Making a good case for cost effectiveness

Professor Dyfrig Hughes
Bangor University

AWTTC
All Wales Therapeutics & Toxicology Centre

CHEME
Centre for Health Economics and Medicines Evaluation

Key elements

- Model population
- Model structure and extrapolation
- Comparator
- Effectiveness
- Utilities
- Resource use
- Costs
- Accounting for uncertainty

Population

- Align with the licensed indication
- Representative of eligible population in Wales
- Uncertainty due to small populations
- How does the modelled population reflect the trial population?
- Are there sub-groups that may be more relevant?

Comparator

- Have all the appropriate comparators been considered?
- Model treatment pathways representative of care in Wales
- Seek (Welsh) clinical opinion

Effectiveness

- Non-inferiority ≠ equivalence
- Conduct indirect treatment comparisons *only* if there are no direct trials of the relevant comparator
  - Informed by a systematic review of the evidence
  - Follow best practice: full details of SR, reasons for inclusion/exclusion, tests for heterogeneity, (in)consistency, etc.

Utilities

- EQ-5D is the preferred measure of HRQL in adults, other methods accepted
  - EQ-5D-5L, CHU9D, disease-specific utilities etc.
- Use primary QoL data from trial where possible
  - Avoid unnecessary mapping
- Consider a separate TTO study if there are no utility data whatsoever
- Check plausibility
  - Utilities (disease state) < population average

Resource use

- “Resource implications should be identified, measured and valued within a Welsh context (i.e. using Welsh data on resource utilisation and unit costs). Submitted economic evaluations that do not include Welsh data are required to include a comment on the validity of using resource data from outside Wales, and make reference to any relevant differences in the healthcare environments. Data from any other UK country, or elsewhere, will not be accepted where Wales-specific data is available.”

Resource use

- Have the relevant resource items been identified?
- Based more on data, less on opinion?
- Relevant to Wales?
  - SAIL Secure Anonymised Information Linkage
  - Opinion from Wales?

Costs

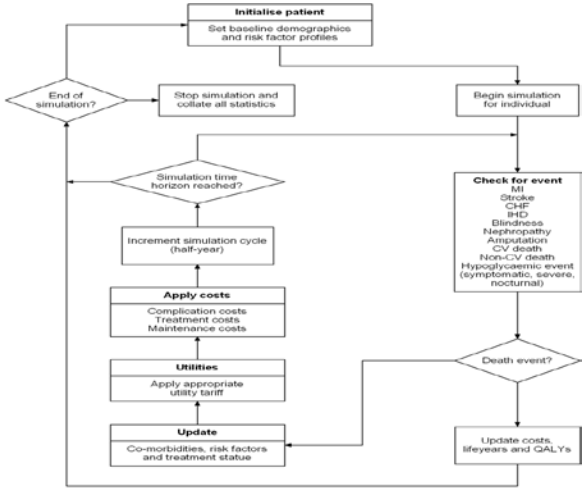
- List price, not discounted (unless part of agreed PAS/WPAS)
- Relevant to Wales where possible
  - Links to data on health and healthcare in Wales
  - http://tinyurl.com/dataNHS

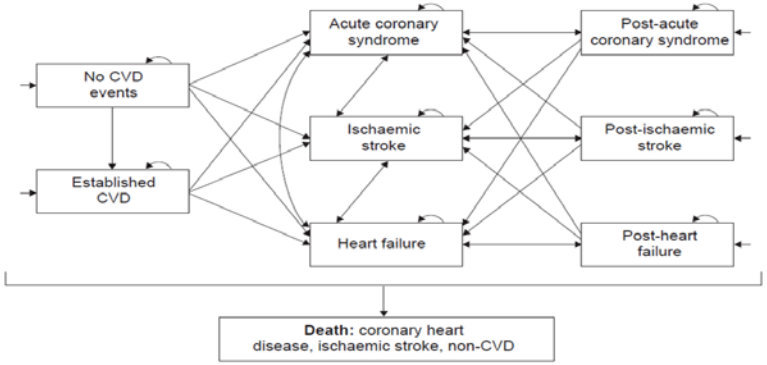
Model structure

- Models for extrapolation of benefit, specification of health states etc should be transparent, validated, subjected to different scenario analyses
- Consider alternative model specifications
  - DES may be more applicable than Markov
  - Is an overly complicated model necessary (reduces transparency)?
- Impact of structural uncertainty on the ICER

