Enhanced Cost-Effectiveness Analysis Using EHR Data for Real World Value

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PRESENTED AT:

BACKGROUND

Background

Health technology assessments for new therapies must rely on data from clinical trials. As these therapies are used in clinical practice, new evidence in the form of real-world data may become available to supplement findings from initial health technology assessments.

Real-world evidence (RWE) generated from electronic health records (EHR) has been shown to be more relevant, timely, and representative for health technology assessment decision-making compared to evidence from clinical trials. We assessed how using EHR-derived RWE ("RWE approach") instead of network meta-analyses of published clinical trial data ("traditional approach") can impact point estimates and uncertainty ranges in cost-effectiveness estimates for advanced non-small cell lung cancer (NSCLC) therapies.

Traditional cost-effectiveness analyses estimate hazard ratios using network meta-analyses of clinical trial data due to lack of head-to-head comparisons between the therapies of interest. If hazard ratio estimates from the network meta-analyses have wide confidence intervals, the resulting cost-effectiveness estimates may have high uncertainty. We hypothesized that the RWE approach would decrease uncertainty in cost-effectiveness estimates compared to the traditional approach.

Research Objectives

1. Calculate incremental cost-effectiveness ratios (ICERs) based on hazard ratios and survival times estimated using a real-world data cohort of patients with NSCLC who would be eligible for the cost-effectiveness study population based on clinical trial inclusion criteria.
2. Compare cost-effectiveness estimates between traditional approach and real-world data approach.

METHODS

Study Design

We replicated a cost-effectiveness analysis of NSCLC therapies developed by the Institute for Clinical and Economic Review in 2016[1] ("traditional"), replacing meta-analysis-derived hazard ratios and survival times from clinical trials with RWE-derived hazard ratios for progression-free and overall survival ("RWE-enhanced").

Data Source

This study used the nationwide Flatiron Health electronic health record (EHR)-derived de-identified database, a retrospective longitudinal database, comprising de-identified patient-level structured and unstructured data, curated via technology-enabled abstraction. During the study period the de-identified data originated from approximately 280 US cancer clinics (~800 sites of care). The data cutoff date for this analysis was November 30, 2020.

Study Population

The analytic cohort included 3,492 adults with EGFR- NSCLC that progressed after first-line treatment with a platinum-based chemotherapy doublet (Figure 1).

Statistical Analysis

The primary outcomes were overall survival (OS) and progression-free survival (PFS). Cox proportional hazards models adjusted for age, sex, race, practice type, performance status, and smoking history were used to estimate hazard ratios for patients who received immunotherapy (atezolizumab, pembrolizumab, nivolumab) vs. chemotherapy (single-agent docetaxel) in the second line of therapy. Parametric exponential models were fit to OS and PFS curves for patients who received chemotherapy. Quality-adjusted life years and costs were estimated according to patient health states (Figure 2), which were simulated based on hazard ratios for OS and PFS, disutilities for adverse events, and costs of medication acquisition and administration. To compare the cost effectiveness of immunotherapy vs, chemotherapy, we report traditional and RWE-enhanced incremental cost-effectiveness ratios (ICERs) and differences in uncertainty as percent change in the size of 95% credible intervals (CrIs).

RESULTS

Results

- The traditional vs RWE-enhanced ICERs were as follows: atezolizumab — $84,000/QALY vs $138,000/QALY; nivolumab — $136,000/QALY vs $123,000/QALY; pembrolizumab — $181,000/QALY vs $110,890/QALY.
- Compared to uncertainty intervals reported for traditionally-calculated ICERs, the RWE-enhanced ICER 95% CrIs were reduced by 37%, 69%, and 83% for atezolizumab, nivolumab, and pembrolizumab respectively.
- Compared to trial patients, real-world patients had longer follow-up time and were more likely to be female or non-white.

Figure 1: Cohort selection criteria for immunotherapy (atezoluzimab, pembrolizumab, nivolumab; light blue) and chemotherapy (docetaxel; dark blue) cohorts. *Patients who received pembrolizumab or atezolizumab were required to be positive for PDL1.

