EE13

"Other similar measures"? – How different really are QALYs from Life years, Health years in total, and Equal value life years?

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Objectives

- The primary objective of this study was to investigate the implications of using alternative outcome measures—LYs, evLYs, and HYT—in health technology assessments, specifically within the context of oncology. 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);
  - evaluated the congruence and differences in the cost-effectiveness of the interventions using these alternative measures; and
  - discussed the potential implications of adopting evLYs, and HYT in HTA processes, considering their advantages and limitations in comparison to QALYs.

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. In particular, HYTs and evLYs:
  - continue to include traditional QALYs within their calculation; and
  - can lead to logical inconsistencies that do not occur with LYs and QALYs.
- Neither QALYs nor the alternative measures can fully capture the value of a treatment to patients or other stakeholders; in fact, the alternative measures seem even worse. Future value assessment research should seek more holistic, patient-centered methodologies to address such issues.

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Background

- QALYs are the predominant measure of health benefit in health technology assessment (HTA) processes.[1] However, there are criticisms on the distributional impacts of this measure, as well as equity and possible discrimination.[2]
- In the US, the use of QALYs has been controversial, making their use less prevalent.[3] The Patient-Centered Outcomes Research Institute (PCORI) is explicitly prohibited from using QALYs in its evaluation.[4] Legislation under consideration in the Senate would ban them "and other similar measures" in federally-funded healthcare programs.
- Alternate measures for valuing health benefits, such as evLYs gained[5,7] and HYT,[6] have been proposed to alleviate QALY-related concerns.

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 PPD™ Evidera™ — three-state (progression free, progressed and dead) partition models (PSMs) were built

Methods (cont.)

- The three selected indications exhibit varying prognoses and utility values, enabling us to evaluate the impact on health outcomes and cost-effectiveness across different levels of disease severity..
  - CML has the best prognosis (five-year survival: >90%),[8] followed by RCC (10-year survival: 10%–40%).[9] NSCLC had the worst prognosis (five-year survival: <1%–10%).[10]
  - Reported minimum health state utilities vary by indication (CML: 0.4; RCC: 0.5; NSCLC: 0.6); progression-free utilities are similar.
- The key inputs for the three economic models are described in **Table 1**.

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 – 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

- We estimated health outcomes (QALYs, LYs, evLYs and HYTs) and total costs. Costs do not change depending on health benefit measure used.
- 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 associated treatment.
- The value of a healthy LY is 0.851, which is the age- and gender-adjusted utility of the healthy US population.[7]
- 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.

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

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

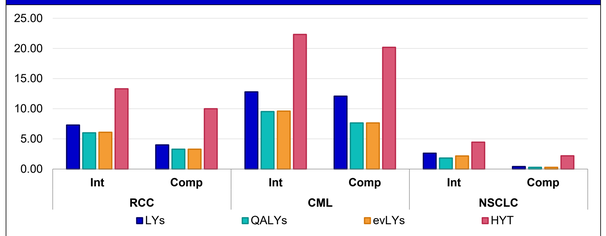
Where: T is the lifetime of the model; t is a particular time period; 1 *and* 0 *relate to the new/comparator treatments;* S_{xt} *is the survival probability for treatment x at time t;* Q_{xt} *is the quality of life for treatment x at time t.*

- 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 and HYT could thereafter be calculated.

Results

- The absolute health benefits using different measures and total costs for the three indications are presented in **Figure 1**.
  - 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, as evLYs are applied only to survival extensions.

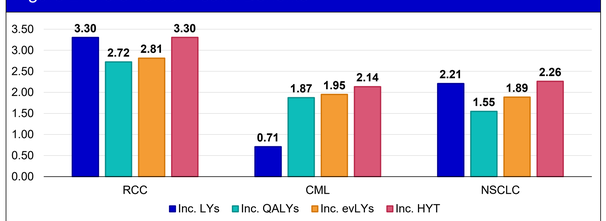
Figure 1. Absolute Health Benefits



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

- The incremental health benefits using different measures for the three indications are presented in **Figure 2**.
- 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
  - very different treatment outcomes relating to time spent in PF/PD health states respectively (*see **Figure 4***).

