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NICE technology appraisals based on single-arm trials in 2022 – what can we learn from them?

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INTRODUCTION

- The number of drug regulatory and reimbursement approvals based on single-arm trials (SATs) is increasing[1]
- While some regulatory and health technology assessment agencies provide guidance and cautionary statements on external comparator (EC) data in submissions, these agencies do not provide a gold-standard methodology on SAT appraisals[2,3]
- EU HTA regulations for 2025 will reinforce EUnetHTA 21 guidance critiquing SAT evidence as insufficient for estimation of the relative treatment effectiveness in the context of the Joint Clinical Assessment (JCA). Therefore, there should be very careful consideration of the underlying assumptions of the methodological approaches[4]

OBJECTIVES

- As National Institute for Health and Care Excellence (NICE) routinely reviews and accepts SAT-based submissions, we sought to characterize NICE 2022 appraisals of SATs, as well as their application of EC data towards indirect treatment comparisons (ITC) and associated critique

METHODS

- From the NICE technology appraisals in 2022 we identified: disease area; population; presence of genetic biomarker; source of EC; type of real-world evidence (RWE); ITC methods used; critique from the External Assessment Group (EAG); and the NICE Committees' final appraisal decision

RESULTS

- Thirteen of 73 technology appraisals (TAs) (recommendations: positive [10]; negative [3]) were based on SATs (Table 1). This represents 18% of all TAs submitted to NICE in 2022 (Figure 1)
- The disease areas of these SAT-based TAs were oncology (11); chronic kidney disease (1); acute hyperkalaemia (1) (Figure 2)
- Eight of 13 TAs were for personalized medicines (i.e. drugs targeting populations defined by genetic profiling or biomarkers)

Table 1. List of NICE TAs in 2022 based on SATs

TA	Title (evidence sample size)
*TA850**	Amivantamab for treating EGFR exon 20 insertion mutation-positive advanced non-small-cell lung cancer after platinum-based chemotherapy (n = 114)
TA816*	Alpelisib with fulvestrant for treating hormone receptor-positive, HER2-negative, PIK3CA-mutated advanced breast cancer (n = 121)
*TA812**	Pralsetinib for treating RET fusion-positive advanced non-small-cell lung cancer (n = 310)
TA809	Imlifidase for desensitisation treatment before kidney transplant in people with chronic kidney disease (n = 46)
TA802	Cemiplimab for treating advanced cutaneous squamous cell carcinoma (n = 219 [pooled from two SATs])
TA796*	Venetoclax for treating chronic lymphocytic leukaemia (n = 406)
TA795	Ibrutinib for treating Waldenström's macroglobulinaemia (n = 823 [RWE])
TA789*	Tepotinib for treating advanced non-small-cell lung cancer with MET gene alterations (n = 275)
TA783	Daratumumab monotherapy for treating relapsed and refractory multiple myeloma (n = 106)
TA781*	Sotorasib for previously treated KRAS G12C mutation-positive advanced non-small-cell lung cancer (n = 250)
TA779*	Dostarlimab for previously treated advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency (n = 129)
TA599	Sodium zirconium cyclosilicate for treating hyperkalaemia (trial 1 n = 251; trial 2 n = 751)
TA760*	Selpercatinib for previously treated RET fusion-positive advanced non-small-cell lung cancer (n = 329)

Key: EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; KRAS, Ki-ras2 Kirsten rat sarcoma; NICE, National Institute for Health and Care Excellence; PIK3CA, Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha; RET, rearranged during transfection; RWE, real-world evidence; SAT, single-arm trial; TA, technology appraisal.
Notes: Appraisals that received negative recommendation are highlighted in red. *Indications that involve genetic biomarkers.

Figure 1. Proportion of NICE TAs in 2022 based on SATs

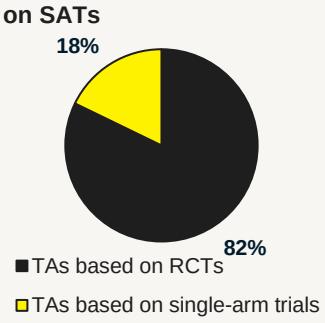
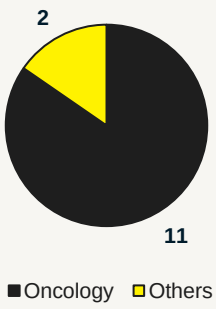


