A Review of survival modeling approaches adopted in NICE technology appraisals (TAs) in Non-Small Cell Lung Cancer (NSCLC)

Shubhram Pandey<sup>1</sup>, Barinder Singh<sup>2</sup>, Akanksha Sharma<sup>1</sup>

<sup>1</sup>Pharmacoevidence, SAS Nagar, Mohali, PB, India, <sup>2</sup>Pharmacoevidence, London, UK



HTA159



### Conclusion

Survival analysis in NICE Technology Appraisals (TAs) needs improvement, with inconsistent model selection and insufficient validation. The extrapolation approach used in submissions is still being determined and cannot accurately capture the complex hazard function. The use of flexible survival modeling techniques with an adjustment of background mortality is recommended by NICE.

## -Background

- Economic evaluations in healthcare involve comparing the costs and health outcomes of different interventions, often using quality-adjusted life-years, which depend on time-to-event data like survival in oncology.
- Trials are often shorter than the desired evaluation timeframe for practical reasons, necessitating the extrapolation of survival data to bridge the gap and avoid approval delays.
- NICE in England evaluates healthcare technology submissions, including clinical and cost-effectiveness evidence from companies. An independent group reviews this, and NICE's Appraisal Committee delivers the final determination, addressing any concerns and reporting the outcome.
- NICE's Decision Support Unit (DSU) released Technical Support Documents 14 and 21 to improve the consistency of survival analysis in Technology Appraisals (TAs). The document provides guidance on selecting survival modeling approaches, but it's unclear if these recommendations are consistently applied in current NICE submissions.<sup>1,2</sup>

# Objective-

This research examined the extrapolation modeling methods in NICE's Technology Appraisals (TAs) for NSCLC therapies post-2016.

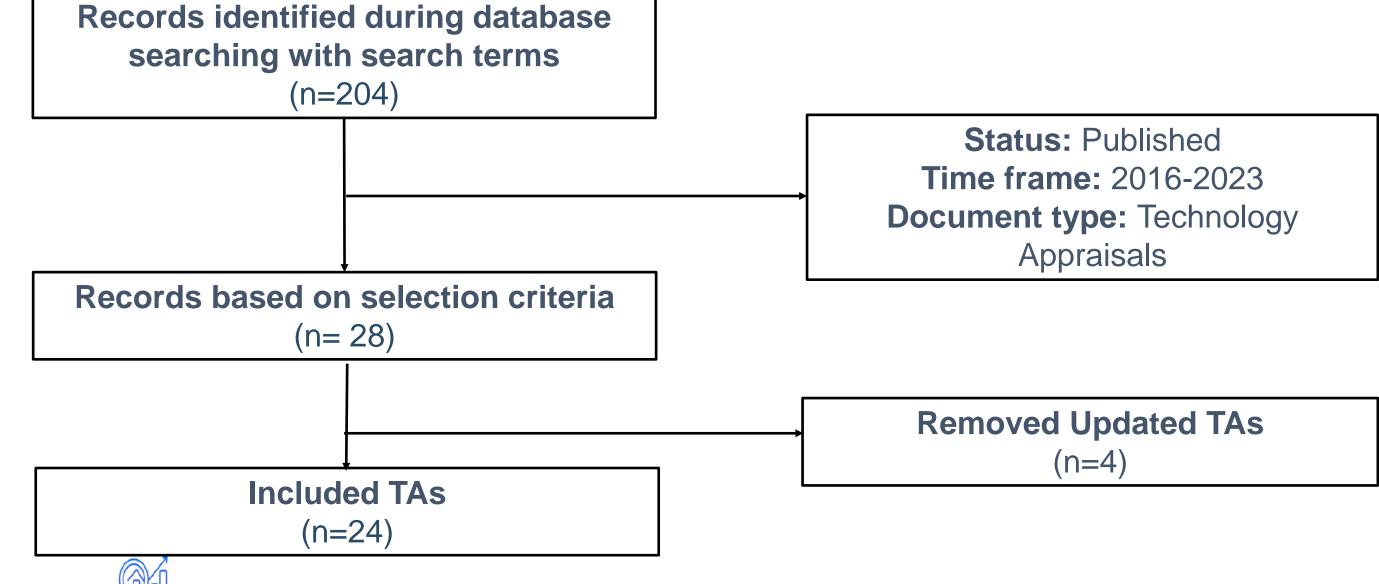
# \_Methodology

- The methods used for the review followed similar reviews of NICE TAs.<sup>2,3</sup>
- "NSCLC" or "non-small cell lung cancer," were used as search terms on the NICE website, with the status of "published," and the published year of 2016-2023.
- The initial TA and the updated ones were counted as one TA.
- A data extraction form was created by the review team to ensure that the necessary information was extracted to meet the aims and objectives of the review.
- The published documents were reviewed and summarized, focusing on the survival modeling approach, fitted statistical distributions, long-term treatment effect, and NICE's final recommendation on the extrapolation approach.