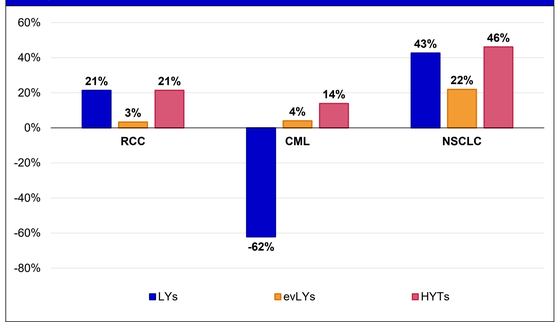
Figure 2. Incremental Health Benefits



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

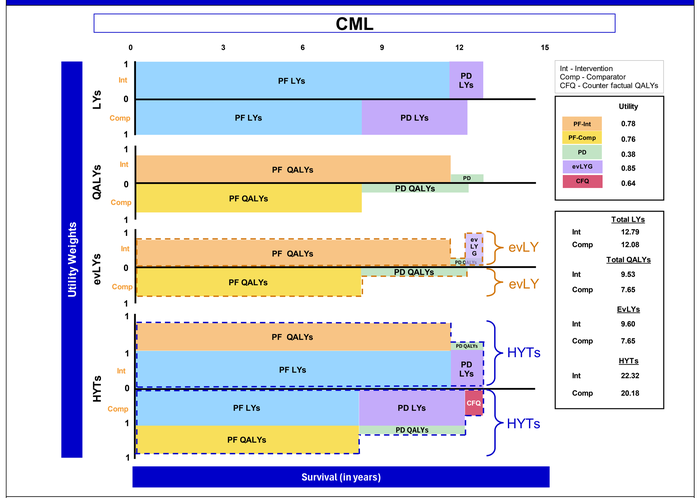
- **Figure 3** presents the relative change in the incremental evLYs and HYTs compared to incremental QALYs.
  - Incremental HYTs consistently yielded the most favorable treatment benefit (13%–46% higher than incremental QALYs); the incremental cost per HYT is always lower than the ICER and such measures.
  - 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.

Figure 3. 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

Figure 4. Graphical Representation of LYs, QALYs Segregated by PF and PD States and Their Impact on evLYs and HYTs



Abbreviations: CML = chronic myeloid leukemia; evLY = equal value life-year; HYT = health years total; LY = life-year; QALY = quality adjusted life-year

- Graphical representation of the alternative measures disaggregated by PF and PD health states for NSCLC and CML are shown in **Figure 4.**
  - It highlights the interplay of how survival time in PF and PD states and the associated utility values impact the values generated for the alternative health measures.

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. In all cases the ordering of treatments remained the same.
- Therefore, on a case-by-case basis, alternative health benefit measures (evLYs and HYTs) might be expected to have a small impact on the cost-effectiveness of the treatment, and thereby on policy decisions.
- However, this may not be the case on a healthcare system-wide level. In practice, LYs, evLYs and HYTs all place less emphasis than QALYs on improved HRQoL. If these approaches were used in place of QALYs in HTA assessments, this could lead to displacement of currently reimbursed treatments by treatments that primarily extend life.
- The proposed alternative outcome measures do not offer a silver bullet to address the drawback of QALYs.[11]
  - the primary justification of using such approaches seems to be to sidestep ethical and practical baggage of using the QALY, rather than any meaningful methodological improvement.
  - both evLY and HYT continue to include traditional QALYs within their calculation, and assumedly therefore cannot overcome ethical and distributional (and potentially legislative) criticisms of using QALYs in cost-utility analyses;
  - these approaches are further associated with logical inconsistencies, as pointed out by Paulden and colleagues.[12]
- If HTA agencies and other decision-makers were to use these alternative health outcome measures in place of, or alongside, traditional cost per QALY/cost-utility analysis approaches, they should:
  - Fully understand their justifications for adopting these measures and the methodological and ethical limitations that would remain.
  - Develop a better understanding of the value these approaches could bring to incorporating patient, provider, and social perspectives into the decision-making process.
- More research is needed to better understand if the results reported here are consistent across indications or whether specific patterns might emerge.