# Reviewing implementation in practice of the NICE Health Technology Evaluation Manual


November 2024

# Executive summary

In 2019, the National Institute for Health and Care Excellence (NICE) initiated a significant review of the methods and processes used to evaluate health technologies. The review concluded in early 2022 with the publication of a new Health Technology Evaluation (HTE) Manual, with NICE stating that *"the changes [contained] will give patients earlier access to innovative new treatments by allowing greater flexibility over decisions about value for money and consideration of a broader evidence base"*.[1] At the time, the Association of the British Pharmaceutical Industry (ABPI) welcomed the changes but raised concerns that they did not sufficiently meet the level of ambition that had been anticipated by many stakeholders, including the pharmaceutical industry (and as set out in the government's Life Sciences Vision), and could therefore risk patients in England not being able to access innovative medicines.[2]

To help monitor the impact of the key changes set out in the HTE Manual, the ABPI launched an initiative – Continuous NICE Implementation Evaluation (CONNIE)[3] – to collect feedback from companies on implementation. More than two years on, the impact is starting to become apparent. This report is the third in the ABPI's CONNIE series, which aims to review company feedback and explore trends. This latest analysis now captures feedback from 72 completed evaluations, which is representative of 76 per cent of all topics that have concluded in the analysis timeframe.

The capped 2024 Voluntary scheme for branded medicines Pricing, Access and Growth (VPAG) presents a five-year opportunity to address the UK's decade-long underinvestment in medicines, without increasing costs to the NHS above agreed limits. In this context, it is more important than ever to ensure NICE's methods and processes are robust, fit for purpose, and can adequately value and support the introduction of new medicines and significant indications into the NHS.

**Key insights from the analysis**

- **Severity modifier:** the severity modifier has been applied in 21 topics (30 per cent of all topics) – which represents a recent increase in utilisation of the severity modifier. The average quality-adjusted life year (QALY) weighting across the entire CONNIE sample is 1.092. The current analysis and a recent NICE analysis use different methodologies to evaluate the implementation of the severity modifier against design.[4] The degree to which there is a gap between opportunity cost neutrality and implementation of the severity modifier depends on the methodology used. **Had the end of life criteria been applied to appraisals following the implementation of the methods review, additional weighting and value of 8.9 per cent for oncology medicines would have been offered over and above what is provided by the severity modifier.**

- **Uncertainty: there was increased utilisation of flexibilities for uncertainty for the specific circumstances where NICE outlined a greater acceptance of uncertainty as part of the methods review**. Companies reported 15 topics (21 per cent) where NICE committees accepted greater uncertainty and it was clear how this impacted decision making – in five topics for innovation, three topics for rarity, one topic for paediatric and five topics for a combination of factors. However, a decision making incremental cost-effectiveness ratio (ICER) threshold at the lower end of the range (e.g. below £25,000) was used in 45 per cent of these topics.
- **Non-reference case flexibilities:** despite 19 topics (26 per cent) making a case for non-reference case flexibilities (e.g. 1.5 per cent discount rates and wider societal perspectives), the NICE committee did not fully grant non-reference case flexibilities in any topic. Two of these topics were ultimately not recommended for use by NICE.
- **Additional flexibilities:** there was an increased number of topics where companies made cases for additional flexibilities such as surrogate endpoints, carer quality of life (QoL) and real-world evidence (RWE). **Encouragingly, in all three flexibilities, companies reported a high rate of acceptance**.
- **Decision making ICER threshold: There are concerns from industry that there has been an increase in the number of appraisals where a decision making ICER threshold to the lower end of the £20,000 - £30,000 per QALY range was used.** Companies report that typically, appraisal committees cite the degree of uncertainty in a given appraisal as the driver behind this. The ABPI will look to explore this in further research.

# Recommendations

1. The ABPI recommends that government steps in and releases NICE from its current constraint of opportunity cost neutrality so that NICE can review the severity modifier to adjust the cut-off levels used to determine the degree of severity – so that more medicines can benefit.
2. NICE recently re-committed to conducting further research into societal preferences on severity but set a timeline of more than two years before this work would report back. The ABPI welcomes NICE's commitment to conducting this research but urges NICE to be more ambitious on timelines, given the potential impact of this delay on patients. We urge NICE to rapidly commission the necessary research and to provide clarity on the process and timelines for this to its stakeholders.
3. There remain concerns from industry about the relationship between uncertainty and the decision making ICER threshold. The ABPI will look to explore this in further research. The ABPI recommends NICE works collaboratively with industry to understand any potential trends in the relationship between uncertainty and decision making ICER thresholds and take action to address if necessary.
4. NICE should bring to life the commitments set out in the HTE Manual to offer non-reference case flexibilities, including allowing relevant topics to use a 1.5 per cent discount rate and evolving methods to allow full inclusion of a wider societal perspective to allow more patients to benefit from innovative medicines.
5. Given mostly positive experiences and a high degree of appraisal committee acceptance reported by companies when using broader methods flexibilities – such as surrogate endpoints, carer QoL and RWE – companies should explore all opportunities to use the flexibilities offered. We recommend that NICE continues to work with companies to encourage their use where appropriate.

# Introduction

Following an extensive review of the methods and processes used in its health technology evaluations, NICE published an updated HTE Manual in January 2022.[5] NICE stated, *"the changes will give patients earlier access to innovative new treatments by allowing greater flexibility over decisions about value for money and consideration of a broader evidence base".*[6] Key changes included:

- Giving additional weight to health benefits in the most severe conditions to allow more equitable access to treatments for these conditions, alongside withdrawing the end of life modifier that was introduced in 2009.
- Adopting new approaches to the evidence NICE considers in its assessments. For example, improving how RWE from the lived experiences of patients can be used in evaluations.
- Allowing more flexibility for NICE's independent committees in cases where it is particularly difficult to generate enough evidence. Sometimes, research into conditions affecting children, rare diseases or where the new treatment is innovative or complex can be problematic. The changes were intended to allow NICE's committees to consider uncertainty more appropriately and to manage the risks to patients and the NHS while preventing inappropriate barriers to valuable innovations.
- Adopting a clearer vision, and clearer principles and routing criteria for treatments for very rare diseases that NICE will evaluate under its Highly Specialised Technologies (HST) Programme. This was intended to improve the efficiency, predictability and clarity when routing topics to the programme and build upon NICE's ambition to provide fairer access to highly specialised medicines and treatments within the NHS.
- Earlier engagement with NHS England and companies about commercial/managed access proposals that allow NHS patients to receive a treatment while further data is collected on its effectiveness. There will also be greater clarity around the circumstances in which NICE committees can make a managed access recommendation.

The ABPI welcomed the changes but raised concerns when the new HTE Manual was published that the outcome of the review did not meet the level of ambition that was anticipated by many stakeholders, including the pharmaceutical industry (as set out in the government's Life Sciences Vision), and that this might negatively impact patient access to some new medicines/indications at a critical time when the UK needs to be seen as an attractive priority launch market on the global stage.[7]

NICE made commitments to closely monitor the impact of the HTE Manual in practice and to adopt a more agile, modular approach to making further updates to its methods and processes. To support these endeavours, the ABPI launched a new initiative – CONNIE – to collect continuous feedback from its members on the implementation of the key changes in the HTE Manual. CONNIE captures member feedback on completed evaluations only. Therefore, CONNIE does not consider feedback on the recent trend of increased NICE terminations or discontinued topics.[8]

In August 2024, the ABPI published the second report presenting the CONNIE data to review the impact of the updated NICE HTE Manual (CONNIE: Round 2).[9] Key insights included: the severity modifier being applied on a more conservative basis than needed to deliver opportunity cost neutrality, as per its design; companies reporting limited evidence of committees accepting greater uncertainty in the evidence base; and no instances of NICE committees granting non-reference case flexibilities.

As companies continue to provide feedback monitoring the implementation of the updated NICE HTE Manual to the ABPI, and the CONNIE database grows, the ABPI plans to publish twice-yearly updates in the CONNIE series to continuously review the impact of the updated NICE HTA Manual. The current report (CONNIE: Round 3) represents the third report in this series.

