EE204

Beyond QALYs: Alternative Cost-Effectiveness Measures in ICER Reports from 2019 to 2025

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Objective

To characterize the alternative cost-effectiveness (CE) measures ICER has historically utilized in value assessments, given heightened interest in CE evidence following Medicare drug price negotiations and CMS restrictions on the use of quality-adjusted life years (QALYs).

Background

- ICER is the most prominent independent HTA organization in the US and conducts CE analyses using a defined Reference Case that is generally aligned with published HTA guidance.[1,2]
- In ICER's Reference Case, three incremental CE measures are routinely reported: cost per QALY gained (primary outcome), cost per life-year (LY) gained, and cost per equal value life-year (evLY) gained.[1]
- Following the Inflation Reduction Act (IRA) and rollout of Medicare drug price negotiations, there is a greater emphasis on CE evidence in the US. However, CMS is restricted from using adjusted life-year measures, including QALYs, increasing the relevance of alternative CE outcomes.[3,4]
- There is limited understanding of how non-QALY cost-effectiveness measures are reported in practice. Describing the use of these alternative outcomes within a reference case framework consistent with international HTA guidance helps clarify when they may add value alongside QALYs, LYs, and evLYs in value assessments.

Methods

- Completed ICER reports published between 2019–2025 were extracted using a standardized grid. Model structure, clinical evidence rating, date of publication, and analytic perspective were recorded.
- For each therapy, all cost inputs and incremental CE ratio denominators (QALYs, LYs, and evLYGs) were catalogued along with any alternative CE outcomes.
  - CE measures were included in the analysis if they were reported in the base case or a co-base case scenario.
- Summary statistics were calculated for the frequency and values of each CE measure.

Results

- A total of 54 ICER reports published between 2019 and 2025 were identified; 52 (96%) reported at least one incremental CE ratio. Of the 52 reports with incremental ratios:
  - All 52 (100%) reported the cost per QALY, 46 (88%) reported cost per LY, and 40 (77%) reported cost per evLYG.
  - A total of 34 (65%) included at least one alternative, non-QALY measure in the base case or co-base case analysis.
- The 34 alternative measures were qualitatively analyzed and grouped into 3 buckets:
  - Cost per time in an improved health state: n=17 (50%)
  - Cost per event or resource use avoided: n=12 (35%)
  - Cost per symptom management outcome: n=5 (15%)
- Use of alternative measures was relatively stable over time, with 3–6 assessments per year (**Figure 1**).
- Across disease areas, neurology and hematology/oncology contributed the largest number of alternative measures, together accounting for 14 of 34 (42%) alternative measure used and commonly employing improved health state time (**Figure 2**).
- Incremental CE ratios for alternative measures varied by type and exhibited highly skewed cost-per-measure distributions (**Table 1**).
- Of the 34 alternative measures, 19 were reported over a specified time period. (**Figure 3**).

Conclusion

The breadth and routine use of alternative CE measures across disease areas suggests ICER already employs a range of patient-and condition-specific measures. As CMS cannot consider QALYs in drug price negotiations, these existing non-QALY metrics offer a foundation for future pricing and coverage decisions. However, substantial variation in definitions, timeframes, and value ranges highlights the need for methodological standardization to improve interpretability and policy relevance.

