Drivers of Negative HTA Decisions: A Data-Driven Review of Cost-Effectiveness Submissions

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01. Introduction

Negative or access-restricted health technology assessment (HTA) recommendations can be challenging for manufacturers and stakeholders. However, understanding the concerns behind these recommendations can help identify evidence gaps and inform future reimbursement submissions.

A dataset of assessment records and supporting documents from England's National Institute for Health and Care Excellence (NICE) and Ireland's National Centre for Pharmacoeconomics (NCPE) was developed to examine these concerns. Comparing findings across the two agencies provides an opportunity to identify common challenges and differences in documented concerns, while accounting for their different appraisal processes and recommendation outcomes.

This study aimed to:

1. Develop an evidence base and interactive dashboard linking findings to original assessment documents.
2. Classify documented reasons for negative and access-restricted recommendations using a common framework.
3. Describe how frequently these concerns were identified in assessments from 2016–2025.
4. Compare decision drivers between NICE and NCPE, focusing on outright-negative recommendations to improve comparability.

02. Methods

Assessment selection	Publicly available NICE and NCPE assessments issued between 2016 and 2025 were reviewed, focusing on a recent ten-year period to improve relevance to current clinical practice and HTA requirements. Eligible recommendations were negative, economic-conditional, restricted or managed-access/research. The main analysis included 581 of 838 eligible assessments for which supporting documents were available.
Identification of concerns	Automated text searches and document review identified concerns across six categories and 22 subcategories covering clinical evidence, cost-effectiveness, economic modelling, comparators or patient populations, robustness of the economic results and supporting analyses, and budget impact or affordability. Document review allowed concerns to be checked, corrected or added. Each recorded concern was linked to supporting text in the original document.
Analysis	Frequencies represented the percentage of included assessments in which each concern was identified. Each assessment counted once per concern and could contribute to several categories. Assessments with no identified concern remained in the analysis. Some concerns may have been missed, so frequencies may underestimate those present.
Agency comparison and dashboard	Direct NICE–NCPE comparisons were limited to outright-negative recommendations. An interactive R Shiny dashboard was developed and allows users to explore the findings and supporting evidence using the same assessment groups and definitions as the main analysis.

03. Decision-driver framework and interpretation

A decision driver was defined as a concern documented in an assessment relating to a negative, conditional, restricted or managed-access recommendation. The framework below groups these concerns into six categories and 22 subcategories. Each assessment could contain concerns in several categories.

Clinical evidence	• Immature survival data • Uncertain treatment effect • Limited follow-up
Comparators or populations	• Inappropriate or omitted comparator • Limitations of indirect comparisons • Uncertain relevance to patient subgroups
Cost-effectiveness	• ICER above an acceptable threshold • Low probability of cost-effectiveness • Price reduction required
Economic modelling	• Survival extrapolation • Utility assumptions • Model structure • Costs
Robustness	• Economic results sensitive to assumptions • Results judged insufficiently robust for decision-making
Budget impact or affordability	• Uncertain eligible population size • High budget impact • Affordability concerns

Percentages describe the proportion of included assessments in which a concern was identified. Repeated references to the same concern within an assessment did not increase its contribution. Each assessment counted once within a category or subcategory, but could contribute to several categories, so percentages should not be added together.

The frequency of a concern does not measure its importance in determining the recommendation. A frequently documented issue may accompany other concerns, while a less frequently reported issue may be decisive in an individual assessment.

A common framework supports comparison of documented concerns while retaining the context of each agency's assessment. Differences in reporting, available documentation and the treatments assessed may influence the observed frequencies.

Direct NICE–NCPE comparisons focused on outright-negative recommendations to improve comparability. These groups contained different assessments and were not matched treatment–indication pairs. Differences should therefore not be interpreted as evidence that one agency applies stricter requirements.

04. Results

Assessments included

Of 838 eligible assessments issued during 2016–2025, 581 had supporting documents available and formed the main analysis; 257 lacked eligible supporting documents and were excluded from the concern analysis. Full review of the available supporting documents was completed for 538 assessments. The remaining 43 were held aside from this review for potential independent validation but remained in the analysis using existing recorded concerns. Included recommendations were outright negative (n=101), economic conditional (n=188), restricted (n=271) or managed access/research (n=21).

