Tackling Heterogeneity in Indirect Treatment comparisons (ITC): A Comparative Review of NICE Submissions in Oncology Versus Non-oncology

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BACKGROUND

Context: Over the years, advanced methods such as network meta-analysis (NMA) have become integral in the realm of evidence synthesis and indirect treatment comparisons (ITC). However, conducting an NMA poses a significant challenge due to the inherent heterogeneity between studies. Heterogeneity in ITC is expected, and various advanced statistical methods exist to address it. However, the utilization of these methods is limited.

Aim: This study aims to: (i) understand how heterogeneity is assessed in NICE single technology appraisal (STA) submissions in recent years, and (ii) compare the approaches to handling heterogeneity in oncology versus non-oncology submissions.

METHODS

- The final guidance of NICE STAs published in the last two years (April 2022-April 2024) were retrieved.
- Terminated, withdrawn and in-development STAs were excluded.
- The STAs were classified into oncology and non-oncology submissions.
- STAs where anchored ITC was conducted were included in the analysis.

RESULTS

- A total of 182 STAs were retrieved from the NICE website during the research period.
- Forty-three of these STAs were either terminated or withdrawn. Seventy oncology and 69 non-oncology submissions were included for the further review (**Fig. 1**).

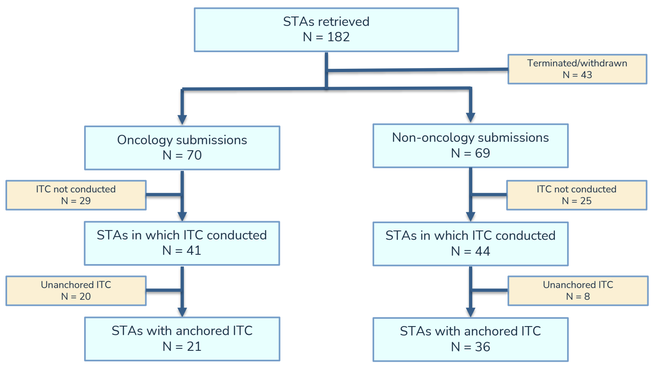

Figure 1: Summary of the inclusion/exclusion of STAs

- **Figure 2** shows the ITCs conducted in oncology and non-oncology STA submissions. ITCs were performed in 41 of 70 oncology submissions and 44 of 69 non-oncology submissions.
- Within submissions reporting ITCs, the anchored ITCs were performed less frequently in oncology submissions (21/41) vs non-oncology (36/44; **Fig. 2**).
- Nearly one-third of the non-oncology submissions did not address or report the evidence of heterogeneity. However, the proportion was relatively smaller in oncology submissions **(Fig. 2).**

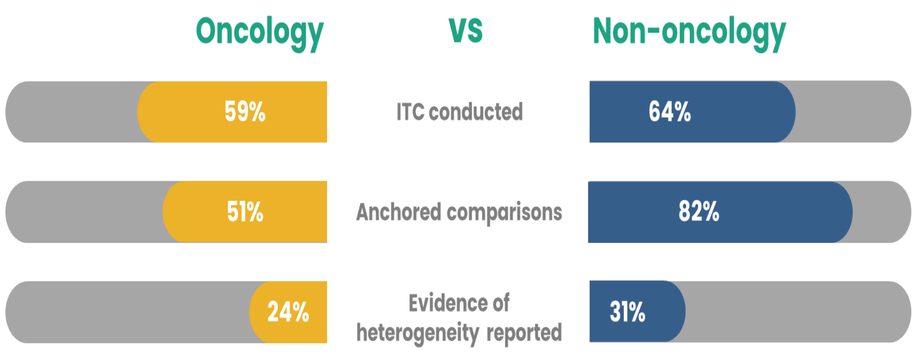

Figure 2: Summary of the ITC in oncology vs non-oncology submissions

- Among the oncology submissions population-adjusted indirect comparison methods (PAICs), including matching-adjusted indirect comparisons (MAIC) and propensity score matching (PSM) [1], were most frequently used to deal with heterogeneity followed by random effects models, assessment using I^2 estimates, identification of treatment effect modifiers and meta-regression **(Fig. 3)**.

Heterogeneity in the ITC in oncology and non-oncology submissions to NICE is addressed poorly.

