To What Extent Does Seeking Clinical Expert Opinion for Model Inputs Reduce the Cost of Uncertainty? A Conceptual Approach Using Expected Value of Perfect Parameter Information (EVPPI)

N. van Hest, M. Griffiths, N. Hearmon

Costello Medical, London, UK

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OBJECTIVES

- This study aimed to estimate the value (with respect to the cost of decision uncertainty) of seeking clinical expert opinion as a source for inputs in health economic models, using a novel application of expected value of perfect parameter information (EVPPI).

BACKGROUND

- Expert opinion offers a valuable approach for generating model inputs in the absence of, or as an alternative to, empirical data.
- Inputs informed by experts may affect decisions taken under uncertainty, through their influence on incremental cost-effectiveness ratio (ICER) point estimates. Decision-makers may explicitly assess this impact through scenario analysis. However, the value of expert opinion in terms of the cost of decision uncertainty is rarely considered.
- This conceptual study demonstrates a novel application of the expected value of perfect parameter information (EVPPI) to determine the value and implications of expert opinion in altering the cost of decision uncertainty.

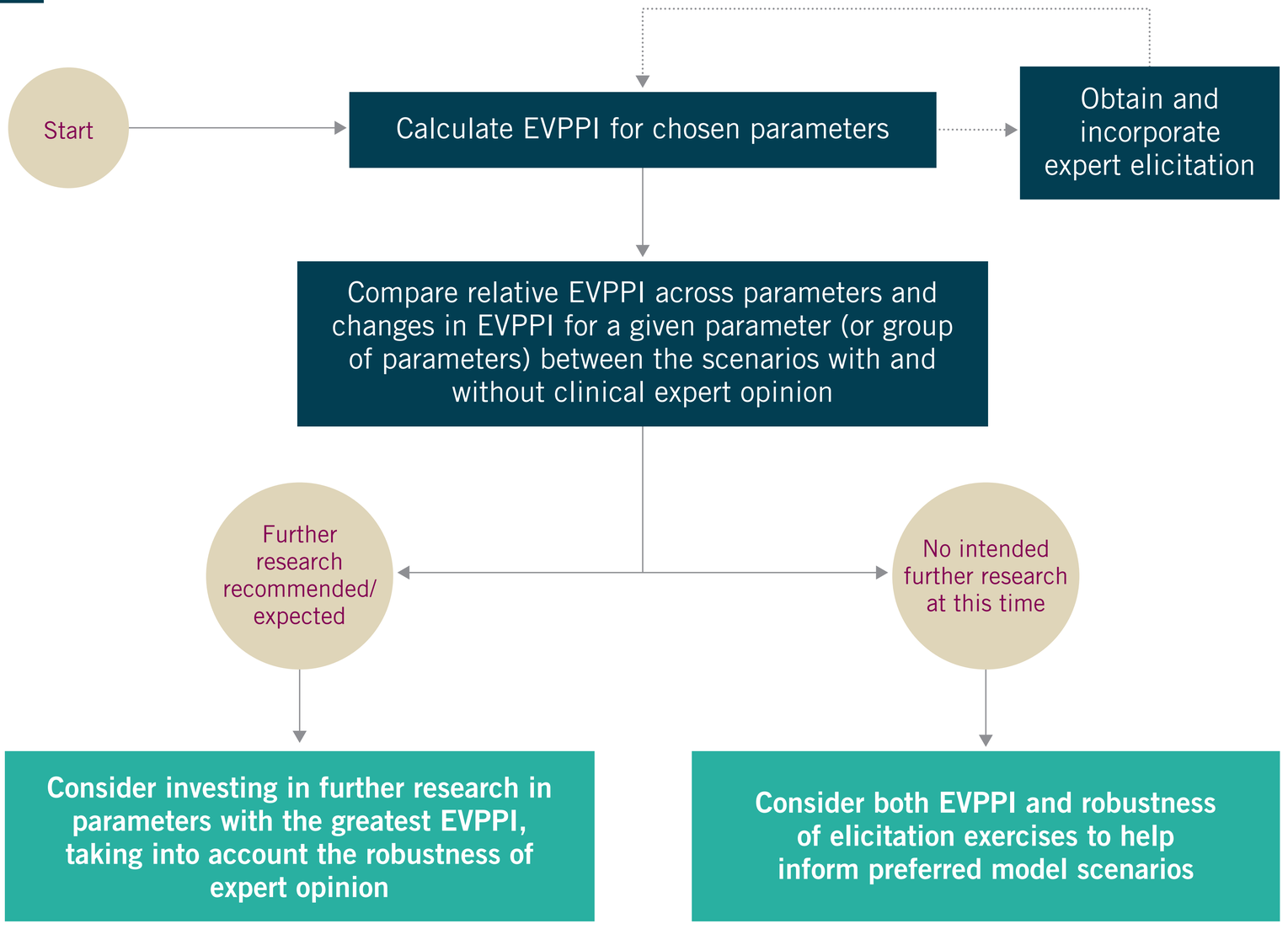
EVPPI

- EVPPI represents the price that a decision-maker would theoretically be willing to pay in order to gain perfect information for a parameter or group of parameters (e.g. by conducting further research).
- It is calculated as the difference between the expected value (e.g. net monetary benefit) of the decision made on the basis of existing evidence for parameters and that made with perfect information.