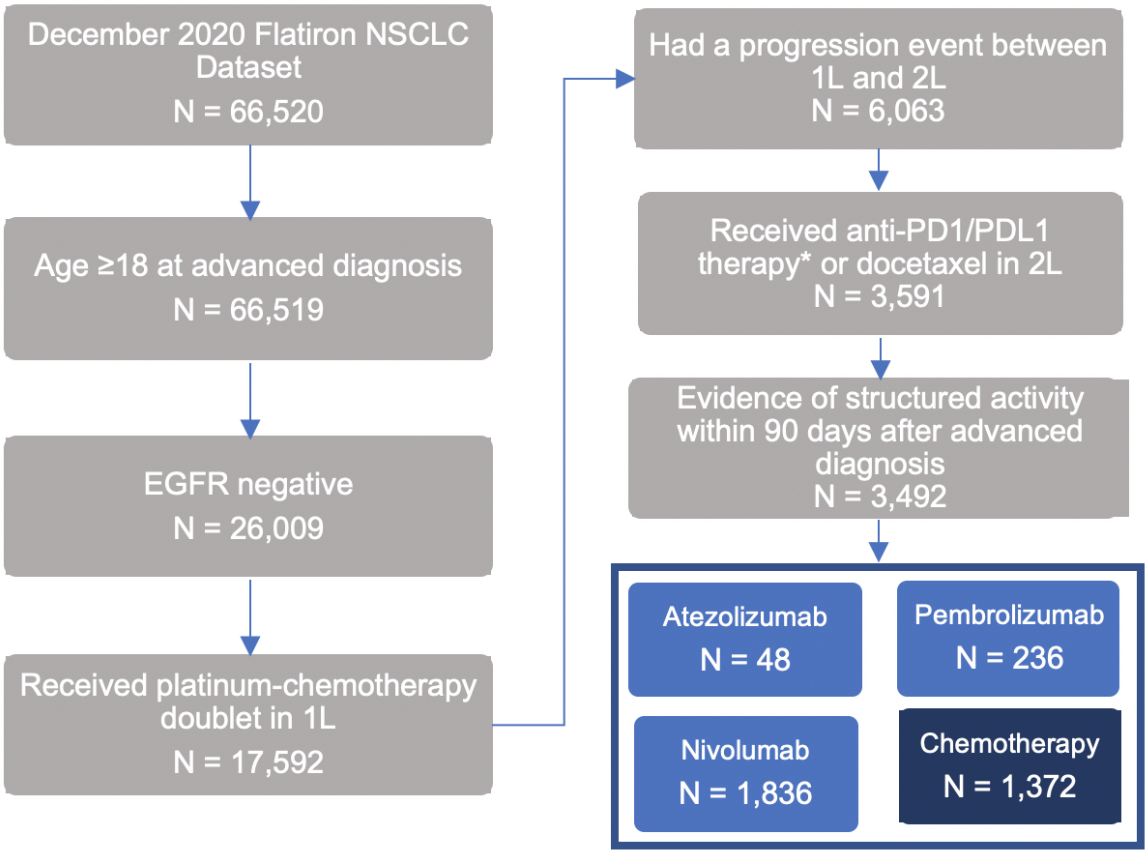


Figure 2: Design of patient health state simulation model.

