EE200

A Comparison of Outcomes Measures in Cost-effectiveness Analysis—Three Applications within Oncology

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Objectives

- The primary study objective was to better understand the measurement outcomes and variability of using alternative outcome measures to quality-adjusted life-years (QALYs) in cost-utility models. To achieve this, we:
  - created health economic models for three oncology indications;
  - compared standard QALYs with alternative measures of life-years (LYs), equal value life-years (evLYs) and health years in total (HYT); and
  - checked for congruence and differences in the cost-effectiveness of the interventions evaluated.

Conclusions

- Among the indications evaluated, this study found that:
  - evLYs and HYTs were consistently higher than QALYs (evLYs only marginally);
  - incremental evLYs generated were similar to incremental QALYs, while incremental HYTs were generally similar to incremental LYs; and
  - the incremental cost per QALY was generally the highest of the incremental costs measured. Nonetheless these results were broadly comparable across all outcome measures.
- The alternative measures could in principle be used alongside the traditional QALY approach, but do not fully remedy the perceived drawbacks of the QALY.
  - Both measures continue to include traditional QALYs within their calculation; furthermore,
  - the evLYs and HYTs can lead to logical inconsistencies that do not occur with LYs and QALYs.
- To that end, a broad understanding of the limitations of alternatives to the QALYs—and of disease-specific variability—is needed by HTA bodies and other access policy decision-makers.

Background

- QALYs are the predominant measure of health benefit in health technology assessment (HTA) processes.[1] However, there are criticisms on the distributional impact of this measure:[2]
  - Disease severity, burden, or other attributes are not considered.
  - They discriminate based on age, disability, or chronic conditions.
- Alternate measures for valuing health benefits, such as evLYs gained[3] and HYT,[4] have been proposed to alleviate QALY-related concerns.
  - evLYs value the gain in LYs at the full value of a healthy LY (adjusted by age and gender), regardless of age, disability, or illness.[3,5]
  - HYTs evaluate outcomes by additively combining LYs and "modified QALYs" (the utility of treatment applied to maximum LYs gained across all comparators).[4]

Methods

- Health economic models were developed for three oncology indications—renal cell carcinoma (RCC), chronic myeloid leukemia (CML), and non-small-cell lung cancer (NSCLC).
  - Utilizing the PfyDICE platform—an in-house model development tool developed for Pfizer by Evidera — the models were built using three-state partition survival models (PSMs).
- The three indications selected display quite different prognoses and utilities. This allows us to assess the impact on health outcomes and cost-effectiveness for different disease severities.
  - CML has the best prognosis (five-year survival: >90%),[6] followed by RCC (10-year survival: 10%–40%).[7] NSCLC had the worst prognosis (five-year survival: <1%–10%).[8]
  - Reported health state utilities vary by indication (RCC: 0.5–0.8; NSCLC: 0.6–0.8; CML: 0.4–0.8).
- The key inputs for the three economic models are described in **Table 1**.
- We estimated traditional health outcomes (LYs and QALYs) and total costs.
- Costs do not change depending on health benefit measure used.

Table 1. Overview of Model Settings and Inputs

Key model sections	Descriptions
Structure	Three-state PSM with PFS, OS, and ToT
Key settings	1. Time horizon: ranged from 20 to 40 years 2. Cycle length: one week to one month 3. Discounting: 3% for both costs and benefits
Efficacy	1. PFS and OS: Parametric fits or KM + parametric fits 2. ToT: Parametric fits, PFS as proxy, and using median TTD
Cost category included	1. Drug costs 2. Administration costs 3. Safety costs 4. Disease management cost 5. Subsequent treatment cost (applied as a one-off cost to incident progressors) 6. End-of-life
Utilities	Utilities by health states (PF: 0.747–0.785; and PD: 0.380–0.610), or time to death utilities (>360 days: 0.824; <30 days: 0.462)

Abbreviations: KM: kaplan–meier; OS = overall survival; PD = progressive disease; PF = progression-free; PFS = progression-free survival; PSM = partitioned survival model; ToT = time on treatment

- evLYs were calculated as the sum of the life extension offered by treatment multiplied by the value of healthy LYs, plus the LYs offered by SOC adjusted with the utility weight of treatment.
  - The value of a healthy LY is 0.851, which is the age- and gender-adjusted utility of the healthy US population.[5]
- HYTs are calculated as the sum of LYs of the treatment and "modified QALYs" - the product of the treatment's utility weight with the maximum LYs across all treatments that are evaluated.

