US Healthcare Databases for Health Economic Modeling in Precision Medicine: An Oncology-Based Comparative Landscape Assessment (CLA)

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Background

- The landscape of innovation is changing rapidly with the rise of genomics and precision medicine. These dramatic advances in healthcare and increasing precision of treatment are translating into real-world shifts in treatment paradigms as well as meaningful improvements in patient outcomes
- Driver mutation-directed therapies are either used in or being developed for many types of cancers.[1] There is an increasing reliance on real-world evidence (RWE) to understand the health economic (HE) impact of these therapies. Also, health technology assessment (HTA) usually involves populating complex decision models that require RWE using diverse range of data sources (e.g., see use of RWE to support regulatory decision-making for medical devices by the FDA)[2]
- Furthermore, novel ways of defining and treating diseases raise key HE modeling questions on precision oncology technologies, such as:
  - What is the comparative effectiveness of a product relative to standard of care (SoC)?
  - What are the current SoC treatment patterns in the real world for rare oncology diseases?
  - What is the current burden of treatment and cost of care in rare oncology conditions?
  - Do patient outcomes and cost trends present differently across genetic alterations within the same rare oncology disease?
- RWE can help inform the answers to the above mentioned questions by providing:
  - Clinical data for comparators given an intervention with single arm trial data;
  - Treatment utilization data to justify comparator selection when no HTA exists and/or clinical practice guidelines are unclear or do not exist;
  - Disease management costs to populate economic models; and
  - Proxy data from similar mutations to fill data gaps on specific mutations

Objective

- To assess the capabilities of US-based retrospective data assets and provide guidance on the optimal sources to use when conducting HEOR research and inform HE modeling studies in precision oncology
  - To elicit a roadmap to aid HE modelers in identifying RWE data assets for needed model inputs in precision oncology

Methods

Overview

- Precision oncology focuses on individual patient's treatment by genetic alteration and stratification in relation to disease susceptibility, diagnosis, prognosis, and treatment response
  - **Main HE modeling inputs included:** Epidemiology, patient and disease characteristics, treatment patterns, costs (e.g., treatment, resource use, adverse events) and healthcare resource utilization (HCRU)
- The comparative landscape assessment (CLA) was conducted using US-based RWE data assets including: IQVIA Real World Adjudicated Claims – US Database (PharMetrics Plus (PMTX+)), Ambulatory Electronic Medical Record (AEMR), Oncology EMR (OEMR), Prescription Claims (Rx), Professional Fee Claims (Dx) and Hospital Charge Data Master (CDM); see **Table 1**
  - This CLA was conducted by reviewing the data dictionaries of the above data sets and discussion with RWE experts
- Precision oncology was selected to exemplify the range of required HE inputs across driver mutation oncology-related diseases
  - Note that the CLA methodology presented in this study could be used in disease areas beyond precision oncology

Landscape Analysis

- The analysis explored the relationship between HE modeling inputs and common RWE outputs as in previous studies[3]
  - **Step 1**: Map out main HE modeling inputs into RWE outputs. See outer square in **Figure 1**
  - **Step 2**: Map out HE modeling inputs into categories of common use in HTA – see intermediate square in **Figure 1**. Categories included:
    - **Epidemiology (Epi):** Incidence and/or prevalence of rare cancers (e.g., ALK non-Small Cell Lung Cancer [NSCLC]), stage of disease, comorbidities
    - **Patient and Disease Characteristics**: Mutation-directed biomarkers, BMI, weight, height, survival, lab values (e.g., Eastern Cooperative Oncology Group [ECOG] and Karnofsky scores), prior lines of treatment, diagnosis, and/or metastatic stage
    - **Treatment Patterns:** Treatments used and utilization (i.e., market share for a unique line of therapy), adherence/persistence, switching, cycles, duration of therapy
    - **Costs and HCRU:** Biomarker screening, resource costs, hospitalization costs and rates, patient out of pocket expenses, adverse events (AE) management costs, HCRU
  - **Step 3:** Categorize the HE input categories in Step 2 into three core decision-making drivers in HE evaluations: Clinical, economic and population. See innermost square in **Figure 1**

Data Asset Evaluation

- To assess the availability and quality of data for precision oncology modeling, the rating scale below was applied to each of the four HE modeling inputs categories above. This rating scale is only intended to serve as a guide for HE modelers when identifying RWE US-based data from the data assets considered in this study
  - **High:** RWE data is easily obtainable and provides a robust estimate in the HE modeling input category
  - **Medium:** RWE data exists but require algorithms to obtain the desired output. Data is not necessarily robust
  - **Low:** RWE data were not found or not useful for HE modeling

