What is driving the increase in terminated NICE appraisals?

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Introduction

Previous research has identified that the proportion of manufacturer-terminated National Institute for Health and Care Excellence (NICE) appraisals has increased over time, and that terminations are disproportionately higher for cancer and rare diseases, as well as multi-indication and combination products (1-4). Increasing termination rates could have a global impact on patient access to new drugs, as terminated NICE appraisals may lead to non-submissions for the same product in other markets (5).

Whilst it is well understood that the number of terminated appraisals is rising, and certain indications or drug types are disproportionately affected, a comprehensive assessment of why the termination rate is increasing has not yet been conducted.

This research sought to explore the drivers behind the increase in terminated NICE appraisals by characterising the reason for all terminated appraisals, and analysing trends by year and indication.

Methods

A database of all terminated NICE appraisals between 2008 and June 2025 was analysed in Excel®. The manufacturer's reasons for terminating the appraisal were first categorised into granular themes, and then consolidated into broader categories related to evidence limitations, economic evidence and cost-effectiveness challenges, administrative factors, manufacturer's decision to focus efforts elsewhere, and National Health Service (NHS) implementation (Table 1).

To account for some years having a much smaller number of submissions than others, appraisals were grouped into 3-year periods. Similarly, indications were grouped into broad categories reflecting International Classification of Diseases 11th Revision (ICD-11) chapters. Descriptive statistics were used to assess general trends in how the rationale for terminating the appraisal changed over time, as well as indication-specific trends. A simple linear regression model was applied to evaluate the statistical significance of changes over time in appraisal termination reasons.

Table 1: Categories of reasons reported by the manufacturer for terminating the NICE appraisal

Broad category	Subcategory	Definition
Evidence limitations	Clinical evidence limitations	Clinical data either do not represent NHS practice; limitations in trial design mean it would not be possible to appraise the clinical and/or economic value; or trial endpoints were not met or not strong
	Insufficient evidence	Not enough evidence to support submission; or the manufacturer is awaiting additional clinical data from key trials
Economic evidence and cost-effectiveness challenges	Economic evidence limitations	Manufacturer identified challenges demonstrating the economic value of the technology arising from clinical data, e.g. stating that there is insufficient evidence available to develop a cost-effectiveness model in line with NICE's methods
	Technology is not or is unlikely to be cost effective	Manufacturer stated that it is unlikely that there is sufficient evidence that the technology is a cost-effective use of NHS resources; or that the technology is unlikely to be cost effective based on manufacturer's evidence
Administrative factors	Marketing authorisation withdrawn/paused	Manufacturer withdrew or withheld marketing authorisation for the treatment
	Drug discontinued	Drug removed from market
	Manufacturer delay	Manufacturer was unable to submit evidence in time; or requested a delay
Focusing efforts elsewhere	Not a worthwhile use of manufacturer's resources to submit	Manufacturer stated that it would not be a worthwhile use of their time and resources to submit evidence; or that they are deciding to focus efforts elsewhere
	Not launching in UK	Manufacturer decided not to launch product in the UK for that indication
Implementation into the NHS	Patient population limitations	Only a small number of patients are eligible for treatment; only a small number of patients in the trial are comparable to UK patients; or it would be challenging to identify the patients most likely to benefit from the treatment
	Lack of clinical need or value of the new technology	The manufacturer identified that there is no clinical need for the treatment after discussion with clinicians; or NICE identified that there is insufficient clinical benefit following reimbursement via the Cancer Drugs Fund (CDF)
	Patient pathway challenges	Manufacturer identified that it is unlikely that the technology will be used at the most suitable point within the treatment pathway
No further reason		Manufacturer did not provide further justification for decision to terminate appraisal

Results

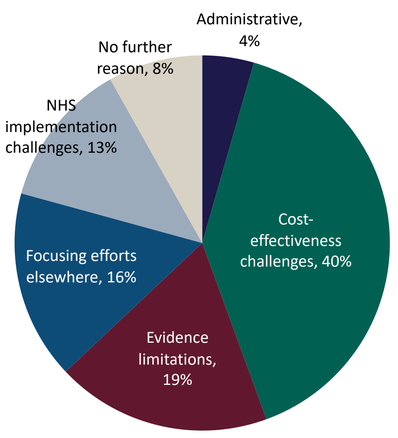
Reasons for termination

10% (135/1,342) of all appraisals between 2008 and 2025 were terminated by the manufacturer. The percentage of terminated appraisals in each year has risen over time, from 3% in 2008/9 to a high of 15% in 2022/23 (data not shown).

The most common reasons for terminating appraisals over the entire time period were that the manufacturer did not think the technology would be a cost-effective use of NHS resources (33%); did not have sufficient clinical evidence (15%); or decided not to launch in the UK (14%).