$$\Delta evLYs = \sum_{t}^{T} 0.851 \times (S_{1t} - S_{0t}) + \sum_{t}^{T} S_{0t} \times (Q_{1t} - Q_{0t})$$

$$\Delta HYTs = \sum_{t}^{T} (S_{1t} - S_{0t}) + \sum_{t}^{T} S_{1t} \times (Q_{1t} - Q_{0t})$$

Where: T is the lifetime of the model; t is a particular time period; 1 and 0 relate to the new/comparator treatments; S_{xt} is the survival probability for treatment x at time t; Q_{xt} is the quality of life for treatment x at time t.

- The incremental health benefits using the different measures are then compared across all three models, to see the magnitude and the direction of change of the incremental outcomes.
- Incremental costs per LY, QALY, evLY gained and HYT gained can thereafter be calculated.

Results

- The absolute health benefits using different measures and total costs for the three indications are presented in **Table 2**.
  - Absolute health outcome measures were highest for CML, followed by RCC, and then NSCLC.
  - The evLYs and QALYs generated by SOC treatments are identical in all cases

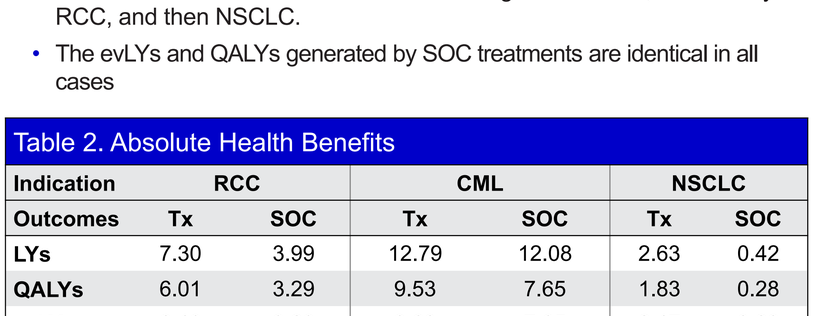
Table 2. Absolute Health Benefits

Indication	RCC		CML		NSCLC	
Outcomes	**Tx**	**SOC**	**Tx**	**SOC**	**Tx**	**SOC**
LYs	7.30	3.99	12.79	12.08	2.63	0.42
QALYs	6.01	3.29	9.53	7.65	1.83	0.28
evLYs	6.10	3.29	9.60	7.65	2.17	0.28
HYT	13.31	10.00	22.32	20.18	4.46	2.20
Costs	$497,439	$241,553	$2,357,574	$2,337,199	$100,885	$11,270

Abbreviations: CML = chronic myeloid leukemia; evLY = equal value life-year; HYT = health years total; LY = life-year; NSCLC = non-small-cell lung cancer; RCC = renal cell carcinoma; QALY = quality-adjusted life year; SOC = standard of care; Tx = treatment

- The incremental health benefits using different measures for the three indications are presented in **Figure 1**.
- The highest incremental health benefits were observed for RCC; they were comparable across CML and NSCLC.
- For CML, in contrast to other indications, the incremental LYs estimated are lower than incremental QALYs. This is because, compared to other indications, CML has:
  - a larger differential in utilities between progression-free (PF) and progressive disease (PD) health states (PF: 0.76–0.78; PD: 0.38); and
  - divergent treatment outcomes relating to time spent in each health state (For the intervention: PF LYs: 11.66, PD LYs: 1.12; for the comparator: PF LYs: 8.05, PD LYs: 4.02)

Figure 1. Incremental Health Benefits

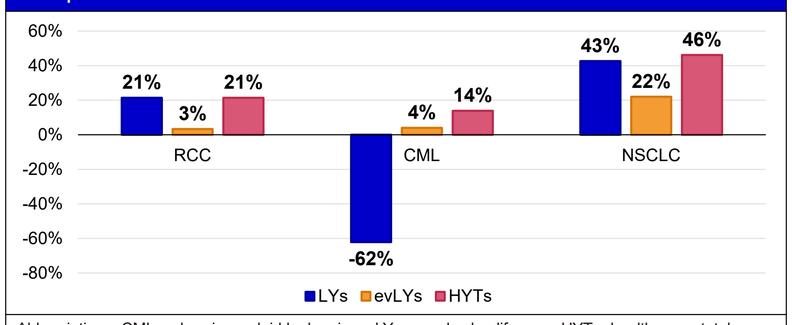


Abbreviations: CML = chronic myeloid leukemia; evLY = equal value life-year; HYT = health years total; Inc. = incremental; LY = life-year; NSCLC = non-small-cell lung cancer; QALY = quality adjusted life-year; RCC = renal cell carcinoma

