SEE Sense: Tools for Conducting Structured Expert Elicitation to Support Healthcare Decision Making

Conflicts of interest and disclosures

Prof Laura Bojke:	PI for MR/N028511/1 “HEE: Developing a reference protocol for expert elicitation in health care decision making”; author of Developing a reference protocol for structured expert elicitation in health-care decision-making: a mixed-methods study. HTA, 2021; 25(37). Member of NICE appraisal committee and York NICE assessment group.
Dawn Lee, MMath, MSc:	Employee of Lumanity. No conflicts of interest relevant to the content of this workshop
James Horscroft, PhD:	Employee of Lumanity. No conflicts of interest relevant to the content of this workshop
Dina Jankovic, PhD:	Researcher on MR/N028511/1 “HEE: Developing a reference protocol for expert elicitation in health care decision making” and co-author of Developing a reference protocol for structured expert elicitation in health-care decision-making: a mixed-methods study. HTA, 2021; 25(37).

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ISPOR US 2022, Monday 16 May 2022

SEE Sense: Tools for Conducting Structured Expert Elicitation to Support Healthcare Decision Making

16 May 2022

Dawn Lee, James Horscroft, Dina Jankovic and Laura Bojke

Agenda

Section	Title	Time
1	Introduction to SEE for HCDM – **Prof Laura Bojke, University of York**	10 mins
2	Current resources for SEE for HCDM – **Dawn Lee, MMath, MSc Lumanity**	10 mins
3	Challenges faced in conducting SEE for HCDM – **James Horscroft, PhD, Lumanity**	10 mins
4	Goals of the online repository – **Dina Jankovic, PhD, University of York**	15 mins
5	Q&A	15 mins

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Key: HCDM, healthcare decision making; SEE, structured expert elicitation

Structured expert elicitation in HCDM
Overview of the landscape

Laura Bojke
Centre for Health Economics
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Poll Question 1

- Have you been involved in an SEE exercise before?

  A: Yes

  B: No

Evidence needs for HCDM

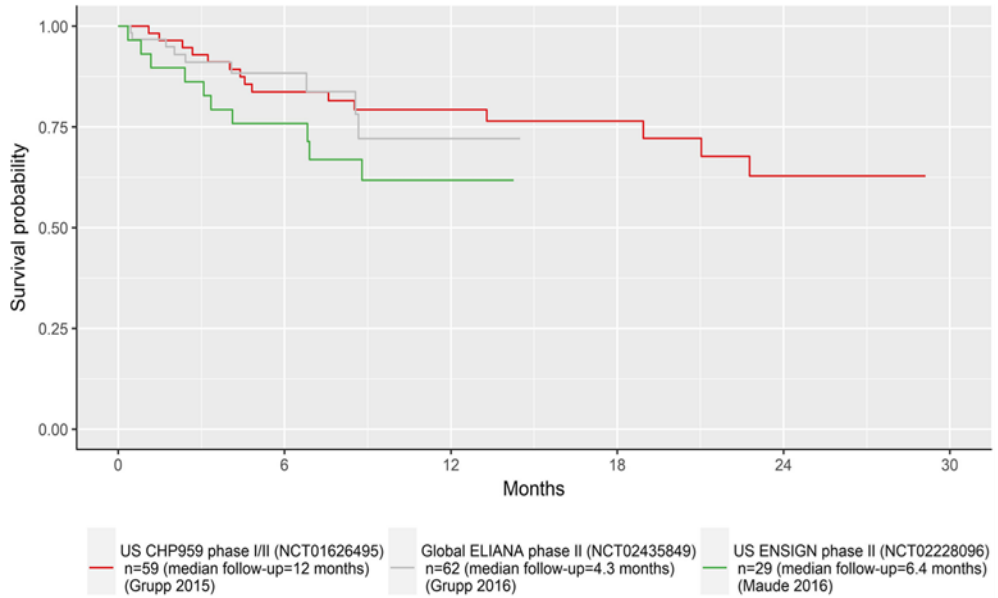
- HCDM and, in particular, Health Technology Assessment (HTA) often requires evidence on the costs and outcomes for competing interventions.
  - Evidence to inform decisions is often uncertain – immature data, under developed evidence base.
  - In some circumstances a decision is not possible with existing evidence.
  - Important to characterise uncertainty in this evidence.
  - Required to make better adoption decisions and inform further data collection.

SEE use in HCDM context.

- Expert judgements used throughout HCDM
- Formal methods (SEE) more often used in HTA, specifically modelling studies
  - Cadham: 40 SEE studies and 112 non-formal (indeterminate) methods
  - Poor reporting on methods
- As part of formal decision making processes
  - Van Hest: Review of 25 company submissions appraised by NICE found that expert judgement is ubiquitously used in company submissions (23/25).
  - 173 expert elicitation informed parameters identified, gathered through five different forms

Example: CAR-T therapy for children/young adults with relapsed/refractory acute lymphoblastic leukaemia

From: Integrating expert opinion with clinical trial data to extrapolate long-term survival: a case study of CAR-T therapy for children and young adults with relapsed or refractory acute lymphoblastic leukemia (Cope, et al, 2019)



- First CAR-T therapy approved by the FDA in this indication.
- Previous assessments of cost-effectiveness showed reimbursement decision was highly sensitive to choice of parametric model.
- Methods adapted from SHELF to obtain survival estimates. Combined with the empirical data to estimate long-term survival curves.

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Example: Health Opportunity costs

- SEE to inform estimates of expected health opportunity costs in the UK NHS.
- Uncertain beliefs on a set of quantities for that are central to an estimate of health opportunity costs for the UK's NHS.
  - Duration of effects
  - Surrogacy
  - Extrapolation
- Elicited beliefs could be used to support other empirical studies.

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Table 2 Summary of the Wuantities Elicited with Diagrammatic Representation

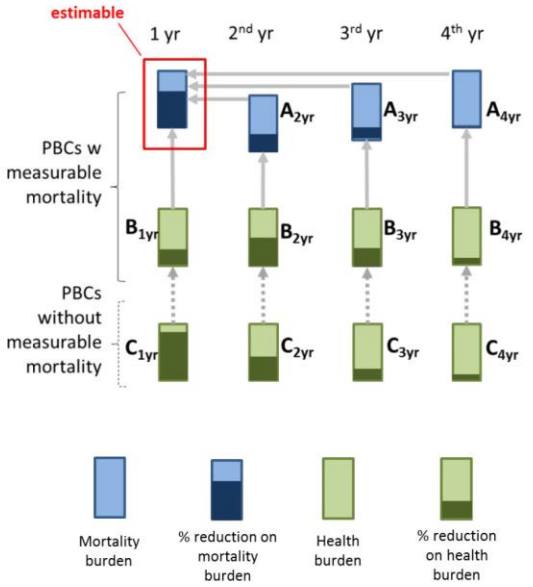
Question	Diagramatic Representation
Section A *Question.* For how many more years (beyond the year of increased expenditure) would you expect disease-specific mortality rates to be reduced? *Question.* From an increase in expenditure in a particular year, how do reductions in mortality rates in subsequent years compare (in proportionate terms) to the reduction observed in the first year? This was elicited separately for the second, third, and fourth years. Refers to quantities A2 yr, A3 yr, and A4 yr, respectively, in the diagram. Section B *Question.* If expenditure is increased in a particular year, how many times bigger (or smaller) are proportionate reductions on quality-adjusted life-year burden when compared with proportionate reductions on mortality burden? We elicited for the year of increased expenditure (first year) and also for any later effects of expenditure on the second, third, and fourth years subsequent to increased expenditure. Refers to quantities B1 yr, B2 yr, B3 yr, and B4 yr, respectively, in the diagram. Section C *Question.* How much bigger (or smaller) are reductions in health burden (quality-adjusted life-years) when expenditure is increased, for example, in "mental health disorders" instead of disease areas with a measured effect of increased expenditure on mortality (average effect across all disease areas in this group). This was elicited for the year of expenditure (first year) and also for any later effects of expenditure on subsequent years (second, third, and fourth years). Refers to quantities C1 yr, C2 yr, C3 yr, and C4 yr, respectively, in the diagram.	

Table 2 Summary of the Quantities Elicited with Diagrammatic Representation

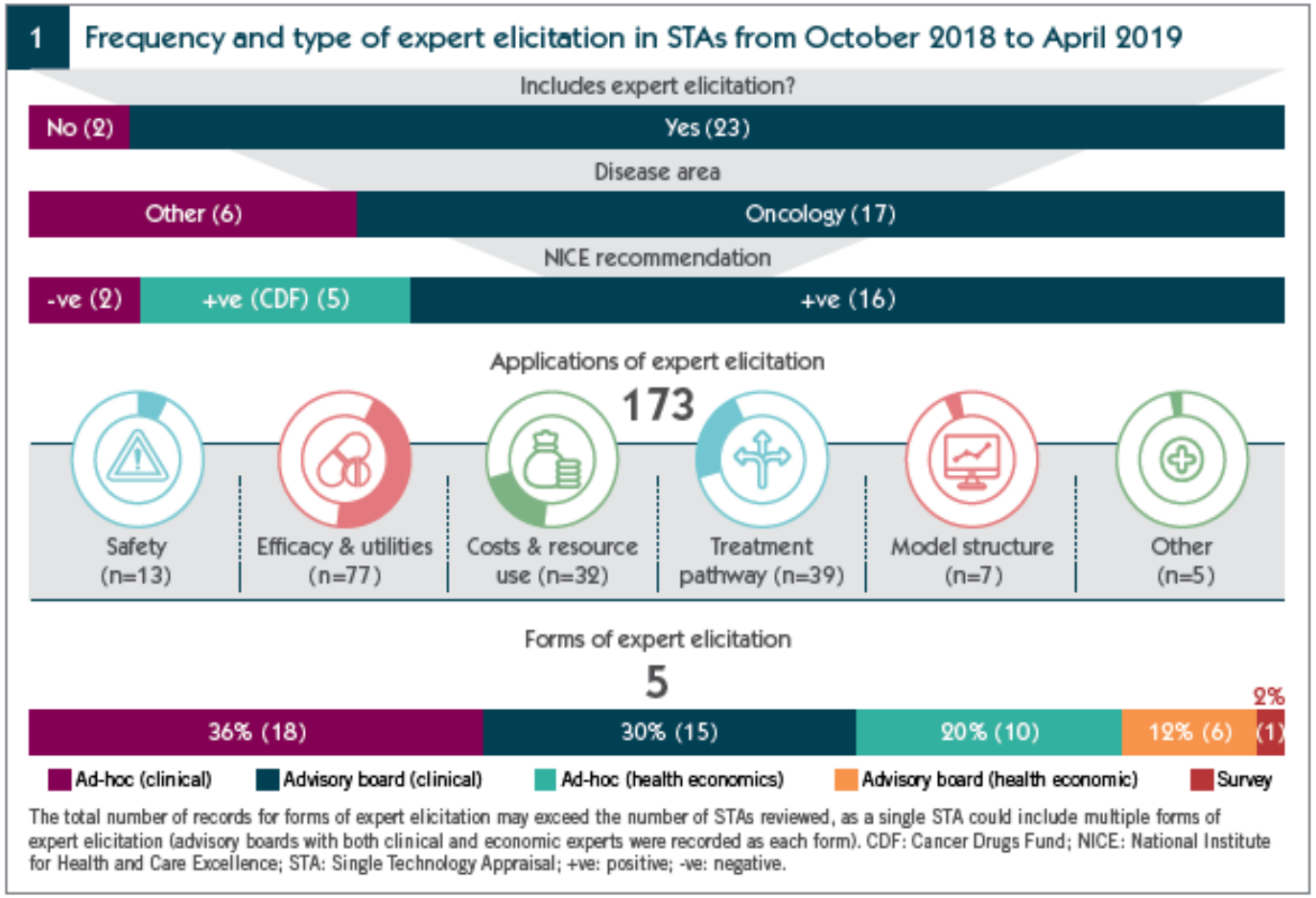
How does SEE work in this context

- Elicitation provides the additional information needed to reach a decision when empirical evidence is lacking.
- Often refers to quantitative processes
  - In HTA experts beliefs used as inputs into HTA evidence generation or interpreting empirical evidence
  - Qualitative belief elicitation also used to support HCDM (*best practice processes TBD*)
- 'Experts' observe outcomes of interest or use skills to generalise from one setting to another – *their beliefs*
- SEE uses methods to enable experts to encode their beliefs in a quantitative manor.