**Note - CONNIE captures company feedback and the analysis presented does not attempt to determine whether modifiers and flexibilities should, or should not, have been applied in any particular evaluation.**

# CONNIE analysis

## 1. Sample

Building on the 39 topics outlined in the previous CONNIE report (CONNIE: Round 2), this latest report (CONNIE: Round 3) includes an additional 33 topics. Therefore, the total sample includes data for 72 topics that have completed their evaluation (to publication of final guidance), up to September 2024, using the updated methods set out in the HTE Manual. The sample includes 53 (74 per cent) single technology appraisals (STA), eight (11 per cent) cost comparison appraisals, three (4 per cent) multiple technology appraisals (MTA), four (6 percent) Cancer Drugs Fund (CDF) / Innovative Medicines Fund (IMF) exit appraisals, and two (3 per cent) HST evaluations.10 The sample represents 76 per cent of all topics using the updated methods set out in the HTE Manual that have concluded in the period to September 2024.

**Date of final guidance publication**

Where analysis of trends over time is of interest, this report presents results within half-yearly time periods. Topics are categorised by the date of publication of final guidance, with half one (H1) covering appraisals with final guidance from April to September and half two (H2) covering appraisals with final guidance from October to March. Table 1 outlines the number of topics from CONNIE Rounds 1-3 reports by date of final guidance publication.

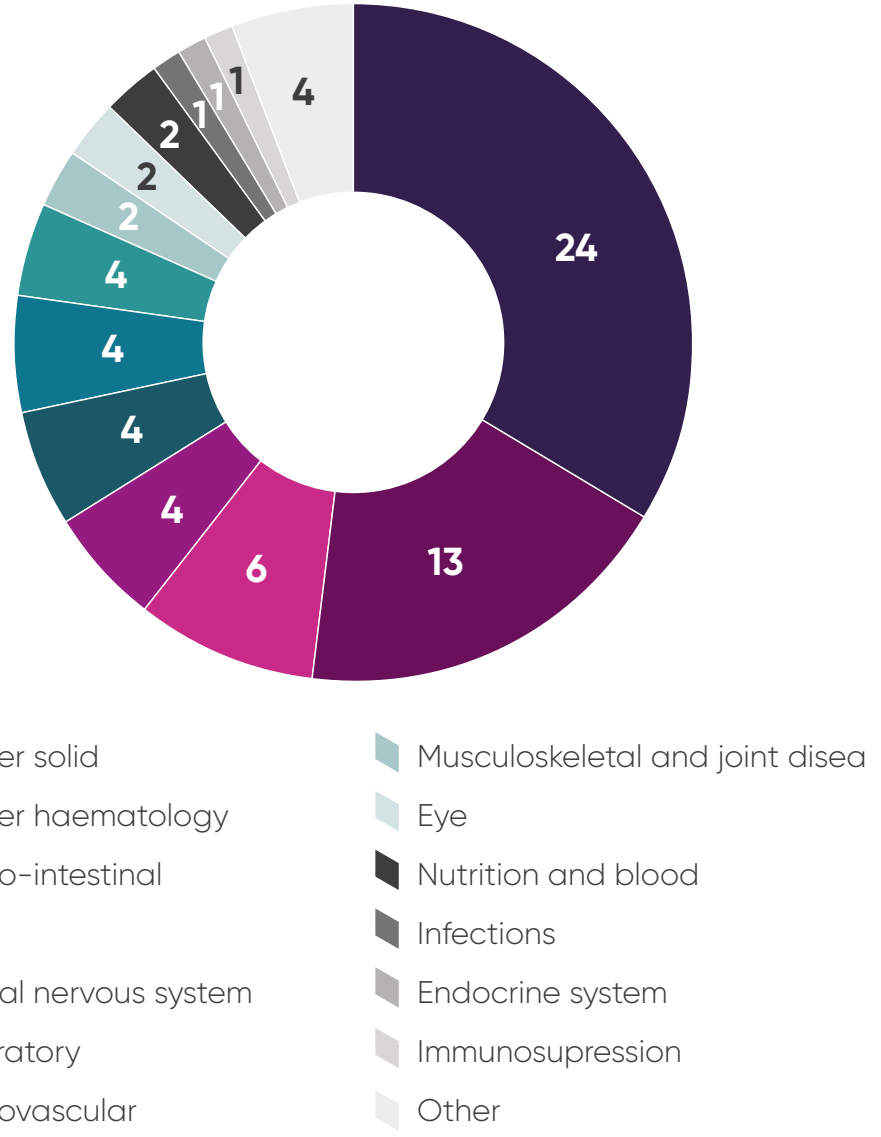
Table 1: CONNIE rounds by date of final guidance publication

| | H2 2022/23 topics (%) | H1 2023/24 topics (%) | H2 2023/24 topics (%) | H1 2024/25 topics (%) | Total |
|---|---|---|---|---|---|
| CONNIE: Round 1 | 7 (78%) | 13 (76%) | 0 (0%) | 0 (0%) | 20 (28%) |
| CONNIE: Round 2 | 2 (22%) | 4 (24%) | 13 (48%) | 0 (0%) | 19 (26%) |
| CONNIE: Round 3 | 0 (0%) | 0 (0%) | 14 (52%) | 19 (100%) | 33 (46%) |
| Total | 9 (100%) | 17 (100%) | 27 (100%) | 19 (100%) | 72 (100%) |

## Sample characteristics

- Thirty-two (44 per cent) new active substances and 40 (56 per cent) licence extensions.
- Fifty-three (74 per cent) monotherapies, 12 (17 per cent) combination therapies with generics, and seven (10 per cent) combination therapies with other branded medicine(s).
- Thirty-eight (53 per cent) common indications, 27 (38 per cent) orphan indications, and seven (10 per cent) ultra-orphan indications.
- Two (3 per cent) ATMPs.
- Thirty-seven (51 per cent) cancer medicines.
- Forty-five (63 per cent) first in class, 13 (18 per cent) second in class, 10 (14 per cent) third in class, two (3 per cent) fourth in class, and two (3 per cent) other/unknown position in class.
- The evidence submissions were reviewed by 11 Evidence Assessment Groups (EAGs).
- The topics covered a representative range of all five NICE appraisal committees.

Figure 1: Breakdown of topics by therapy area



# 2. NICE guidance outcomes

Fifty-two topics (72 per cent) were fully recommended, nine (13 per cent) were optimised, four (5 per cent) were recommended for use in the CDF/IMF and seven (10 per cent) were not recommended (Table 2). H1 2024/25 saw the first instance of NICE recommending a topic in the IMF for its intended use – etranacogene dezaparvovec for adults with severe or moderately severe haemophilia B without a history of FIX inhibitors.[11]

To validate the CONNIE dataset, a comparison of technology appraisal outcomes was conducted against outcomes of all NICE appraisals in the comparable time period. Largely, the CONNIE dataset is representative of a typical NICE sample with respect to outcomes. The CONNIE dataset outcomes reflect a higher proportion of fully recommended topics and a lower proportion of optimised topics – this is likely because companies are reporting some optimised appraisals as recommended in CONNIE feedback.

CONNIE only captures data for completed evaluations, so the results and insights in this report do not include topics that NICE has terminated. Given a recent increasing trend of NICE terminations, some results in this sample may be prone to selection bias with an increasing number of appraisals with unfavourable access conditions excluded due to them being terminated.

