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NICE technology appraisals of oncology treatments

A review of economic modeling approaches, recommendation decisions and the potential impact of the new severity modifier

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The appraisal of oncology treatments is a key activity conducted by the National Institute for Health and Care Excellence (NICE). As part of the Department of Health and Social Care in England, NICE provides evidence-based best practices to help get the best care to patients while ensuring value for the taxpayer.[1]

The assessments and recommendations made by NICE have a profound impact on the accessibility of cancer treatments in England and Wales and often serve as a reference point for health technology assessment (HTA) bodies worldwide. To help manufacturers (drug development sponsors) incorporate market access planning and navigate the complex landscape of HTA evaluation of innovative oncology treatments, this white paper provides an overview of NICE assessment methods and discusses target indications, health economic modeling approaches, cost-effectiveness estimates and recommendation decisions.

NICE recommendation types for oncology treatments

Of the 978[2] technology appraisals (TAs) published by NICE between 2000 and August 2024, nearly half (464; 47.4%)[3] have been for oncology indications. NICE appraisal committees can make five types of recommendations for oncology treatments:

1. Recommended for use
2. Optimized recommendation (recommended for smaller group than stated in marketing authorization)
3. Recommended for use in Cancer Drugs Fund[4] (The CDF is a dedicated fund for promising oncology treatments that require further evidence to demonstrate cost-effectiveness)
4. Research use only
5. Not recommended

An overview of NICE process and methods

To assess the value for money of healthcare technologies, NICE generally considers interventions to be cost-effective if their incremental cost-effectiveness ratio (ICER) is £20,000 to £30,000 per quality-adjusted life year (QALY) gained.[5] However, in recognition that some interventions address areas of particular clinical unmet need, for example, severe, rare or life-limiting diseases, NICE has established modifiers to its general willingness-to-pay threshold. In 2009, end-of-life (EoL) criteria[6] were introduced for technologies that extend life at the end of life, such as treatments with survival benefits in terminal cancer. To meet EoL criteria, a treatment had to be indicated for patients with short life expectancy (usually <24 months), with evidence supporting an extension of life (usually an additional three months) compared with current treatment. The cost-effectiveness of treatments meeting these criteria was assessed at a willingness-to-pay threshold of £50,000 per QALY gained.

In 2022, NICE published updated methods[7] that introduced a severity modifier to replace the EoL criteria. The severity modifier is based on the concept of the proportional and absolute QALY shortfall. NICE proposed that the shortfall be calculated based on the difference in the quality-adjusted life expectancy (QALE) of a person with and without a particular disease (at a given age):

Absolute shortfall = expected total QALY loss
Proportional shortfall = percentage of the QALYs that are lost

The resulting QALY shortfall determines which of three severity levels is applied to weight the willingness-to-pay threshold (Table 1). This, in turn, results in modified cost-effectiveness thresholds of £30,000, £36,000 and £50,000 by severity level, respectively.

Table 1: QALY weights for three severity levels

QALY weight	Proportional QALY shortfall	Absolute QALY shortfall
1	Less than 0.85	Less than 12
x 1.2	0.85 to 0.95	12 to 18
x 1.7	At least 0.95	At least 18

Considering the influential role of NICE TAs in oncology, it is important for manufacturers to understand how submission evidence is reviewed and appraisal recommendations are made. Critical components include the health economic modeling approach taken, the impact of EoL status and new severity modifier on assessments, as well as the degree of alignment between cost-effectiveness estimates and the ultimate recommendation decisions.