When grouped into broader categories as in Table 1, 40% of appraisals were terminated due to cost-effectiveness challenges; 19% due to evidence limitations; and 16% due to the manufacturer deciding to focus their efforts elsewhere (Figure 1).

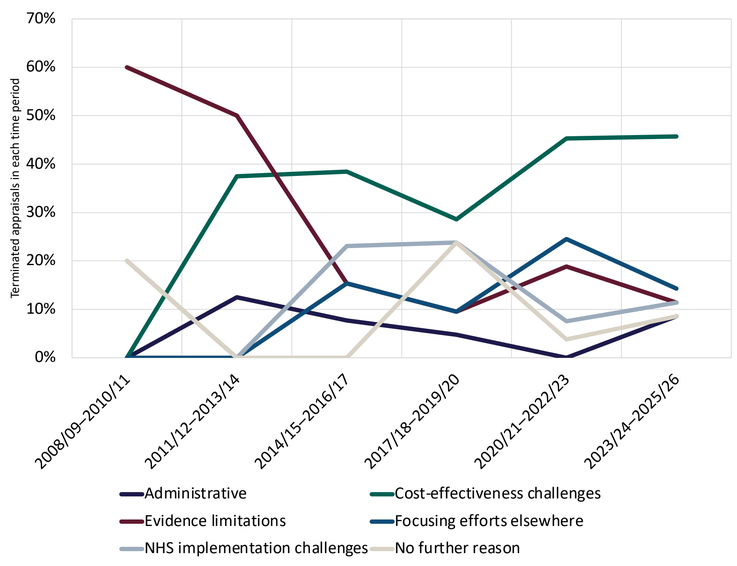
Figure 1: Reasons for termination for all appraisals between 2008 and 2025



Evolution of reasons for termination over time

A time series analysis found that the percentage of appraisals terminated due to cost-effectiveness challenges rose from 0% in the period 2008/09–2010/11 to 46% in the period 2023/24–2025/26. The percentage of terminations due to clinical evidence and NHS implementation challenges generally declined over time (Figure 2).

Figure 2: Reasons for termination in each time period



A linear regression was conducted to assess whether there was a statistically significant trend in reasons for appraisal termination over time (Table 2). There was a statistically significant ($p<0.05$) reduction over time in the percentage of appraisals being terminated due to clinical evidence limitations. An increase in the percentage of appraisals in each time period being terminated for cost-effectiveness challenges and for the manufacturer focusing efforts elsewhere approached significance at the 0.05 level. The percentage of appraisals terminated due to NHS implementation challenges declined over time, but this decline was not statistically significant.

Table 2: Linear regression results to identify statistically significant trends in appraisal termination reasons over time