Table 2: NICE guidance outcomes for CONNIE topics

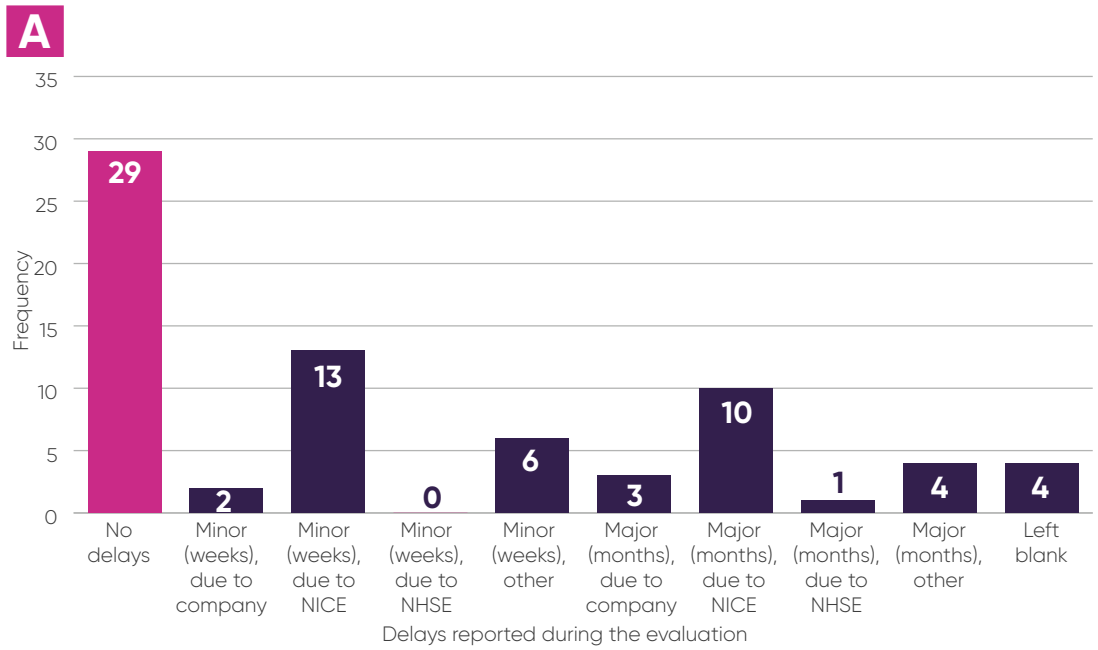
| | H2 2022/23 topics (%) | H1 2023/24 topics (%) | H2 2023/24 topics (%) | H1 2024/25 topics (%) | Total |
|---|---|---|---|---|---|
| Recommended | 7 (78%) | 11 (65%) | 18 (67%) | 16 (84%) | 52 (72%) |
| Optimised | 1 (11%) | 3 (18%) | 4 (15%) | 1 (5%) | 9 (13%) |
| Recommended – CDF/IMF | 1 (11%) | 1 (6%) | 1 (4%) | 1 (5%) | 4 (5%) |
| Optimised – CDF/IMF | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Not recommended | 0 (0%) | 2 (12%) | 4 (15%) | 1 (5%) | 7 (10%) |
| Total | 9 (100%) | 17 (100%) | 27 (100%) | 19 (100%) | 72 (100%) |

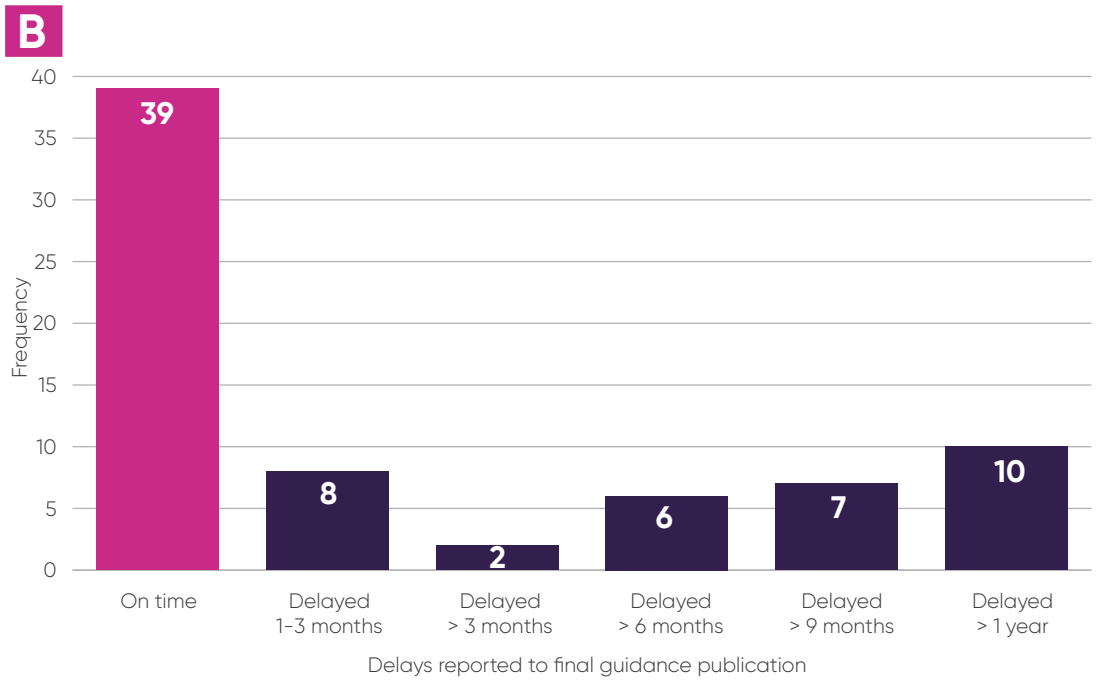
# 3. Process steps and timing

Evaluation scheduling (reported as companies receiving an invitation to participate) was on time for 53 topics (76 per cent). Ten topics (14 per cent) were delayed by NICE and seven topics (10 per cent) were delayed by companies.

Some delays were reported during the evaluation process for 39 topics (54 per cent), these were predominantly due to NICE (23 topics, 32 per cent, as per Figure A). There were also delays to publication of final guidance in 33 topics (46 per cent, as per Figure B) and in 23 of these topics (32 per cent), delays were greater than six months.

Figure 2: Delays reported during the evaluation (A) and to final guidance publication (B)




## Scoping

Topics are scoped at the beginning of the evaluation process to define what questions the evaluation will answer and what will and will not be included, providing a framework and defining the issues for consideration. NICE has flexibility to vary the consultation timing for developing the scope and to determine the degree of engagement that is required. Thirty-five topics (49 per cent) had no scoping engagement, indicating they were probably not in a new or complex disease area/care pathway. Of the 37 topics where scoping was held, 14 topics (15 per cent) had a full workshop, five topics (7 per cent) had a short/abbreviated workshop, and 18 topics (25 per cent) had a call instead of a workshop. Recently, NICE has moved away from short/abbreviated

workshops (4/26 – 15 per cent until September 2023 vs 1/36 – 2 per cent after September 2023) and towards full workshops (3/26 – 11 per cent until September 2023 vs 11/36 – 24 per cent after September 2023).

### Technical engagement

Technical engagement is a process step to allow discussions between a company, the EAG and the NICE technical team to identify and consider any evidence gaps, issues and potential resolutions ahead of the committee meeting. It can also be used to consider any commercial or managed access proposals.11 Forty-four topics (61 per cent) had technical engagement (see Table 3). The technical engagement step is no longer a mandatory part of the process, but the ABPI considers it a high-value process step and that it should be utilised when there are significant uncertainties and/or questions about the evidence base. Results indicate there is a recent trend towards less use of technical engagement – noting that for the first time there have been five topics (7 per cent) where the company has requested technical engagement and NICE has rejected this request. Where technical engagement was used, it was considered helpful in most (75 per cent).