Results

- Epidemiology (PMTX+, OEMR), patient/disease characteristics (PMTX+, AEMRs, CDM), resource utilization (PMTX+, Rx, CDM, Dx), treatment patterns (PMTX+, Rx, CDM, Dx) and control cohort information (AEMRs) are reported in various data assets. However, information on genotypes are not consistently reported in the US
- Across databases, there is substantial data on treatment patterns; however, information on resource use, costs and disease status is more limited, suggesting the need to link across databases to cover all categories; see **Figure 2**
  - When linking CDM, Dx and Rx, data (deterministically or probabilistically) on treatment patterns and costs of oncology populations in both inpatient and outpatient settings can be available
    - This type of information is also available in the PMTX+ database; however this is primarily restricted to a commercial population that is <65 years of age
  - OEMR is a powerful tool for use in models as outcomes include treatment patterns, epidemiology, disease status, patient characteristics and AEs. However, linking to other databases (e.g., PMTX+) is required to capture costs alongside inputs for HCRU
  - Finally, AEMR was not found appropriate for precision oncology since more oncology-focused sources are available (e.g., OEMR)
    - Dx database provides information primarily only in outpatient settings
- HE modeling inputs in precision oncology requires patient data with detailed health records including information on mutations or other genetic alterations. Information related to patient clinical characteristics (etiology, genetics, performance scores, companion diagnostics use) can be rare and unstructured, so studies require novel approaches such as using high-quality linked databases or enriching RWE databases with patient or provider surveys

Limitations

- Only six US-based IQVIA RWE data assets were reviewed in this analysis. Although other data assets available and data coverage in the US were not considered, the findings of this study are generalizable to other similar data assets, contingent of a review of relevant data dictionaries and database characteristics. This study format could be expanded to include those data assets in future iterations
- HE modeling is contingent on the disease being modeled, model type (e.g., budget impact analysis [BIM], cost-effectiveness analysis [CEA]), patient population, and model settings (e.g., perspective, outpatient/inpatient). Thus, the HE modeling input categories in this study may not be applicable to all models
- This study looks at availability of concepts to support modeling in precision oncology but does not explicitly map HTA acceptance or approval trends

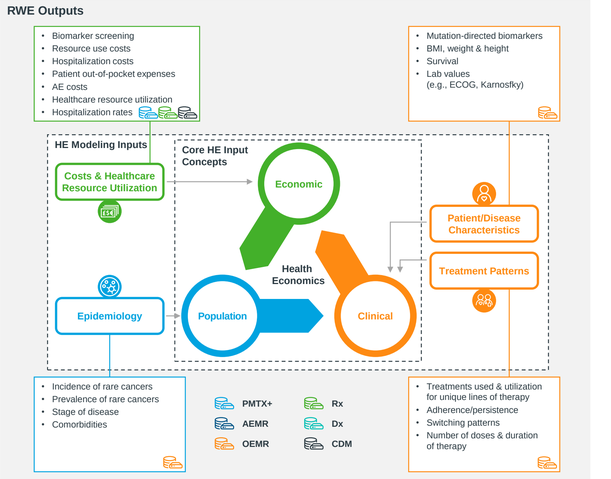
Table 1. RWE Data Assets for HE Modeling

Data Asset	Description	Coverage	Key data Elements	Limitations	Precision Oncology Modeling Inputs
Pharmetrics Plus (PMTX+)	• Adjudicated plan level data including complete inventory of a patient's prescriptions, hospital and medical claims • Provides information on paid amounts and out-of-pocket expenditures most relevant for economic modeling	• >150M enrollees with medical coverage with ~40M active in most recent year • ~ 20M with pharmacy/medical coverage with 3 or more years continuous enrollment • Data from 90% of US hospitals, 80% of all US doctors, and representation from 85% of the Fortune 100 companies • 3-4 month lag period	• Inpatient and outpatient diagnoses and procedures, retail and mail order prescription records, pharmacy and medical benefit, inpatient stay and provider details	• Most relevant for commercial population due to under-representation of Medicare, Medicaid, and of over 65 population • Lab test results and drug utilization in hospital not available	• **Epidemiology:** Incidence/prevalence (not rare cancers), comorbidities • **Patient and disease characteristics:** Prior lines of treatments, diagnosis and/or metastatic stage (using ICD codes) • **Treatment patterns:** Treatments used and utilization (i.e., market share for a unique line of therapy), adherence/persistence, switching, cycles, duration of therapy • **Costs and HCRU:** Biomarker screening, resource costs, hospitalization costs and rates, patient out-of-pocket expenses, AE management costs, HCRU
Ambulatory Electronic Medical Record (AEMR)	• Processed and aggregated detailed patient interactions from electronic systems by physician practices and clinics. Updated on monthly basis • Provides detailed disease information, specifically on patient health metrics and disease status • Can be linked to other databases to explore cost outcomes	• ~50 million patient records sourced from an "opt-in" provider research network • Records collected across 40K physicians from large practices and physician networks • ~50% of the contributing physicians are primary care practitioners and the remaining are specialists	• Patient demographics, vitals, risk factors, prescribed/ administered drugs, diagnoses, procedures, lab tests ordered & results and recording of patient care episodes	• No inpatient or cost data • Smaller patient size may limit generalizability of outcomes	• **Epidemiology:** Incidence and/or prevalence of cancers (not rare cancers) and stage of disease • **Patient and disease characteristics:** BMI, weight, height, survival, lab values (cancer related may not be prevalent), diagnosis, and/or metastatic stage

Table 1. RWE Data Assets for HE Modeling (contd.)