METHODS

- A partitioned survival model **(see Figure 1)** was constructed based on a recent National Institute for Health and Care Excellence (NICE) single technology appraisal for which expert opinion informed alternative values for several parameters **(see Table 1)**.[1]
- The EVPPI of each parameter supported by clinical opinion was calculated for a scenario with and without expert input, and the difference between these scenarios was determined.

3 Valuing clinical expert opinion with EVPPI



EVPPI: expected value of perfect parameter information.

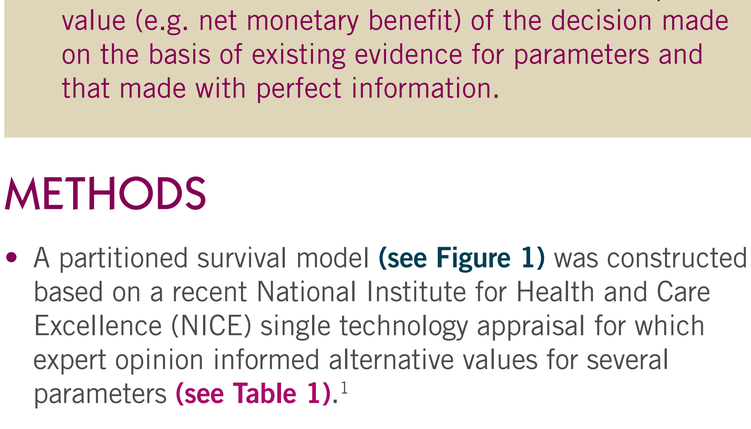
RESULTS

- **Figure 2** indicates the change in EVPPI for each parameter between scenarios, interpretable as the extent to which utilisation of expert opinion across all investigated parameters has altered each parameter's contribution to the cost of decision uncertainty.
- Expert opinion had a mixed effect on the cost of decision uncertainty; the EVPPI associated with the intervention's overall survival (OS) curve was reduced by £3,681, however the EVPPI of the comparator's OS curve increased by £11,954. The EVPPI of other parameters, which were previously zero, increased to between £8–925 with expert opinion.

APPLICATIONS

- This approach demonstrates a novel application of EVPPI, whereby the difference in the relative contribution of key parameters to the cost of decision uncertainty when seeking or not seeking clinical expert opinion is examined. **Figure 3** summarises both the process and potential applications of this approach.
- This methodology may provide valuable additional information to the decision-maker alongside more common considerations of the impact of expert-elicited inputs on cost-effectiveness point estimates. It illustrates that the adoption of clinical expert opinion can considerably change both the absolute EVPPI of parameters, and the EVPPI values relative to one another.
- When faced with multiple, equally robust model scenarios from various expert elicitation approaches, this EVPPI methodology could provide useful further information to the decision-maker when selecting and justifying which scenarios to pursue.
- Furthermore, it reiterates the importance of evaluating the trust placed in expert opinion, as this expert opinion can influence not only the decision (i.e. by altering the ICER, and hence likelihood of being evaluated as cost-effective), but also change which parameters are identified as priorities for future research. Given the increasing trend towards managed access agreements with further data collection requirements, and hence the potential for a shift towards increasing utilisation of EVPPI to direct research priorities, the approach outlined here could be an important step in checking the extent to which expert opinion is influencing EVPPI-driven decisions over such research.
- Likewise, if decision-makers have greater confidence in the clinical expert opinion (e.g. if it has been gathered through rigorous methods, such as a Delphi panel, as opposed to ad-hoc validation), standard applications of EVPPI can be used with greater confidence at this stage of research:
  - As a useful tool in avoiding performing costly research on parameters with low EVPPI (e.g. OS extrapolation of Treatment A);
  - To provide supporting evidence on where additional research would be better placed (e.g. OS extrapolation of Treatment B).