Table 3: Number of topics with technical engagement

| Technical engagement | ABPI CONNIE analysis H2 2022/23 topics (%) | ABPI CONNIE analysis H1 2023/24 topics (%) | ABPI CONNIE analysis H2 2023/24 topics (%) | ABPI CONNIE analysis H1 2024/25 topics (%) | ABPI CONNIE analysis total topics (%) |
|---|---|---|---|---|---|
| Technical engagement helped to resolve key issues | 0 (0%) | 4 (24%) | 2 (7%) | 0 (0%) | 6 (8%) |
| Technical engagement resolved some issues | 4 (44%) | 8 (47%) | 11 (41%) | 4 (21%) | 27 (38%) |
| Technical engagement did not resolve issues | 1 (11%) | 3 (18%) | 7 (26%) | 0 (0%) | 11 (15%) |
| No technical engagement (agreed by company) | 4 (44%) | 2 (12%) | 6 (22%) | 11 (58%) | 23 (32%) |
| No technical engagement (despite company request) | 0 (0%) | 0 (0%) | 1 (4%) | 4 (21%) | 5 (7%) |
| Total | 9 (100%) | 17 (100%) | 27 (100%) | 19 (100%) | 72 (100%) |

## Appraisal committee meetings

The average number of committee meetings per topic was 1.56 (see Table 4) with a trend of an increased number of committee meetings observed in more recent time periods (1.68 in H2 2023/24 and 1.63 in H1 2024/25). A potential driver of this could be appraisal committees being increasingly risk averse and preferring to go to second committee meetings before making a decision. Resolving some uncertainties/ questions at the technical engagement stage can support better use of committee meeting time and ensure focus on what matters to the committee decision making.

Table 4: Number of appraisal committee meetings needed to conclude each topic

| Appraisal committee meetings | ABPI CONNIE analysis H2 2022/23 topics (%) | ABPI CONNIE analysis H1 2023/24 topics (%) | ABPI CONNIE analysis H2 2023/24 topics (%) | ABPI CONNIE analysis H1 2024/25 topics (%) | ABPI CONNIE analysis total topics (%) |
|---|---|---|---|---|---|
| 1 | 5 (56%) | 12 (71%) | 9 (33%) | 9 (47%) | 35 (49%) |
| 2 | 1 (11%) | 4 (24%) | 15 (56%) | 9 (47%) | 29 (40%) |
| 3 | 1 (11%) | 1 (6%) | 1 (4%) | 0 (0%) | 3 (4%) |
| 4 | 0 (0%) | 0 (0%) | 0 (0%) | 1 (5%) | 1 (1%) |
| Left blank | 2 (22%) | 0 (0%) | 2 (7%) | 0 (0%) | 4 (6%) |
| Total | 9 (100%) | 17 (100%) | 27 (100%) | 19 (100%) | 72 (100%) |
| Average number of committee meetings | 1.43 | 1.35 | 1.68 | 1.63 | 1.56 |

# 4. Severity modifier

One of the biggest changes made in the updated HTE Manual was the removal of the end of life modifier and its replacement with a new severity modifier. The ABPI supported broadening NICE's definition of 'severity' beyond just imminently life-threatening conditions.

However, in the absence of evidence to clearly define the magnitude of societal value for health benefits in severe diseases, the severity modifier was implemented in an opportunity cost neutral way and designed to have an overall magnitude similar to that applied under the end of life modifier for its initial implementation until it could be evolved further using an evidence-based approach informed by research. By definition and design, this represents a retrograde step for access to cancer medicines for cancer patients.

In NICE's retrospective analysis (of 364 decisions between January 2011 and November 2019), approximately 18 per cent received the end of life QALY weighting (x1.7).12 In designing the new severity modifier to be opportunity cost neutral, NICE estimated 8.2 per cent of decisions should receive the higher QALY weighting, 30.5 per cent should receive the lower QALY weighting and 61.3 per cent should receive no weighting.[13]

This approach caused the ABPI and our members significant concerns, as the proportional and absolute QALY shortfall cut-offs that NICE applied were seen as too challenging to adequately support access to medicines that treat very severe conditions. This ultimately means that patients risk losing access to innovative medicines in England.

Table 5 shows the results for the CONNIE data for company-reported utilisation of the severity modifier against NICE's intended design for the severity modifier. Across the sample, 4.7 topics (7 per cent) received the higher QALY weighting (x1.7), 15.6 topics (22 per cent) received the lower QALY weighting (x1.2), and 49.7 topics (71 per cent) received no QALY weighting.[14]

Previous reports in the CONNIE series have reported strong alignment between the company-proposed, EAG-proposed, and committee-assigned QALY weights. However, the data shows a recent trend towards misalignment. Before 1 April 2024, there was alignment between companies and appraisals committees on the severity modifier in 49/52 topics (96 per cent); after 1 April 2024, there was alignment in 12/19 topics (63 per cent). Companies cited factors like conservative committee modelling assumptions and a paucity of evidence in rare disease spaces as explanations for the misalignment.

Table 5: Percentage of topics applicable for severity modifier when designed, compared to percentage of topics the severity modifier was applied to in its implementation (committee-assigned QALY weights)

| Technical engagement | Design | Implementation | | | | |
|---|---|---|---|---|---|---|
| | Severity modifier design[15] | ABPI CONNIE analysis H2 2022/23, topics (%) | ABPI CONNIE analysis H1 2023/24, topics (%) | ABPI CONNIE analysis H2 2023/24, topics (%) | ABPI CONNIE analysis H1 2024/25, topics (%) | ABPI CONNIE analysis total, topics (%) |
| Higher QALY weight (x1.7) | 8.2% | 2 (25%) | 0.2 (1%) | 1 (4%) | 1.5 (8%) | 4.7 (7%) |
| Lower QALY weight (x1.2) | 30.5% | 0 (0%) | 2.8 (16%) | 5.3 (21%) | 7.5 (39%) | 15.6 (22%) |
| No QALY weight (x1.0) | 61.3% | 6 (75%) | 14 (82%) | 19.7 (76%) | 10 (53%) | 49.7 (71%) |
| Total | 100% | 8 (100%) | 17 (100%) | 26 (100%) | 19 (100%) | 70 (100%) |

**Box 1: NICE Board decision on severity modifier**

The NICE Board met on 25 September 2024 to discuss the implementation of the severity modifier. As part of the preparation for this meeting, NICE published a board paper reviewing the implementation of the severity modifier, which aimed to assess whether the severity modifier is operating as intended, including whether it has been opportunity cost neutral compared to the end of life modifier it replaced – as estimated by average QALY weighting (implementation average QALY weighting 1.125 vs opportunity cost neutrality average QALY weighting 1.122).[4] The NICE analysis has some methodological differences to the ABPI CONNIE analysis, which are explored further in Appendix 1. The paper concluded that the severity modifier is operating as intended and based on the data to date, it has remained opportunity cost neutral compared to the end-of-life modifier. Therefore the recommendation to the board was that no change to the severity modifier is required.

In the public board meeting it was discussed whether – in light of the VPAG cap – there is a case to make changes to the severity modifier, given any additional net spend this would cause would ultimately be returned by industry through VPAG rebates. The NICE board outlines that NICE cannot make any make any adjustments to the severity modifier that would exceed opportunity cost neutrality as NICE is not in a position to implement actions that are cost inflationary without the agreement of the Department of Health and Social Care and ministers. Ultimately, the board aligned with the recommendations of the NICE team and did not recommend a further update to the severity modifier but stated that NICE would continue to monitor it's implementation. NICE set a trigger of two consecutive quarters below

1.10 (currently 1.125) – representing an average QALY weighting gap of 0.022 from opportunity cost neutrality – as a sufficient trigger to reinvestigate.

The board also confirmed – as per recommendations in previous CONNIE reports – that further research into societal preferences on severity is required. NICE has begun scoping this work with plans to tender this work by December 2024 and anticipates it will take two years to report results.

Another way to review whether the modifier is being implemented as opportunity cost neutral is to look at the average QALY weighting granted per topic (Table 6). The increased use of the severity modifier in H1 2024/25 has increased the average QALY weighting in the total Round 3 CONNIE sample to 1.092 (vs. 1.073 in Round 2).

The initial design of the severity modifier was less than true opportunity cost neutrality when compared to end of life. The gap between the severity modifier design and true opportunity cost neutrality represents value that was lost in the original design.

The ABPI has discussed with NICE the methodological differences between the NICE and the ABPI CONNIE analyses – as outlined in more detail in Appendix 1.[4] A key difference in methodologies to measure average QALY weighting between the ABPI CONNIE analysis and NICE analysis is whether the denominator used in the analysis is in 'topics' (the ABPI CONNIE analysis) or 'decisions' (NICE analysis).

