Case for Clear Communication and Justification of Survival Extrapolation Methodology: A Review of NICE Submissions in Oncology

Noor-E Zannat.[1], Alana M. Stilla.[1], Michael J. Zoratti[1,2], David Wennersbusch[1], Sean Harrigan[1], Leah Yang[1], Eve H. Limbrick-Oldfield[1], Steve Kanters[1]

[1]RainCity Analytics, Vancouver, BC, Canada

[2]Department of Health Research Methods, Evidence, and Impact; McMaster University, Hamilton, ON, Canada

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Background

- Survival extrapolation is required in health economic evaluations in order to assess the long-term costs and benefits of interventions beyond clinical trial periods.[1]
- Multiple approaches to extrapolation are used in practice, with selection guided by data characteristics to find the best fit.
- However, while the choice of extrapolation method can have important impacts on analyses, the methods used to justify the choice of extrapolation techniques are often poorly described in technology appraisals.[1]

Objective

- The purpose of this review was to describe how survival models are chosen in National Institute for Health and Care Excellence (NICE) technology appraisals in oncology and the impact these choices have on the findings of cost-effectiveness analyses.

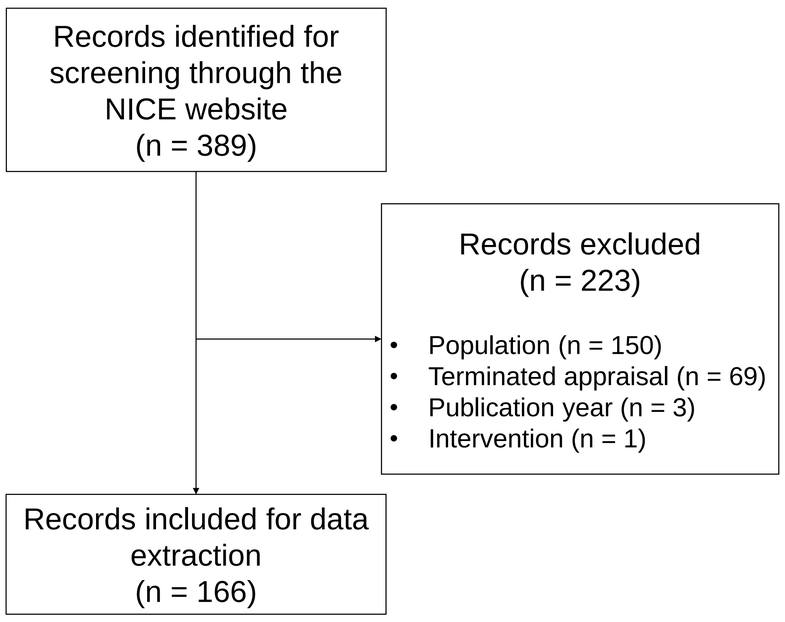
Methods

- A targeted literature search was conducted to identify NICE technology appraisals for pharmacological interventions in oncology published between 01 January 2018 and 16 June 2023.
- Descriptive statistics were used to characterize the type of survival models used in extrapolation in base-case analyses, the methods used to justify the base-case extrapolation approach, and the impact of alternative survival models on cost-effectiveness results in scenario analyses (as presented in the appraisal).

Results

- The search yielded 389 records, of which 166 records were eligible for inclusion (**Figure 1**).