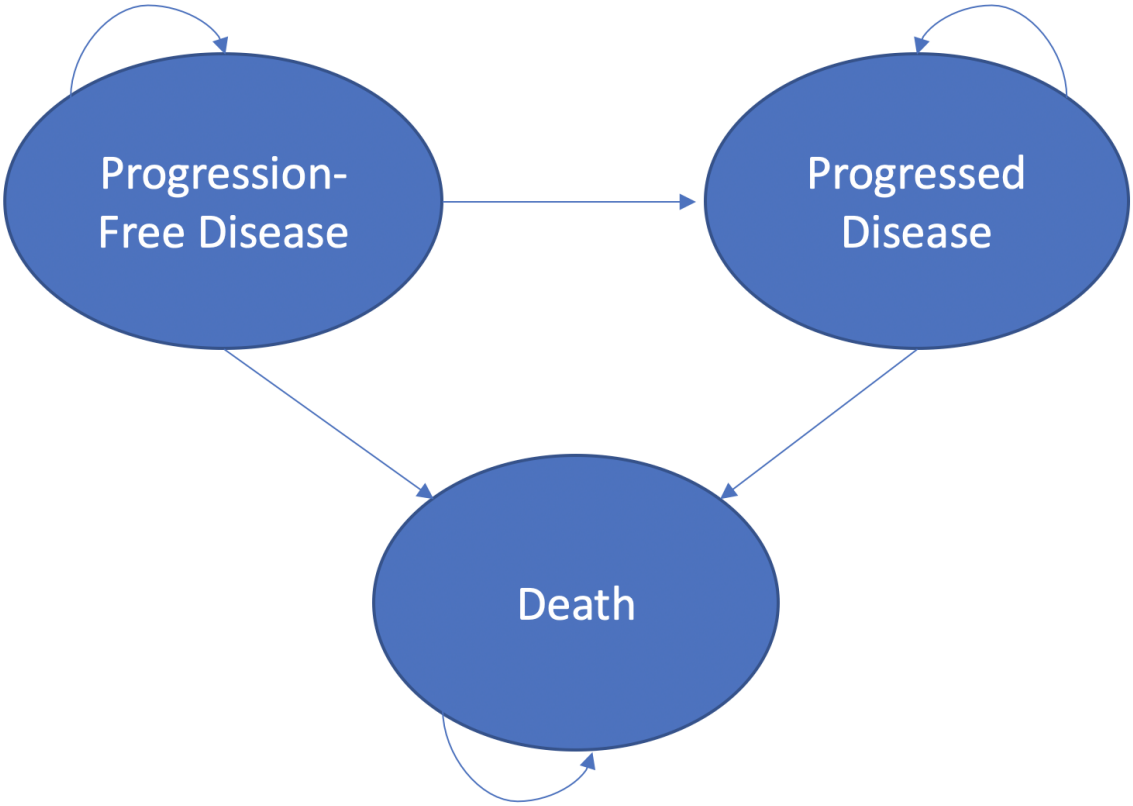


Figure 3: Clinical and demographic characteristics of clinical trial (POPLAR[2] for atezolizumab, CheckMate 017[3] for nivolumab, and KEYNOTE-010[4] for pembrolizumab) and RWE populations. *Data not reported in trial publication.