When using topics as the denominator, as per the ABPI CONNIE analysis, there is an average QALY weighting gap of 0.065 between opportunity cost neutrality (1.157) and implementation of the severity modifier (1.092). When using decisions as the denominator, as per the NICE analysis, there is no average QALY weighting gap between opportunity cost neutrality (1.122) and implementation of the severity modifier (1.125) – as outlined in NICE's board paper.[4] Therefore, the degree to which there is a gap between opportunity cost neutrality and implementation of the severity modifier depends on the methodology used.

The most representative methodology to estimate average QALY weighting would be to use the weighted number of patients in each topic as the denominator. However, due to practical constraints, this is not considered feasible. Both methodologies presented – using topics and decisions – are different ways to approximate a weighted average of patient numbers. Both have limitations. While the differences in the average QALY weighting gap between implementation and opportunity cost neutrality across the topics and decisions methodologies warrants further investigation, the ABPI recognises NICE used the decisions methodology for the design of the severity modifier and is therefore maintaining this approach to monitor implementation.

Table 6: Severity modifier average QALY weightings design vs implementation

| Source | | Average QALY weighting calculated with topics as denominator | Average QALY weighting calculated with decisions as denominator |
|---|---|---|---|
| Design | Opportunity cost neutrality | 1.157 | 1.122 |
| | Severity modifier design | 1.139 | 1.116 |
| Implementation | NICE analysis | 1.102 | 1.125 |
| | ABPI CONNIE analysis total | 1.092 | -- |
| | ABPI CONNIE analysis H2 2022/23 | 1.175 | -- |
| | ABPI CONNIE analysis H1 2023/24 | 1.041 | -- |
| | ABPI CONNIE analysis H2 2023/24 | 1.068 | -- |
| | ABPI CONNIE analysis H1 2024/25 | 1.134 | -- |

Companies reported that 14 topics (20 per cent) would have met NICE's end of life criteria meaning had NICE not updated it's methods from end of life to the severity modifier, the sample average QALY weighting would have been 1.140. Therefore, the current CONNIE sample average QALY weighting (1.092) is a 4.2 per cent reduction. Replicating the same analysis using the NICE assumptions results in a 3.7 per cent reduction (with 24 per cent of topics meeting end of life criteria). Had the end of life criteria been applied to appraisals following the implementation of the methods review, additional weighting and value for oncology medicines would have been offered over and above what is provided by the severity modifier.

When considering oncology specifically, of the 37 oncology topics in CONNIE, 4.7 topics (13 per cent) received the higher x1.7 QALY weighting, 11.6 topics (31 per cent) received the lower x1.2 QALY weighting and 20.7 topics (56 per cent) received no weighting, which represents an average QALY weighting of 1.152.[14] Companies reported that 14 of these topics (38 per cent) would have met NICE's end of life criteria meaning had NICE not updated it's methods from end of life to the severity modifier, the same oncology topics would have had an average QALY weighting of 1.265. Therefore, the current CONNIE sample average QALY weighting (1.152) is an 8.9 per cent reduction – representing the magnitude of the retrograde step for access to cancer medicines for cancer patients. There were two oncology appraisals in the sample that would have met the end of life criteria but only received a x1.2 QALY weighting under the severity modifier and were subsequently not recommended by NICE – resulting in no access for oncology patients. In both instances, the failure to obtain a x1.7 weighting was cited as a critical factor in the medicine not being recommended.

Table 7: Average QALY weighting for oncology topics under end of life versus severity modifier design

| | Higher QALY weight (~x1.7), topics (%) | Lower QALY weight (x1.2), topics (%) | No QALY weight (x1.0), topics (%) | Average QALY weighting |
|---|---|---|---|---|
| ABPI CONNIE analysis, oncology topics under severity modifier | 4.7 (13%) | 11.6 (31%) | 20.7 (56%) | 1.152 |
| ABPI CONNIE analysis, modifier oncology topics would have received under end-of-life criteria | 14 (38%) | 0 (0%) | 23 (62%) | 1.265 |

NICE implemented the severity modifier with the intention to be opportunity cost neutral to end of life. The ABPI understands this is a constraint placed on NICE by government. At the time, the ABPI raised concerns that an opportunity cost neutral implementation would be damaging for patients.

The ABPI recommends that government steps in and release NICE from its current constraint of opportunity cost neutrality so that NICE can review the severity modifier to adjust the cut-off levels used to determine the degree of severity – so that more medicines can benefit. We feel going beyond opportunity cost neutrality is justified because of the reasons set out below:

- Some patients are missing out on access to crucial medicines that would have been reimbursed under the end of life criteria
- Due to VPAG, the NHS is protected against going past opportunity cost neutrality. Any overspend in the medicines budget will ultimately be paid back via higher industry rebate rates
- OHE research – 'Understanding UK societal preferences for health gains by disease severity'[16] – indicates that societal preferences for treating patients with severe disease start at a much earlier degree of severity than NICE's current severity modifier design. These results give cover to be able to go beyond opportunity cost neutrality in the knowledge that lower cut-offs are likely to be backed by further societal preference research.

The degree to which patient access to medicines for treating patients with severe disease is prioritised relative to less severe disease should represent societal preferences. In 2022, NICE committed to further research into societal preferences on treating severe disease to provide the evidence base for the severity modifier to further evolve to reflect societal preferences. As part of NICE's 25 September 2024 board meeting, NICE re-committed to this research but set a timeline of more than two years before this work would report back. The ABPI welcomes NICE's commitment to conducting this research but urges NICE to be more ambitious on timelines, given the potential impact of this delay on patients. We urge NICE to rapidly commission the necessary research and to provide clarity on the process and timelines for this to its stakeholders.

Following NICE's 2022 commitments to conduct this research, the ABPI has commissioned the Office of Health Economics (OHE) to conduct research to explore the likely results of societal preferences outlined in the OHE report – 'Understanding UK societal preferences for health gains by disease severity'[16]. The results indicate that NICE's current severity modifier is not well aligned with the UK public's preference for prioritising health gains in more severe health states. Societal concern begins at a substantially lower shortfall threshold than NICE's current severity modifier. If NICE's (ultimate) objective is for the priority assigned to new medicines and technologies to reflect societal preferences, results suggest a need for NICE to reassess its criteria for the severity modifier.

# 5. Managing uncertainty

The HTE Manual states:

"6.2.34 The committee will be mindful that there are certain technologies or populations for which evidence generation is particularly difficult because they are:

- rare diseases
- for use in a population that is predominantly children (under 18 years old)
- innovative and complex technologies

In these specific circumstances, the committee may be able to make recommendations accepting a higher degree of uncertainty. The committee will consider how the nature of the condition or technology(s) affects the ability to generate high-quality evidence before applying greater flexibility."[5]

Companies reported 15 topics (21 per cent) where the committee accepted greater uncertainty and it was clear how it impacted decision making (Table 8). Of these 15 topics, greater flexibility was given in five topics for innovation, three topics for rarity, one topic for paediatric and five topics for a combination of factors.

Table 8: Uncertainty management

| | H2 2022/23 topics (%) | H1 2023/24 topics (%) | H2 2023/24 topics (%) | H1 2024/25 topics (%) | Total |
|---|---|---|---|---|---|
| Greater acceptance and clear how impacted decision making | 0 (0%) | 2 (12%) | 4 (15%) | 9 (47%) | 15 (21%) |
| Claimed to be greater acceptance but unclear how impacted decision making | 1 (11%) | 1 (6%) | 0 (0%) | 0 (0%) | 2 (3%) |
| Unsure if greater flexibility/acceptance of uncertainty was applied | 4 (44%) | 4 (24%) | 5 (19%) | 4 (21%) | 17 (24%) |
| No flexibility/greater acceptance applied | 3 (33%) | 10 (59%) | 17 (63%) | 6 (32%) | 36 (50%) |
| Left blank | 1 (11%) | 0 (0%) | 1 (4%) | 0 (0%) | 2 (3%) |
| Total | 9 (100%) | 17 (100%) | 27 (100%) | 19 (100%) | 72 (100%) |

A key result from CONNIE: Round 1 was that no companies reported committees accepting greater uncertainty in the evidence base and it being clear how this had impacted decisions. The results displayed in Table 8 show a continuation of the trend observed in Round 2 – an increasing number of companies reporting greater acceptance of uncertainty and it being clear how this impacted decision making. Experience from companies suggests this result may be driven by improved explicit communication from NICE about existing uncertainty management rather than improved acceptance of uncertainty management from NICE committees.