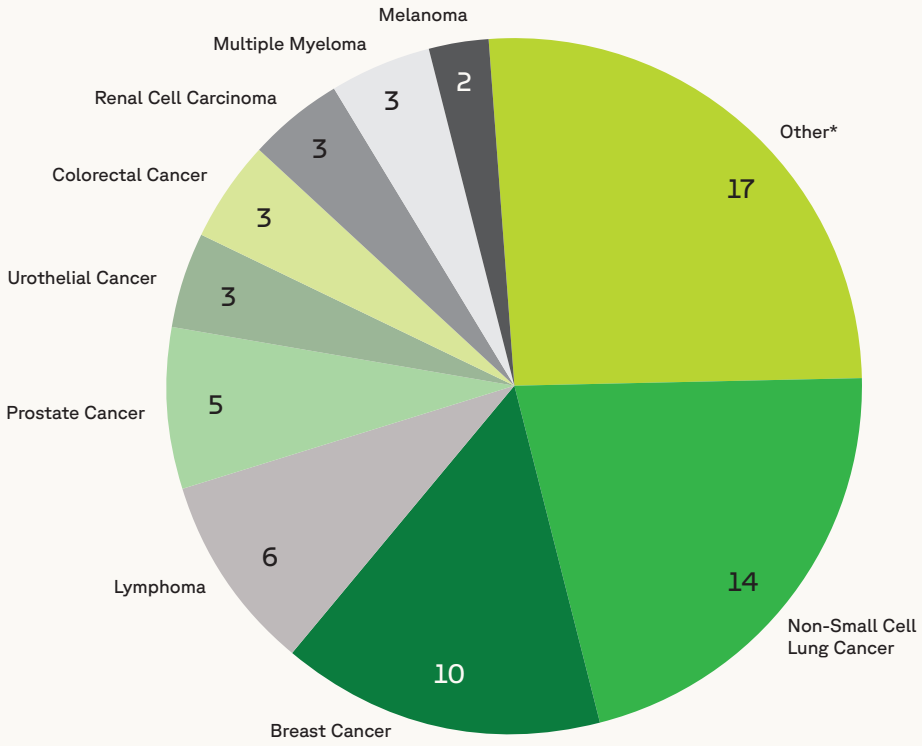
A two-year review of NICE technology appraisals

To explore technology appraisal (TA) recommendations, we conducted a review of 66 TAs of oncology drugs published by NICE over two years between June 1st, 2021 and May 31st, 2023, spanning the time during which the current severity modifier was introduced.

Target indications

Of the 66 TAs included in the review, non-small-cell lung cancer (NSCLC) was the most common indication and was the focus of 14 submissions (Figure 1). Breast cancer and lymphoma were the next most common, with 10 TAs and six TAs respectively. The frequency of appraisals in these indications may reflect the substantial burden they present, and the continued focus on more effective treatments for patients with these diagnoses. Additionally, eight cancer drugs were submitted in multiple indications. For example, nivolumab was considered in 12 TAs, and pembrolizumab in 10 TAs.

Figure 1: Target indications of submissions



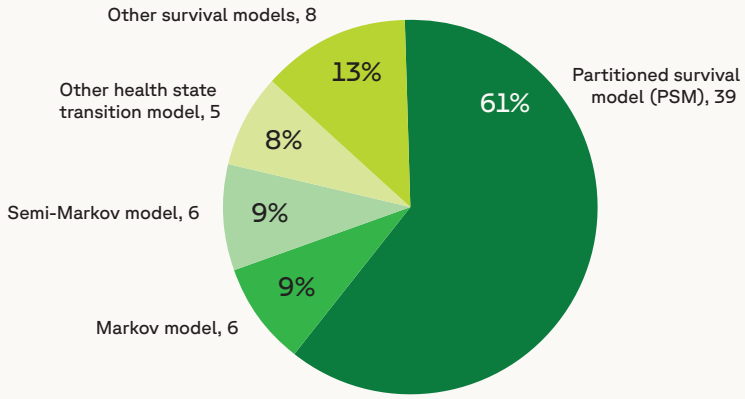
** The "Other" area in this figure groups 17 target indications that received just one technical appraisal each. These are: Hepatocellular Carcinoma, Gastric/Gastro-esophageal Junction/Esophageal Adenocarcinoma, Pleural Mesothelioma, Cutaneous Squamous Cell Carcinoma, Thyroid Cancer, Esophageal/Gastro-Esophageal Junction Cancer, Esophageal Squamous Cell Carcinoma, Ovarian, Fallopian Tube and Peritoneal Cancer, Endometrial Cancer, Gastric Cancer/Gastro-esophageal Junction Adenocarcinoma, Uterine Fibroids, Squamous Cell Carcinoma, Cholangiocarcinoma, Gastrointestinal Stromal Tumor Esophageal Cancer, Cervical Cancer and Esophageal and Gastro-esophageal Junction Cancer.*