- **Figure 2** presents the relative change in the incremental evLYs and HYTs compared to incremental QALYs.
  - Incremental HYTs consistently yielded the most favorable treatment benefit (13%–46% higher than incremental QALYs).
  - Incremental evLYs and QALYs were generally closely aligned, except for NSCLC (22% increase incremental evLYs vs. QALYs). This is due to the its larger relative extension in survival and lower differential between PF/PD utility values, as compared to other indications.

Results (cont.)

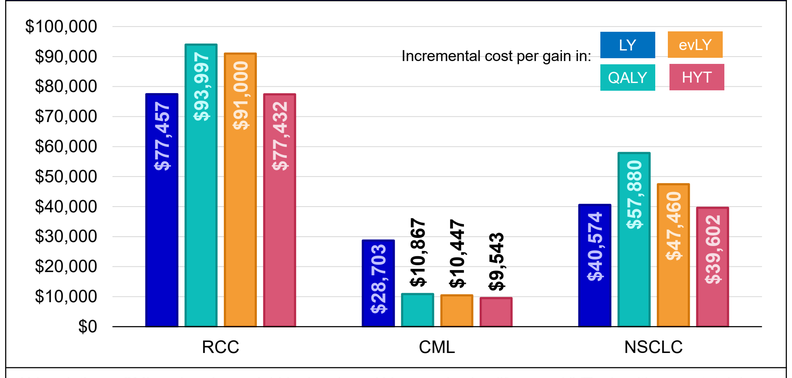
Figure 2. Relative Change in Incremental LYs, evLYs and HYTs, compared to Incremental QALYs



Abbreviations: CML = chronic myeloid leukemia; evLY = equal value life-year; HYT = health years total; LY = life-year; NSCLC = non-small-cell lung cancer; QALY = quality adjusted life-year; RCC = renal cell carcinoma

- The incremental costs per health benefit gained are shown in **Figure 3**.
- Incremental cost per HYT gained is consistently the lowest, as the incremental HYT gained is highest among of the alternative measures (**Figure 1**).
- Nonetheless, the incremental costs per health measures calculated are similar regardless of measure used. This indicates that the different measures are unlikely to affect the cost-effectiveness of a treatment versus SOC.

Figure 3. Incremental costs per Health Benefit Gained



Abbreviations: CML = chronic myeloid leukemia; evLY = equal value life-year; HYT = health years total; Inc. = incremental; LY = life-year; NSCLC = non-small-cell lung cancer; QALY = quality-adjusted life-year; RCC = renal cell carcinoma

Discussion

- Across the three indications, incremental evLYs were closely aligned with incremental QALYs, while incremental HYTs were closely aligned with incremental LYs, except in the case of CML.
- Therefore, alternative health benefit measures (evLYs and HYTs) are expected to have a minimal impact on the cost-effectiveness of the treatment—and thereby on policy decisions.
- The proposed alternative outcome measures have their own drawbacks:
  - evLYs are biased in favor of treatments that extend LYs, because they apply a single uniform utility to the life extension. They may therefore diminish the perceived value for treatments that impact only quality of life and do not provide any survival extension;
  - HYTs add incremental LYs to incremental QALYs that already account for these LYs; while "modified QALYs" attribute additional value to the treatment with lower survival—but such benefit is hypothetical and never accrues to patients;
  - both measures continue to include traditional QALYs within their calculation, and assumedly therefore cannot overcome ethical criticisms of using QALYs in cost-utility analyses; and
  - these approaches are associated with logical inconsistencies, as pointed out by Paulden and colleagues.[10]
- If such alternative health outcome measures were used by HTA agencies and other decision makers in place of, or in parallel with, traditional cost per QALY/cost-utility analysis approaches:
  - it behoves such bodies to fully understand both their own justifications for doing so, and what methodological and ethical limitations would remain in place;
  - there needs to be better understanding of what value such approaches could bring to incorporating patient, provider and social perspectives into the decision-making process; and
  - it is clear that more research is needed to better understand if the results reported here are consistent across indications—and otherwise what specific patterns might emerge.

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