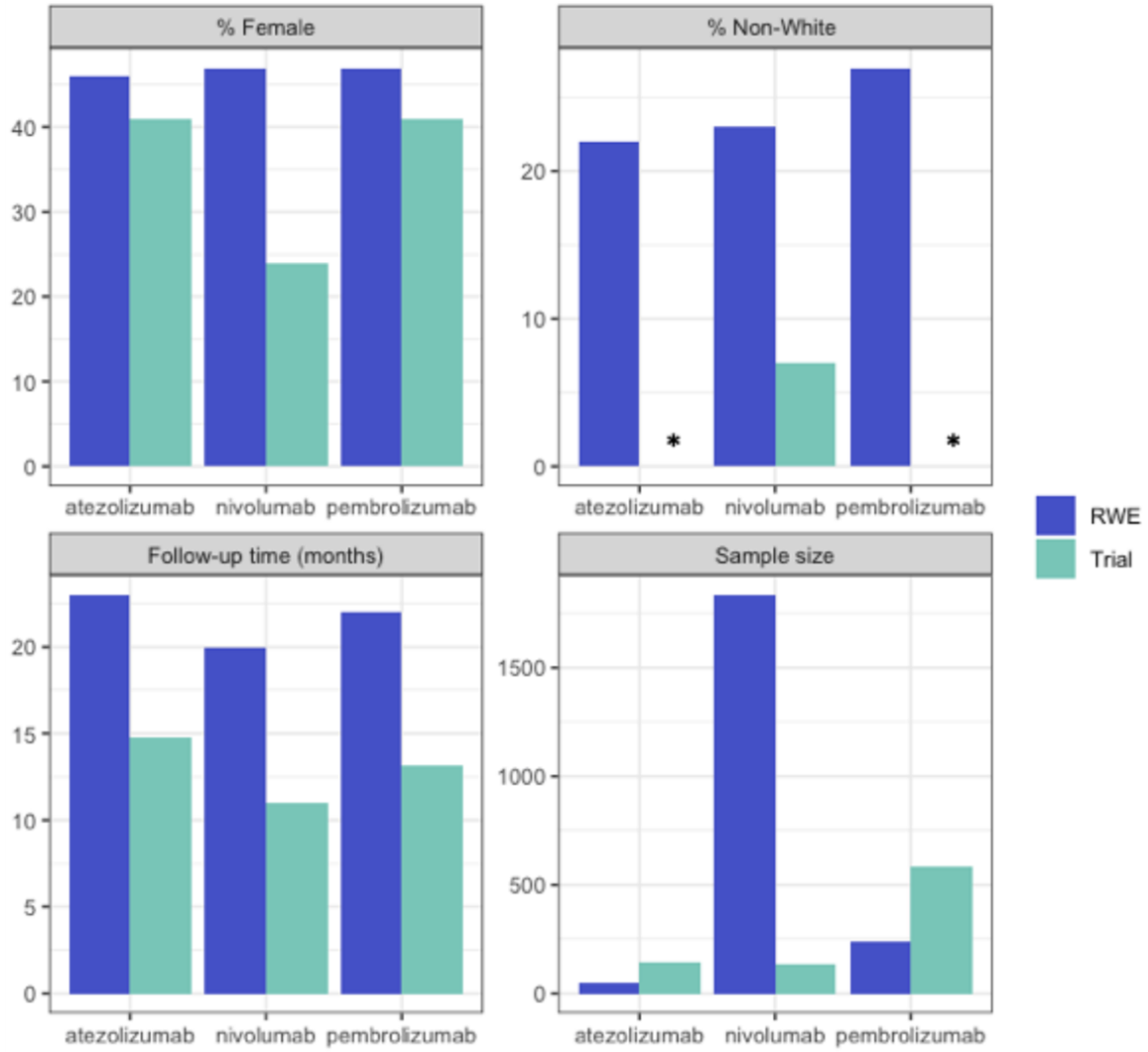
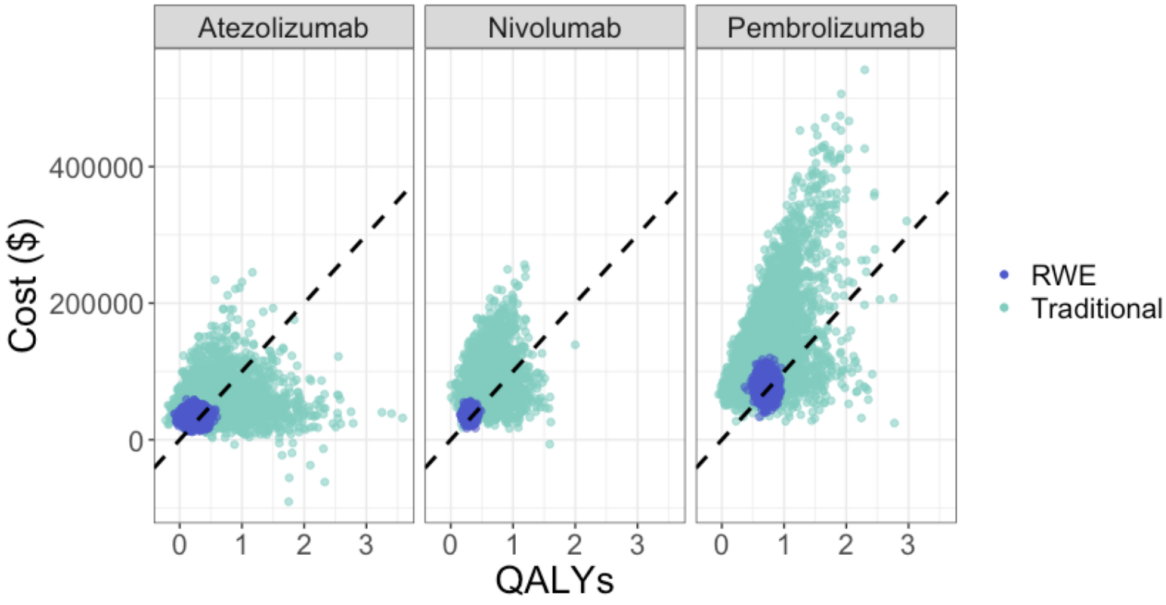