Figure 2. Disease area



RESULTS

- The sources for EC arms in the submissions were from randomized controlled trials (RCTs), RWE, or both (Figure 3)
- Types of RWE included registries, database studies, and chart reviews (Figure 4)

Figure 3. Sources of EC data used in the submissions

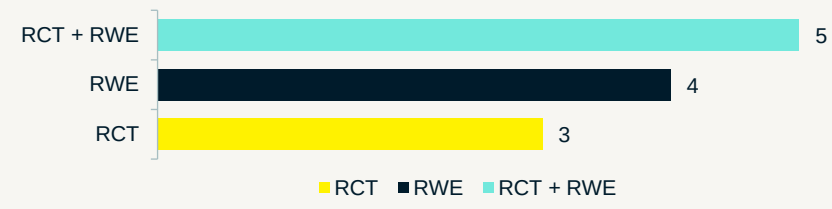
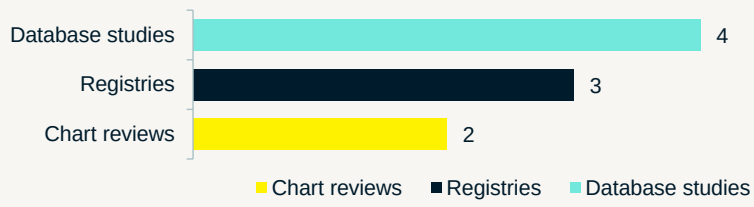


Figure 4. Type of RWE used to create the EC



- EC creation included different propensity score (weighting) approaches, subset or pooling of RWE, and covariate adjustment (Figure 5)
- A great variety of ITC methods were used across the submissions (Figure 6)
- Critique focused on the robustness of forming the EC, although negative feedback concerning adjustment methods (or lack thereof) was not always associated with the final decision

Figure 5. Methods to create the EC arm

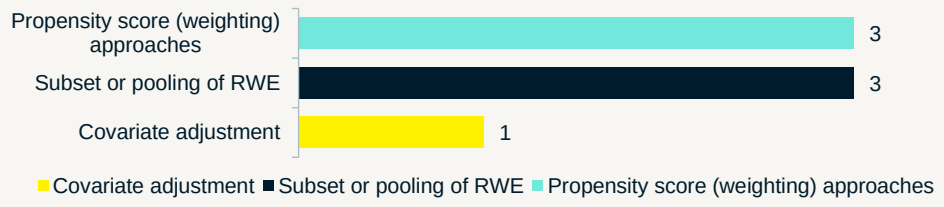
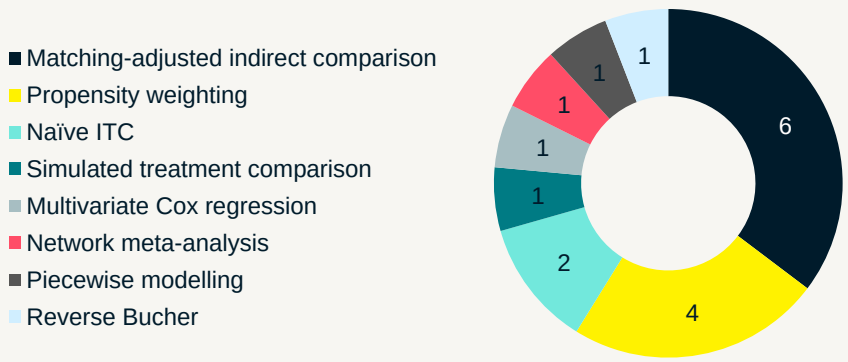


Figure 6. ITC methods



CONCLUSIONS

- In recent years, there has been an increase of SATs in NICE submissions. The methods used to create EC varied. This was likely due to the available evidence
- While submission characteristics (such as EC population and ITC methods) aligning with NICE Technical Support Documents appeared better received over naïve approaches, there is still a lack of centralized guidance towards selecting the most robust methods for submissions with SATs
- A roadmap on how to manage EC challenges given the available evidence would be valuable to inform submission strategy, which will be particularly important for the JCA from 2025

REFERENCES

1. Patel et al. Value Health. 2021; 24(8):1118-1125.
2. European Medicines Agency. ICH Topic E 10. 2001.
3. National Institute for Health and Care Excellence. ECD9. 2022.
4. EUnetHTA 21 Practical Guideline D4.3.2 Direct and Indirect Comparisons. 2022.

An electronic version of the poster can be viewed by scanning the QR code.

Poster presented at the 2023 ISPOR EU; 12–15 November 2023; Copenhagen, Denmark.