A Portfolio Modeling Framework for HEOR Decision Making

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Background

- Portfolio prioritization in drug development requires consistent assessment of disease burden, unmet need, and the potential value of future therapies across multiple indications.
- Conventional decision frameworks often rely on clinical or commercial signals alone and may not provide a standardized basis for cross-indication comparison.
- A scalable health economic framework that quantifies life-year (LY) and quality-adjusted life-year (QALY) shortfall relative to standard of care (SoC) and the general population can support more transparent and methodologically consistent portfolio decision-making.

Objectives

- To develop and apply a standardized, scalable portfolio modeling framework to estimate LY and QALY shortfall, as well as potential health gains of new therapies versus SoC and the general population across multiple indications. The framework is intended to support health economics and outcomes research (HEOR)-informed portfolio prioritization.

Methods

- A standardized Microsoft Excel-based portfolio model was developed to compare unmet need consistently across multiple indications within a common framework. The tool is designed for early-stage use, incorporating dropdown selections, minimal data entry requirements, and the ability to rapidly add and evaluate multiple indications within a unified structure.
- Model structures are selected based on indication characteristics, including partitioned survival, state-transition, and response-based approaches, depending on disease natural history and available clinical endpoints.
- Standardized methods are applied to ensure cross-indication comparability, including parametric survival extrapolation, assignment of health state utilities, and benchmarking against age- and sex-matched general population outcomes. SoC efficacy and survival inputs are derived from pivotal trials, with supporting evidence from clinical guidelines and health technology assessment (HTA) submissions.
  - For long-term extrapolation, published Kaplan-Meier (KM) curves are digitized using Engauge Digitizer, validated against the original plots, and used to reconstruct individual patient data (IPD) following the method of Guyot et al.[1] The reconstructed IPD are then used to fit standard parametric survival models (i.e., exponential, Weibull, lognormal, loglogistic, Gompertz, gamma, and generalized gamma).
  - Where appropriate, cure assumptions may be applied with a user-specified cure timepoint. Standardized mortality ratios (SMRs) may be applied to general population mortality to supplement survival or transition estimates where data are limited or immature. Overall survival (OS) is capped by general population mortality at all times.
- Treatment effects for hypothetical future interventions are modeled by applying assumed hazard ratios (HRs) to SoC to estimate potential incremental benefit. HRs may be derived from expected median survival or landmark outcomes relative to SoC.
- Utility values are assigned by health state using published sources. Where appropriate, additional QALY adjustments may be applied (e.g., adverse events or route of administration), and QALYs are adjusted by age and sex.
- The model generates both indication-level and portfolio-level outputs, including LY and QALY shortfall and incremental LY/QALY gains. Automated reporting enables comparison across multiple indications and supports drill-down analyses at the individual indication level.
- **Figure 1** presents a high-level overview of the portfolio modeling tool, and **Figure 2** demonstrates relevant input specifications using oncology indications as a case study.

Results

- The framework generates both indication-level and portfolio-level outputs, including LY and QALY shortfall and estimated incremental health gains for hypothetical future interventions relative to SoC.
- Application to oncology case-study indications demonstrates that the framework enables direct and methodologically consistent comparison of unmet need across indications, rather than evaluating each in isolation. LY and QALY shortfall vary substantially, with the greatest unmet need observed in advanced, late-line, poor-prognosis settings with limited effective SoC, and the lowest shortfall in earlier-stage or more favorable settings where current therapies provide improved long-term outcomes.
- The model also estimates incremental LY and QALY gains for hypothetical interventions, enabling comparison of both current unmet need and the potential value of future innovation across indications.
- By jointly evaluating shortfall and projected gains, the framework identifies settings with the greatest potential health impact and differentiates higher- and lower-priority opportunities, as illustrated in **Figure 3**.
- Overall, the results demonstrate that the framework distinguishes indications with high residual disease burden from those where current SoC has already reduced the gap to expected life expectancy and quality of life, supporting portfolio-level prioritization.

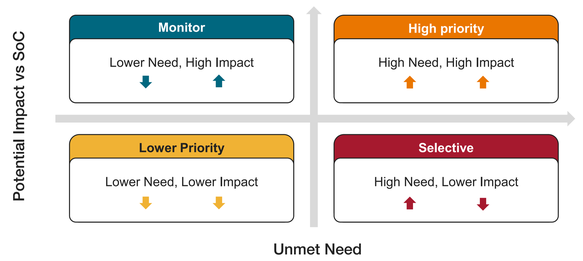
Figure 1. Overview of the Portfolio Modeling Tool

Abbreviations: LY = life-year; QALY = quality-adjusted life-year; SoC = standard of care

Figure 2. Inputs Specifications for Oncology Indications (Case Study)

Abbreviations: DF = disease free; DM = distant metastasis; EF = event free; HR = hazard ratio; LR = local recurrence; LY = life-year; PD = progressed disease; PF = progression free; QALY = quality-adjusted life-year; SMR = standardized mortality ratio; SoC = standard of care

Figure 3. Portfolio Prioritization Framework Based on Unmet Need and Potential Impact



Abbreviation: SoC = standard of care

Strengths and Limitations

- This framework addresses a key portfolio-planning challenge: how to compare unmet need across diverse indications within a single analytic approach. In the absence of such a framework, cross-indication assessments often rely on heterogeneous methods, assumptions, and outputs, limiting comparability and complicating portfolio-level decision-making.
- Designed for early-stage settings with limited data, the framework supports structured evaluation even when key inputs must be informed by assumptions or estimated medians. It integrates standardized methods for model structure selection, long-term survival extrapolation, utility assignment, population benchmarking, and reporting, ensuring methodological consistency across indications.
- The tool supports both portfolio-level summaries and indication-specific analyses, enabling efficient comparison across multiple indications as well as drill-down into individual cases. Its scalable design allows for rapid incorporation of additional indications, while semi-automated reporting facilitates streamlined review.

Conclusions

- This framework extends beyond estimating LY and QALY shortfall to support portfolio-level prioritization. By enabling consistent comparison of disease burden and unmet need across indications, it identifies where future interventions may deliver the greatest health gains and supports more informed decision-making.

References

1. Guyot P, et al. *BMC Med Res Methodol*. 2012;12(1):9.

Disclosures

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