FIGURE 1

Count of alternative CE measure types used by year

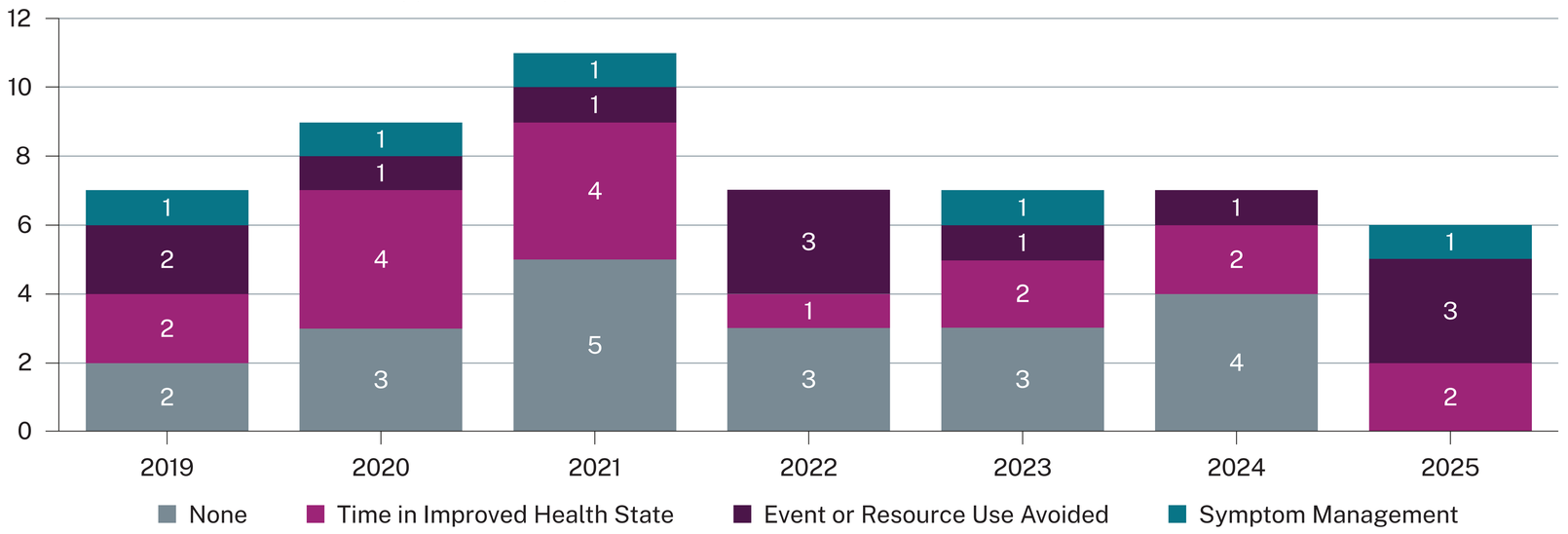

FIGURE 2

Count of alternative measure types used by disease area

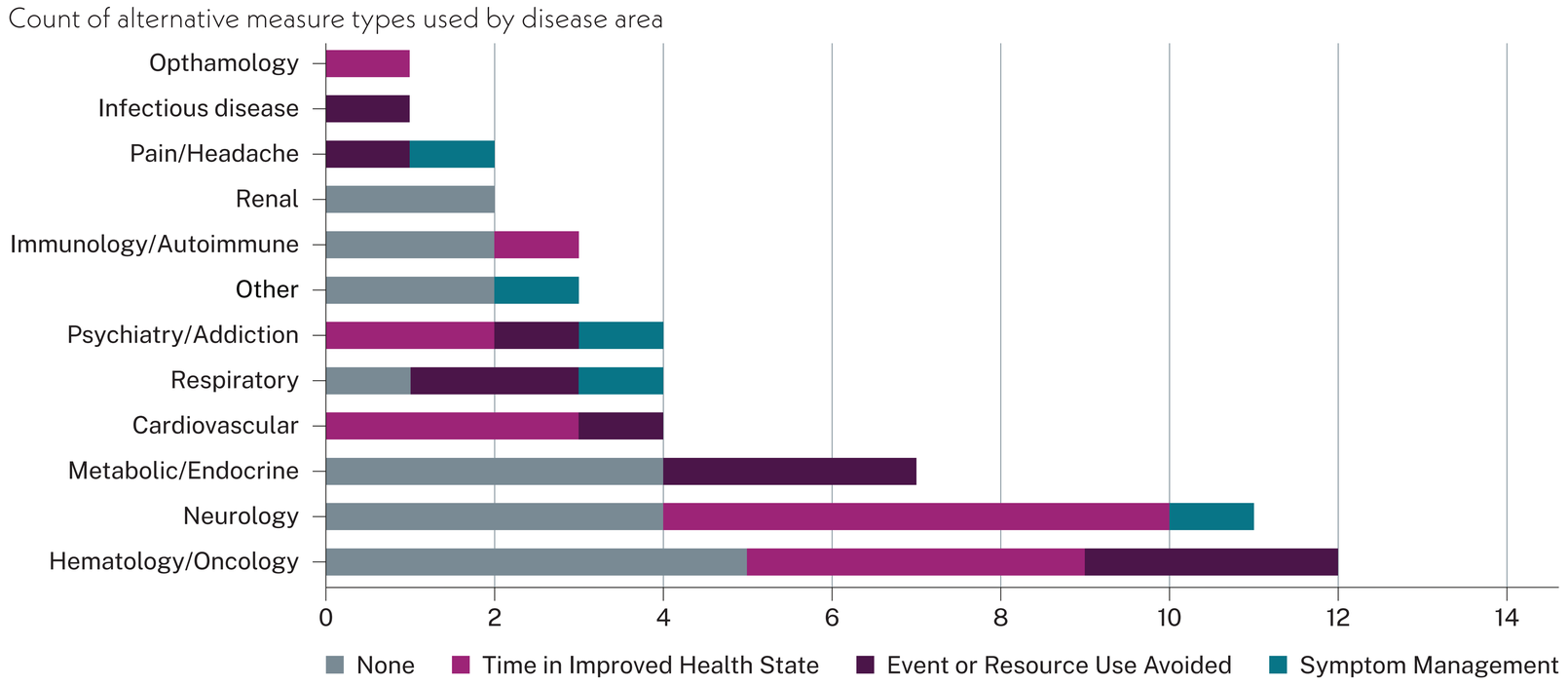

TABLE 1

Summary statistics of incremental CE ratios for alternative measures

Alternative Measures	Mean (SD)	Range	Median (IQR)
Time in Improved Health State	$560,153 ($604,779)	$600 — $1,831,000	$313,500 ($31,000 — $1,133,000)
Event or Resource Use Avoided	$238,102 ($274,820)	Less costly, more effective — $675,000	$73,000 ($5,800 — $540,500)
Symptom Management Outcome	$7,324,567 ($13,900,159)	$5 — $31,922,000	$500 ($168 — $18,311,000)
Total	$1,580,731 ($5,705,018)	Less costly, more effective — $31,922,000	$189,000 ($15,800 — $675,000)

Three reports included event or resource use avoided measures with less costly, more effective, or dominated result values; a value of −$1 was used in the summary statistic calculations for these measures. For reports with multiple therapies, numerical CE measure values were recorded for the therapy with the highest clinical evidence rating.

FIGURE 3

Time period over which alternative CE measures were reported

