MSR148

Missing Health State Utility Values in NICE Oncology Appraisals: A Systematic Review of Utility Data Reporting and Handling Practices

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Background

- Health State Utility Values (HSUVs) are key to quality-adjusted life-year (QALY) estimation in National Institute for Health and Care Excellence (NICE) oncology appraisals and influence reimbursement decisions[1,2].
- Trial-derived HSUVs in oncology are often incomplete due to reasons such as attrition and declining patient-reported outcomes (PRO) and health-related quality of life (HRQoL) completion as disease progresses, which risks biased QALY estimates[3,4].
- In the wider utility/cost-effectiveness analysis (CEA) literature, analyses frequently apply mixed-effects models or multiple imputation under a missing at random (MAR) assumption, while missing not at random (MNAR) approaches (pattern-mixture/selection or reference-based imputations) are less commonly reported. How missing data practices map specifically to oncology submissions merits focused review[3,5,6,7].
- NICE guidance emphasises transparent reporting of missing data, clear justification of missingness assumptions, and sensitivity analyses[1,2].
- Several recent TAs have either proactively adopted or have been prompted by EAGs[8,9] to incorporate sensitivity analyses based on missing data assumptions. These include multiple imputation (n=4) and pattern-mixture modelling (n=1), which aimed at testing the robustness of the MAR assumption and exploring potential MNAR scenarios.

Objectives

The study objectives are listed as follows:

1. Quantify how often NICE oncology submissions use trial-based HSUVs.
2. Document which statistical approaches are used to handle missing HSUVs and whether MAR/MNAR assumptions are assessed or justified.
3. Assess acceptability of those approaches to NICE/EAG reviewers and alignment with NICE guidance.
4. Record the frequency and scope of MNAR-focused analyses in submissions.
5. Derive practical recommendations for reporting standards and MNAR sensitivity analysis strategies for future oncology submissions.

Methods

We conducted a systematic review of oncology NICE technology appraisals (TAs) published between 1 June 2023 and 31 May 2025.

Two reviewers independently screened committee papers to determine whether trial-based HSUVs (e.g., EuroQol five-dimension - EQ-5D, or mapped utilities) were reported, as well as the level of missingness (if applicable).

Double data extraction was also performed on statistical methods used to handle missingness in trial-based HSUVs (e.g., complete-case analysis, mixed model for repeated measures, multiple imputation, pattern-mixture model, last observation carried forward), as well as EAG commentary on assumptions/robustness of the missingness handling methods. We also assessed whether missingness-related issues impacted the appraisal outcomes.

Results

- Of 68 unique NICE oncology TAs identified by the systematic review during the study period, 62 reported trial derived HSUVs (Figure 1).
- Over 50% of the appraisals reported the proportion of complete utility data (n=39), though many did not explicitly assess whether missingness was at random or provide justification of the MAR assumption, unless prompted by the EAG. In addition, missingness in trial-derived HSUVs was noted by the EAG as an issue in 31 TAs, with MAR assumption and request for imputation being the most common theme of EAG critique (Table 1).
- The most common approach for utility analysis of trial data was a **mixed model for repeated measures** (n=45, Figure 1), which assumes that data are MAR. However, when data patterns suggested informative dropout (e.g., when a significant number of patients discontinued around progression), alternative trial-level analyses or non-MAR scenarios were seldom pursued as part of the base-case analysis.
- **Time-to-death regression** featured in some submissions to handle missing HSUVs (n=6). However, this approach was frequently critiqued by EAGs when it misaligned with the economic model's health-state structure (e.g., progression-based states in partitioned survival or state-transition models), potentially biasing state-specific utility values.
- Several recent TAs have either proactively adopted or have been prompted by EAGs[8,9] to incorporate sensitivity analyses based on missing data assumptions. These include **multiple imputation** (n=4) and **pattern mixture modelling** (n=1), which aimed at testing the robustness of the MAR assumption and exploring potential MNAR scenarios.

Figure 1. Sankey diagram showing a breakdown of 68 NICE oncology TAs identified during the study period, stratified by whether trial-based HSUVs were reported, type of utility analysis methods applied, and whether the EAG noted an issue with utility missingness.

