HTA238

Uncovering the Hidden Rare Disease Gap within NICE Appraisals

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Objectives

The National Institute for Health and Care Excellence's (NICE's) Highly Specialised Technologies (HST) programme aims to secure more equitable treatment access for very rare, and often very severe, diseases (1). It recognises that, in order to achieve this, a higher incremental cost-effectiveness ratio (ICER) threshold is required which starts at £100k/quality-adjusted life year (QALY). However, orphan medicines that do not meet the strict criteria for HST are instead evaluated by the Single Technology Appraisal (STA) programme which uses a lower ICER threshold of £20k-£30k/QALY.

Interestingly, previous research has found no significant differences between the proportion of positive NICE STA recommendations for orphan and non-orphan medicines despite the unique challenges faced by orphan medicines (2, 3). This research aimed to investigate this further by evaluating NICE recommendations for orphan medicines when controlling for different confounding variables.

Methods

STAs published within the study period (July 2016–January 2022) were identified. Terminated appraisals were excluded. Data including appraisal type, date, decision outcome, end-of-life criteria and orphan status were extracted for each STA. Analysis was conducted to compare decision outcomes. A positive recommendation was defined as a positive recommendation by NICE, regardless of any restrictions or managed access agreements.

Results

There were 300 STAs identified during the study period, of which 71 (23.7%) were identified as having orphan status. Figure 1 provides a summary of STAs included in our analysis.

Considering all STA outcome decisions, orphan and non-orphan STAs had negative recommendation rates of 7.04% and 9.61%, respectively (Figure 2a and 2d). However, within orphan medicines, non-cancer medicines fared considerably worse than cancer medicines with negative recommendation rates of 13.33% and 5.36%, respectively (Figure 2c and 2b).

Figure 1: Summary of Single Technology Appraisals (STAs) included in analysis

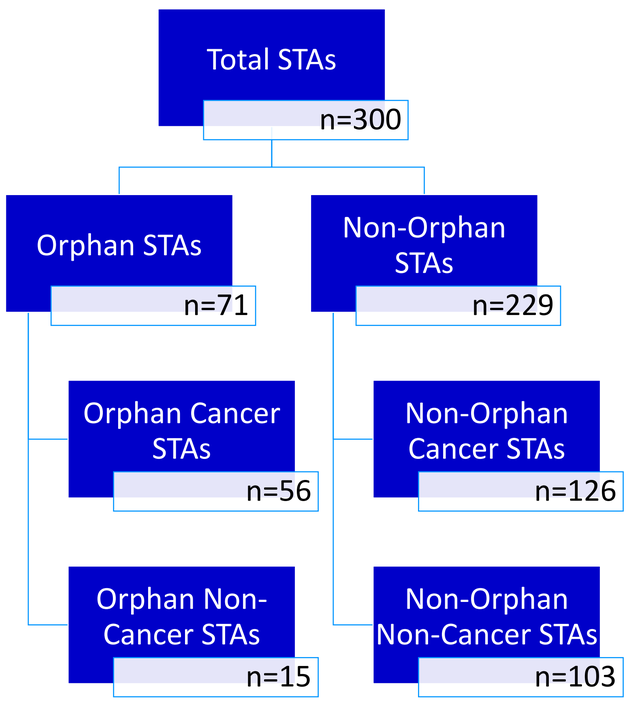
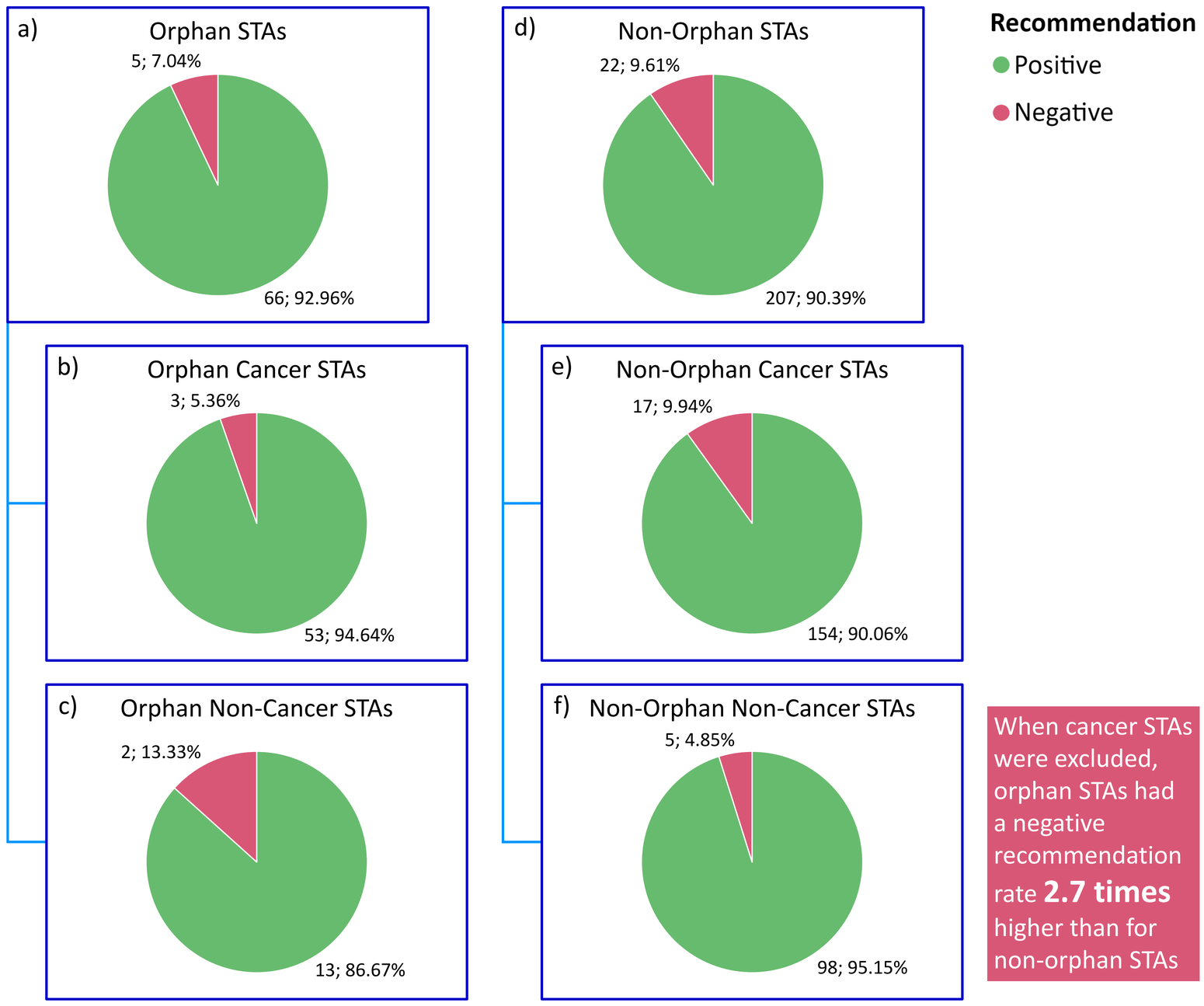


