Poster #HTA71

The Acceptance of Using External Data to Inform Survival Extrapolations for Oncology Health Technology Assessments by NICE

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Background

- Pivotal trial data in oncology is often immature at the time of health technology assessments.[1] The National Institute for Health Care and Excellence (NICE) technical support document 21 (TSD21) (2020) and real-world evidence (RWE) framework (2022) provide guidance and support for the use of external data for survival extrapolations to decrease uncertainty around long-term survival estimations.[2]
- This study provides an update of a previous review on the use of external data for survival extrapolation in oncology NICE technology appraisals (TAs) in the past year, comparing it with previous years.[3]

Objective

To evaluate the frequency, methods, and acceptance of using external data for survival extrapolation in oncology NICE TAs since the release of TSD21, in accordance with NICE's RWE framework, and to compare these trends with previous years.

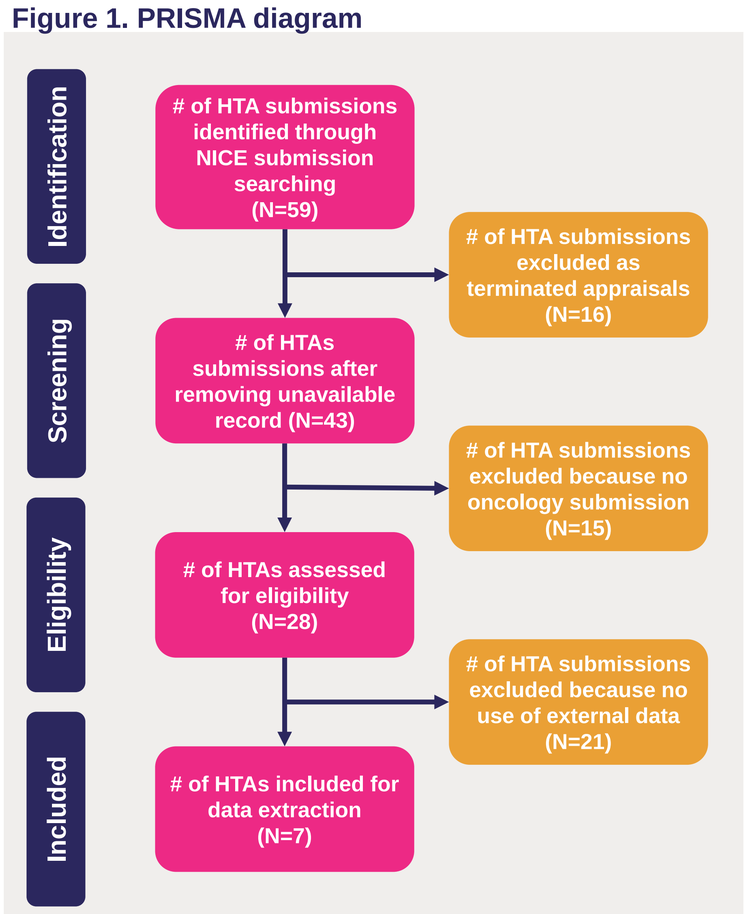
Methods

- A review update was conducted on all oncology NICE TAs that were published between May 2023-May 2024.
- Screening and data extraction were conducted by two independent reviewers. Any outstanding issues were resolved with the help of a third independent assessor.
- Eligible TAs were subjected to a full-text review if they were indicated for oncology and utilized external data for survival extrapolation. Terminated TAs were excluded.
- The following items were extracted:
  - indication
  - intervention
  - comparator
  - extrapolation
  - method
  - type of external data
  - NICE recommendation, and critique
- The findings were then compared to those of the original review (2001-mid 2023).

Results

- **Figure 1** presents an overview of the review process. A total of 59 HTA submissions were identified as part of the review update (2023-2024).
- Seven out of 28 oncology TAs met the inclusion criteria.

