MSR140

Current trends in survival extrapolation methods: A review of NICE health technology appraisals for oncology drugs

Luis Fernandes[1], Damilola Victoria Tomori[1], Chih-Yuan Cheng[1], Nasuh C. Buyukkaramikli[1], Joanne Holden[2], Feng Pan[3]

[1] Janssen Pharmaceutica N.V., Beerse, Belgium
[2] Janssen-Cilag Limited, High Wycombe, UK
[3] Janssen Global Services LLC, Raritan, NJ, USA

BACKGROUND

- Economic evaluation of novel oncology drugs generally requires the extrapolation of overall survival (OS) data from registrational trials beyond their duration to model lifetime health benefits
- Although the National Institute for Health and Care Excellence (NICE) Decision Support Unit (DSU) provided recommendations on survival extrapolation for NICE technology appraisals (TAs) in the Technical Support Documents (TSD) 14 and 21, different extrapolation approaches are available which may produce distinct estimates of health benefits and thus of incremental cost-effectiveness ratios (ICERs)[1,2]
- No review on trends of OS extrapolation methods used in NICE oncology TAs has been conducted after publication of the TSD 21

OBJECTIVES

This study surveyed oncology technology appraisals appraised to NICE and aimed to

- Summarize the OS extrapolation methods used by companies in NICE oncology submissions for interventions
- Understand Evidence Review Groups' (ERGs) critiques and Appraisal Committees' (ACs) preferences for such extrapolation methods

METHODS

- We reviewed NICE Single Technology Appraisals (STAs) of oncology products completed between November 2019 and December 2022 and in which partitioned survival models (PSM) with OS extrapolation were used in company submissions
- Information on the extrapolation methods and corresponding suitability assessments as recommended by NICE in TSD 14 and 21 were extracted for each STA, along with ERGs' critiques and Committees' preferences
  - Methods recommended in TSD 14 are described as "Standard parametric methods"
- Methods recommended in TSD 21 are described as "Flexible methods"
- The data were extracted by three reviewers. Where there were discrepancies in opinion, consensus was reached through discussion

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FIGURE 1. Cases of PSMs with OS extrapolation in STAs