Figure 2: NICE Single Technology Appraisal (STA) recommendations for orphan and non-orphan STAs



When cancer STAs were excluded, orphan STAs had a negative recommendation rate **2.7 times** higher than for non-orphan STAs

Figure 2a and 2d compare STA recommendations for all orphan and non-orphan STAs. Figures 2b and 2c present the breakdown for orphan STAs when isolating or excluding cancer STAs, respectively. Figures 2e and 2f present the equivalent breakdown for non-orphan STAs. Each data label represents number of appraisals and the corresponding percentage (n; %).

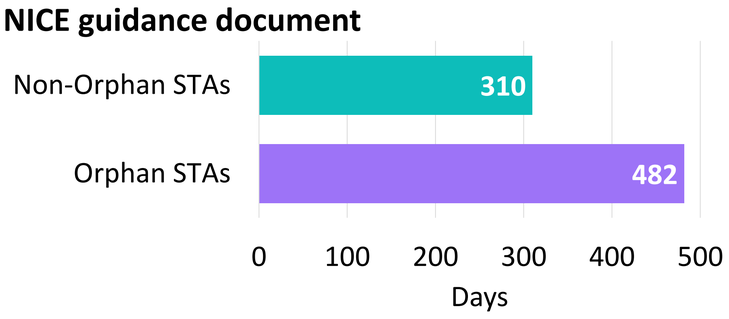
When subsequently focusing on cancer medicines, it was identified that 100% of orphan medicines meeting end-of-life criteria (£50,000/QALY) achieved a positive recommendation (Table 1). When cancer medicines were then excluded, orphan medicines had a negative recommendation rate 2.7 times higher than for non-orphan medicines (13.33% versus 4.85%) as shown in Figure 2c and 2f.

Table 1: Orphan Single Technology Appraisals (STAs) evaluated at different incremental cost-effectiveness ratio (ICER) thresholds

Recommendation	£20,000 - £30,000 / QALY ICER threshold	£50,000 / QALY End-of-life ICER threshold
Positive	46 (90.2%)	20 (100%)
Negative	5 (9.88%)	-

Lastly, the average time to access, defined as the time from European Medicines Agency (EMA) marketing authorisation to the publication of final NICE guidance, was found to be 172 days longer for orphan STAs compared to non-orphan STAs (Figure 3).

Figure 3: Average time from European Medicines Agency (EMA) marketing authorisation to final NICE guidance document



Conclusion

This research provides evidence of a 'rare disease gap' for orphan non-cancer medicines, previously masked by the inclusion of cancer medicines.

Excluding cancer medicines, not only did orphan medicines experience a higher negative recommendation rate than non-orphan medicines, but orphan medicines in general were further disadvantaged by a longer time to access. This is supported by a previous publication (3).

This research also demonstrated that the end-of-life criteria (£50,000/QALY) has potentially influenced access for orphan cancer medicines. In 2022, the end-of-life criteria was replaced with a new severity modifier and therefore future work should evaluate the success of this and the new Innovative Medicines Fund (IMF) in reducing inequity in access for orphan medicines.

Finally, a higher ICER threshold for rare diseases outside of the HST programme might help reduce the 'rare disease gap' identified in this research.

References

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2. Foxon G, Craddy P, Wilson C. Does Orphan Drug Status Confer Any Benefits for Products Undergoing HTA Appraisal By NICE in England? [Internet]. ISPOR. 2021. Available from: https://www.ispor.org/heor-resources/presentations-database/presentation/euro2021-3408/113077

3. Clarke S, Ellis M, Brownrigg J. The impact of rarity in NICE's health technology appraisals. Orphanet Journal of Rare Diseases. 2021;16(1).