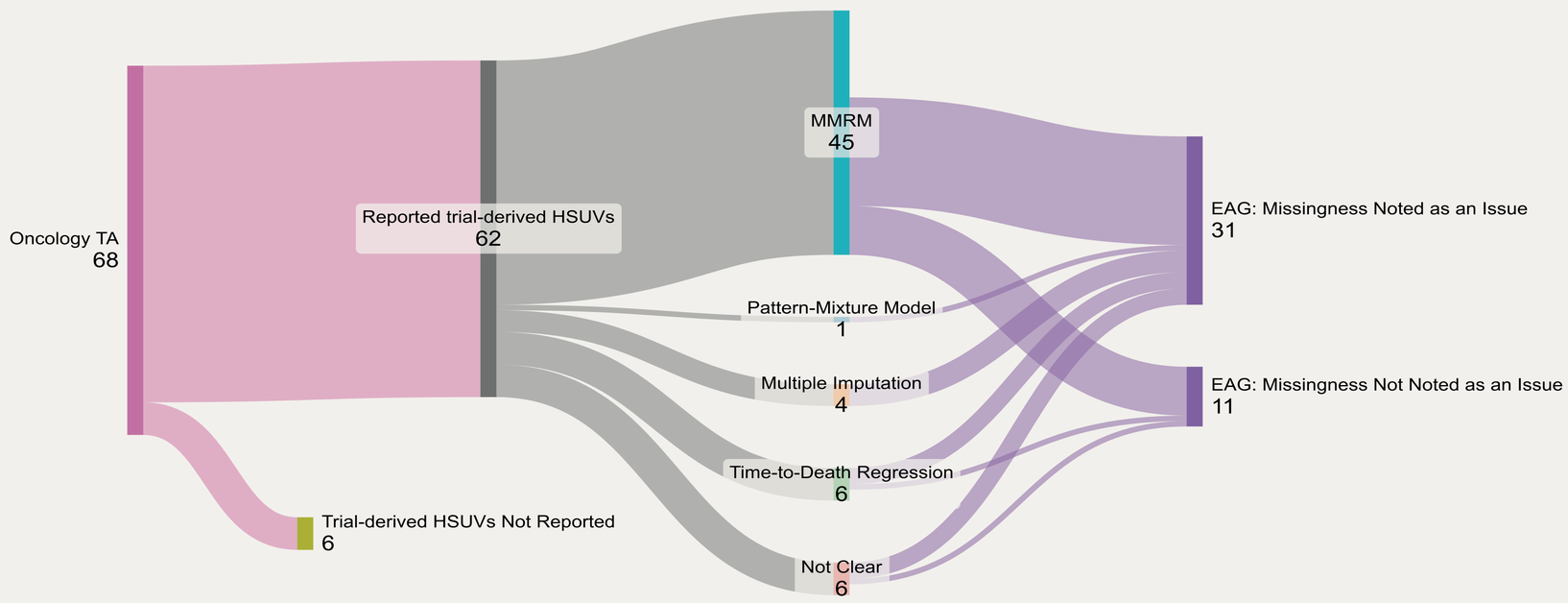

Table 1. Most common EAG comments and issues raised, with regards to utility analysis and missingness of utility values.

Nature of Issue	Summary of EAG Commentary	Example TA IDs
MAR assumption & request for imputation	MAR assumption challenged by EAG, as it may be implausible under attrition. EAG request missing-data imputation and/or MNAR sensitivity analyses.	TA931, TA1030
Declining completion & sparse post-progression utilities	Completion drops over time and progressive disease (PD) observations are very few, so PD utility is uncertain/implausible.	TA950, TA1059
Transparency & diagnostics on utilities/missingness	EAG request pattern of missingness by arm/timepoint, covariate lists, full regression output, and explicit MAR justification and to clarify mapping/value-set choices.	TA1001, TA1012

Discussions

- Using mixed models for repeated measures under the MAR assumption is a pragmatic approach for trial-based HSUVs, but the MAR assumption should be explicitly justified and routine sensitivity analysis exploring MNAR assumption should be undertaken — particularly in oncology, where informative missingness is plausible.
- Transparency in missing HSUVs reporting is crucial: company submissions should feature number and proportion of missing HSUVs at each given timepoint, as well as contrasts between completers and non-completers to document and justify missingness assumptions. In addition, providing outputs such as pairing trial-level HRQoL analysis (both base-case and sensitivity analyses) to economic model inputs may help EAGs to assess impact of missingness on final estimates and ensure a clear audit trail.
- For manufacturers, having proactive plans in place or early dialogue with NICE around missingness diagnostics, plausible MNAR scenarios, and model-method alignment can pre-empt later critiques.
- Limitations of this study include that: (1) findings reflect only what was reported in NICE committee papers, with some analyses potentially undertaken but undocumented; (2) heterogeneity across tumour types and utility instruments was not explicitly explored, which may influence missingness patterns and generalisability.
- Future directions: NICE oncology submissions could strengthen transparency and robustness by pre-specifying a utility analysis plan[10] which incorporates missingness diagnostics, including at least one MNAR-compatible sensitivity analysis[11,12], aligning trial analyses with model health states, and adopting a standardised reporting checklist with audit trail and early engagement with NICE.

Conclusion

- Missing utility data, which often stem from lack of post-progression utility measurements and low patient compliance, remain a common challenge in NICE oncology appraisals.
- Despite available statistical approaches when utility data are missing not at random, these are infrequently applied in company submissions.
- EAGs support decision-making by highlighting assumptions around missing data and encouraging greater transparency in reporting.
- Assessment of the level and type of missing utility data is vital in NICE oncology submissions. Where missingness may be not at random, approaches such as pattern mixture modelling, joint longitudinal models, or Bayesian methods can improve robustness, with structured sensitivity analyses used to test assumptions and quantify impact on cost-effectiveness estimates.

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