Figure 1. PRISMA diagram

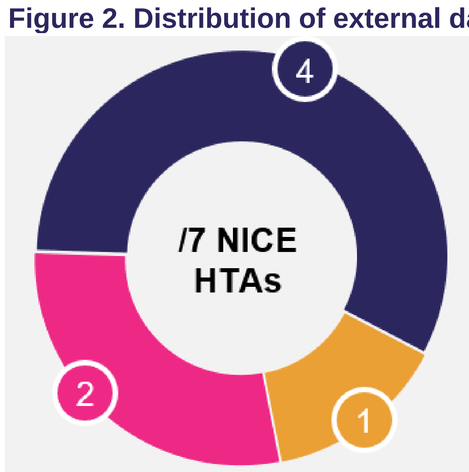


Abbreviations: HTA, Health Technology Assessment; NICE, National Institute for Health Care and Excellence

- Two, five, three, and three TAs used registry data, external clinical trial data, general population mortality, and key opinion lead opinion to inform survival extrapolations, respectively (**Figure 2**).
- Clinical trial data was used most frequently (5/7), primarily to inform one or more health state transition probabilities or to support survival extrapolations for an external control arm (**Table 1**).

Results (continued)

Figure 2. Distribution of external data types used in NICE TAs



More than 70% of the submissions used multiple types of external data.

28.6%	57.1%	14.3%
One type of external data	Two types of external data	Three types of external data

Registry data	2/7	28.6%
Clinical trial	5/7	71.4%
General population mortality	3/7	42.9%
KOL input	3/7	42.9%

Abbreviations: HTA, Health Technology Assessment; KOL, key opinion leader; NICE, National Institute for Health Care and Excellence

Table 1. TA's using external data in 2023-2024

TA	Technology	Indication	Pivotal trial	NICE Assessment	Type of external data used	Key critiques
TA977[4]	Dabrafenib with trametinib	Glioma	TADPOLE	Recommended	Registry data, Clinical trials	- SickKids institutional PLGG database used for long-term extrapolations for PFS - SIOP-LGG 2004 cohort study and ACNS0423 trial used for multiple TPs and rate of malignant transformation - EAG recommended more complex modeling, like two-knot normal splines, for ACNS0423 trial extrapolation to better reflect observed outcomes
TA975[5]	Tisagen-lecleucel	B-cell acute lymphoblastic leukaemia	ELIANA	Recommended	KOL input, Clinical trials	- Company used only ELIANA data, while the EAG recommended pooling with ENSIGN and B2101J for a more representative survival estimate - Arguing that relying on clinical experts' expectations for long-term PFS and OS might not be optimal - Company updated base-case with pooled dataset (using ELIANA, ENSIGN and B2101J trials)
TA967[6]	Pembrolizumab	Hodgkin lymphoma	KEYNOTE-087	Recommended	Registry data, KOL input, General population mortality, *UK life tables to model cure*	- Registry data: EAG highlighted the observational nature and biases in SACT, noting it reflects real-world practice but lacks randomized trial rigor - KOL input: EAG noted that SEE helps estimate parameters without direct data, but it is subjective and adds uncertainty - UK Life Tables for cure state: EAG found use overly optimistic and arbitrary, exploring a standard mortality ratio of 1.5, as actual survival might be lower than general population for this group
TA928[7]	Cabozantinib	Thyroid cancer	COSMIC-311	Not recommended	KOL input, *for blended survival analysis*	- EAG recognizes that blended survival analysis could address OS extrapolation issues found in standard models - However, EAG and committee noted the blended survival analysis poorly fit COSMIC-311 data - Committee criticized the lack of transparency around the blended survival analysis
TA909[8]	Lorlatinib	Non-small-cell lung cancer	CROWN	Not recommended	Clinical trials	- EAG accepted the use of PROFILE 1001 and 1005 data for PPS due to immature OS data from CROWN, though this adds uncertainty to the CEA - EAG stressed considering this uncertainty when interpreting model results and making decisions
TA891[9]	Ibrutinib with venetoclax	Chronic lymphocytic leukaemia	CAPTIVATE & GLOW	Recommended	Clinical trials, General population mortality, *to cap long-term extrapolations*	- EAG noted that external data from ECOG1912 and RESONATE-2 informed and validated parametric models - Concerns over patient and treatment differences between these external and pivotal trial - EAG advised caution with HRs from differing populations, as these differences could affect extrapolation validity
TA886[10]	Olaparib	Breast cancer	OlympiA	Recommended	Clinical trials, *to inform two TPs* General population mortality, *to inform TP*	- No comment or critique on use of external data