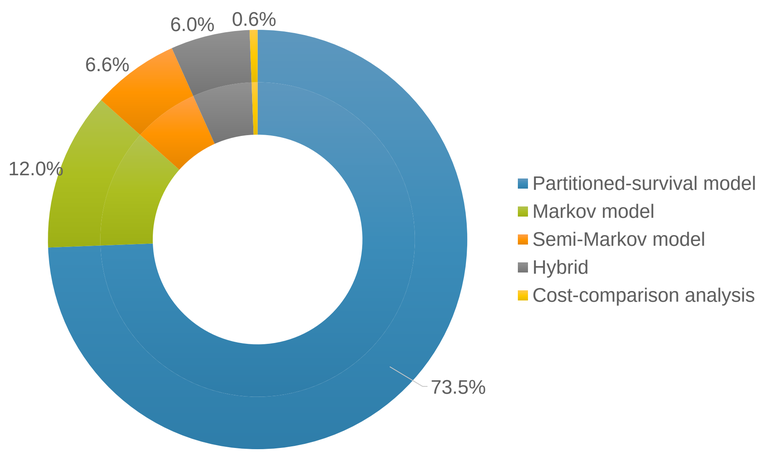
Figure 1. PRISMA flow diagram



Overview of trends

- Non-small-cell lung cancer (19%), breast cancer (12%), and lymphoma (12%) were the most commonly evaluated indications.
- Partitioned-survival models (73.5%) were most frequently utilized in economic analyses, while Markov models (12%), semi-Markov (7%), and hybrid models (6%) were used less frequently (**Figure 2**).
- The time horizons studied varied from 3 years to lifetime.

Figure 2. Overview of model structures



Survival extrapolations

- Overall survival (84%) and progression-free survival (77%) were the most commonly extrapolated survival outcomes, followed by time to treatment discontinuation (25%) and time on treatment (14.5%).
- The choice of survival models in base-case analyses varied (**Figure 3**), though standard parametric models were utilized for survival extrapolation in most of the appraisals.
- In nearly all appraisals, model suitability was evaluated through a combination of goodness-of-fit statistics (98%), visual inspection (94%), and clinical validity (82%), whereas log-cumulative hazard plots (57%) and external data (28%), such as separate clinical trials in a similar patient group, were considered less frequently (**Figure 4**).

Figure 3. Extrapolation techniques

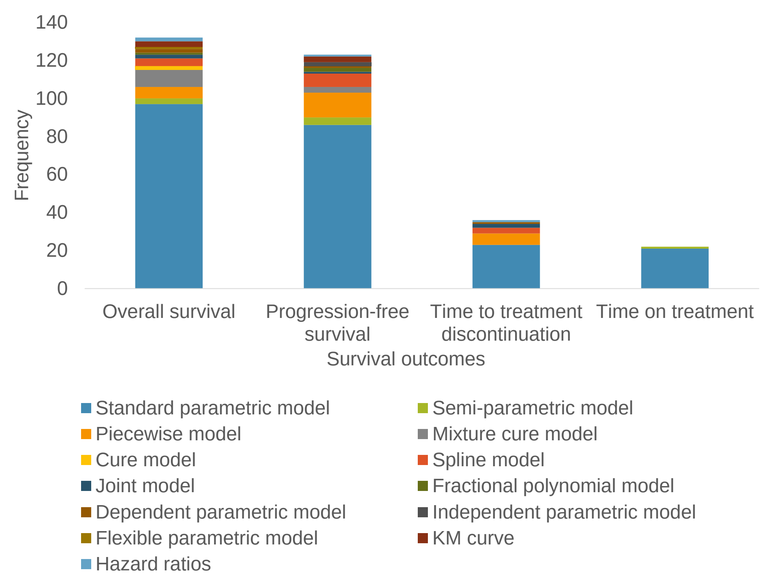
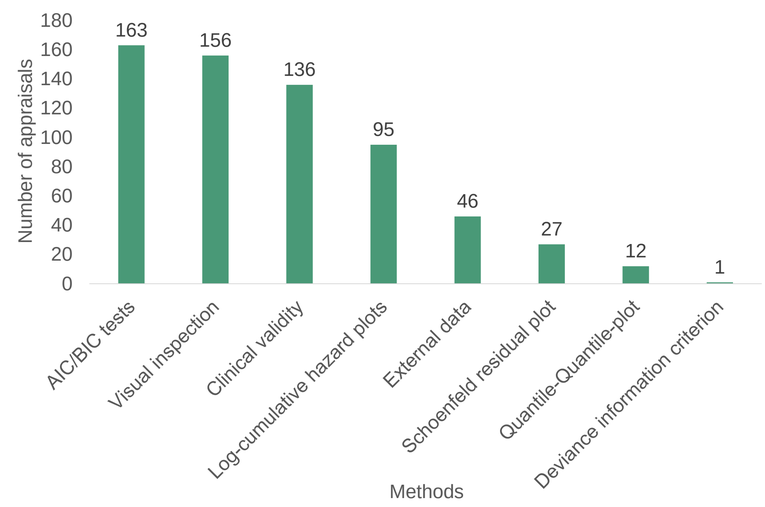