Guidance on SEE by HTA decision makers

- NICE Reference Case Update
  - Expert elicitation can be used to provide evidence.
  - Structured methods are preferred because they attempt to minimise biases and provide some indication of the uncertainty.
  - Should adhere to existing protocols (such as the Medical Research Council protocol).
- 14 country-specific, HTA methods guides were reviewed. Most mention expert opinion may be used to inform cost-effectiveness assessments. Most do not specify methods or requirements for SEE.

SEE as part of formal decision making processes



- Predominately part of HTA processes
- Large number of elicitation part of Ad-boards.
- Using non-structured processes.
- Best practice standard practices not utilised.
- Poor reporting

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What are the requirements of SEE for HCDM?

- Judgements are required for decision making in health.
  - To ensure accountability in decisions, these judgements should be made explicit and incorporated transparently into the decision making process.
  - Inherently Bayesian view on decision-making.
- Multiple methods exist for SEE.
  - Lack of empirical evidence on which methods are appropriate
- HCDM processes may involve complexities and impose constraints that are relevant for SEE.
  - What are the considerations for SEE in this context?

Guiding principles for SEE informing HCDM

1. Transparency
2. Provide useful information for the decision problem
3. Aim for consistency but respect the constraints of the decision-making context
4. Reflect uncertainty at the individual expert level
5. Recognize and act on biases.
6. Suitable for experts who possess substantive skills and who are less likely be trained in probability and statistics
7. Recognize where adaptive skills are required
8. Recognize, and act on, between-expert variation
9. Promote high performance.

Poll Question 2

- What types of quantities would you consider eliciting using SEE? (choose all that are relevant)

  A: Simple probabilities (proportions) of events

  B: Treatment effects on probabilities or odds

  C: Rate and hazard type parameters

  D: Weights (likelihood) for alternative scenarios, e.g. survival extrapolations

  E: Resource use/costs

  F: Quality of life measures

  G: Information relevant for model structuring

2.

Resources for Conducting Structured Expert Elicitation

Dawn Lee, Lumanity

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No single resource covers all steps

Steps involved in structured expert elicitation (SEE)

- **Preparation and design**
  - Selection of quantities
  - Selection of methods to encode and validate judgements
  - Selection of experts
  - Training and preparation for experts
- **Design and execution of elicitation session**
- **Aggregation and reporting**
  - Behavioral aggregation
  - Mathematical aggregation ~
  - Fitting of distributions
  - Reporting
  - Use within economic analyses ~
- **Decision maker interpretation** ✖

Consensus building & brainstorming software:
- Within3, Miro, Visio, FacilitatePro, IdeaBoardz, Survey Monkey, Qualtrics etc.

Methodological resources:
- MRC protocol, SHELF

Online literature databases:
- PubMed, clinicaltrials.gov, societies, meetings, journals, social media, etc.

Tools for training:
- Vancouver e-learning course

Tools for elicitation:
- SHELF (and MATCH Uncertainty Elicitation Tool)
- Excalibur (uses Cooke's classical model)
- Numerous Excel examples (such as EXPLICIT)
- Examples outside of HE field (Unicorn, Elicitator, UncertWeb, etc.)

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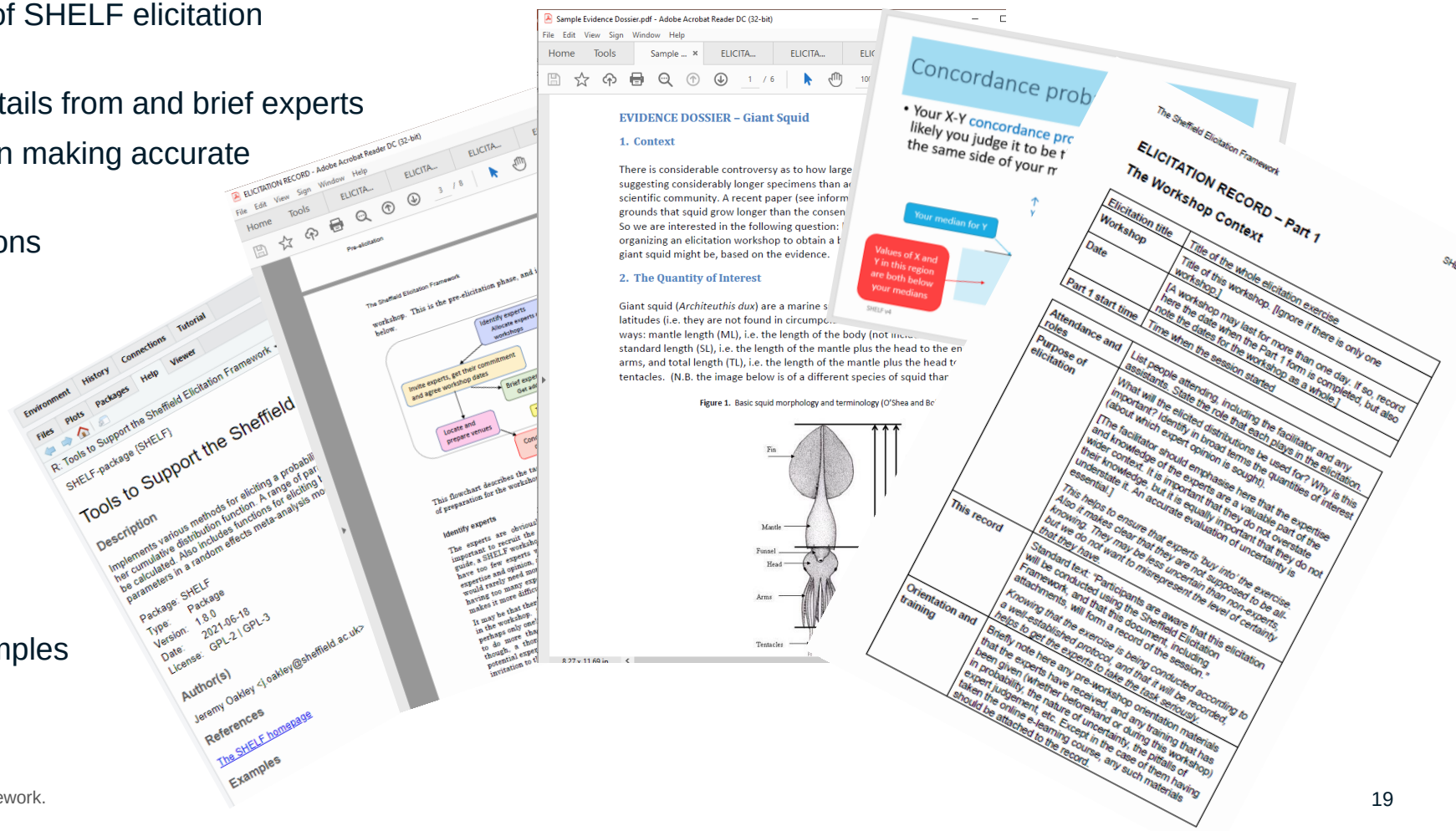
Key: HE, health economics; MATCH, Multidisciplinary Assessment of Technology for Healthcare; MRC, UK Medical Research Council; SHELF, Sheffield Elicitation Framework.

References: COST 151304 European Cooperation in Science and Technology. Selection of structured expert judgement software. Available at: https://www.expertsinuncertainty.net/Software/tabid/4149/Default.aspx. Access date: 12 April 2022.

Sheffield Elicitation Framework (SHELF)

Resources available

- Advice for coordinators and facilitators of SHELF elicitation workshops
- Sample documents for use to gather details from and brief experts
- PowerPoint slide sets to guide experts in making accurate judgements
- Templates for recording SHELF elicitations
  - Continuous
  - Discrete
  - Multivariate:
    - Extension
    - Dirichlet
    - Copula
- Sample SHELF elicitation records
- R package including vignettes and examples
- Inbuilt Shiny front-end



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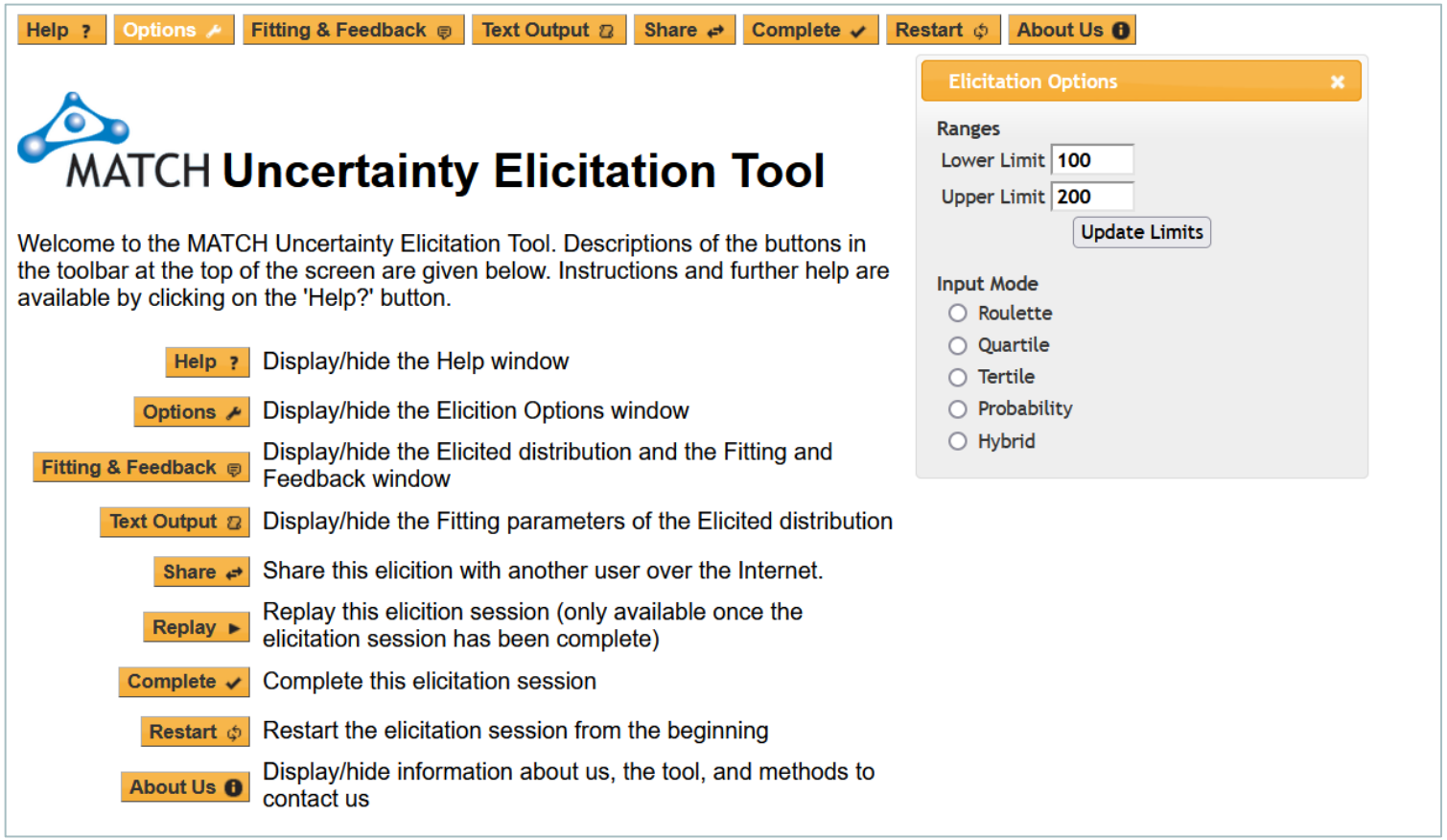
Key: SHELF, Sheffield Elicitation Framework.

MATCH

R / Shiny app based upon SHELF

- All methods begin by asking for plausible upper and lower limits
- Four types of method are then available in MATCH:
  - Roulette
  - Quartile
  - Tertile
  - Probability
- Hybrid option combines estimation of a median with the probability method



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MATCH

R / Shiny app based upon SHELF

- Tertile and quantile methods work in a similar manner
- Experts can find the judgements difficult
- Suitable for individuals or groups
- Software fits a number of distributions to expert judgements and allows user to check back fit

Reminder to hit enter after putting in answers!