Compared to non-oncology submissions, the use of advanced methods such as PAICs to assess heterogeneity is more common in recent oncology submissions to the NICE.

- The common approaches used to deal with heterogeneity in non-oncology submissions included random effects model followed by subgroup analysis, baseline risk adjustment, meta-regression [2] and anchored MAIC **(Fig. 3)**.

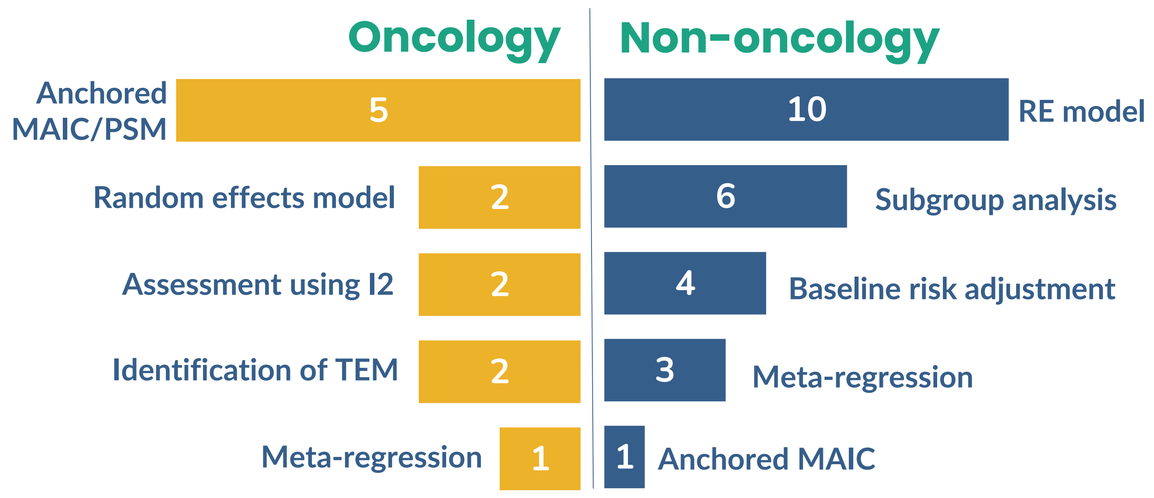

Figure 3: Approaches to handle heterogeneity in oncology and non-oncology STAs

- The population adjusted methods (MAIC/PSM) were more frequently used in the oncology submissions as compared to non-oncology submission. The identification of treatment effect modifiers(TEM) was carried out more frequently in oncology submissions **(Fig. 4).**

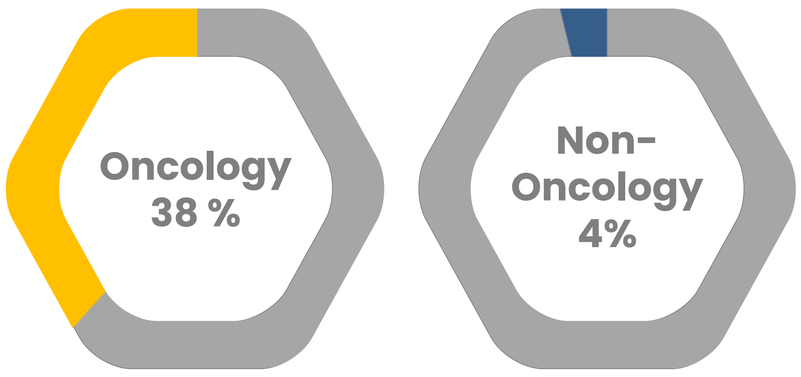

Figure 4: Use of PAICs in oncology vs non-oncology submissions

DISCUSSION

- ➢ Heterogeneity in evidence synthesis is an inevitable challenge that must be addressed effectively. While various methodologies and guidelines are available to investigate and manage heterogeneity, adherence to these frameworks has been limited in recent oncology and non-oncology submissions to NICE.
- ➢ In oncology submissions, advanced methods such as PAICs are more commonly employed, likely due to the limited number of available trials. Properly addressing heterogeneity is essential to mitigate potential biases in effect estimates and to facilitate robust decision-making processes.

References

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2. Phillippo, D.M., Ades, A.E., Dias, S., et al. NICE DSU Technical Support Document 18: Methods for population-adjusted indirect comparisons in submission to NICE. 2016. Available from http://www.nicedsu.org.uk

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