Health economic modeling approaches

The choice of modeling approach impacts the estimate and assessment of cost-effectiveness and the subsequent recommendations made by NICE. It represents a critical element for healthcare manufacturers seeking to understand and navigate the appraisal process effectively. Of the 66 TAs included in this review, the vast majority (n=64) used cost-utility analysis (CUA). The remaining two TAs used cost-minimization analysis (CMA) with clinical trial or indirect comparison evidence provided to prove similar benefits between the intervention and comparator.

Of the TAs using CUA, the most commonly used modeling approach used by 39 TAs (61%) was the partitioned survival model (PSM). The rest of the CUA used Markov and semi-Markov models (12 TAs, 18%) or other health state transition and survival models (Figure 2). The heterogeneity in the choice of modeling approaches may reflect the different underlying characteristics of the various cancer types, such as the rapidly progressing nature of some cancers as opposed to less progressive conditions in which patients spend longer time in chronic health states.

Figure 2: Cost-utility analysis (CUA) modeling approaches



Appraisal recommendations

The recommendations made in the TAs are summarized in Figure 3.

Of the 66 assessed TAs:

36 (55%) did not meet the EoL criteria, of these:

- 31 (86%) were recommended
- 3 were recommended in the CDF
- 1 was recommended with managed access
- 1 was not recommended

30 (45%) met the EoL criteria, of these:

- 22 (73%) were recommended
- 3 were recommended in the CDF
- 5 were not recommended

All recommended drugs had ICERs under the relevant willingness-to-pay thresholds, i.e., £20,000 to £30,000 per QALY gained when EoL criteria were not applicable, or £50,000 per QALY gained when EoL criteria were applicable. For drugs that were recommended in the CDF, had managed access, or were not recommended, the calculated ICERs either exceeded these thresholds or were subject to significant uncertainty (Table 2). This indicates a close alignment between NICE recommendation decisions and the comparison of ICER estimates to willingness-to-pay thresholds.

