

Structured Expert Elicitation in HTA Submissions: A Practical Guide Using the Example of Pembrolizumab for Treating Relapsed or Refractory Classical Hodgkin Lymphoma

Alan Lamb, Sam Barton, Rob Fordham, Ari Asaadi, Kayla Engelbrecht, Ross Maconachie
MSD (UK) Limited, 120 Moorgate, London, EC2M 6UR, UK

Background and objectives

NICE TA540 (2018)¹

- Pembrolizumab recommended for managed access in Cancer Drugs Fund (CDF) for treatment of relapsed or refractory classical Hodgkin Lymphoma (cHL)
- Data to be collected in CDF and KEYNOTE-087 trial on survival outcomes and stem cell transplant (SCT) rates on pembrolizumab

CDF exit (2024)²

- Cost-effectiveness of pembrolizumab reevaluated using new data to address uncertainties
- Limited data for some key parameters or model outputs, including cure rate after SCT, proportion of patients on standard care (chemotherapy) who receive SCT and overall survival (OS) on standard of care in the licensed patient population → **expert opinion required**

NICE health technology evaluations: the manual (2022): “Expert elicitation may use either structured or unstructured methods.” [...] “Structured methods are preferred because they attempt to minimise biases and provide some indication of the uncertainty.”

Medical Research Council (MRC) protocol and principles³

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

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

- 1 Transparency
- 2 Fitness for purpose
- 3 Consistency
- 4 Reflecting uncertainty at the individual level
- 5 Recognising and acting on biases
- 6 Suitability for experts with substantive skills
- 7 Recognising where adaptive skills are required
- 8 Recognising and acting on between-expert variation
- 9 Promoting high performing experts

Challenges when conducting a SEE

- There are several challenges a manufacturer may face when conducting a Structured Expert Elicitation (SEE) exercise to support an HTA submission:

Timeline pressure

Recruitment and availability of suitable clinical experts

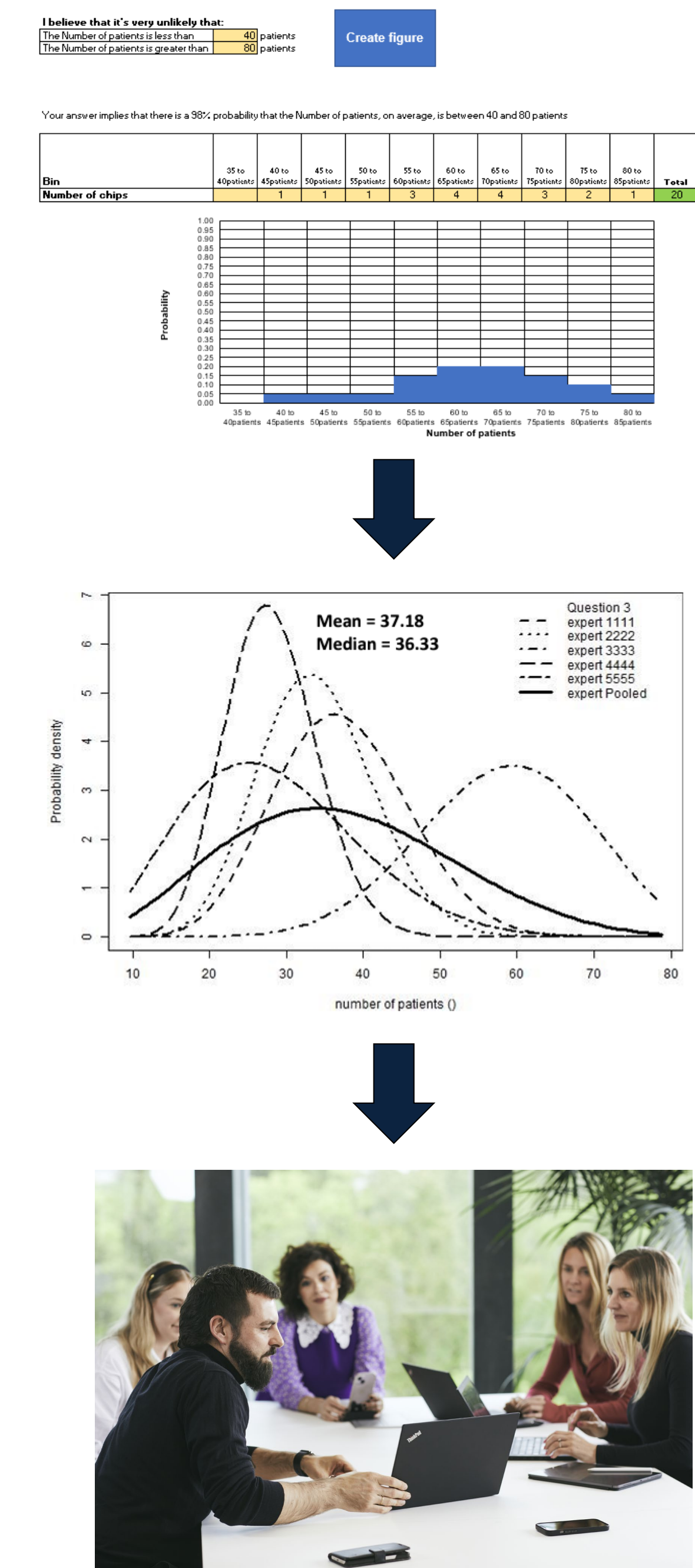
Methods of survey delivery and IT security and data protection constraints