Figure 4: For RWE-enhanced (purple) and traditional (green) cost-effectiveness models, the simulated ICERs resulting from probabilistic sensitivity analyses comparing atezolizumab, nivolumab, and pembrolizumab to chemotherapy. The dashed reference line indicates an ICER of $100,000/QALY.



CONCLUSIONS

Conclusions

- This proof-of-concept demonstrated how clinical depth, longer follow-up time, and larger sample sizes in EHR-derived data may reduce uncertainty in cost-effectiveness analysis.
- The approach has potential to inform dynamic value-based pricing and highlights the importance of reassessments once RWE is available.
- Future studies could explore the opportunity to inform patient-level microsimulation models with EHR-derived data.

Limitations

- Sample size in the three immunotherapy cohorts varied based on how many patients received each therapy in the Flatiron Health database. RWE-enhanced cost effectiveness analysis is best suited for therapies with high uptake in real-world populations.
- For the purposes of this analysis, only the inclusion criteria listed in Figure 2 were implemented; clinical trial criteria involving other variables (ex. Baseline ECOG, sites of metastasis) were not implemented.
- Population adjustment methods such as matching were not applied to the real-world dataset. Bias-variance trade-offs should be considered before applying matching.

References

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ABSTRACT

Background: Real-world evidence (RWE) generated from electronic health records (EHR) has been shown to be more relevant, timely, and representative for health technology assessment decision-making compared to evidence from clinical trials. We assessed how using EHR-derived RWE instead of published clinical trial data can impact point estimates and uncertainty ranges in cost-effectiveness estimates for advanced non-small cell lung cancer (NSCLC) therapies.

Methods: We replicated a cost-effectiveness analysis of NSCLC therapies developed by the Institute for Clinical and Economic Review in 2016 (“traditional”), replacing meta-analysis-derived hazard ratios from clinical trials with RWE-derived hazard ratios for progression-free and overall survival (“RWE-enhanced”). Cox proportional hazards models adjusted for age, sex, race, practice type, performance status, and smoking history were used. The study used the Flatiron Health database, a nationwide (US-based) longitudinal, de-identified EHR-derived database. We compared the cost-effectiveness of immunotherapy (atezolizumab, pembrolizumab, nivolumab) vs. chemotherapy (single-agent docetaxel) in the second line of therapy. The analytic cohort included 3,492 adults with EGFR- NSCLC that progressed after first-line treatment with a platinum-based chemotherapy doublet. We report traditional and RWE-enhanced incremental cost-effectiveness ratios (ICERs) and differences in uncertainty as percent change in the size of 95% credible intervals (CIs).

Results: The traditional vs RWE-enhanced ICERs were as follows: atezolizumab — $84,000/QALY vs $138,000/QALY; nivolumab — $136,000/QALY vs $123,000/QALY; pembrolizumab — $181,000/QALY vs $110,890/QALY. Compared to uncertainty in traditional ICERs, 95% CIs for RWE-enhanced ICERs were reduced by 37%, 69%, and 83% for atezolizumab, nivolumab, and pembrolizumab respectively.

Conclusions: This proof-of-concept demonstrated how clinical depth, longer follow-up time, and larger sample sizes in EHR-derived data may reduce uncertainty in cost-effectiveness analysis. The approach has potential to inform dynamic value-based pricing and highlights the importance of reassessments once RWE is available.