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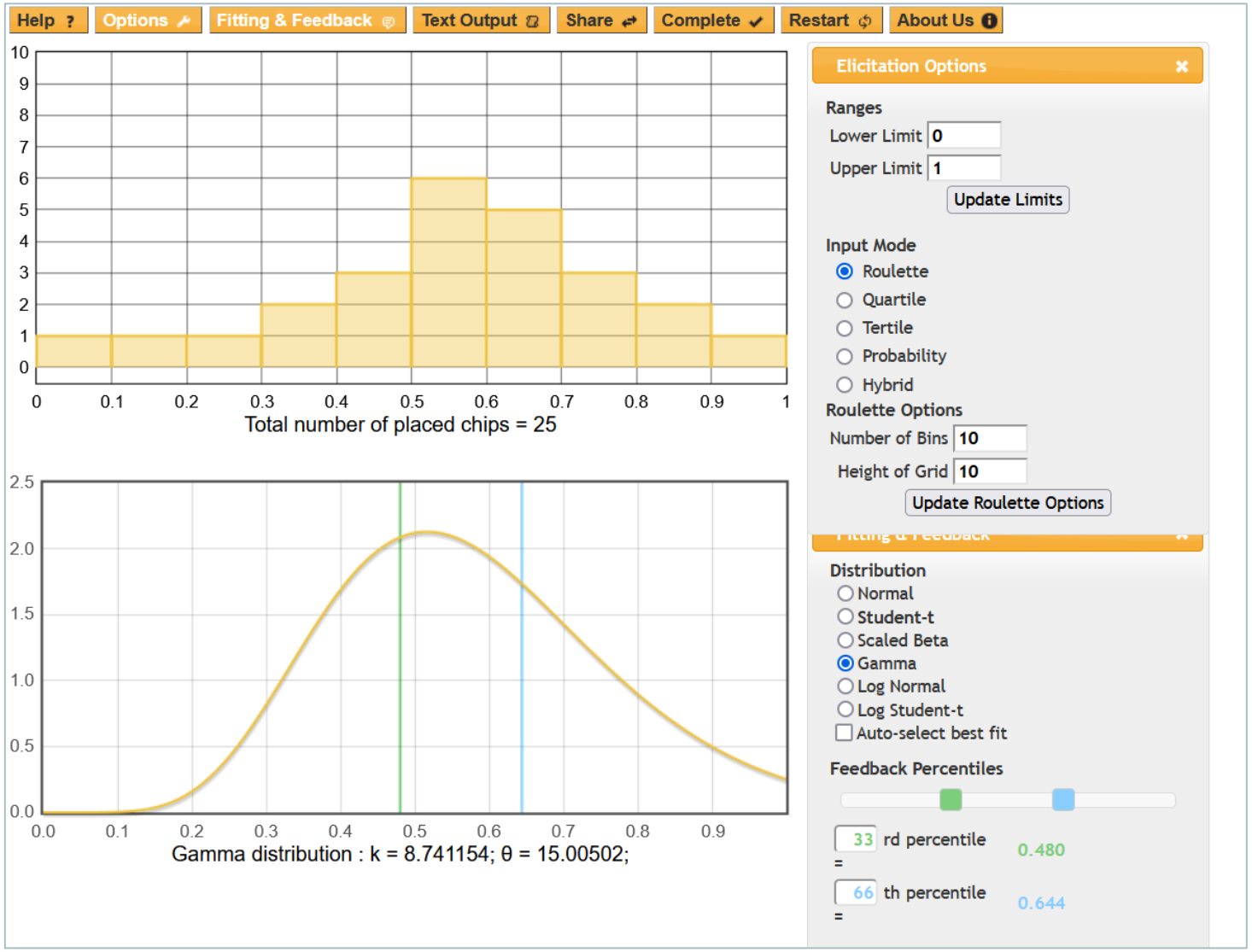
Key: MATCH, Multidisciplinary Assessment of Technology for Healthcare; SHELF, Sheffield Elicitation Framework.

Reference: Morris et al. *Environmental Modelling & Software.* 2014; 52:1-4. Available at: http://optics.eee.nottingham.ac.uk/match/uncertainty.php.

MATCH

R / Shiny app based upon SHELF

- The Roulette method involves the placing of counters (probs) on the grid
- Recommended:
  - 10–12 columns
  - 20–25 probs
- Less challenging for experts but subject to bias: range–frequency compromise
- Suitable for individuals only



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MATCH

R / Shiny app based upon SHELF

- The probability method is used to facilitate group judgements
- Three values are asked for:
  - Probability X < X1
  - Probability X > X2
  - Probability X < X0

- **All good in theory but:**
  - Server/loading issues mean it isn't reliable for use in interviews
  - It is not user friendly enough to leave experts to use independently
  - Experts cannot see the impact of their judgements on end outcomes (e.g. overall survival)
  - No aggregation

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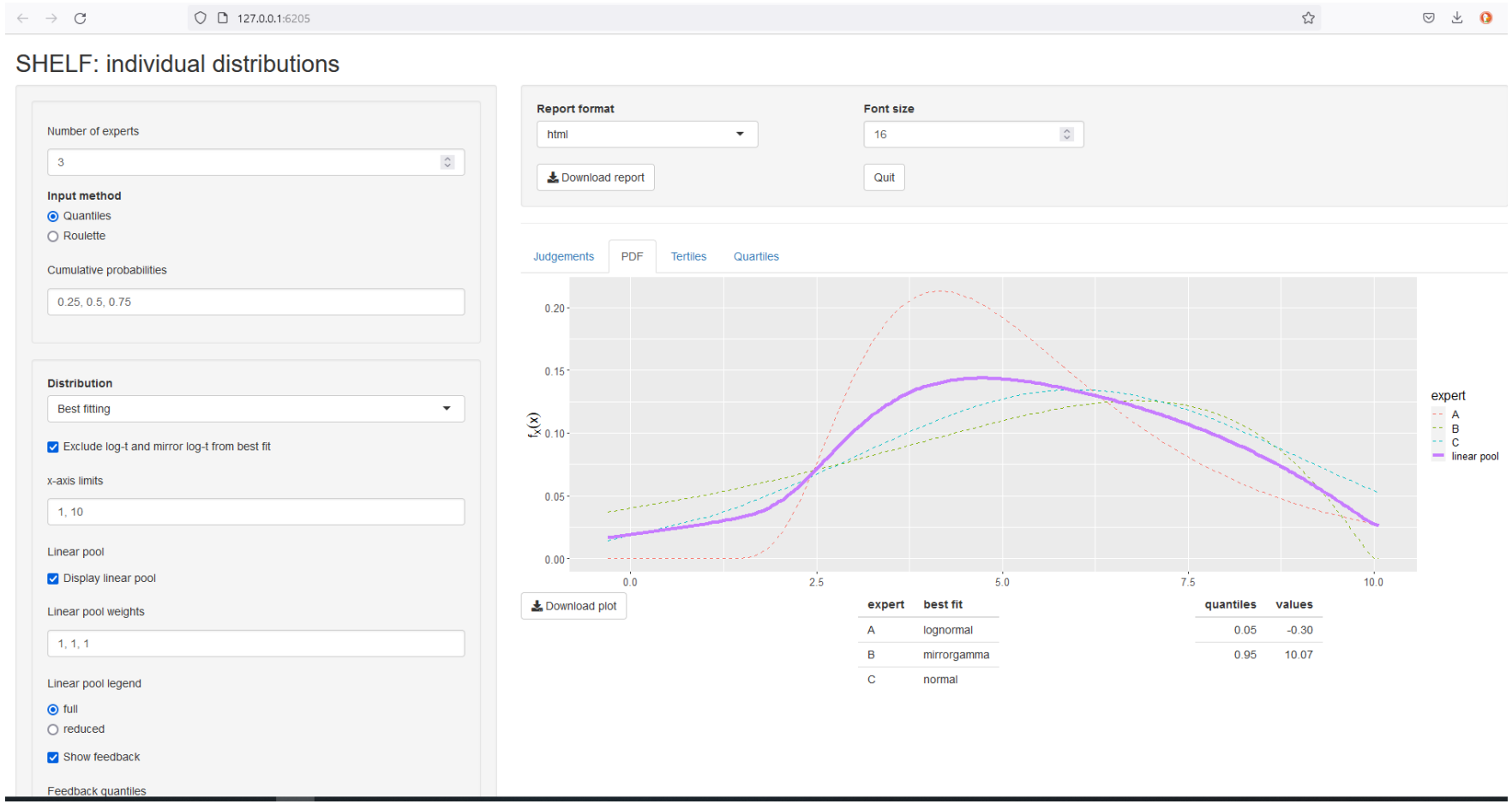
Inbuilt SHELF Shiny front-end

- Less intuitive
- More reliable
- Allows presentation of aggregation
- Report download provides parameters for all fitted distributions
- Samples from linear pooling can only be accessed within R



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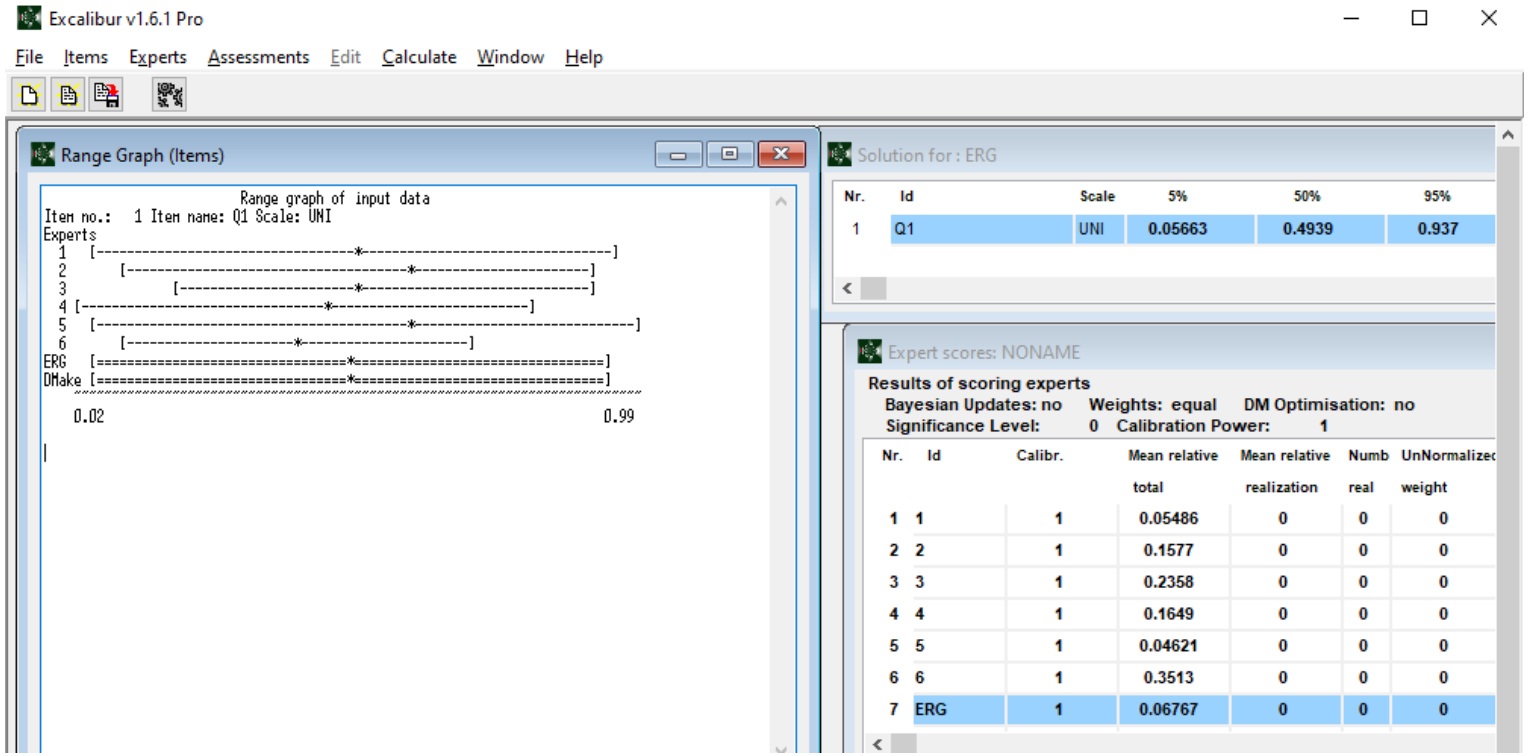
Excalibur

- Excalibur is a software package for structured expert judgement elicitation using Cooke's classical model
- Version compiled April 2004
- Free to use (up to 20 experts and up to 100 items)
- Minimally maintained by LightTwist Software
- User-weights, equal weights and performance-based weights are supported

Not simple to use!



