating NMA results in a Markov model

- Markov structure used to calculate time in each states
- Costs and health outcomes assigned to each state
- Differences in time in each state drive differences across interventions

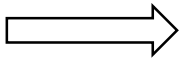


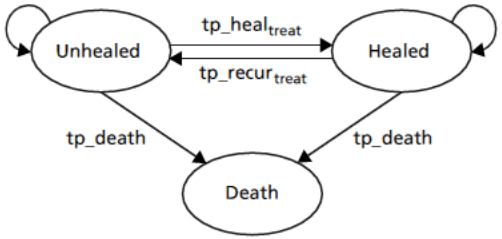
Example: Venus leg ulcers

- VenUS IV clinical trial compared four-layer bandage (4LB) with two-layer hosiery (HH) for management of venous leg ulcers.
- Decision problem included wider set of comparators
    1. Conducted NMA of alternative high-compression treatments
    2. Constructed decision model to assess cost-effectiveness
- Effects of treatment
    - Time to healing – all treatments have different rate (NMA)

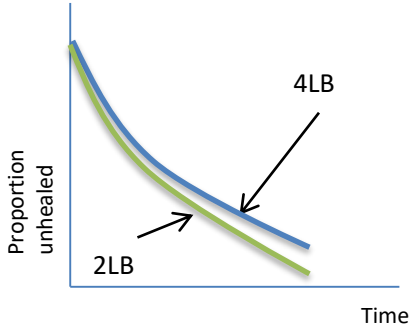
Example: Venous leg ulcers

		Base-case analysis Including VenUS IV (1)	
HRs		HR	95% CrI
Treatment effects (vs. 4LB)	SSB	0.88	0.76 to 1.03
	HH	1.05	0.85 to 1.29
	Paste	0.77	0.41 to 1.42
	2LB	1.40	0.65 to 3.05
	Ba	1.19	0.43 to 3.47
	BHeH	0.93	0.34 to 2.62
	BzeaH	1.33	0.42 to 4.51
	HV	1.00	0.23 to 4.22





- NMA Hazard ratios modify hazard "rate" of healing
  Example: $h_{2LB} = h_{4LB} \cdot HR_{2LBvs.4LB}$
- Essentially "shifts" the survival curve for time to healing
- Computationally achieved by modifying transition probabilities



Synthesis of other parameters

- Focus so far on relative effectiveness
  - Drive incremental differences between interventions
- Multiple source of evidence may also be available for other parameters
  - Natural history or 'baseline' event rate (e.g. remission rate with fluoxetine)
  - Costs/resource use
  - Utilities (health related-quality of life weights)

Reference: Saramago P, Manca A, Sutton AJ. Deriving input parameters for cost-effectiveness modeling: taxonomy of data types and approaches to their statistical synthesis. Value in Health. 2012 Aug 31;15(5):639-49.

Evidence synthesis for the baseline (natural history)

- Synthesis methods - effectively weighted pooling
- Recommend conducted separately from NMA
  - So that NMA unaffected by assumptions in baseline model
- Exploration of heterogeneity may be important
  - May be possible if subgroup data or individual patient data (IPD) available

Reference: Dias S, Welton NJ, Sutton AJ, Ades AE. Evidence synthesis for decision making 5: the baseline natural history model. Medical Decision Making. 2013 Jul;33(5):657-70.

Evidence synthesis of cost and resource use data

- Rarely done
- Require data specific to a jurisdiction
- Potential limitations to synthesis:
  - Methodological heterogeneity e.g. data collection strategies, methods of measurement
  - Temporal changes e.g. prices, technology
  - Differences between health systems

Evidence synthesis of utility data

- Methodological heterogeneity is a major issue
  - Different instruments (descriptive systems, valuation methods/populations)
- Guidance from NICE recommends synthesis only if studies share similar populations and use the same instrument and valuation
- Synthesis methods not well developed, generally weighted pooling

Reference: Papaioannou D, Brazier J, Paisley S. NICE DSU Technical Support Document 9: the identification, review and synthesis of health state utility values from the literature. University of Sheffield. 2011 Oct. Available from: http://www.nicedsu.org.uk/TSD9%20HSUV%20values_FINAL.pdf

Summary

- Relative effects from (network) meta-analysis need to be translated into absolute estimates for decision making
- The specific methods depend on the outcome scale and the model structure
- Decision model provides framework to incorporate results from (network) meta-analysis and translate these into policy relevant outcomes (costs, QALYs)
- Need to consider role and appropriateness of synthesis for other input parameters