Table 1: List of Technology Appraisals included

NICE TA	Intervention	Type of model	OS extrapolation	PFS extrapolation	Cure fraction assumption	Waning
TA403	Ramucirumab	Parametric	Log-logistic	Generalised gamma	No	Assumption No
TA411	Necitumumab	Parametric	Log-logistic	Log-logistic	No	No
TA406	Crizotinib	Parametric	Weibull	Generalised gamma	No	No
1/1-100	Pemetrexed for the	raiametric	VVCIDUII	Generalised gamma	IVO	IVO
TA190	maintenance	Parametric	Exponential	_	No	No
TA529	Crizotinib	Parametric	Exponential	Log-normal	No	No
TA531	Pembrolizumab	Parametric	Exponential	Exponential	No	No
TA584	Atezolizumab	Parametric	Weibull	Weibull	No	No
TA628	Lorlatinib	Parametric	Exponential	Exponential	No	No
TA638	Atezolizumab	Parametric	Log-logistic	Log-logistic	No	No
TA643	Entrectinib	Parametric	Exponential	Exponential	No	No
1710-13	Littleetiiiib	rarametric	Ехропении	spline 1-knot	110	110
TA655	Nivolumab	Parametric and splines	spline hazard 2-knot	normal	No	Yes
	Pembrolizumab with	r arametric and spinies	Spinie nazara z knot	Homai	110	163
TA683	pemetrexed	Parametric	Log-normal	Weibull	No	No
TA705	Atezolizumab	Parametric	Weibull	Generalised gamma	No	No
	710000110011100	rararre	Trona an	spline 1-knot	110	
TA713	Nivolumab	Parametric and splines	Log-normal	normal	No	No
TA724	Nivolumab	Parametric and splines	spline normal 2 knots	spline odds 2 knots	Yes	No
TA760	Selpercatinib	Parametric and splines	spline 1-knot normal	Gompertz	No	No
	Pembrolizumab with	,		2 3 3 1 1 p 2 3 2 2		
TA770	pemetrexed	Parametric	Log-logistic	Log-normal	No	Yes
TA781	Sotorasib	Parametric	Log-normal	Log-normal	No	Yes
TA789	Tepotinib	Parametric	Log-logistic	Log-logistic	No	No
TA802	Cemiplimab	Parametric	Log-normal	Log-normal	No	No
TA812	Pralsetinib	Parametric	Exponential	Generalised gamma	No	No
TA818	Nivolumab	Parametric	Log-logistic	Generalised gamma	No	Yes
TA823	Atezolizumab	Parametric	0 1 2 0 1 2 1 2	Log-logistic	Yes	No
TA855	Mobocertinib	Parametric	Gen-gamma	Exponential	No	Yes