Ensuring adherence to local compliance requirements

Prioritisation of questions to include. Which questions are truly essential?

Parallel development of economic models means SEE questions may have to be developed with imperfect understanding of how outputs will be used

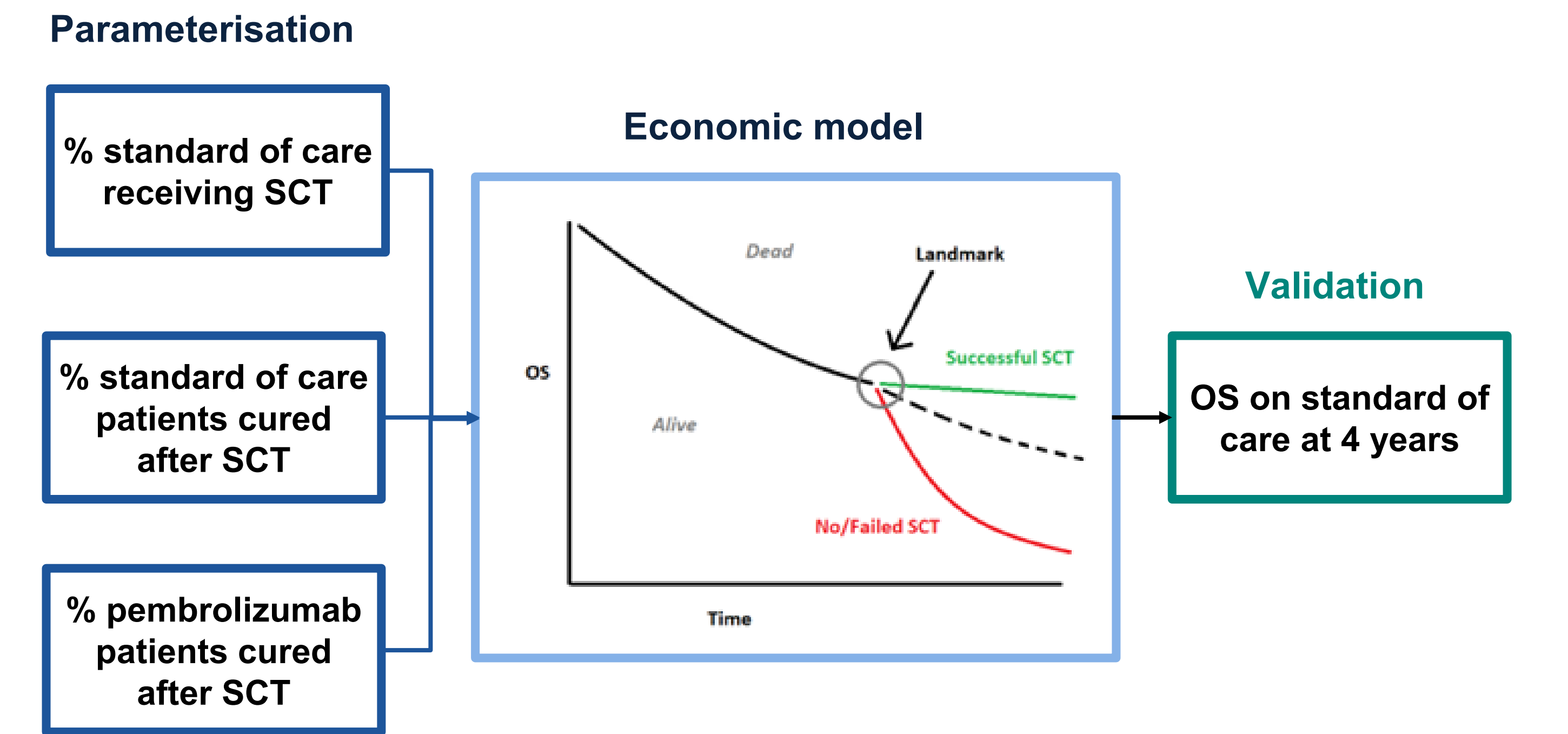
Methods and tools



Methods and tools used	Key learning during implementation	Principles supported
STEER adaptable training slide deck ⁴ and Excel survey tool ⁵ using fixed interval method (chips and bins) to elicit opinion	<ul style="list-style-type: none">Use of publicly available structured expert elicitation resources (STEER) allowed rapid development of high-quality training material and survey questionsUse of Excel tool complicated process of collating responses. R-Shiny application may provide smoother user experience and ease timeline pressureFree-text boxes provided valuable insights on rationales for estimated values	<div>23467</div>
STEER R-Shiny application ⁶ to aggregate responses via linear pooling	<ul style="list-style-type: none">Publicly available STEER R packages allowed rapid pooling and analysis of results – uncertainty in estimates clearly demonstratedAlternative distributions or presentation of results omitting outliers or grouping similar responses could be explored where appropriateCrucial for exploring inter-expert variability in next stage	<div>1238</div>
Group discussion to explore inter-expert variability and gain consensus on preferred estimates	<ul style="list-style-type: none">A consistent framework was developed to explore inter-expert variability and utilised experts' free-text responses to frame discussion.Consistency in approach minimises the risk of bias in group discussions. This framework could be repurposed to use in future SEE exercisesProvides potential to achieve consensus on preferred distributions where appropriate	<div>123458</div>

Parameters elicited and application in NICE appraisal

- Parameters estimated in the SEE were either **used as input parameters** for the economic model or **used to validate model outputs**
- Parameters from pooled distributions were used in probabilistic sensitivity analyses



Conclusions

- Leveraging publicly available Structured Expert Elicitation Resources (STEER), including training decks, survey templates and Excel tools **enabled rapid development of a robust SEE exercise conducted in alignment with the “gold standard” MRC protocol**
- The outputs from the SEE **were successfully used as inputs and to validate an economic model** developed to support an HTA submission to NICE
- Contrasting the committee conclusions on the evidence presented using unstructured and structured techniques (see below) to elicit expert opinion for the same indication indicates that **NICE committees may be more accepting of evidence generated using a structured approach**

Committee conclusions: unstructured expert opinion vs SEE

TA540 – unstructured opinion (pooling of 2 clinician surveys)

“there is **considerable uncertainty** about whether the rates of allogeneic stem cell transplant used in the models are an accurate reflection of transplant rates in UK clinical practice.”

TA967 (CDF exit) – SEE

“the company's assumptions for the 'successful stem cell transplant' health state [based on results of the SEE] **were acceptable.**”