References: LightTwist Software. Excalibur. Available at: https://lighttwist-software.com/excalibur/.

Use within economic analyses

Examples are limited

Stevens and Orr, 2021: method illustrated using breast cancer data[1]

- Contrasts the retrospective and prospective use of experts' beliefs in choosing between survival models
- "Conclusion: The retrospective use of experts' beliefs to validate a model is potentially misleading, may not achieve its intended objective and is an inefficient use of information"
- **"**Further research is required to develop guidance on the elicitation of experts' beliefs about parameters in standard and other survival models, the generation of practical examples and formulating prior model probabilities"

Cope et al., 2019: tisagenlecleucel (CAR-T) for relapsed or refractory pediatric acute lymphoblastic leukemia[2]

- Conversion of elicited survival at four timepoints to discrete interval hazards for each timepoint following trial end
- Each set of expert-specific discrete hazard estimates were individually added to original set from the trial and the Weibull, Gompertz and fractional polynomial models fitted. Results then combined (not clear how)
- Model based on expert elicitation close to observed later datacut

> **"ERG conclusion:** The expert elicitation was clearly reported and appears to have been well-conducted. The exercise was double-blinded, but there is still potential for bias through the expert identification process, which included cemiplimab study investigators and their contacts. We therefore agree with the company's decision to use PFS and OS distributions fitted to empirical data alone for their base case analysis and we focus on these results in this report."
>
> NICE TA592[5]

NICE model for the evaluation and purchase of antimicrobials

- EEPRU elicited expert opinion for some patient populations
- Outcomes: 30-day mortality, LoS in hospital, and the type of ward
- Validated with published literature
- Used within NICE's accepted base case

Guyot et al., 2017[4]

- Expectation that hazard ratio is a smooth function with a monotonic decrease followed by a monotonic increase over Years 0–5
- Introduced external data on the hazard ratio taking the value of 1 at time points t = 6…35 years, each with a standard error of 0.1

$$HR(t) \sim N\left(\frac{h_{1,RCT}(t)}{h_{0,RCT}(t)}, 0.1^2\right),\ t = 6 \ldots 35 \text{ years}$$

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Key: CAR-T, chimeric antigen receptor T-cell therapy; ERG, Evidence Review Group; OS, overall survival; PFS, progression-free survival.

References: 1. Stevens and Orr. https://arxiv.org/abs/2109.06760. 2021. | **2.** Cope et al. *BMC Med Res Methodol*. 2019; 19(1):182. | 3. Soares et al. *Statistics in Medicine. 2011; 30(19):2363-2380* | **4.** Guyot et al. *Med Decis Making*. 2017; 37(4):353-66. | 5. NICE. Cemiplimab for treating metastatic or locally advanced cutaneous squamous cell carcinoma [TA562]. 2019. Available at: https://www.nice.org.uk/guidance/TA592.

Gaps in existing resources

No end-to-end solution exists. Gaps include the following:

- KOL identification resources tailored to SEE
- Guidance on compliance processes during recruitment and for materials
- Template for protocol
- Available resources assume face-to-face elicitation; required amendments for a virtual setting are not clear
- Available resources for on-the-day elicitation either:
  - Are not publicly available (Excel examples)
  - Require knowledge of R (more advanced SHELF methods)
  - Are not user friendly (EXCALIBUR)
  - Do not allow immediate feedback and review of distributions and their impact on end outcomes
- Lack of code for mathematical aggregation methods
  - Linear pooling is not the only option available
- Paucity of use cases demonstrating application within health economic analysis
  - Time-to-event data application is a particular gap
- No guidance for decision makers

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Key: KOL, key opinion leader; SEE, structured expert elicitation; SHELF, Sheffield Elicitation Framework.

Poll Question 3

What software would you prefer for future tools to aid in the conduct of SEE?

A. Word
B. Excel
C. R
D. Web app

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3.

Challenges faced in SEE for HCDM

James Horscroft, Lumanity

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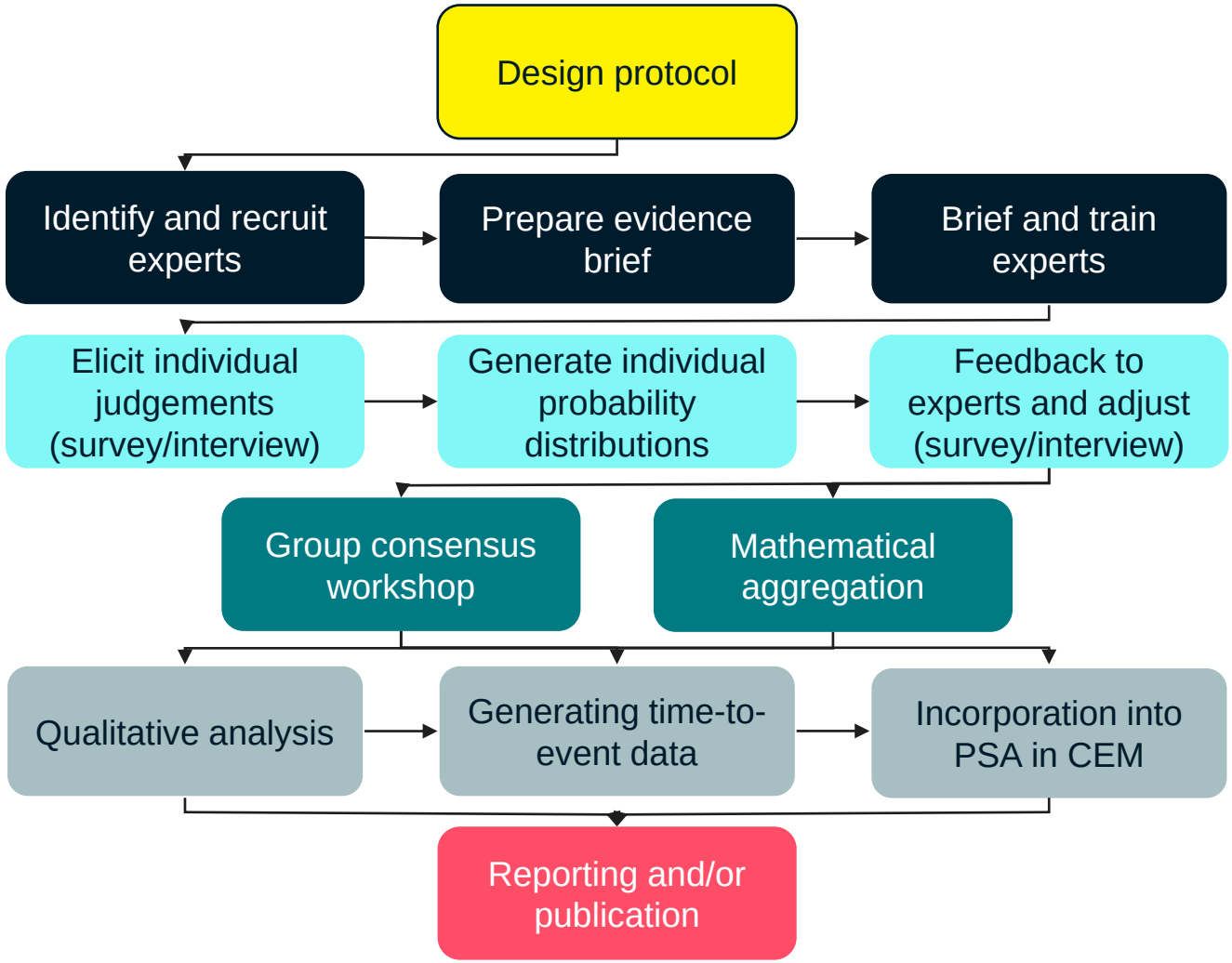
How is SEE conducted?

SEE requires a multi-disciplinary collaborative approach

1. Protocol
2. Preparation
3. Individual elicitation
4. Aggregation
5. Modelling/analysis
6. Reporting



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Key: CEM, cost-effectiveness model; PSA, probabilistic sensitivity analysis; SEE, structured expert elicitation

Case study 1: Survival rates in an oncological indication

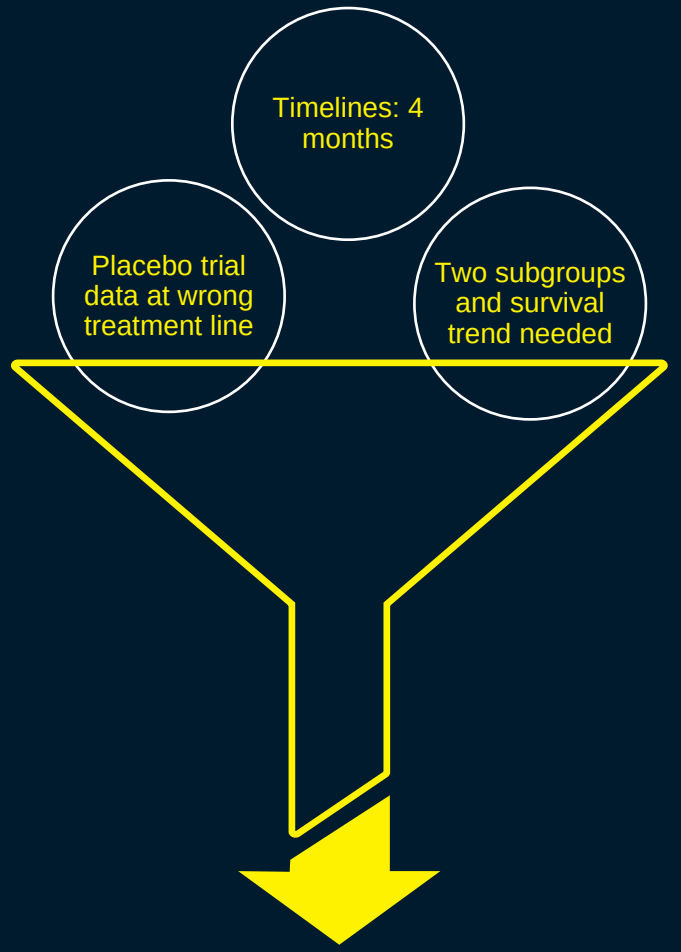
The challenge

- 4 months from project initiation to submission deadline
- Single-arm trial, so best supportive care (BSC) data lacking
- Placebo arm of a separate trial available, but at a different line of therapy
- Patients with/without genetic markers with vastly differing survival
- Shape of survival extrapolation of interest – proportional hazards likely not appropriate

The outcome

- Consensus probability distributions for survival at two timepoints in two subgroups
- Indicated that the Committee may have previously overestimated BSC survival

Goal: to explore long-term survival for patients receiving best supportive care for a NICE reappraisal



Approach: SHELF study to elicit survival rates at two timepoints for two subgroups of patients receiving best supportive care