There remain company concerns about the relationship between NICE's implementation of greater acceptance of uncertainty and the decision making ICER threshold. Companies that reported greater acceptance of uncertainty cited in comments that a decision making ICER threshold towards the lower end of the range was used and there remains significant committee challenge. In the topics where companies reported greater acceptance of uncertainty and a decision making ICER threshold was reported:[17]

- a decision making ICER threshold of below £20,000 per QALY was used in two topics (18 per cent)
- the lower end of the decision making ICER threshold range (e.g. £20,000 - £25,000 per QALY) was used in three topics (27 per cent) – one of which used a x1.7 severity modifier
- the upper end of the decision making ICER threshold range (e.g. £25,000 - £30,000 per QALY) was used in four topics (36 per cent)
- a decision making ICER threshold of above £30,000 per QALY was used in two topics (18 per cent) – one of which was an HST appraisal

The relationship between the implementation of the acceptance of uncertainty and the decision making ICER threshold is explored further in Section 7.

# 6. Non-reference case flexibilities

**Non-reference case flexibilities**

The updated HTE Manual intended to allow greater flexibility in decision making, where this was deemed appropriate, along with permitting the consideration of a broader evidence base.[5] Companies made a case for non-reference case flexibility in 19 topics (26 per cent) – in seven topics (10 per cent) companies made a case for a 1.5 per cent discount rate to be applied and in six topics (8 per cent) companies made a case for adopting a wider societal perspective (the remaining six were not specified).

Despite companies making a case in 19 topics, the NICE committee did not fully grant non-reference case flexibilities in any topic. In three topics, the committee partially accepted the company case for some degree of an inclusion of wider societal impact. There rremain no cases in the CONNIE sample of a NICE committee accepting a case for a 1.5 per cent discount rate. In one appraisal, the committee indicated it was plausible the criteria for a 1.5 per cent discount rate could be met but required further data collection while the medicine was in the IMF. Therefore, a 3.5 per cent discount rate was subsequently used.

NICE's decision not to change the reference case discount rate despite an evidence-based case for change was disappointing and something that the ABPI is seeking to resolve. The retention of a 3.5 per cent discount rate in the reference case puts greater emphasis on being able to utilise the non-reference case flexibility. The analysis shows that committees continue not to apply this which reflects NICE's restrictive criteria for non-reference case discounting. This risks limiting patient access to treatments that have long-term health benefits and societal cost savings outside of the health system.

NICE should bring to life the commitments set out in the HTE Manual to offer non-reference case flexibilities, including allowing relevant topics to use a 1.5 per cent discount rate and evolving methods to allow full inclusion of a wider societal perspective to allow more patients to benefit from innovative medicines.

## Surrogate endpoints

Surrogate endpoints sometimes need to be used to demonstrate treatment effect when final clinical endpoints are unavailable. The HTE Manual recognises this and advises on the type of evidence that should be provided to demonstrate the relationship between the surrogate and the final endpoint. Seventeen topics (24 per cent) used surrogate endpoints for main treatment effect parameter(s), and these were accepted or partially accepted by the committee in 16 topics (22 per cent) (see Table 9). In 12 topics, the surrogate endpoints were used to predict the final endpoint in the cost-effectiveness model. It is encouraging to see a continuation of the trend observed in recent CONNIE reports of committees applying flexibility for accepting an increasing number of surrogate endpoints when final endpoints are not available and that companies are providing good quality evidence to demonstrate the surrogate relationship.

Table 9: Surrogate endpoints used for main treatment effect parameter(s)

| | | H2 2022/23 topics (%) | H1 2023/24 topics (%) | H2 2023/24 topics (%) | H1 2024/25 topics (%) | Total |
|---|---|---|---|---|---|---|
| No surrogate endpoints submitted | | 8 (89%) | 12 (71%) | 20 (74%) | 11 (58%) | 51 (71%) |
| PFS (for OS) | Submitted and accepted | 0 (0%) | 2 (12%) | 1 (4%) | 2 (11%) | 5 (7%) |
| | Submitted and partially accepted | 0 (0%) | 0 (0%) | 1 (4%) | 0 (0%) | 1 (1%) |
| | Submitted and not accepted | 0 (0%) | 1 (6%) | 0 (0%) | 0 (0%) | 1 (1%) |
| Other surrogate endpoints | Submitted and accepted | 1 (11%) | 2 (12%) | 4 (15%) | 1 (5%) | 8 (11%) |
| | Submitted and partially accepted | 0 (0%) | 0 (0%) | 1 (4%) | 1 (5%) | 2 (3%) |
| | Submitted and not accepted | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Left blank | | 0 (0%) | 0 (0%) | 0 (0%) | 4 (21%) | 4 (6%) |
| Total | | 9 (100%) | 17 (100%) | 27 (100%) | 19 (100%) | 72 (100%) |

### Carer quality of life (QoL)

The HTE Manual states:

4.3.17 "Evaluations should consider all health effects for patients, and, when relevant, carers. When presenting health effects for carers, evidence should be provided to show that the condition is associated with a substantial effect on carer's health-related quality of life and how the technology affects carers."

In the previous reports in the CONNIE series, companies reported limited experience of the utilisation of carer QoL. In the latest data, companies reported a total of 10 topics (14 per cent) where carer health-related quality of life (HRQoL) was included in the submission – these were accepted (four topics) or partially accepted (four topics) by the committee for direct use in ICER calculations in most topics of topics.

The ABPI is encouraged to see a recent increase by committees of utilisation and acceptance of flexibilities for carer HRQoL. The ABPI continues to encourage companies, where relevant, to generate and submit evidence to support the evaluation of medicines that impact carer QoL to ensure the full benefit of all health effects can be considered in NICE evaluations, in line with NICE guidance.

### Real-world evidence (RWE)

Another key update to the HTE Manual was to provide more flexibility for considering broader evidence sources used in evaluations. CONNIE captures whether RWE has been used to estimate treatment effect as a) a primary source, b) an adjustor of the primary source, or c) a validator of the primary source. Companies used RWE as the primary source to estimate treatment effect in six topics (eight per cent), as an adjustor to the primary source in three topics (four per cent), and as a validator of the primary source in 20 topics (28 per cent) (Table 10). Of the 29 topics where RWE was used, companies reported some degree of acceptance from committees in 16 topics (55 per cent) and no acceptance from committees in two topics (7 per cent), with 11 topics unclear/unsure/left blank. Successful utilisations of RWE that were accepted by committees include using RWE to inform the comparator arm as an external control and to define transition probabilities in a Markov model.

The current results reflect a trend of increased company submission of RWE in appraisals. Further, when RWE is submitted, there is strong evidence that committees are willing to accept the usage of RWE in line with guidance updates from the methods review.