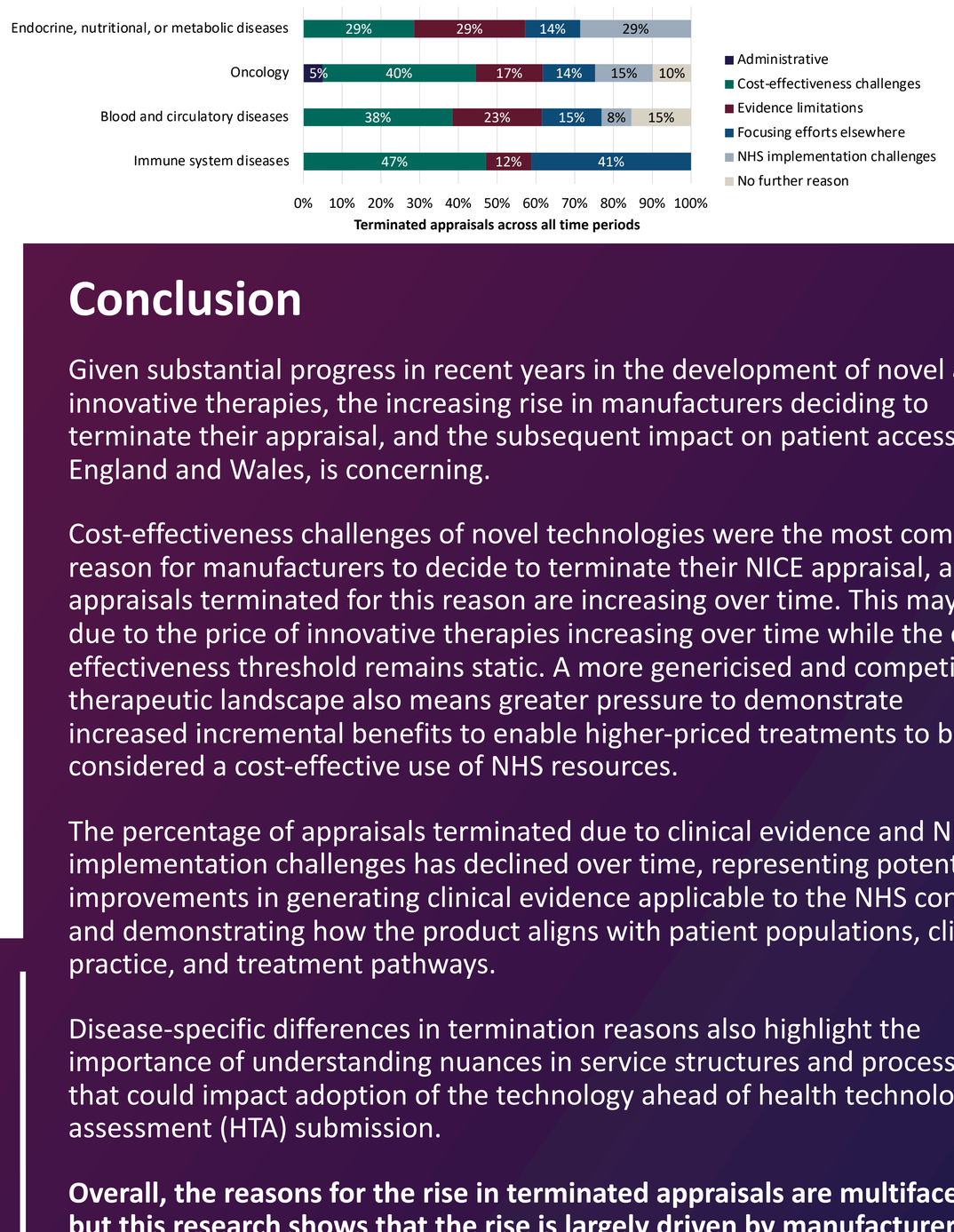
	Coefficients	Standard error	t-stat	p-value	Lower 95%	Upper 95%
Cost-effectiveness challenges	0.07	0.03	2.30	0.08	-0.01	0.15
Evidence limitations	-0.10	0.03	-3.11	**0.04**	-0.19	-0.01
Focusing efforts elsewhere	0.04	0.02	2.48	0.07	0.00	0.08
NHS implementation	-0.01	0.03	-0.22	0.84	-0.08	0.07

Indication-specific trends

An analysis of the reasons for appraisal termination for indications with the most appraisals (oncology [n=81], immune system diseases [n=17], blood and circulatory diseases [n=13], endocrine, nutritional, or metabolic diseases [n=7]) found that almost half of immunology appraisals were terminated due to cost-effectiveness challenges, compared with 40% of oncology and blood and circulatory disease appraisals, and 29% of endocrine, nutritional, or metabolic disease appraisals (Figure 3).

Appraisals terminated due to clinical evidence limitations were most prevalent in endocrine, nutritional, or metabolic diseases. 41% of appraisals for immune system diseases were terminated due to manufacturers' decisions to focus efforts elsewhere – some of which may be due to commercial reasons. 29% of endocrine, nutritional, or metabolic disease appraisals were terminated due to NHS implementation challenges compared with 8% in blood and circulatory diseases and 15% in oncology, suggesting differences in the readiness of healthcare systems for such therapies.

Figure 3: Reasons for termination across indications



Conclusion

Given substantial progress in recent years in the development of novel and innovative therapies, the increasing rise in manufacturers deciding to terminate their appraisal, and the subsequent impact on patient access in England and Wales, is concerning.

Cost-effectiveness challenges of novel technologies were the most common reason for manufacturers to decide to terminate their NICE appraisal, and appraisals terminated for this reason are increasing over time. This may be due to the price of innovative therapies increasing over time while the cost-effectiveness threshold remains static. A more genericised and competitive therapeutic landscape also means greater pressure to demonstrate increased incremental benefits to enable higher-priced treatments to be considered a cost-effective use of NHS resources.

The percentage of appraisals terminated due to clinical evidence and NHS implementation challenges has declined over time, representing potential improvements in generating clinical evidence applicable to the NHS context and demonstrating how the product aligns with patient populations, clinical practice, and treatment pathways.

Disease-specific differences in termination reasons also highlight the importance of understanding nuances in service structures and processes that could impact adoption of the technology ahead of health technology assessment (HTA) submission.

Overall, the reasons for the rise in terminated appraisals are multifaceted, but this research shows that the rise is largely driven by manufacturers being unable to demonstrate the cost effectiveness of new products. This emphasises the importance of early HTA strategy and cost-effectiveness modelling to increase the chance of a successful HTA and ensure patient access to new healthcare innovations.

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Abbreviations

CDF, Cancer Drugs Fund

HTA, health technology assessment

ICD-11, International Classification of Diseases 11th Revision

NHS, National Health Service

NICE, National Institute for Health and Care Excellence