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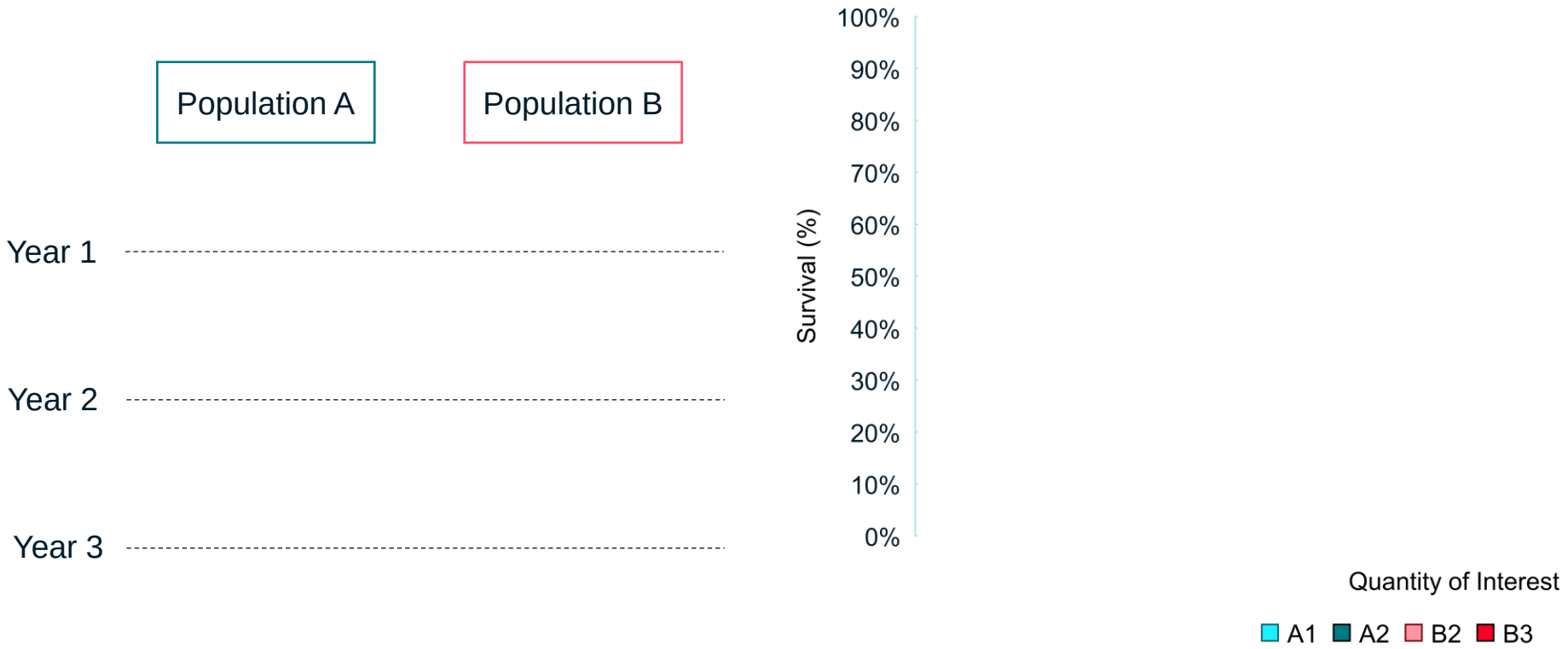
Key: BSC, best supportive care; SHELF, Sheffield Elicitation Framework.

Case study 1: Survival rates in an oncological indication

Quantities of interest and results



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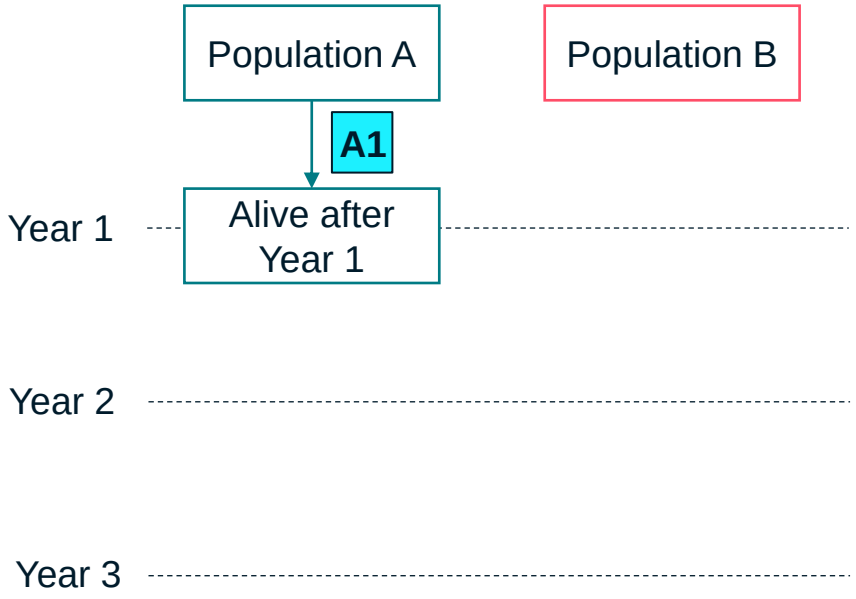
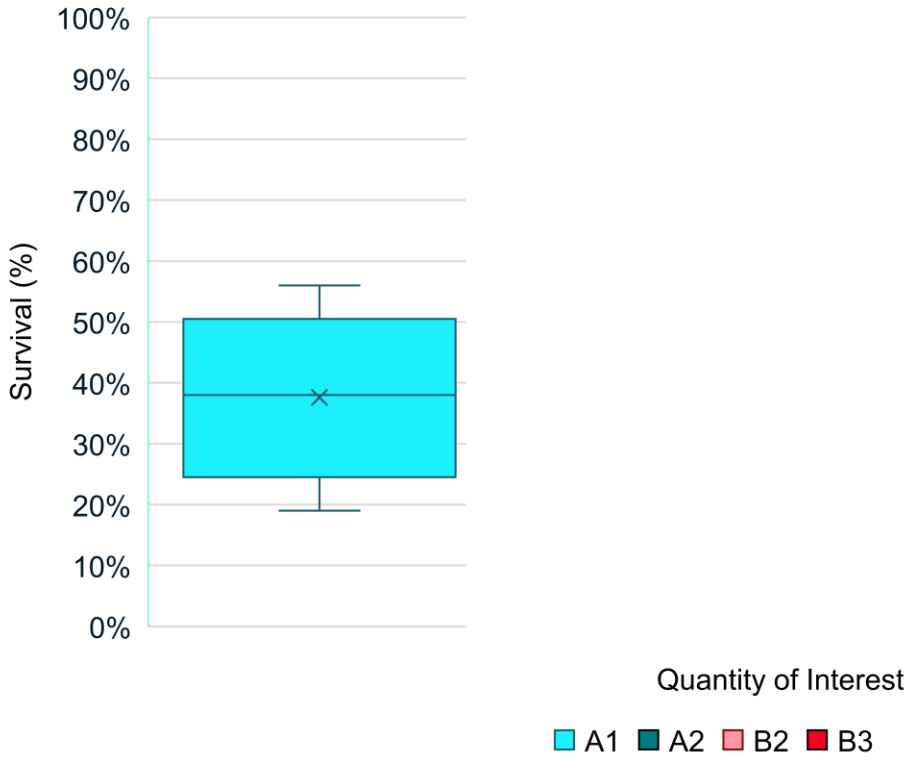
Notes: Error bars represent the 95% confidence intervals (5th and 95th percentile); boxes represent the interquartile range (25th and 75th percentile) and the mid-line represents the median (50th percentile).

Case study 1: Survival rates in an oncological indication

Quantities of interest and results





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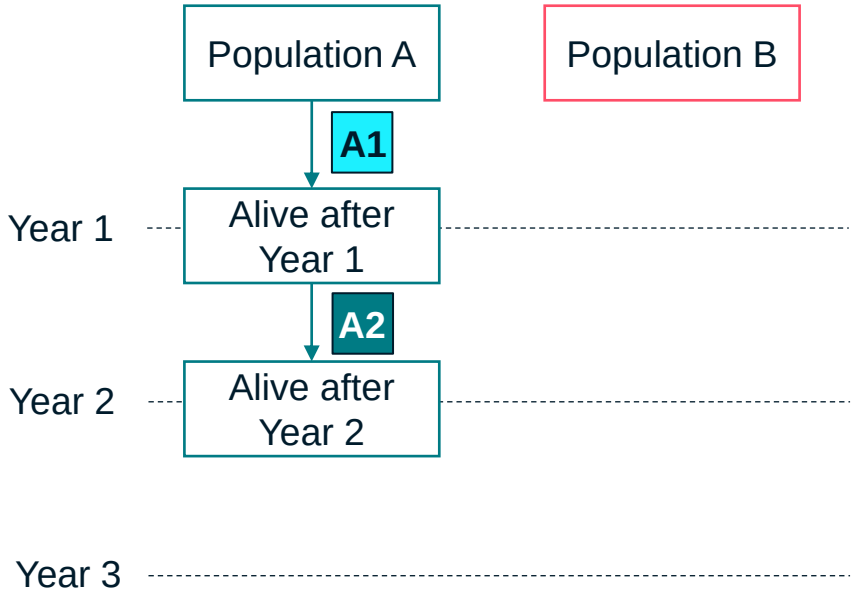

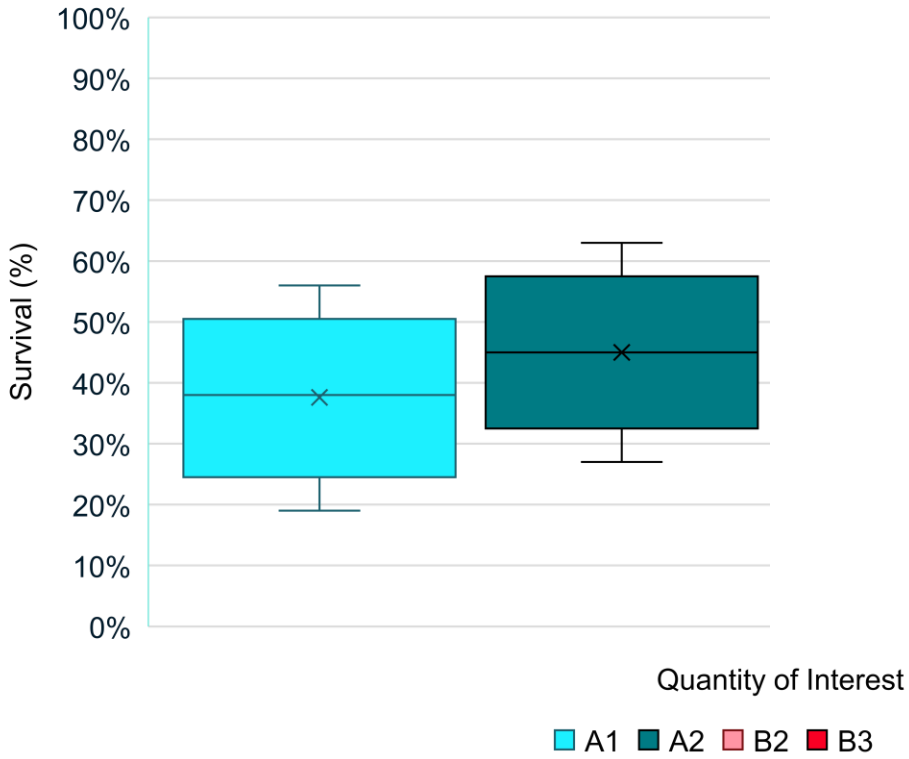

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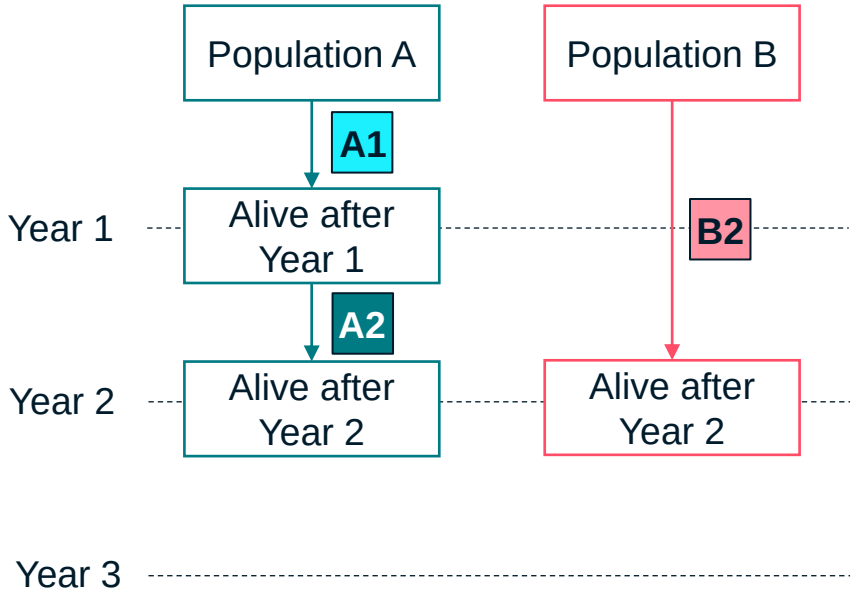