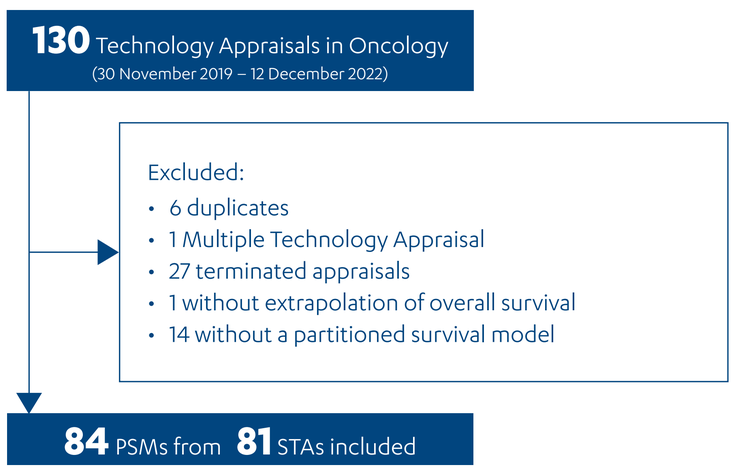


FIGURE 2. Extrapolation methods considered in initial company submission

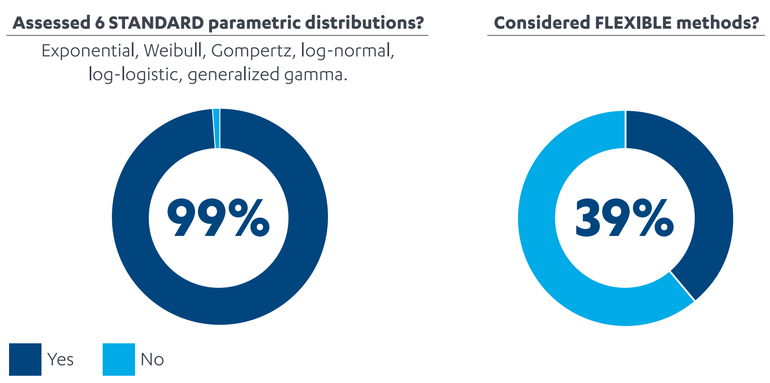
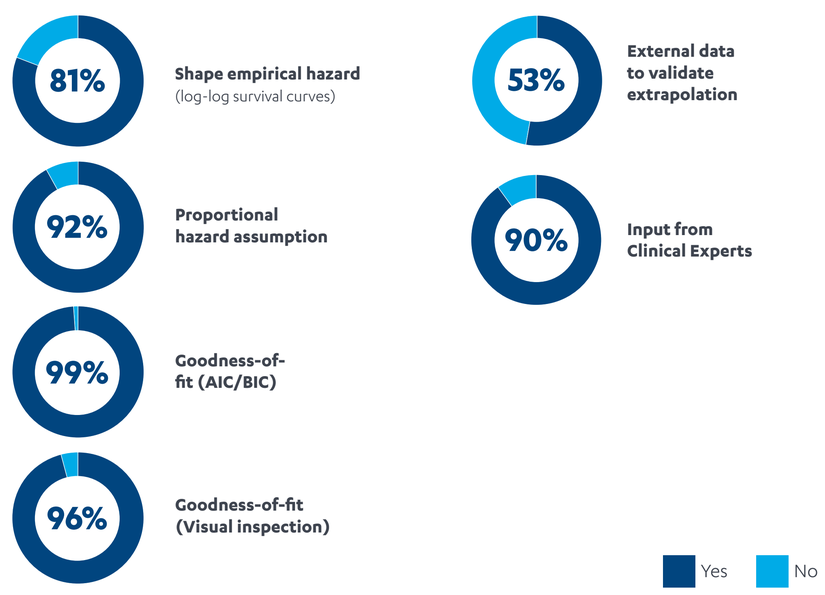


FIGURE 3. Companies are generally compliant with best practices stated in NICE TSD 14



RESULTS

- 84 PSMs from 81 STAs were included in the review (Figure 1)
- Most cases considered all common standard parametric distributions (99%, 83/84), and 39% (33/84) further assessed flexible methods (Figure 2)
- The suitability of extrapolation methods was verified using relative statistical goodness-of-fit (99%, 83/84), visual inspection (96%, 81/84), tests of proportionality of the hazard (92%, 77/84), clinical expert validation (90%, 75/84), shape of the hazard (81%, 68/84), and comparison with external data (53%, 45/84) (Figure 3)
- Weibull (18/67) and log-logistic (18/67) were the most frequently selected base-case standard parametric distributions (67/84) by companies, whereas flexible methods were preferred in 20% (17/84) of the cases, particularly piecewise models (7/17) (Figure 4)
- ERGs preferred Weibull (15/59) and exponential (12/59) standard parametric distributions (59/84) for the base-case, and flexible methods in 23 out of 84 PSMs (Figure 5)
- In circumstances where ERGs and companies (45/84) differed on the choice of base-case extrapolation approach, Committees preferred ERGs' base-case assumptions (25/45) more often than companies' (12/45), or were indifferent between the two (8/45) (Figure 6)

CONCLUSION

- Most company submissions followed NICE TSDs 14 and 21 in their extrapolation approach
- Standard parametric methods were widely used, and flexible methods were typically used when standard approaches provided poor fitting to observed survival estimates
- ERGs and companies differed on the base-case approach in over half of the cases. Committees' preferences for ERG's base-case approach in such cases likely led to different cost-effectiveness estimates

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DISCLOSURES:
The study is funded by Janssen Pharmaceutica NV. CYC, DVT, LF, NCB, JH, and FP are employees of Janssen Pharmaceuticals and may hold stock in Johnson & Johnson