Table 10: RWE used by company

| | H2 2022/23 topics (%) | H1 2023/24 topics (%) | H2 2023/24 topics (%) | H1 2024/25 topics (%) | Total |
|---|---|---|---|---|---|
| RWE used to estimate treatment effect – primary source | 1 (11%) | 1 (6%) | 0 (0%) | 4 (21%) | 6 (8%) |
| RWE used to estimate treatment effect – adjustor of primary source | 0 (0%) | 0 (0%) | 2 (7%) | 1 (5%) | 3 (4%) |
| RWE used to estimate treatment effect – validator of primary source | 3 (33%) | 4 (24%) | 7 (26%) | 6 (32%) | 20 (28%) |
| RWE not used to estimate treatment effect | 5 (56%) | 11 (65%) | 17 (63%) | 8 (42%) | 41 (57%) |
| Left blank | 0 (0%) | 1 (6%) | 1 (4%) | 0 (0%) | 2 (3%) |
| Total | 9 (100%) | 17 (100%) | 27 (100%) | 19 (100%) | 72 (100%) |

# 7. Decision making and commercials

### Commercial flexibility

Companies reported that in 20 topics (28 per cent), a medicine required additional commercial flexibility for a positive recommendation – three of these topics were in the CDF / IMF. The most common flexibility required was indication-based pricing (13 topics – two of these topics were in the CDF / IMF).

In 16 of these topics (80 per cent), companies reported having to give additional flexibility by coming in at or below the lower end of the ICER threshold.' as per tracked change in word document.

### Committee decision making ICER: company vs. EAG assumptions

The results show a trend of increasing clarity for companies on what the committee's preferred decision making ICER was. Results indicate that until September 2023 this clarity was provided in 14/23 topics (61 per cent) and after September 2023 this clarity was provided in 33/41 topics (80 per cent). This clarity over the sharing of ICERs forms part of a concerted effort by NICE following collaborative work with industry. The ABPI welcomes the additional clarity that this provides in the appraisal process.

Across an appraisal, companies put forward and develop a series of modelling assumptions that comprise a cost-effectiveness model from which an ICER can be calculated. Across the appraisal process, an EAG will critique the company modelling assumptions and put forward their own set of (typically more conservative) modelling assumptions that result in a separate (typically higher) ICER. It is the role of an appraisal committee to determine which modelling assumptions to use to inform the cost-effectiveness model and ICER that are used for decision making.

When clarity over the decision making ICER used is provided, companies can to make a judgement on whether the appraisal committee used an ICER for decision making that was closer to the company's or EAG's ICER (Table 11). Companies reported that in 51 per cent of topics, the appraisal committee used an ICER that was closer to the EAG estimate and in 49 per of topics the appraisal committee used an ICER that was either closer to the company or was a mid-point. This indicates that while committees do lean towards EAG ICERs, that impact does not appear to be severe.

Table 11: If there was clarity over the decision making ICER, do you consider this ICER was closer to the company or EAG estimate of cost-effectiveness? Or in the middle?

| | H2 2022/23 topics (%) | H1 2023/24 topics (%) | H2 2023/24 topics (%) | H1 2024/25 topics (%) | Total |
|---|---|---|---|---|---|
| Closer to company estimate | 0 (0%) | 3 (27%) | 6 (30%) | 3 (27%) | 12 (27%) |
| Mid-point ICER landed on | 1 (33%) | 2 (18%) | 3 (15%) | 4 (36%) | 10 (22%) |
| Closer to EAG estimate | 2 (67%) | 6 (55%) | 11 (55%) | 4 (36%) | 23 (51%) |
| Total | 3 (100%) | 11 (100%) | 20 (100%) | 11 (100%) | 45 (100%) |

### Decision making ICER threshold

The appraisal committee will use an ICER threshold for decision making during an appraisal. Under normal circumstances, NICE will adopt a decision making ICER threshold in the £20,000 - £30,000 per QALY range. Within this range, the NICE committee determines the decision making ICER threshold depending on the degree of uncertainty around the ICER and aspects that relate to uncaptured benefits and non-health factors. Table 12 demonstrates the committee decision making ICER thresholds in the CONNIE dataset. A decision making ICER threshold below £25,000 per QALY was used in 29 topics (54 per cent) and a decision making ICER threshold above £25,000 per QALY was used in 25 topics (46 per cent).

Table 12: Committee decision-making ICER threshold

| | H2 2022/23 topics (%) | H1 2023/24 topics (%) | H2 2023/24 topics (%) | H1 2024/25 topics (%) | Total |
|---|---|---|---|---|---|
| Below £20,000 | 1 (20%) | 4 (31%) | 6 (26%) | 2 (15%) | 13 (24%) |
| £20,000-£25,000 | 0 (0%) | 5 (38%) | 8 (35%) | 3 (23%) | 16 (30%) |
| £25,001-£30,000 | 2 (40%) | 3 (23%) | 8 (35%) | 7 (54%) | 20 (37%) |
| Above £30,000 | 2 (40%) | 1 (8%) | 1 (4%) | 1 (8%) | 5 (9%) |
| Total | 5 (100%) | 13 (100%) | 23 (100%) | 13 (100%) | 54 (100%) |

Consistent anecdotal evidence from companies suggests there has been a recent shift in the distribution of decision making ICER thresholds towards the lower end of the £20,000 – £30,000 per QALY range compared to pre-2022. Common feedback received by companies is that NICE typically cites the degree of uncertainty in a given appraisal as the driver behind this. The current results indicate a distribution of decision making ICER thresholds that is balance across the £20,000 – £30,000 per QALY range. However, data is only provided following the 2022 methods review so a historical comparison to explore any shifts in this distribution is not feasible. Further research is required to explore any potential longer-term shifts in the distribution of decision making ICER thresholds.

Concerning uncertainty, there are examples of topics where NICE has communicated greater acceptance of uncertainty, but committees are still using decision making ICER thresholds at the lower end of the £20,000 - £30,000 per QALY range. Similarly, there are several examples where a severity modifier is applied and the decision making ICER threshold is at the lower end of the threshold range. Companies have suggested that the impact of uncertainty driving to the lower end of the ICER threshold has, in some instances, negated any additional benefit from a severity modifier.

There remain concerns from industry about the relationship between uncertainty and the decision making ICER threshold. Specifically, there are concerns that there has been an increase in the number of appraisals where a decision making ICER threshold to the lower end of the £20,000 - £30,000 per QALY range was used compared to pre-2022. Companies report that typically, appraisal committees cite the degree of uncertainty in a given appraisal as the driver behind this. The ABPI will look to explore this in further research. The ABPI recommends NICE works collaboratively with industry to understand any potential trends in the relationship between uncertainty and decision making ICER thresholds and take action to address if necessary.

# Conclusion

This is the third report in the CONNIE series to monitor the impact of the 2022 HTE Manual.

The report details some positive company experiences with the implementation of the methods review in areas such as surrogate endpoints, carer QoL, RWE, and additional clarity over the decision making ICER.

However, there remain significant concerns over the severity modifier. Despite the Round 3 results demonstrating increased utilisation of the severity modifier, there is further evidence of a retrograde step for access to cancer medicines with patients missing out on access to crucial medicines that would have been reimbursed under the end-of-life criteria. Industry has substantial concerns that NICE's opportunity cost neutral restriction is risking patients in England not being able to access innovative medicines. Recent research from the OHE indicates that societal preferences for treating patients with severe disease start at a much earlier degree of severity than NICE's current severity modifier design. Results suggest a need for NICE to reassess its criteria for the severity modifier and there are concerns from industry and patient groups around the timelines NICE has put forward to conduct this research.

Furthermore, while there is an indication of NICE appraisal committees allowing greater acceptance of uncertainty in some topics – there remain industry concerns about the relationship between NICE's implementation of greater acceptance of uncertainty and the decision making ICER threshold.

The ABPI will continue to work collaboratively with its members and NICE to evolve NICE methods and processes to support improved patient access across the UK.