1 Partitioned survival model structure



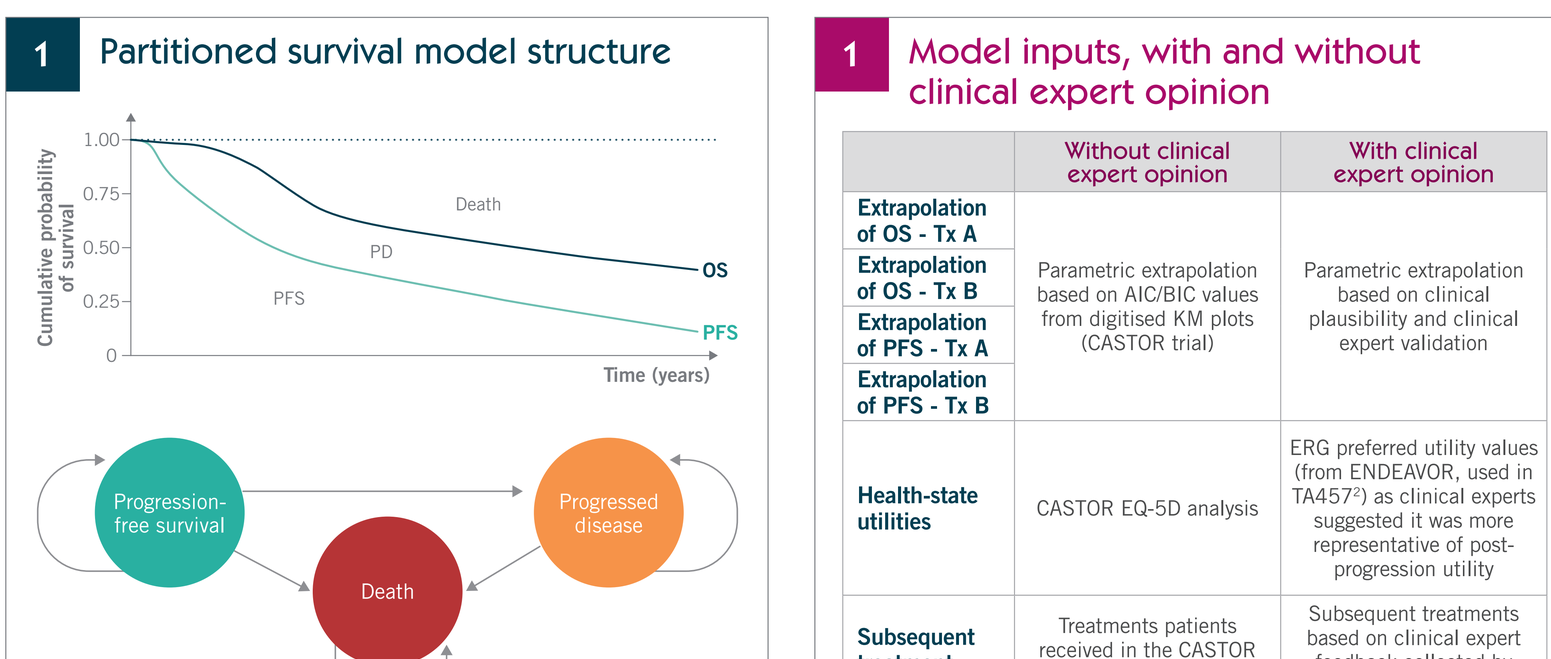
OS: overall survival; PFS: progression-free survival; PD: progressed disease.

1 Model inputs, with and without clinical expert opinion

	Without clinical expert opinion	With clinical expert opinion
Extrapolation of OS - Tx A	Parametric extrapolation based on AIC/BIC values from digitised KM plots (CASTOR trial)	Parametric extrapolation based on clinical plausibility and clinical expert validation
Extrapolation of OS - Tx B		
Extrapolation of PFS - Tx A		
Extrapolation of PFS - Tx B		
Health-state utilities	CASTOR EQ-5D analysis	ERG preferred utility values (from ENDEAVOR, used in TA457[2]) as clinical experts suggested it was more representative of post-progression utility
Subsequent treatment	Treatments patients received in the CASTOR trial	Subsequent treatments based on clinical expert feedback collected by the ERG

AIC: Akaike information criterion; BIC: Bayesian information criterion; ERG: evidence review group; KM: Kaplan-Meier; OS: overall survival; PFS: progression-free survival; Tx: treatment.

2 EVPPI of parameters, with and without clinical expert opinion



Based on 1,000 probabilistic sensitivity analysis iterations and 100 EVPPI simulations (results stable at this number of simulations). EVPPI is presented per patient. EVPPI: expected value of perfect parameter information; OS: overall survival; PFS: progression-free survival; Tx: treatment.

References

1. National Institute for Health and Care Excellence 2019. Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma (TA573). Available at: https://www.nice.org.uk/guidance/ta573 [Last accessed 10 September 2019];
2. National Institute for Health and Care Excellence 2019. Carfilzomib for previously treated multiple myeloma (TA457). Available at: https://www.nice.org.uk/guidance/ta457 [Last accessed 3 October 2019].

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