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Assessing the Impact of the NICE Methods Review on Rare Diseases

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BACKGROUND

- Treatments in the rare disease space face significant barriers to access compared to non-rare diseases (Box 1)[1].
- Due to these barriers to access, HTA agencies globally face significant challenges ensuring there remains equity in access to treatments for patients who suffer from rare diseases.
- NICE is responsible for HTA in England that determines which treatments should be reimbursed by the NHS and hereby made available to patients.
- In November 2020, NICE published The Case for Change in which NICE presented its vision to "remain cutting edge and future proof" and to "support the attractiveness of the United Kingdom as a first launch country"[2].
- The report presented a number of proposals that outlined how NICE would achieve its vision.
- In reference to rare diseases, NICE acknowledged "rare diseases have particular challenges in collecting evidence" and commented that in the case of rare diseases, NICE's assessment methods should "not be seen as a criticism or a barrier to accessing new technologies".
- However, these barriers for rare diseases are well known and can lead to inequity in access between patients with rare and non-rare diseases.
- Following the publication of The Case for Change NICE subsequently updated its methods and processes via updating the NICE HTA manual[3]. From February 2022, all subsequent NICE appraisals were subject to the updated methods and processes.

Box 1: Summary of barriers to access for rare diseases[1]

- Evidence generation is problematic as patient populations are small and often heterogeneous making it difficult to recruit and identify trial participants.
- There is generally a lack of epidemiological and natural history data.
- Validated endpoints to predict long-term effects can be lacking.
- There is often a lack of consensus on comparators or no active comparator.
- Companies need to cover the costs of R&D and earn a return on investment which necessitates charging a high price per patient; cost recovery can be particularly challenging for small companies.

OBJECTIVE

- To assess the impact that the proposals in NICE's The Case for Change report had on reducing inequity in access for rare diseases via the NICE methods review.

METHODS

- The proposals in NICE's The Case for Change report were examined and the proposals with the highest potential to remove barriers to reducing inequity in access for rare diseases were identified.
- For each proposal, the resulting update in the NICE methods review was identified and the associated impact on access for rare diseases was critiqued.
- A simple framework was constructed to evaluate the extent to which each update was able to achieve the aim of reducing inequity in access for rare diseases.
- Updates were categorized as either having "no impact" (red), "partial impact" (orange) or "full impact" (green).

RESULTS

- The following updates in the methods review were identified as having a significant impact on rare disease technologies:
  - The introduction of decision modifiers
  - A greater acceptability of uncertainty in some circumstances, including for rare diseases
  - A greater acceptability of real world evidence (RWE)
  - Updates to the HST eligibility criteria
  - Changing the discount rate from 3.5% to 1.5%, for both costs and health effects
- Table 1 outlines the subsequent impact that the proposals had on removing access barriers for rare diseases.
- Although the overall impact of the methods review is likely to be positive for rare diseases, it's unlikely to be sufficient to overcome substantial access barriers in rare diseases.
- Most notably, the HST eligibility criteria had the most potential to impact inequity for rare diseases. However, with the restrictive HST criteria, there is only additional flexibility for a small number of rare diseases.
- There are no allowances for rare diseases that do not meet the criteria and therefore the updates did not address the perceived cliff edge for rare diseases not deemed rare enough for HST.

Table 1. Assessing the impact of the NICE methods review on reducing inequity in access in rare diseases

Proposal	NICE HTA manual update	Description of impact	Impact
Greater acceptability of RWE	• Greater acceptance of RWE to resolve knowledge gaps and facilitate access to treatments • Supported by the RWE framework to help deliver on this ambition[4]	• A positive signal to accept RWE in addressing address evidence gaps • Uptake from industry has been limited so far but positive case studies where RWE was used are reported[5,6]	Positive impact
Introduction of the decision modifiers	• Giving additional weight to health benefits in the most severe conditions to allow more equitable access to treatments for these conditions ○ 1.7x QALY weighting for the most severe diseases ○ 1.2x QALY weighting less severe diseases	• Moving from end-of-life criteria to a severity modifier is a more equitable approach that may benefit some rare disease treatments, but is unlikely to result in faster reimbursement or address concerns around access of treatments of rare diseases[7] • The severity modifier was designed to be neutral in terms of QALY weighting and cost-neutral for NICE • No modifier for rarity was included	Partial impact
Greater acceptability of uncertainty in some circumstances, including for rare diseases	• Greater flexibility for NICE committees in cases where evidence generation is difficult (e.g. rare diseases) • NICE's committees to consider uncertainty appropriately in order to manage the risks to patients and the NHS while preventing inappropriate barriers to valuable innovations	• A pragmatic approach to uncertainty is welcome but there is a lack of transparency as to how allowances are made for the greater acceptance of uncertainty, with industry questioning its role in decision-making	Partial impact
Updates to the HST eligibility criteria	• The HST criteria revised to provide greater clarity, precision and predictability for the routing of topics.	• New criteria generally more restrictive with additional flexibility for a small number of appraisals. Uncertainty remains. • Only a small proportion of appraisals are eligible – a large proportion of rare disease appraisals do not qualify for HST	Partial impact
Changing the discount rate (3.5% to 1.5%)	• Proposal not carried forward as part of methods review - discount rate remained at 3.5% for both costs and health effects	• No impact	No impact

DISCUSSION

- The UK is a world-leader for rare disease technology patient access. However, there are industry concerns that the UK's status is under threat due to an increasingly unfavourable UK HTA landscape.
- Industry's pipeline of complex, innovative technologies for rare diseases continues to grow. As a result, it is increasingly important that NICE update its methods to adapt to the current and future landscape with a view to increasing equity of access for patients with rare diseases.
- NICE must help play a part in supporting access to rare disease medicines to enable companies to further invest in disease areas of high unmet need with small patient populations.
- NICE's inaction on this matter could lead to further inequity for patients with rare diseases. Considerations for further action are highlighted in Box 2.

Box 2: Considerations for further action on addressing challenges of rare disease HTA

Inclusion of a rarity modifier

- The methods review included no specific modifier for rarity with NICE concluding there was no robust evidence that society values more highly health benefits in rare diseases.
- Subsequent research from BIA (2023) indicated there is public belief that the cost-effectiveness thresholds used for rare diseases should reflect the challenges associated with developing these treatments[8].
  - 75% of focus groups participants felt that funding decisions for treatments of rare diseases should apply cost-effectiveness thresholds that fall between those for very rare treatments and those for more common diseases.

Further modular updates to address rare disease challenges

- Changes to NICE assessment methods need to go further if NICE is to achieve its stated aim of not being seen as a barrier to accessing new technologies in rare diseases.
- Future modular updates should aim to address the challenges of rare diseases to ensure the UK remains a global leader in access to rare disease technologies and reducing inequity in access for rare diseases.

CONCLUSIONS

- Although some updates in the NICE methods review were able to partially reduce inequity in access rare diseases, the NICE methods review did not go far enough to fully address the issue.
- This risks future access in rare diseases. It is crucial to recognise that more work remains to be done to ensure that access barriers are adequately addressed.
- Future modular updates should look to specifically address the issue of rare diseases to ensure that the UK remains a world-leader in access for rare disease technologies.

DISCLOSURES

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