# Recommendations

**Recommendations**

1. The ABPI recommends that government step in and release NICE from its current constraint of opportunity cost neutrality so that NICE can review the severity modifier to adjust the cut-off levels used to determine the degree of severity – so that more medicines can benefit.
2. NICE recently re-committed to conducting further research into societal preferences on severity but set a timeline of more than two years before this work would report back. The ABPI welcomes NICE's commitment to conducting this research but urge NICE to be more ambitious on timelines, given the potential impact of this delay on patients. We urge NICE to rapidly commission the necessary research and to provide clarity on the process and timelines for this to its stakeholders.
3. There remain concerns from industry about the relationship between uncertainty and the decision making ICER threshold. The ABPI will look to explore this in further research. The ABPI recommends NICE works collaboratively with industry to understand any potential trends in the relationship between uncertainty and decision making ICER thresholds and take action to address if necessary.
4. NICE should bring to life the commitments set out in the HTE Manual to offer non-reference case flexibilities, including allowing relevant topics to use a 1.5 per cent discount rate and evolving methods to allow full inclusion of a wider societal perspective to allow more patients to benefit from innovative medicines.
5. Given mostly positive experiences and a high degree of appraisal committee acceptance reported by companies when using broader methods flexibilities – such as surrogate endpoints, carer QoL and RWE – companies should explore all opportunities to use the flexibilities offered. We recommend that NICE continues to work with companies to encourage their use where appropriate.

**The ABPI will continue working with its members to collect feedback and help support NICE's monitoring of the impact of the key changes made in the HTE Manual.**

**We would like to thank our members for supporting us with evidence generation and NICE for continuing to engage in a collaborative way to support our joint ambition to ensure the methods and processes used to evaluate technologies enable timely patient access to clinically and cost-effective medicines.**

# Appendix

## Appendix 1: Methodological differences between ABPI CONNIE analysis and NICE

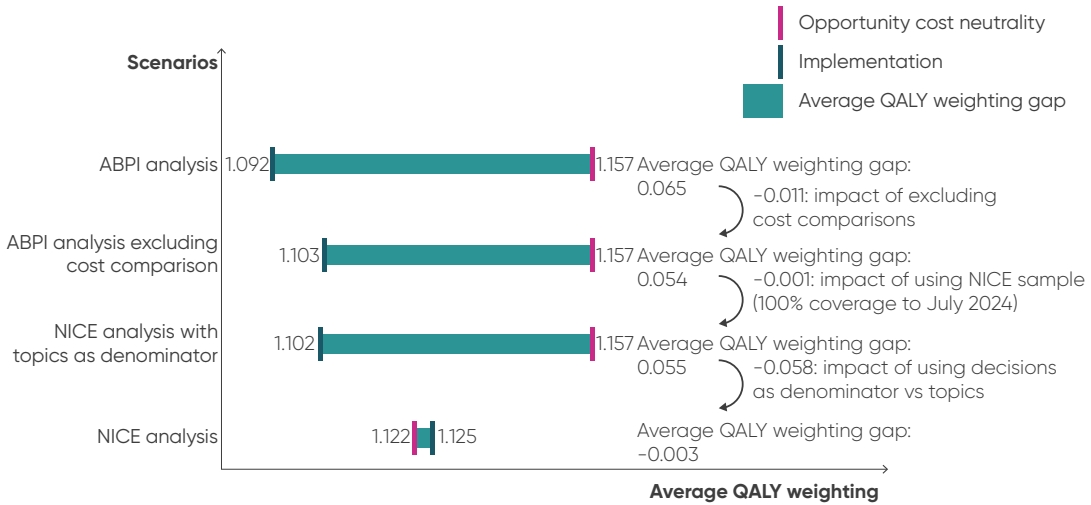
On 24th September 2024 ahead of the NICE Board meeting, NICE published a Board paper reviewing the implementation of the severity modifier which aimed to assess whether the severity modifier is operating as intended, including whether it has been opportunity cost neutral compared to the end-of-life modifier it replaced. The analysis in that report, whilst comparable to the current ABPI CONNIE analysis on the severity modifier (Section 4), comes to an alternative conclusion regarding whether the severity modifier has been implemented in an opportunity cost neutral manner. The reasons for this are due to differing methodological approaches to the analysis which have since been reconciled and understood through cooperative engagement between NICE and ABPI. The NICE analysis addresses these methodological differences. The methodological differences are outlined in more detail in Table 13.

Table 13: Methodological differences

| | NICE analysis[18] | ABPI CONNIE analysis |
|---|---|---|
| Time frame | Completed appraisals until July 2024 | Completed appraisals up until September 2024 |
| Coverage | Full coverage | Coverage of appraisals submitted by members representing 76% of all appraisals |
| Inclusion of cost comparisons | Does not include cost comparisons in average QALY weight calculations | Does include cost comparisons in average QALY weight calculations (n=8) |
| Denominator used in calculations (topics vs decisions) | Considers the number of independent decisions. For example, in a topic with one subgroup with a x1.2 modifier and one subgroup with a x1.7 modifier, NICE would count this as n=1 for x1.2 and n=1 for x1.7 in average QALY weighting calculations. | Considers the number of independent topics. For example, in a topic with one subgroup with a x1.2 modifier and one subgroup with a x1.7 modifier, ABPI would count this as n=0.5 for x1.2 and n=0.5 for x1.7 in average QALY weighting calculations. |
| Total sample | 91 decisions across 62 topics | 70 topics |

The impact that these methodological differences have on the average QALY weighting gap is outlined in Figure 3. Starting with the ABPI analysis (average QALY weighting gap) each scenario demonstrates the impact of a given methodological change on the average QALY weighting gap. Of the disparity in average QALY weighting gap between the ABPI analysis and the NICE analysis, 16% is explained by the inclusion/exclusion of cost comparisons, -1% is explained by differences in time frame/coverage and 85 per cent us explained by the denominator used in calculations (topics vs decisions).

Figure 3: Impact of methodological differences on average QALY weighting gap



# Endnotes


1 NICE, 'NICE publishes new combined methods and process manual and topic selection manual for its health technology evaluation programmes', January 2022, available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation

2 HM Government, 'Life Sciences Vision', 2021, available at https://www.gov.uk/government/publications/life-sciences-vision

3 To find out more about CONNIE, please contact the ABPI's Value and Access team.

4 NICE, 'Review of the implementation of the severity modifier', 25 September 2024. Available at: https://www.nice.org.uk/get-involved/meetings-in-public/public-board-meetings/public-board-meeting-agenda-and-papers--september-2024

5 NICE, 'NICE health technology evaluations: the manual', 31 January 2022, available at https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation

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7 ABPI, 'ABPI analysis on NICE's changes for evaluating new medicines: Next steps', 31 January 2022, available at https://www.abpi.org.uk/media/blogs/2022/january/abpi-analysis-on-nice-s-changes-for-evaluating-new-medicines-next-steps

8 Recent data demonstrates the EFPIA 2024 Patient W.A.I.T. Indicator. https://efpia.eu/news-events/the-efpia-view/efpia-news/new-data-from-efpia-reveals-multiple-factors-leading-to-unequal-access-to-medicines-for-patients-across-europe/

9 ABPI, CONNIE: Round 2, 14 August 2023, available at: https://www.abpi.org.uk/publications/reviewing-implementation-in-practice-of-the-nice-health-technology-evaluation-manual-connie-august-2024/

10 All percentages represent proportion of total CONNIE sample (n=72) unless otherwise stated

11 CSL Behring, NICE recommends CSL Behring's HEMGENIX®, 27 June 2024. https://www.cslbehring.de/en-us/news/2024/pm-hemgenix-managed-access-uk

12 NICE, 'Review of methods for health technology evaluation programmes: proposals for change', August 2021.

13 Proportional QALY shortfall (PS) must be between 0.85 and 0.95 or absolute QALY shortfall (AS) must be between 12 and 18 for a medicine to receive a x1.2 QALY weighting. PS must be at least 0.95 or AS must be at least 18 for a medicine to receive a x1.7 QALY weighting.

14 Decimals denote the weight applied when a topic contains multiple severity modifier decisions across populations as outlined in Appendix 1

15 The severity modifier design is in decisions, not topics. No equivalent design has been released by NICE in topics

16 OHE report, https://www.ohe.org/publications/understanding-societal-preferences-for-priority-by-disease-severity-in-england-wales/

17 In four topics the company did not report an ICER decision making threshold

18 As per the primary+ subsample

**The Association of the British Pharmaceutical Industry**

A company limited by guarantee registered in England & Wales number 09826787

Registered office 2nd Floor Goldings House, Hay's Galleria, 2 Hay's Lane, London, SE1 2HB

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