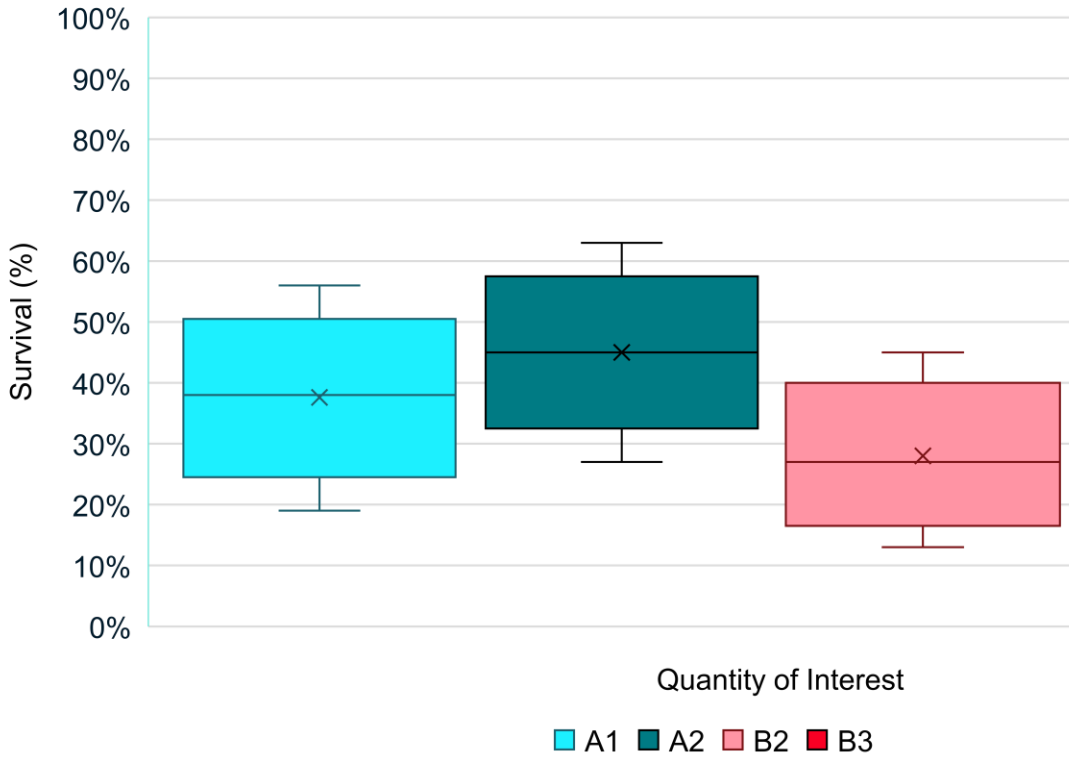

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Case study 1: Survival rates in an oncological indication

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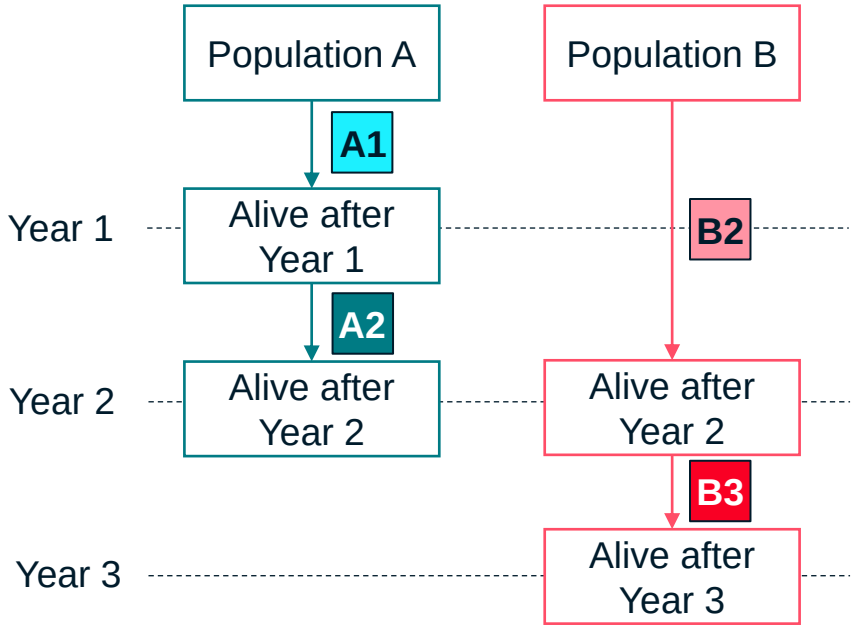

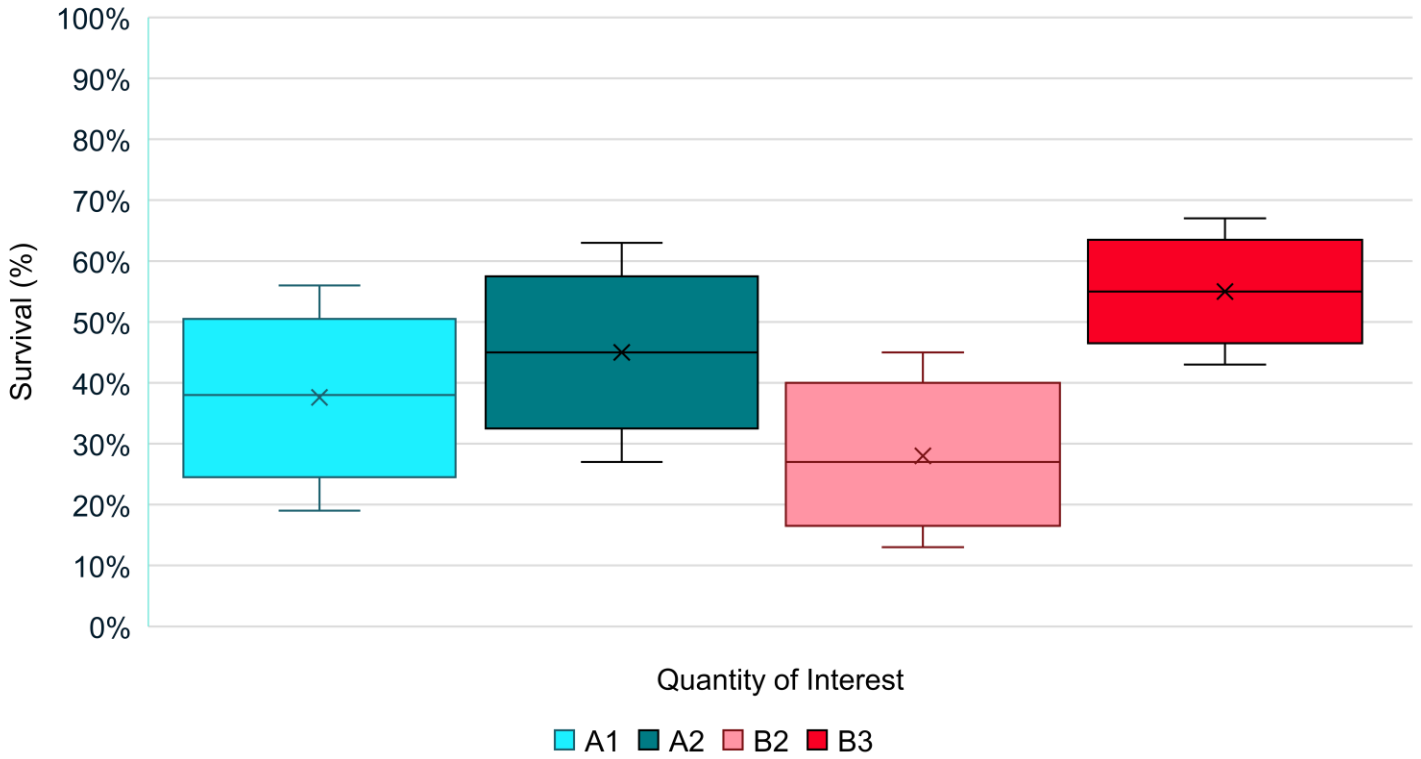

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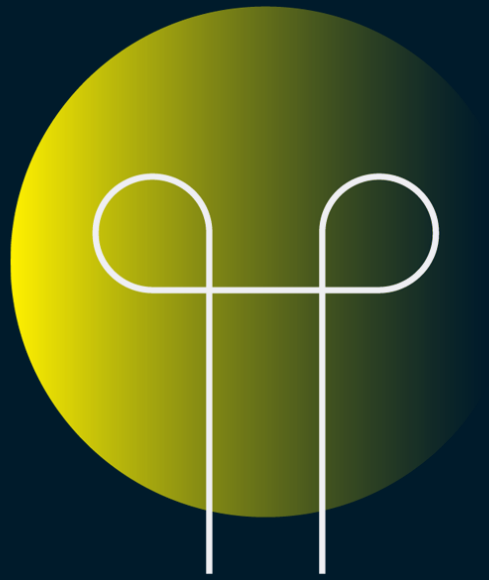
Case study 1: Survival rates in an oncological indication

Key challenges



01 Training materials developed internally due to lack of readily understandable training materials.

02 ‘Roulette’ elicitation tool developed internally due to lack of user-friendly tools.

03 Unable to show impact of survival rates at multiple timepoints in real-time.

04 Unable to overlay results on Kaplan–Meier data in real-time.

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Key: SEE, structured expert elicitation

Case study 2: Hospitalization for an infectious disease

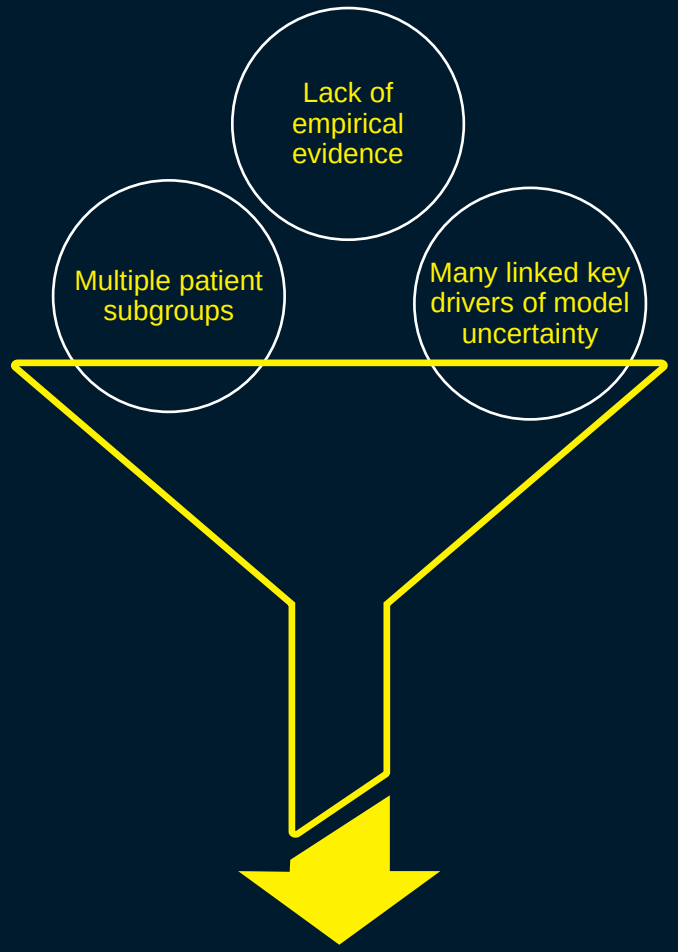
The challenge

- 6 months from project initiation to submission deadline
- Natural history data severely lacking for paediatric indication
- Hospitalization identified as a key driver of the ICER, as it was linked to both costs and mortality
- Mortality per hospitalization also uncertain
- Originally 12 patient subgroups, condensed down to four

The outcome

- Consensus probability distributions for hospitalization in four patient subgroups
- Consensus point-estimates (non-probabilistic) for mortality

Goal: to elicit key model inputs for an economic model to support a submission to the JCVI in the UK



Approach: probabilistic Delphi to elicit hospitalization rates in four patient subgroups