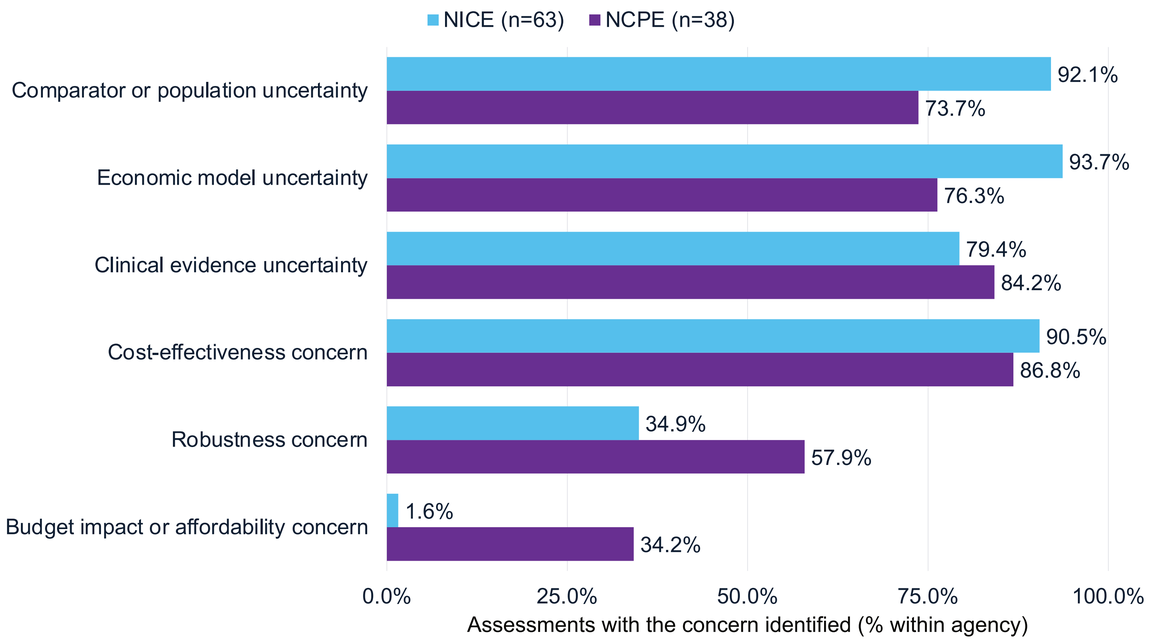
Four decision-driver categories were documented in more than 70% of assessments: comparator or population uncertainty (77.8%), economic-model uncertainty (77.5%), clinical-evidence uncertainty (73.7%) and cost-effectiveness concerns (70.9%). An ICER above the acceptable threshold was the most frequently identified specific concern (65.6%). Other common concerns included population or subgroup uncertainty (53.9%), uncertain treatment effect (51.6%) and limitations of indirect comparisons (48.4%). Utility assumptions (31.3%) and survival extrapolation (30.8%) were also frequently questioned.

Concerns commonly occurred together

96.6% Of assessments with a cost-effectiveness concern, 398 of 412 also had clinical, economic-model or comparator/population uncertainty.

Overall, 468 of 581 assessments (80.6%) contained concerns in at least three broad categories.

Figure 1: Decision-driver categories in outright-negative decisions only



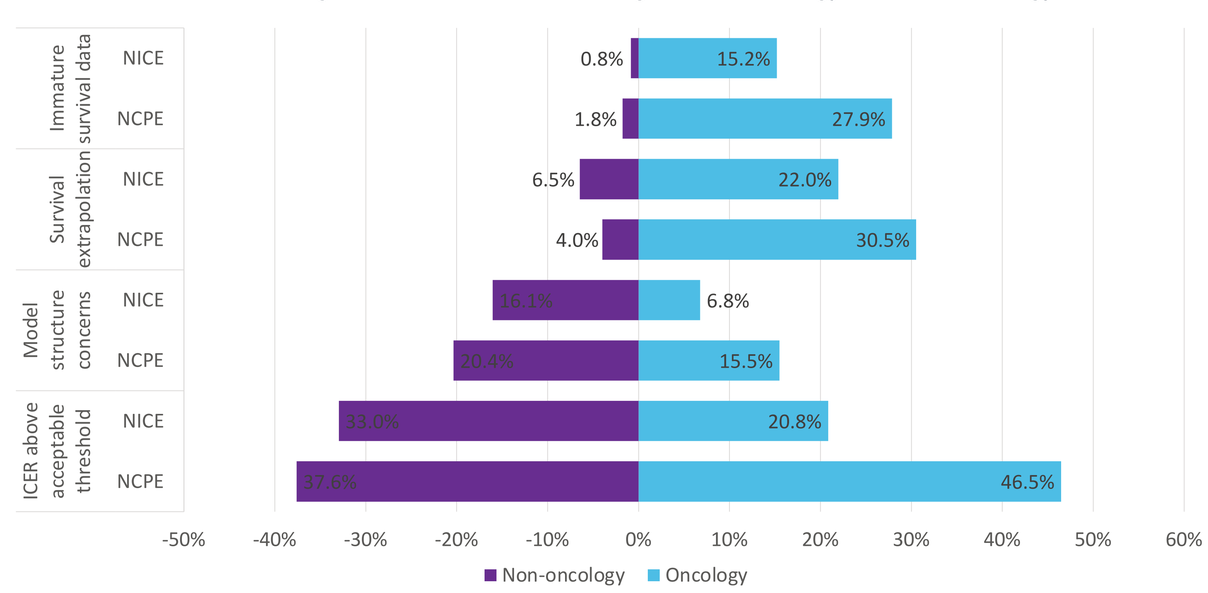
The agency comparison included 38 NCPE and 63 NICE outright-negative assessments. These were separate agency cohorts and were not matched by treatment and indication. Cost-effectiveness concerns were common for both NCPE (86.8%) and NICE (90.5%). NICE more frequently documented comparator or population uncertainty (92.1% vs 73.7%) and economic-model uncertainty (93.7% vs 76.3%), while NCPE more frequently documented robustness concerns (57.9% vs 34.9%) and budget-impact or affordability concerns (34.2% vs 1.6%).

