Assessing the likelihood of receiving a positive recommendation within the indicated patient population at marketing authorisation through NICE's STA process

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Introduction

: As medicines have evolved over recent decades to have increased precision, pharmaceutical companies have been able to target treatments to those patient groups who will benefit most from certain drugs. At the same time, the importance of robust health economic modelling, the ability of HTA bodies to scrutinise clinical trial data, and tightening national health budgets, means HTA agencies are increasingly offering recommendations to drugs with refined patient populations whose ICERs fall within the acceptable cost-effectiveness range.

In early 2019, The National Institute for Health and Care Excellence (NICE), England's primary HTA body, stated that 82% of its technology appraisal recommendations were positive – a figure that has remained constant over the year. This statistic is encouraging for patients in the English NHS. However, examining closer the types of recommendations that NICE deems as 'positive' is less reassuring. This is particularly true when we consider the likelihood of positively recommended drugs reaching the entire patient population indicated at their marketing authorisation.

NICE states that by 'positive', it means that recommended medicines were approved either in line with their licence or with some modifications. It is the approvals with modifications that limit patient access to certain health technologies in the NHS. Modifications may come in the following recommendations: 'Optimised' (including in the Cancer Drugs Fund) and 'Only in Research'.

The majority of modified recommendations that do not receive a full recommendation are 'optimised'. This means, according to NICE, that the technology is recommended for a smaller group of patients than originally stated by the marketing authorisation. This happens when the NICE committee that is appraising the technology decides that the drug is only cost-effective as a treatment option for a specific group of patients.

In this instance, some patients who appeared to be eligible for a drug at the time of its marketing authorisation, are not granted access to it. Yet, NICE discourages companies from this notion of 'sub-grouping' at the clinical trial stage, stating that *"post hoc data 'dredging' in search of subgroup effects is to be avoided and will be viewed sceptically"*.

Objectives

: This study reviews 20 years of NICE data, to assess the likelihood that a technology will be approved for the full patient population indicated at marketing authorisation via NICE's Single Technology Appraisal (STA) process. The objective of the study is to provide a detailed breakdown of the types of recommendation a technology might receive by NICE.

References

1. https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/data/appraisal-recommendations
2. https://www.nice.org.uk/process/pmg9/resources/guide-to-the-methods-of-technology-appraisal-2013-pdf-2007975843781
3. https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/types-of-recommendation
4. https://www.nice.org.uk/about/what-we-do/patient-access-schemes-liaison-unit

Methods

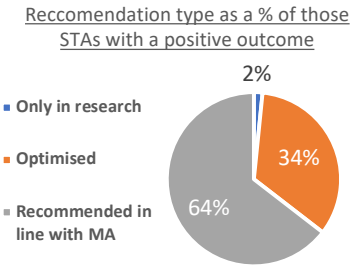
: Twenty years of NICE's publicly available technology appraisal data was reviewed in March 2019. All Multiple Technology Appraisals (MTAs) were removed from this study. MTAs are currently less frequently used by NICE. Of the 419 remaining STAs, 42 appraisals were withdrawn in the event where a company did not complete an evidence submission. This left 377 completed STAs in total. 313 STA recommendations were positively recommended, the remaining 64 technologies that were not recommended were discarded from this study. The study analysed the 313 individual STAs to distinguish the type of recommendation that each was awarded and to assess whether a recommendation was made for a sub-group (an optimised recommendation). Where individual STAs included recommendations for numerous indications, this study considers each indication as a separate STA. NICE's data on technology appraisals with Patient Access Schemes (PAS) and Commercial Access Agreements (CAA) was also analysed. This assisted the aim of the study by further categorising the type of recommendation NICE awarded to the 313 positive STAs.

Results

: The research found that 83.06% of the 377 completed STAs were granted a positive recommendation. 5 (1.33%) of the total number of appraised STAs (including those not recommended) were recommended only in research; 106 (28.13%) received an optimised recommendation.

202/377 technology appraisals (53.58%) received a recommendation that is indicated to treat the full patient population, as stated in the technology's marketing authorisation. The remaining positively recommended technologies either received a recommendation for a patient population smaller than the one indicated at the time of marketing authorisation or were recommended for research only (29.46%).

In total 111 of the positive recommendations received a 'modified' recommendation. 42 of these received a standard optimised recommendation. 48 drugs received an optimised recommendation accompanied by a simple discount PAS (a fixed pricing agreement that is lower than the list price of the treatment, or a percentage discount from the list price). This accounted for 12.73% of the total number of appraised STA drugs. Only 11 of the 111 drugs with modified recommendations were approved via the Cancer Drugs Fund.



Discussion

: There is a regular occurrence of recommendations indicated to treat a smaller patient population than indicated at marketing authorisation (28.13%). This shows that the English appraisal system is adept at assessing cost-effectiveness, ensuring that patient populations who will benefit most from the drug, manage to do so. This is, naturally, the role of the HTA agency, and not the licensing authority.

It is somewhat contradictory that NICE should encourage companies not to sub-group and cut data so that a product becomes cost-effective, whilst NICE, as shown in this study, are inclined to take the step itself. There is some ambiguity as to why NICE can sub-group but companies cannot. One possible reason is the point of patient equity. Manufacturers should strive to treat entire patient populations, rather than sub-groups that show superior clinical outcomes.

Just over a quarter of recommendations are optimised and this may have an impact on the commercial attractiveness of the UK market. If less patients receive a drug than a company had expected, this will impact profitability.

Conclusion

: This research has shown that the 82% figure NICE quotes is accurate, in the sense that this is the proportion of technology appraisals that it awards a 'positive' recommendation to. However, it is clear that drugs recommended for refined patient populations form a large part of the 82%.

The community would benefit from further research to investigate, in depth, those technologies that received optimised recommendations. It may be the case that certain disease areas are more likely than others to receive optimised recommendations. The outcomes of such a study may assist companies in developing their clinical development programme, and so help to avoid the issue of refining patient populations later on in the STA pathway.

Recommendation Type	Number	% of those with positive outcome	% of total appraised
Only in Research	4	1.28	1.06
Only in Research - PAS (Simple Discount)	1	0.32	0.27
Optimised	42	13.42	11.14
Optimised - PAS (Complex - Free Stock)	4	1.28	1.06
Optimised - PAS (Complex - Time Cap)	1	0.32	0.27
Optimised - PAS (Simple Discount)	48	15.34	12.73
Optimised - (CDF) - CAA	8	2.56	2.13
Optimised - CAA (PAS Withdrawn)	3	0.96	0.8
Total	**111**	**35.48**	**29.46**

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