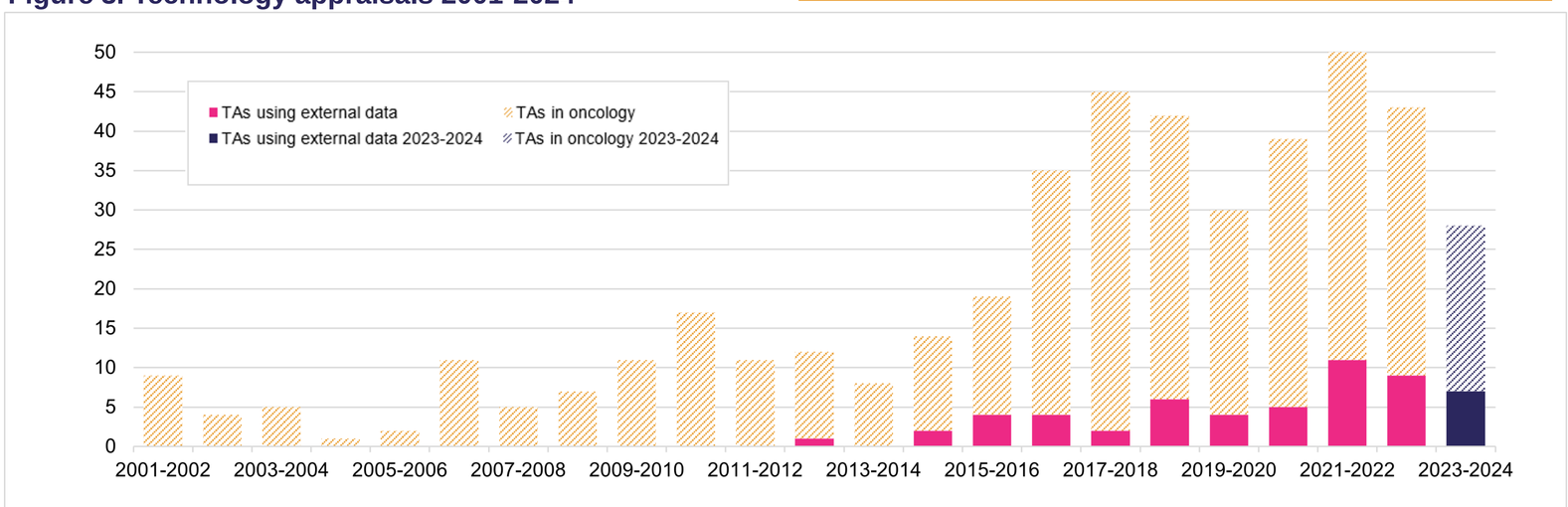
Abbreviations: CEA, cost-effectiveness analysis; EAG, Evidence Assessment group; HR, hazard ratio; KOL, key opinion leader; OS, overall survival; PFS, progression free survival; PPS, post-progression survival; SACT, Systematic Anti-Cancer Therapy; SEE, structured expert elicitation; TA, Technology Assessment; TP, transition probability; UK, United Kingdom

- A similar trend was observed compared to previous years: 25% compared to 23-26% in 2021-2023 of the TAs used external data to quantitatively inform survival extrapolations (**Figure 3**).
- In 2023-2024, two TAs received negative recommendations, not solely due to the use of external data for survival extrapolation but primarily due to other analytical aspects.
- NICE's primary concerns included the robustness and relevance of external data sources, specifically regarding population differences, the fit of survival estimates, and potential biases due to methodological transparency issues.

Conclusions

- The proportion of oncology TAs using external data for quantitative survival extrapolations **remained consistent** with previous years.
- Despite the guidance from TSD21 and the RWE framework, **key concerns** raised by NICE, such as **transparency** and **data reliability**, persist.
- The guidance has not fully alleviated complexity around the use of external data in survival extrapolations.

Figure 3. Technology appraisals 2001-2024



Abbreviations: TA, Technology Assessment

References
1. Naci, H., et al. (2024).The Lancet Oncology, 25(6), 760-769.; **2.** Rutherford, et al. (2020). NICE DSU TSD21: ScHARR, University of Sheffield.; **3.** Reitsma, F., et al. (2023). Value in Health, 26(12), S336.; **4.** NICE. Technology appraisal guidance [TA977]. 2024. **5.** NICE. Technology appraisal guidance [TA975]. 2024. **6.** NICE. Technology appraisal guidance [TA967]. 2024. **7.** NICE. Technology appraisal guidance [TA928]. 2023. **8.** NICE. Technology appraisal guidance [TA909]. 2023. **9.** NICE. Technology appraisal guidance [TA891]. 2023. **10.** NICE. Technology appraisal guidance [TA886]. 2023.

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