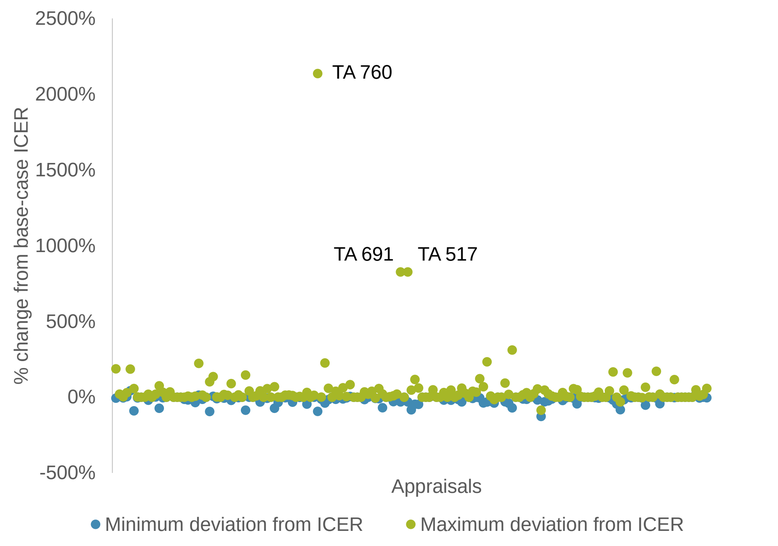
Figure 4. Methods cited in the justification of survival model selection



Scenario analysis results

- Alternative survival models were utilized to explore uncertainty in most appraisals (93%), though the results of cost-effectiveness analyses in scenario analyses were redacted in 30/166 (18%) evaluations.
- When scenario analyses were conducted to evaluate the impact of different extrapolation methods, the incremental cost-effectiveness ratio (ICER) varied considerably from the base-case value, ranging from -127% to 2,136% (**Figure 5)**, highlighting the methodological significance of this decision.
- The use of alternative extrapolation methods (Gompertz vs Exponential distribution in the base-case; Exponential vs Spline models in the base-case) for overall survival produced increases from the base-case ICERs which exceeded 800%.[2-4]

Figure 5. Percentage change from base-case ICER in scenario analysis



Conclusions

- This targeted review revealed the important impact that survival extrapolation methods have on the results of cost-effectiveness analyses.
- In defending their choice of survival extrapolation methodology, investigators commonly provided at least three of the justification metrics recommended by the NICE Decision Support Unit Technical Support Document 14.[1]
- To promote a systematic and transparent approach to survival analysis, particularly in the context of technology appraisals with economic evaluations, clear justifications should be provided for the selection of survival models and these assumptions should be thoroughly evaluated for goodness-of-fit and considerations of clinical plausibility.

References

[1]NICE Decision Support Unit Technical Support Document 14: Survival analysis for economic evaluations alongside clinical trials – extrapolation with patient-level data. 2011.
[2]NICE Single Technology Appraisal (TA 760). October 2020. https://www.nice.org.uk/guidance/ta760/documents/committee-papers. Accessed October 19, 2023.
[3]NICE Single Technology Appraisal (TA 691). February 2018. https://www.nice.org.uk/guidance/ta691/documents/committee-papers-2. Accessed October 19, 2023.
[4]NICE Single Technology Appraisal (TA 517). February 2018. https://www.nice.org.uk/guidance/ta517/documents/committee-papers. Accessed October 19, 2023.

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Contact: nzannat@raincity-analytics.com

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