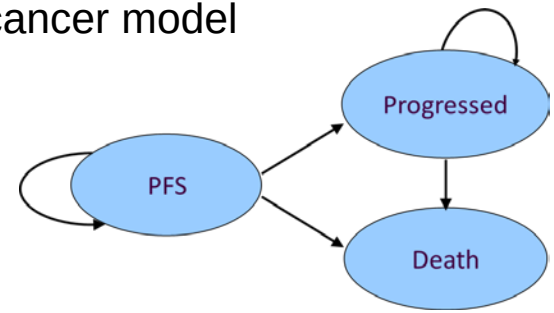
Model structure – designs

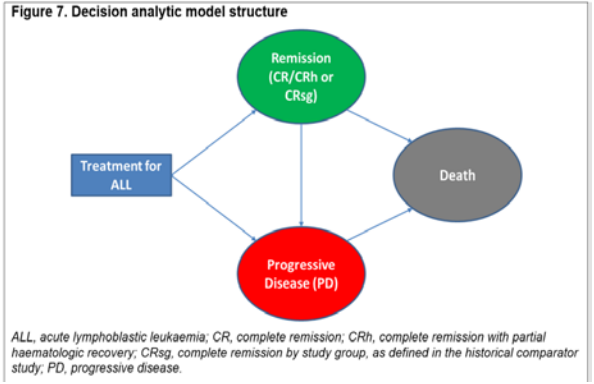
Standard diabetes model





Standard cancer model





Time horizon

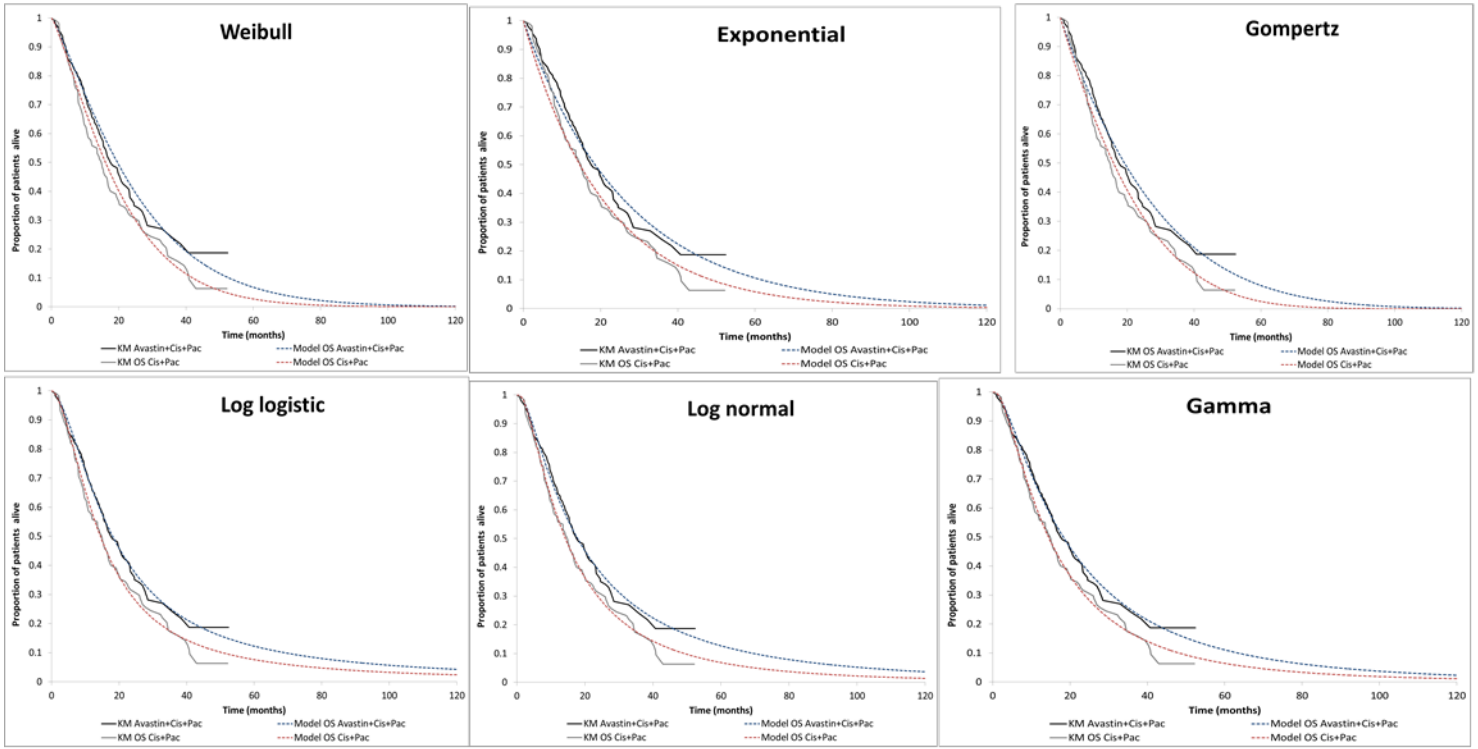
- Long enough to capture full differential effects on health and costs
  - Differential mortality = lifetime horizon
  - Explore alternatives
  - Links to extrapolation of trial data and curve fitting