FIGURE 4. Extrapolation methods used as base case in initial company submission

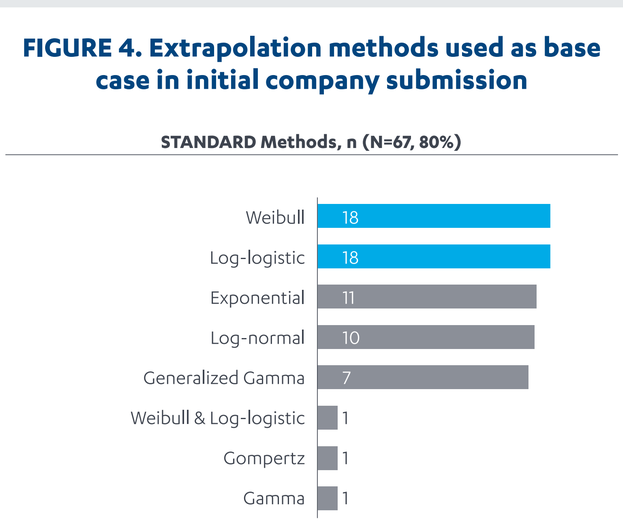
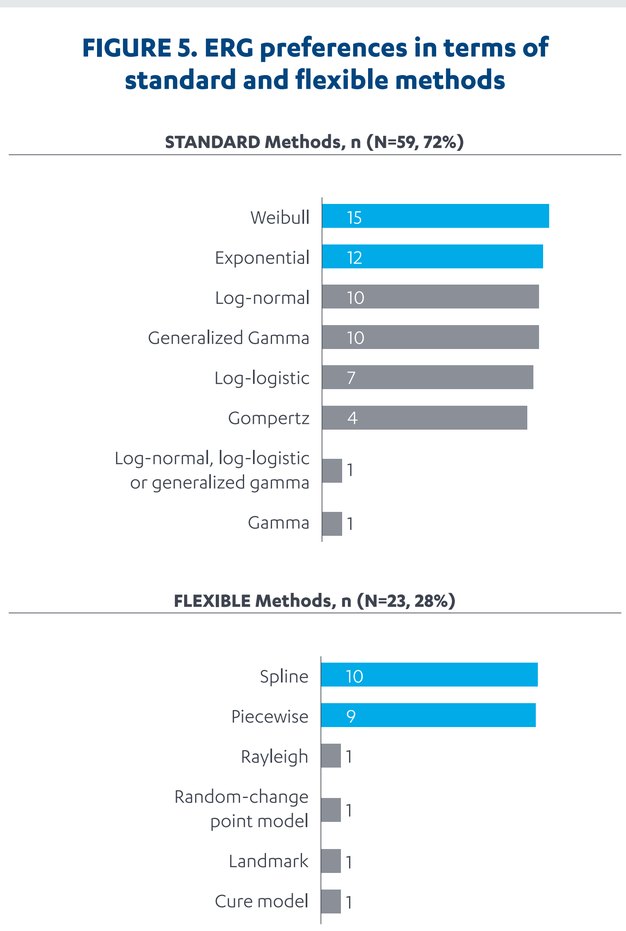
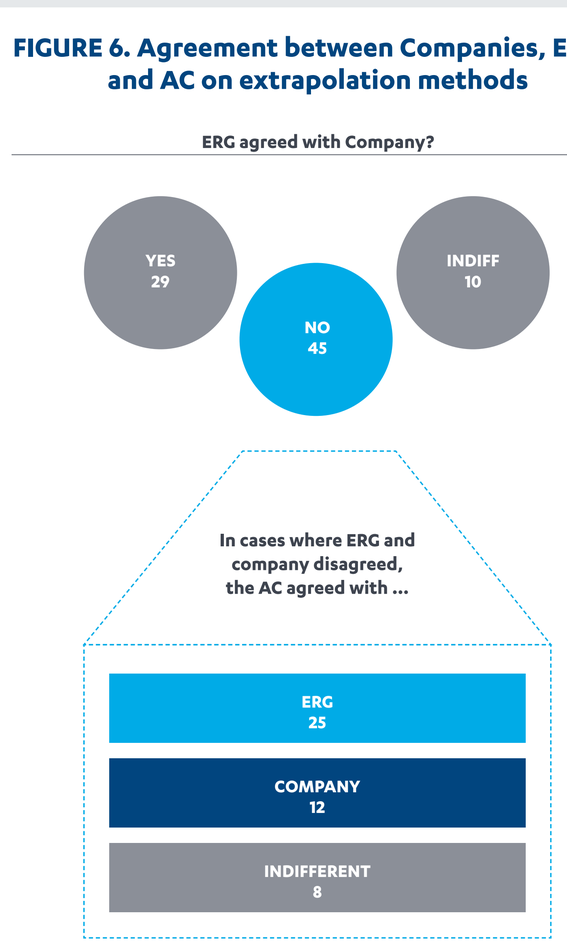


FIGURE 5. ERG preferences in terms of standard and flexible methods



Notes: In 2 cases, the ERG did not expressed its preferred approach. ERG, Evidence Review Group

FIGURE 6. Agreement between Companies, ERGs, and AC on extrapolation methods



Notes: AC, Appraisal Committees; ERG, Evidence Review Group

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[1] Latimer N. NICE DSU Technical Support Document 14: Survival Analysis for Economic Evaluations Alongside Clinical Trials – Extrapolation With Patient-Level Data, Version 2: National Institute for Health and Care Excellence, Decision Support Unit, 2013.;
[2] Rutherford MJ, Lambert PC, Sweeting MJ. et al. NICE DSU Technical Support Document 21: Flexible Methods for Survival Analysis: National Institute for Health and Care Excellence, Decision Support Unit, 2020.