Figure 3: The number and proportion of submissions meeting EoL criteria

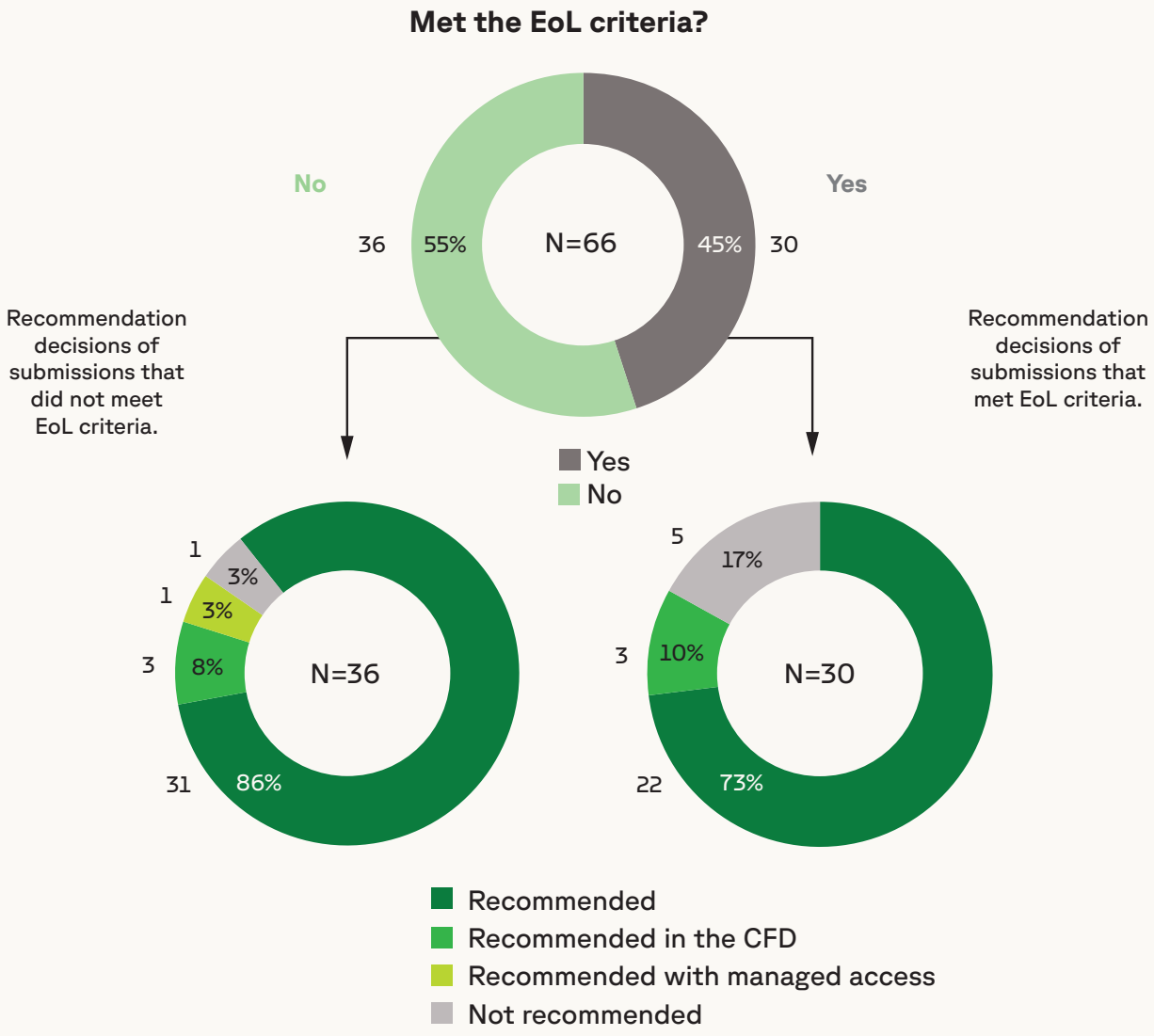


Table 2: Drugs not meeting the willingness-to-pay thresholds

Drug name	Indication	Recommendation	ICER (per QALY gained)
Did not meet EoL criteria			
Atezolizumab	NSCLC	Recommended in CDF	In range of £20,000 to £30,000
Osimertinib	NSCLC	Recommended in CDF	In range of £20,000 to £30,000
Selpercatinib	Thyroid cancer	Recommended in CDF	Higher than considered acceptable use of NHS resources
Trastuzumab deruxtecan	Breast cancer	Recommended with managed access	>£30,000
Abiraterone	Prostate cancer	Not recommended	>£30,000
Met EoL criteria			
Sotorasib	NSCLC	Recommended in CDF	Higher than considered acceptable use of NHS resources
Dostarlimab	Endometrial cancer	Recommended in CDF	£49,454; £61,306
Selpercatinib	NSCLC	Recommended in CDF	£76,210
Tafasitamab with lenalidomide	Lymphoma	Not recommended	Higher than considered acceptable use of NHS resources
Ripretinib	Gastrointestinal stromal tumor	Not recommended	>£100,000
Amivantamab	NSCLC	Not recommended	>£50,000
Pralsetinib	NSCLC	Not recommended	Higher than considered acceptable use of NHS resources
Nivolumab with ipilimumab and chemotherapy	NSCLC	Not recommended	Higher than considered acceptable use of NHS resources

Abbreviations: CDF, Cancer Drugs Fund; EoL, end-of-life; ICER, incremental cost-effectiveness ratio; NHS, National Health Service; NSCLC, non-small cell lung cancer; QALY, quality-adjusted life year

Regarding the association between model approach and EoL status, it was observed that TAs used survival models had a higher proportion meeting EoL criteria than those used Markov or semi-Markov models (Table 3). This may be due to survival models being chosen (as compared with Markov or semi-Markov models) because they better capture disease states with shorter survival periods, i.e., those more likely to meet EoL criteria.