Extrapolation

- Don’t choose parametric function based on one that makes ICER look lowest!
- Different parametric functions
  - Diagnostics, visual inspection
  - Based on fit to the observed data
- Duration of treatment benefit in extrapolated phase
  - Nil
  - Same as treatment phase and continues at the same level
  - Diminishes in the long term
- Plausibility
  - 12 week trial => lifetime benefit?
  - Expert clinical opinion on plausibility

Visual fits of the data

Parametric functions for OS compared with observations in the clinical study



Goodness of fit statistics

Summary of goodness of fit of parametric functions for OS

Parametric Model (OS)	Drug A		Drug B	
	AIC	BIC	AIC	BIC
Weibull	305.02	310.51	303.60	**309.07**
Exponential	307.07	309.82	308.09	**310.83**
Log Logistic	300.69	306.18	300.71	**306.19**
Log Normal	301.21	306.70	297.77	**303.24**
Gamma	302.79	311.02	299.72	**307.93**
Gompertz	**308.55**	**314.04**	**307.83**	**313.30**

Uncertainty

- “...medicines with presented ICERs less than £20,000 per QALY gained may not be recommended if AWMSG are not persuaded by the **plausibility** of the inputs to the economic modelling and/or the **certainty** around the estimated ICER”
- “Above a most **plausible** ICER of £20,000 per QALY gained, judgements about the acceptability of the medicine as an effective use of NHS resources will specifically take account of ...the degree of **certainty** surrounding the calculation of ICERs...”

Uncertainty

- Structural uncertainty
  - Scenario analyses
  - If in doubt, present the data for each and every scenario & let the committees decide which they consider to be plausible
- Parameter uncertainty
  - Sensitivity analyses on all key parameters
    - Tornado diagrams, multi-way analyses
  - Probabilistic Sensitivity Analysis
    - C/E plane, % in each quadrant, CEACs
    - Probability C/E at thresholds of £20k and £30k per QALY

Top tips (1)

- Use primary QoL data and avoid unnecessary mapping
- Avoid cost minimisation analyses
  - Only applicable when there is evidence of equivalence in all dimensions of health, including impact on health-related quality of life (HRQL), survival, as well as adverse events, patient preference and adherence

Top tips (2)

- Model treatment pathways representative of care in Wales
  - Seek (Welsh) clinical opinion if appropriate
  - Remove reference to Scotland or the SMC!
- Conduct indirect treatment comparisons *only* if there are no direct trials of the relevant comparator
  - Informed by a systematic review of the evidence

Top tips (3)

- If in doubt, present the data for each and every scenario
  - Let the committees decide which they consider to be plausible
- Conduct PSA for each scenario
  - Report Pr (cost effective) at threshold values
  - Report Pr (in each quadrant)

Diolch yn fawr - Thank you

AWTTC
All Wales Therapeutics & Toxicology Centre

www.awttc.org

All Wales Therapeutics and Toxicology Centre
Academic Building
University Hospital Llandough
Penlan Road
Penarth
Vale of Glamorgan
CF64 2XX

PAMS Patient Access to Medicines Service

WNPU Welsh National Poisons Unit

WeMeReC Welsh Medicines Resource Centre

Yellowcard Centre Wales

WAPSU Welsh Analytical Prescribing Support Unit