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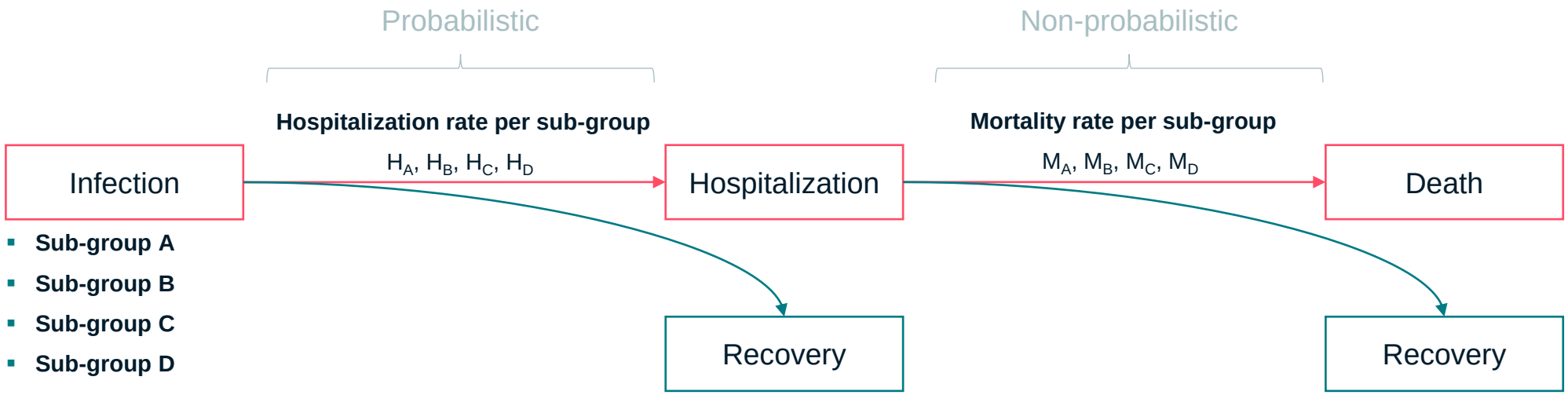
Key: ICER, incremental cost-effectiveness ratio; JCVI, Joint Committee on Vaccination and Immunisation, UK

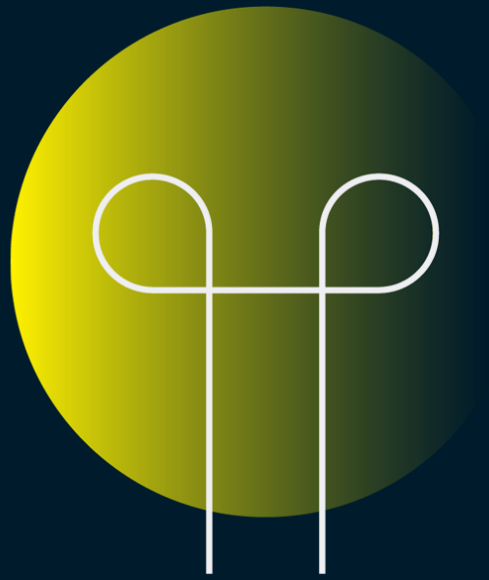
Case study 2: Hospitalization for an infectious disease

Quantities of interest



Case study 2: Hospitalization rates for an infectious disease

Key challenges



01 **Scheduling for training and consensus workshop under tight timelines.**

02 **SEE did not fit into pre-defined categories for compliance processes.**

03 **No user-friendly tools for experts to provide judgements.**

04 **Unable to instantly feed back probability distributions.**

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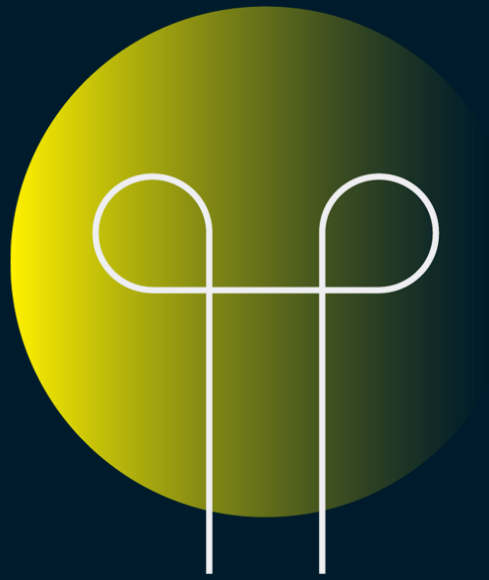
Key: SEE, structured expert elicitation

Conclusions

Many of the challenges faced could be resolved through additional tools and guidance



01 **There are a lack of readily understandable training materials.**

02 **There are a lack of tools that are user-friendly and allow immediate feedback and review of probability distributions.**

03 **There are a lack of tools that generate graphical representations of results in-line with empirical evidence.**

04 **Industry compliance approval processes are still adjusting to SEE.**

Key: SEE, structured expert elicitation

Poll Question 4

What would motivate you to use SEE rather than informal elicitation methods to fill data gaps in key drivers of your economic analysis?

A. SEE is preferred or required by HTA decision makers
B. SEE is more robust and reduces bias
C. SEE characterizes uncertainty for incorporation into probabilistic sensitivity analysis
D. Availability of user-friendly tools that make SEE more accessible
E. The anticipated impact of an SEE study on the incremental cost effectiveness ratio
F. Availability of clearer SEE guidance to make best use of time and resources
G. I am unlikely to use SEE to fill data gaps in key drivers of economic analyses

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Open source resources for structured expert elicitation (SEE)

Dina Jankovic
Centre for Health Economics
University of York, UK

UNIVERSITY of York

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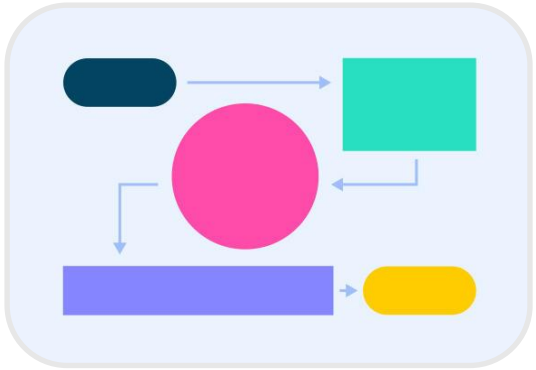
Centre For Health Economics

Open source resources for SEE



1. **Step-by-step guide** for conducting SEE

2. **Databased of existing SEE** applied in cost-effectiveness modelling

3. **Open access templates** for developing new SEE exercises

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1. Step-by-step guide for conducting SEE

Adapt the published reference case methods for SEE in healthcare decision-making

Developing a reference protocol for structured expert elicitation in health-care decision-making: a mixed-methods study

Health Technology Assessment, No. 25.37

Laura Bojke, Marta Soares, Karl Claxton, Abigail Colson, Aimée Fox, Christopher Jackson, Dina Jankovic, Alec Morton, Linda Sharples, and Andrea Taylor.

Author Information

Southampton (UK): NIHR Journals Library; 2021 Jun.

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2. Database of existing SEE applied in cost-effectiveness modelling

			Approach and method of elicitation			Conduct		Analyses	
Study	Type of strategy under investigation	Type of parameter(s) elicited	VIM or FIM	Method (summaries elicited)	Aggregation approach	Mode of administration	Format/software	Pooling	Fitting
Garthwaite et al. [14]	Treatment	Event probabilities, time to event, dependency	VIM	Median and quartiles	Mathematical	Individual face-to-face and remote	Interview and specialized software	No pooling	Independently elicited quantities: NR; dependency elicitation: yes, generalized linear model
Leal et al. [10]	Diagnostic/screening	Event probabilities, relative effectiveness, diagnostic accuracy	FIM	Four complementary intervals	Mathematical	Remote (email) and individual face-to-face	Excel-based		Yes, maximum likelihood
Girling et al. [15]	Treatment	Event probabilities, time to event	VIM*	NR	Consensus	Group face-to-face	NR	–	Yes, method NR
Stevenson et al. [16]	Prevents transmission	Event probabilities, time to event, relative effectiveness	NR	NR	NR	NR	NR	NR	NR

Update of review by Soares, et al. "Experiences of structured elicitation for model-based cost-effectiveness analyses." *Value in health* 21.6 (2018): 715-723.

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3.1: Open-source templates: training and preparation

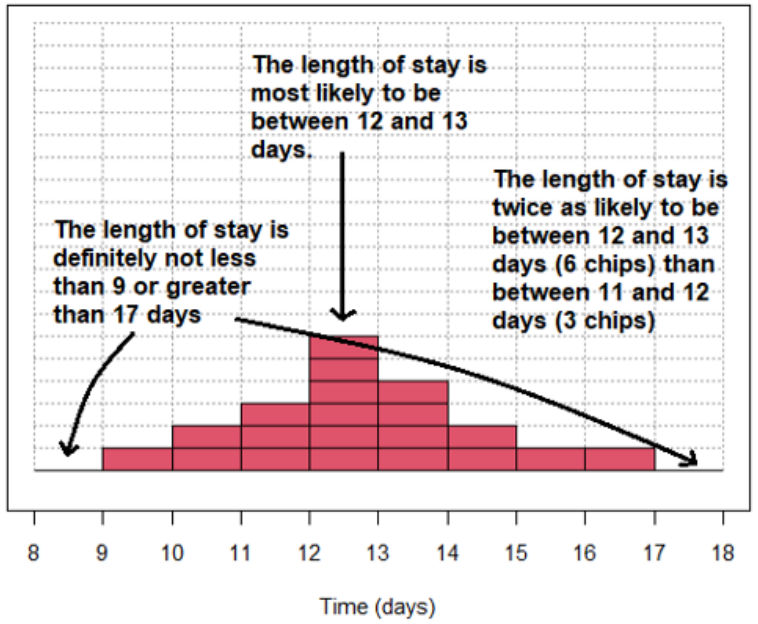
- Consent forms
- Training materials
- Elicitation protocols

Example 1. How long is the average length of stay in hospital after a myocardial infarction (MI), in the UK?

I believe that it's very unlikely that:

- the average length of stay is shorter than 9 days
- the average length of stay is longer than 17 days.

Please add **20 chips** to the grid below to express your uncertainty. The more chips you place in a particular bin the more certain you are that the proportion lies in that bin.



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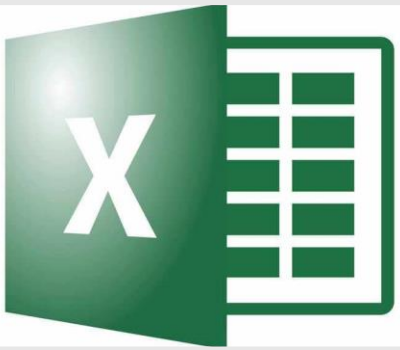
3.2. Open-access resources: conducting SEE