Table 3: Proportion of TAs meeting the EoL criteria across different model types

Modeling approaches	% meeting the EoL criteria
Partitioned survival model	56.4%
Markov model	16.7%
Semi-Markov model	16.7%
Other health state transition model	0.0%
Other survival models	75.0%

Abbreviations: EoL, end-of-life; TA, technology appraisal

The impact of the new severity modifier

Of the 66 assessed TAs in our review timeframe, only three TAs discussed severity modifiers. In two instances, the 1.7 QALY weight was applied and in the other, no QALY weight was applied. Of note, the 1.7 QALY weighting was applied to Trifluridine-tipiracil but it did not meet the EoL criteria in the first submission because it did not extend survival by more than three months. Upon the introduction of the severity modifier, the company resubmitted evidence for review with the proportional and absolute QALY shortfall at 96.84% and 11.33[8], respectively, which qualified for the 1.7 QALY weighting (as the proportional QALY shortfall was at least 95%).

To further explore how the EoL and severity modifier criteria might be applied to the same product, we analyzed the theoretical impact of the severity modifier on products we considered to meet EoL criteria. To do this, we first calculated the oldest patient age at which products could qualify for x1.2 and x1.7 QALY weights under severity modifier criteria. This was estimated using the ScHARR (University of Sheffield) QALY shortfall calculator[9], assuming a 50:50 male:female patient population and a 3.5% discount rate for health outcomes (Table 4). The QALE with the disease (on standard of care) was set to be 1.7 and 0.85 respectively to reflect scenarios of 24 and 12 months' survival at an average 0.85 health utility.

Table 4: Highest age at baseline to still qualify for x1.2 and x1.7 QALY weight

QALY weight	1.7 QALE (24 months survival scenario)	.85 QALE (12 months survival scenario)
x 1.2	63 years	79 years
x 1.7	35 years	46 years

Abbreviations: QALE, quality-adjusted life expectancy; QALY, quality-adjusted life year

The illustration revealed that for a treatment that would result in 12 months' survival to be eligible for the x1.7 QALY weighting, the maximum age of patients at the model baseline would be 46 years. In this scenario, the proportional QALE shortfall would be 95% given an expected discounted 17.07 QALE without the disease (equivalent to 29.88 undiscounted QALE).

This finding starkly contrasts the patient demographic profile for the 22 drugs in our review that were considered to meet EoL criteria with patient age information available. For these drugs, the patient age at baseline in modeling scenarios ranged between 53 and 75 years. Notably, half of drug submissions targeted patient groups aged over 63 years, which indicates that for these drugs meeting the past EoL criteria, the application of the x1.2 QALY weight would become the new norm under the severity modifier criteria assuming they are associated with 24 months' survival. Consequently, this adjustment would lower the cost-effectiveness threshold to £36,000 from £50,000 for these drugs. Under the scenario for diseases where patients have an expected 24 months' survival at baseline, the maximum age at baseline to qualify for the 1.7 QALY weight would be even lower at 35 years; this is a threshold that none of the reviewed recent EoL products would meet.

Implications for manufacturers

Our review has demonstrated that PSM was the most commonly used modeling approach in NICE TAs for oncology indications over the past two years. A lack of correlation between the choice of modeling approach and appraisal recommendations suggests that the selection of modeling approach should be primarily guided by the unique characteristics and available data of the specific oncology drug and indication under consideration. Our review also provides confirmation that NICE recommendations for oncology TAs were fully aligned with published ICER thresholds, suggesting an important role for transparent value-based pricing strategies.

When considering the severity modifier criteria, it was found that most of the drugs meeting the previous EoL criteria may expect a willingness-to-pay threshold decrease from £50,000 per QALY gained to £36,000. This has implications for patient access to cutting-edge oncology treatments within England and Wales. By adjusting the QALY weight based on the patient's age and life expectancy, the updated assessment criteria potentially reduce NICE's willingness-to-pay threshold for innovative cancer therapies. Specifically, treatments targeting older patient groups, who represent the majority of cancer patients, may face greater challenges in qualifying for the highest level of QALY weight adjustment. These findings highlight an important challenge for reimbursement and pricing strategy for manufacturers with an oncology portfolio and demonstrate the need for careful market access planning.

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