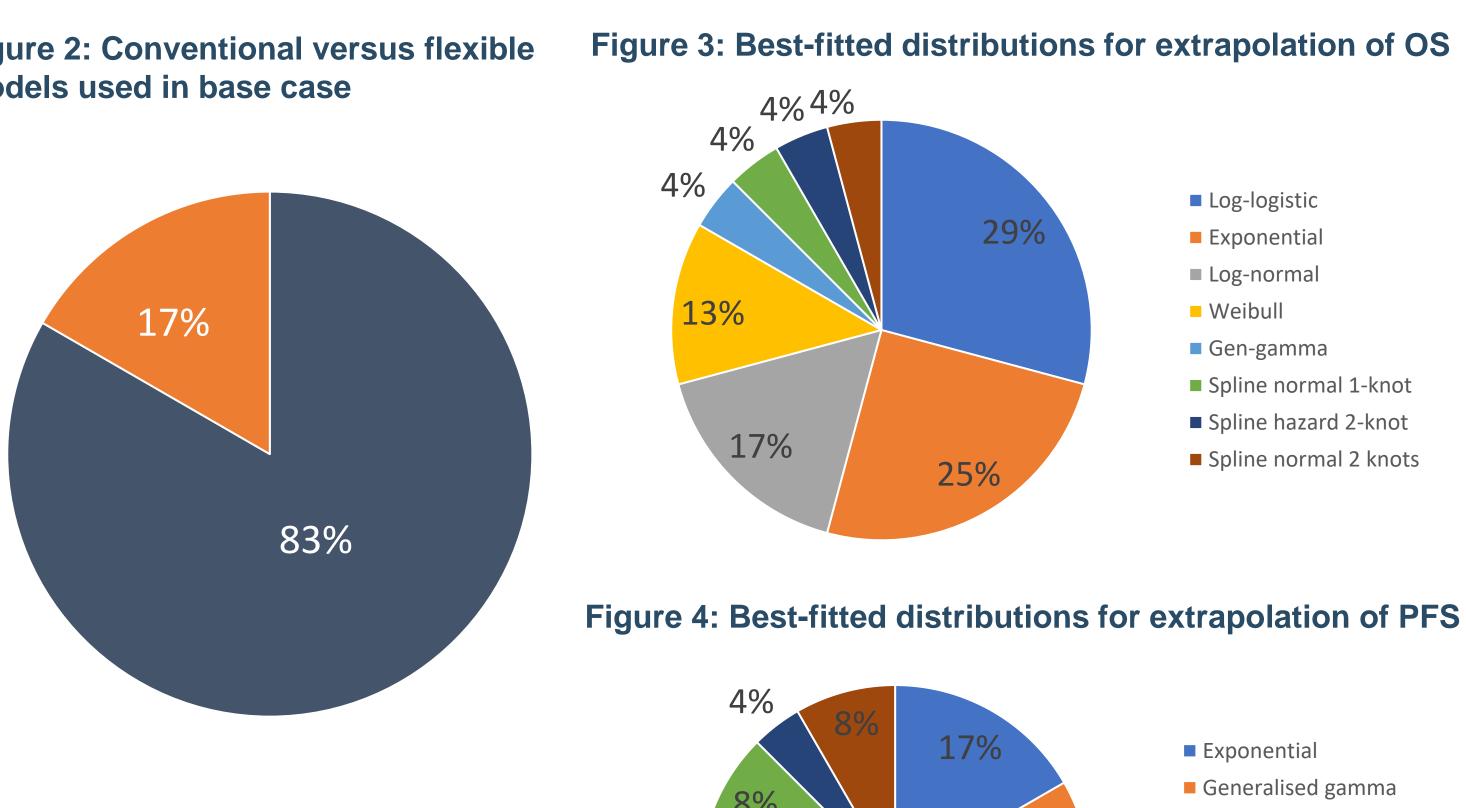
Figure 1: Flow of TAs through the process



# Results

- Atezolizumab (N=5) and Nivolumab (N=4) were the most evaluated therapies in 24 TAs.
- The conventional parametric modeling approach was used in 20 TAs for OS and PFS extrapolation, while four TAs employed a flexible parametric modeling approach (spline-based).
- For OS, Exponential (N=6) and log-logistic (N=7) were best-fit distributions, and for PFS, Generalized gamma (N=5) and Log-logistic (N=4) were preferred.
- "Waning" (N=5) and "Cure" (N=3, in more recent TAs) assumptions were explored for long-term treatment effects in the base case.
- The extrapolation methods and fitted distributions in most TAs were frequently criticized by ERGs but used for decision-making.

Figure 2: Conventional versus flexible models used in base case



■ Conventional parametric 17% ■ Flexible models

Gompertz Log-logistic Log-normal ■ Spline normal 1-knot ■ Spline odds 2 knots

■ Weibull

## \_References

1. Latimer N. NICE DSU Technical Support Document 14: undertaking survival analysis for economic evaluations alongside clinical trials—extrapolation with patient-level data. 2011. Available

https://www.ncbi.nlm.nih.gov/books/NBK395885/pdf/Bookshelf\_NBK395885.pdf. 2. Rutherford M. NICE DSU Technical Support Document 21: Flexible Methods for

- Survival Analysis. 2020. Available https://www.sheffield.ac.uk/media/34188/download?attachment
- 3. Kearns B, Ara R, Wailoo A, et al. Good practice guidelines for the use of statistical regression models in economic evaluations. Pharmacoeconomics. 2013;31(8):643-52.



SP, BS and AS the authors, declare that they have no conflict of interest