Of the 13 NCPE assessments with a budget-impact or affordability concern, nine included uncertainty regarding eligible population size. Explicit high-budget impact concerns occurred in 4/38 NCPE and 1/63 NICE assessments.

Results by therapeutic area

The pattern of concerns differed by therapeutic area. Immature survival data and survival extrapolation were more frequently identified in oncology assessments than in non-oncology assessments, while model-structure concerns were more frequent outside oncology. Above-threshold ICERs occurred at similar frequencies in both groups. These descriptive findings highlight the importance of addressing treatment-area-specific evidence and modelling uncertainties when preparing submissions.

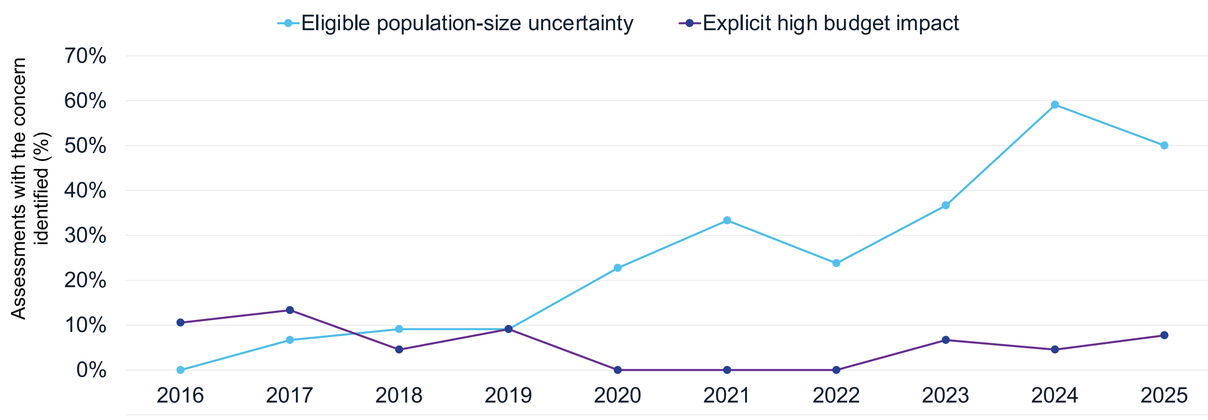
Figure 2: Decision-driver categories in oncology and non-oncology indications



Results over time

In NCPE assessments, uncertainty about eligible patient population size became more frequently identified over the study period, although annual frequencies fluctuated. Explicit high budget-impact concerns remained relatively uncommon. Both concerns were rarely identified in the included NICE documents. This pattern suggests that estimating the number of eligible patients became a more prominent documented issue in NCPE assessments, without a corresponding increase in explicit high budget-impact concerns. The findings highlight the importance of supporting population estimates with clear epidemiological evidence and assumptions about treatment eligibility. Other concerns showed varying patterns over time. Changes in document availability, reporting and the mix of assessments may influence these descriptive findings.

Figure 3: Population-size uncertainty and high budget impact concerns over time (NCPE only)



05. Conclusions

Negative, conditional and access-restricted HTA recommendations commonly contained several overlapping concerns. Cost-effectiveness concerns usually occurred alongside uncertainty about the clinical evidence, comparators, patient populations or economic model.

Among outright-negative recommendations, cost-effectiveness concerns were frequent for both NICE and NCPE. Other concern profiles differed, although these comparisons involved different sets of assessments and should not be interpreted as differences in agency stringency.

The analysis identifies recurring concerns that warrant attention when developing evidence and preparing economic submissions. Linking recorded concerns to the original assessment documents supports interpretation and further investigation. The findings describe documented concerns and do not establish which issues determined the final recommendation.

Abbreviations *HTA: Health Technology Assessments; ICER: incremental cost-effectiveness ratio; NCPE: National Centre for Pharmacoeconomics; NICE: National Institute for Health and Care Excellence*

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