- Easy to assemble and deliver
- Lacks flexibility



- Flexible
- Fairly user-friendly
- Requires macros

- Flexible
- User-friendly
- Requires basic knowledge of R

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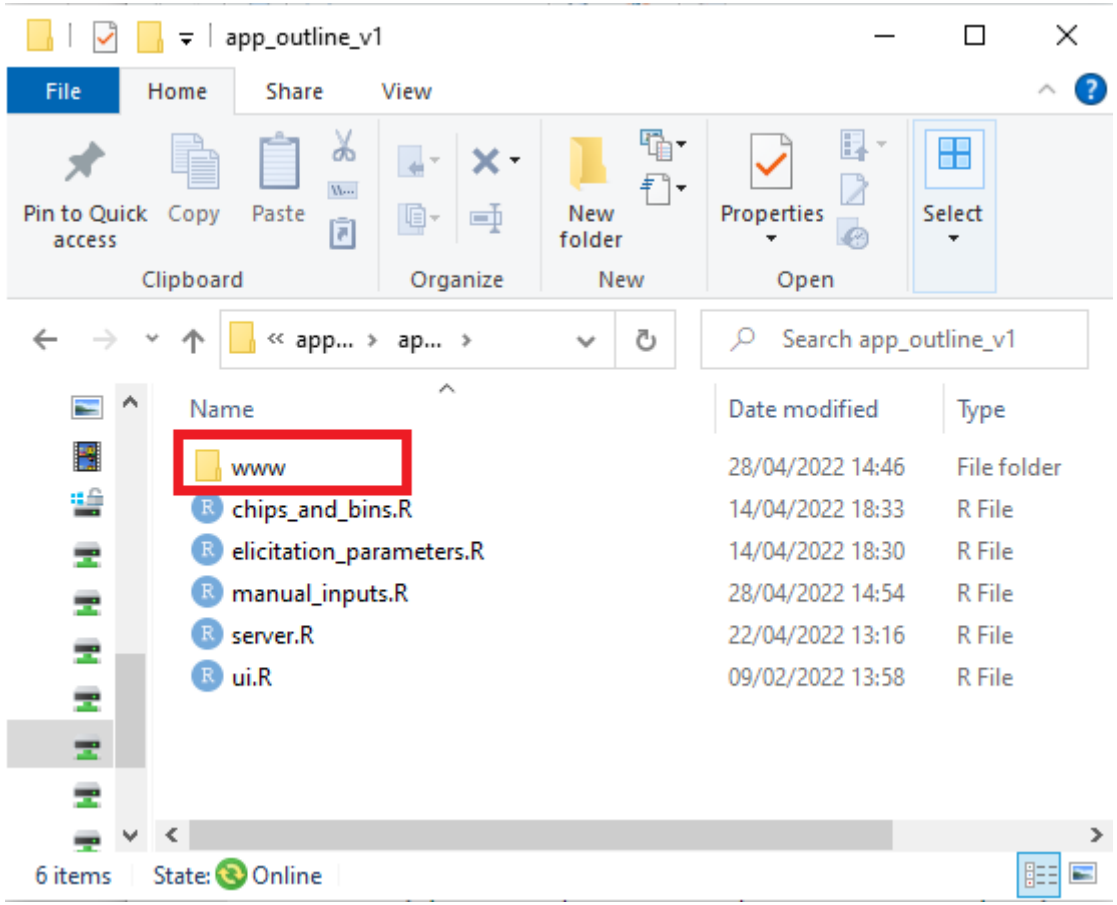
R-based tool: overview



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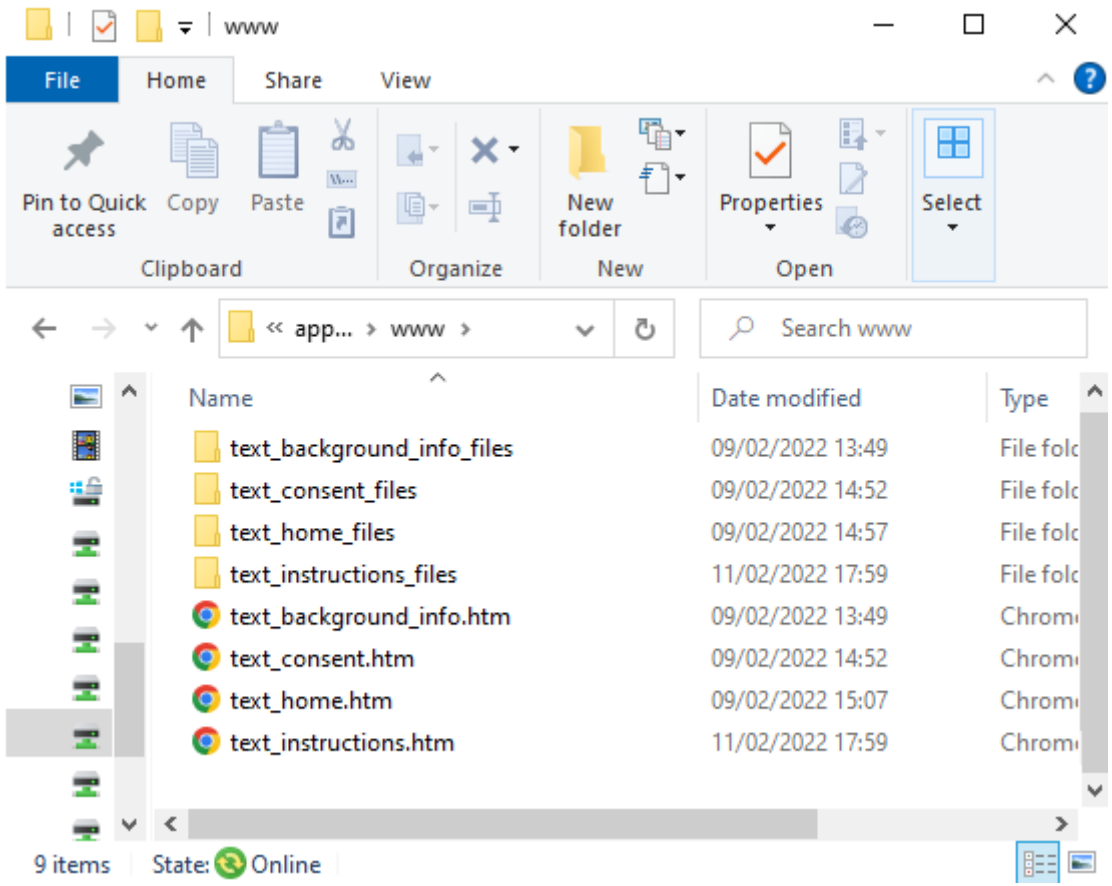

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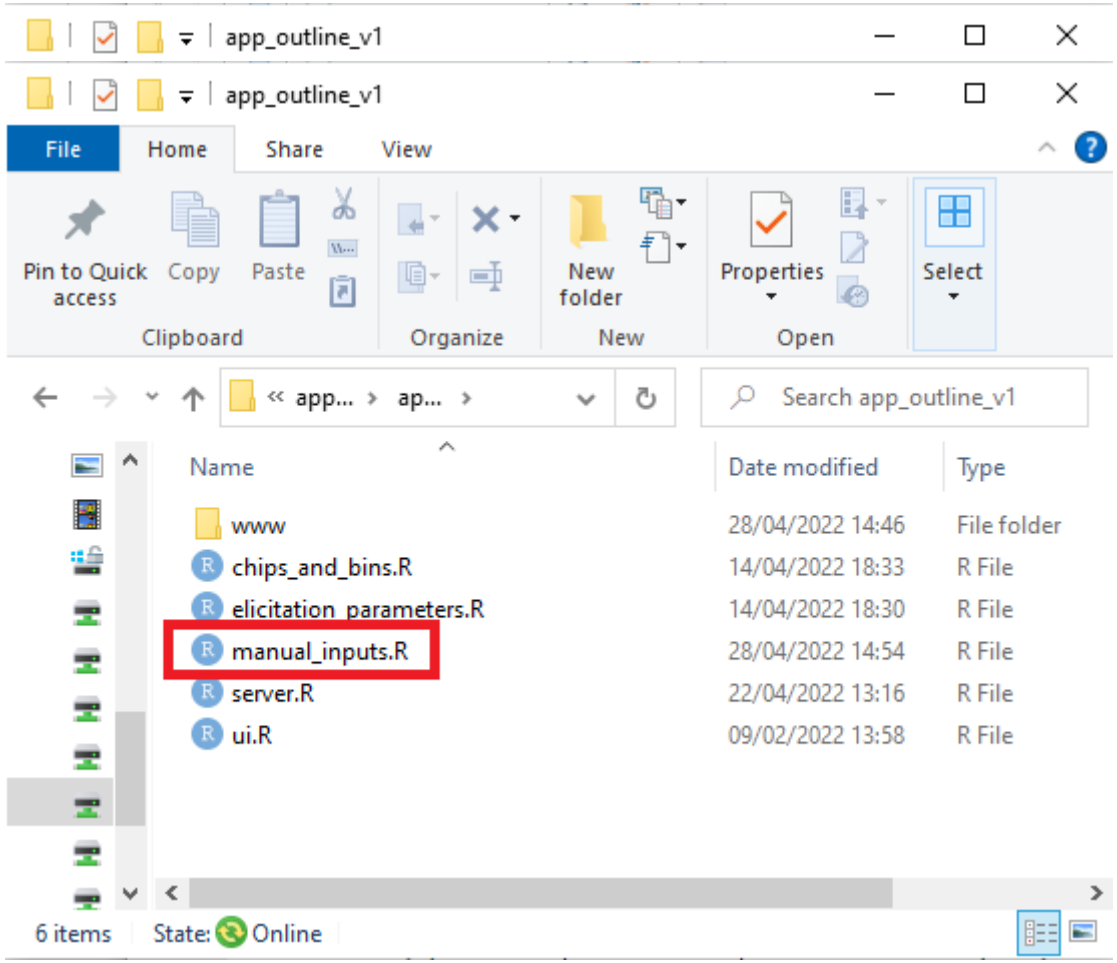

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11
12 tot_eli_ques <- 4
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15 # quantities being elicited e.g. proportion, rate, duration
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40   how much more effective is Drug B after 6 months of treatment?"
41 )
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40:66 (Top Level) R Script

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Application example

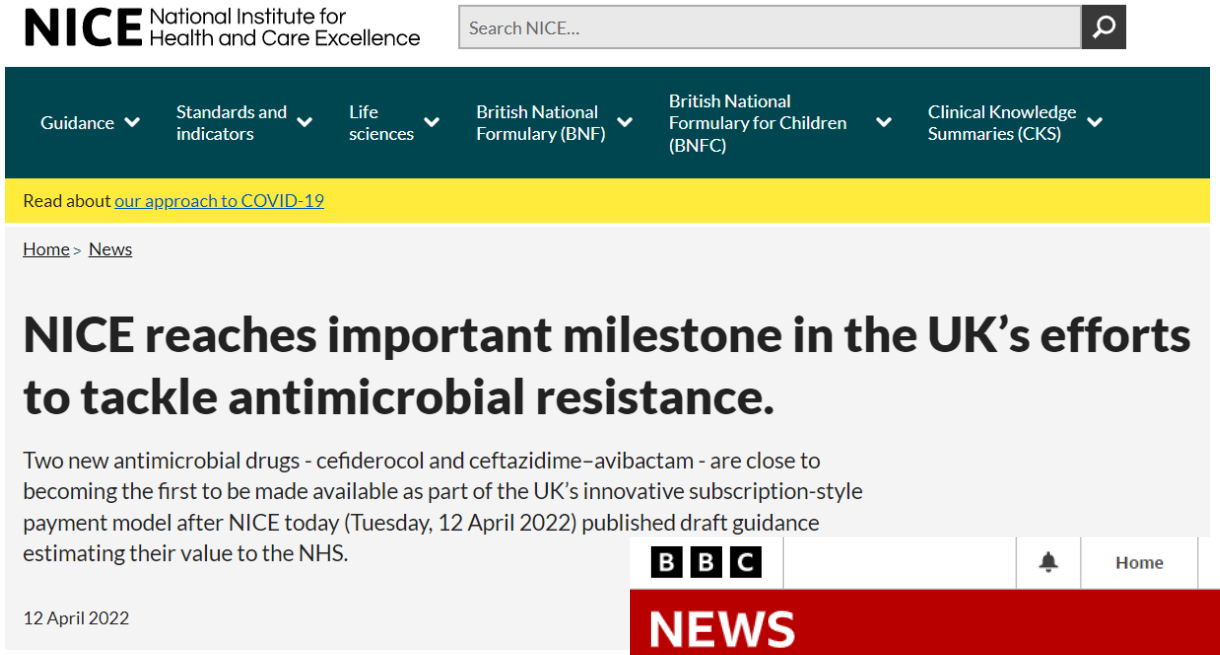
Assessing the value of antimicrobials

Case study: an economic evaluation of two antimicrobials, conducted to inform a novel funding model by NHS England & NHS Improvement

Model: outcomes conditional on in vitro susceptibility to microbials

Experts' beliefs: elicited 30-day mortality and length of hospital stay in patients who are susceptible/resistant to antimicrobials in specific settings.

Assessing the value of antimicrobials



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NICE reaches important milestone in the UK's efforts to tackle antimicrobial resistance.

Two new antimicrobial drugs - cefiderocol and ceftazidime–avibactam - are close to becoming the first to be made available as part of the UK's innovative subscription-style payment model after NICE today (Tuesday, 12 April 2022) published draft guidance estimating their value to the NHS.

12 April 2022

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Health

Two new drugs to fight superbugs available on NHS soon

12 April | Comments

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5.

Q&A

Any questions?

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SEE Sense: Tools for Conducting Structured Expert Elicitation to Support Healthcare Decision Making

Any further queries please do get in touch

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James Horscroft, PhD: james.horscroft@lumanity.com

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