Abbreviations: CE: cost-effectiveness; **CMS:** Centers for Medicare & Medicaid Services; **evLY:** equal value life year; **evLYG:** equal value life year gained; **FDA:** Food and Drug Administration; **HTA:** health technology assessment; **ICER:** Institute for Clinical and Economic Review; **IRA:** Inflation Reduction Act; **ISPOR:** International Society for Pharmacoeconomics and Outcomes Research; **LY:** life year; **QALY:** quality-adjusted life year; **US:** United States of America.

References: [1]ICER (2023) Value Assessment Framework. Available at: https://icer.org/our-approach/methods-process/considering-clinical-real-world-and-unpublished-evidence/ [Last accessed 9 April 2026]; [2]ICER (2025) ICER's Reference Case for Economic Evaluations: Elements and Rationale. Available at: https://icer.org/wp-content/uploads/2024/02/ICER_Reference-Case_For-Publication_102325.pdf [Last accessed 9 April 2026]; [3]Congress (2022) Inflation Reduction Act of 2022, Pub. L. 117 169, §§11001–11002: Medicare Drug Price Negotiation Program. Available at: https://www.cms.gov/files/document/revised-medicare-drug-price-negotiation-program-guidance-june-2023.pdf [Last accessed 9 April 2026]; Social Security Administration (2010) Social Security Act §1182 (42 U.S.C. 1320e-1): Limitation on use of comparative clinical effectiveness research in Medicare. Available at: https://www.ssa.gov/OP_Home/ssact/title11/1182.htm [Last accessed 9 April 2026].

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