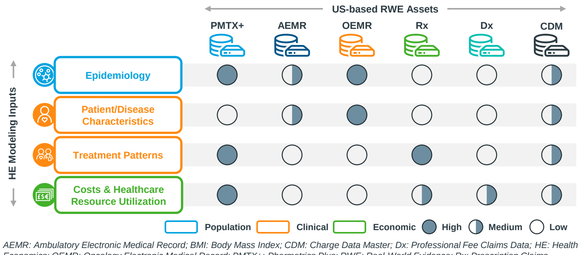
Data Asset	Description	Coverage	Key data Elements	Limitations	Precision Oncology Modeling Inputs
Oncology EMR	• Detailed clinical data from the EMR systems of medium and large community based, oncology practices	• ~905K cancer patients from community oncology practices of ~1400 physicians from ~320 hospitals/clinics • Updated on monthly basis	• Cancer staging and progression, lab results, treatment (injectables/oral) dosing, treatment regimen and intervals, vitals, mortality	• No inpatient or cost data • Smaller patient size	• **Epidemiology:** Incidence and/or prevalence of rare cancers (e.g., ALK Non-Small Cell Lung Cancer [NSCLC]) and stage of disease • **Patient and disease characteristics:** Mutation-directed biomarkers, BMI, weight, height, survival, lab values (e.g., Eastern Cooperative Oncology Group [ECOG] and Karnofsky scores), diagnosis, and/or metastatic stage
Prescription Claims (Rx)	• Prescription claims by retail, mail order and specialty pharmacies across the US	• ~1.6B Rx/year representing 85% of all US pharmacies • National Council for Prescription Drug Programs (NCPDP) claims include those reimbursed by cash, Medicare, Medicaid and other third-party transactions • Data available within 12 days of being dispensed	• Prescribed medication, date written and filled, quantity dispensed, days supply, refills, switching, payment/ charges, payer type	• Lack of diagnosis codes • Only requires that the pharmacy is continuously enrolled • Not possible to apply continuous enrollment, so proxies need to be implemented	• **Treatment patterns:** Treatments used and utilization (i.e., market share for a unique line of therapy), adherence/persistence, switching, cycles, duration of therapy • **Costs and HCRU:** Treatment utilization and costs
Professional Fee Claims (Dx)	• Pre-adjudicated claims with diagnosis and procedure information from office-based physicians and specialists • Costs are unadjudicated and reported as charges	• >1B fee claims per year representing over 870K practitioners per month • 95% of claims available within 3 weeks of service date	• Administered drug, charge amounts, diagnosis, procedures, lab and diagnostic tests performed	• Some lab/diagnostic test results not available; cash patients unavailable • Primarily captures the office setting only • Unadjudicated claims • Not possible to apply continuous enrollment, so proxies need to be implemented	• **Costs and HCRU:** Resource costs, office visit costs
Charge Data Master (CDM)	• Hospital data collected from revenue cycle management vendors who provide revenue cycle management systems to hospitals; data contains all of the underlying patient information that is used to create Diagnosis Related Groups (DRGs)/claims • Explores costs and resource use in inpatient setting only and needs to be linked to Dx and Rx databases for outpatient and pharmacy information	• Records from hospital CDM files from over 450 hospital, covering 7M inpatient & 60M annual outpatient visits including ER visits • Data lag time of 6 weeks following end of each calendar month	• Inpatient and outpatient encounters within a facility, linked to individual departments, with detailed drug, procedure, diagnosis, and applied charge data for the entire stay	• Lab results and information from specialty hospitals not available • Only includes charges • Not possible to apply continuous enrollment, so proxies need to be implemented	• **Epidemiology:** Comorbidities • **Patient and disease characteristics:** Prior lines of treatment, diagnosis • **Treatment patterns:** Treatments utilization (i.e., market share for a unique line of therapy), • **Costs and HCRU:** Resource costs, hospitalization costs and rates, patient out-of-pocket expenses, AE management costs, HCRU

Figure 1. Mapping HE Modeling Inputs and RWE Data Assets Outputs



AE: Adverse Event; AEMR: Ambulatory Electronic Medical Record; BMI: Body Mass Index; CDM: Charge Data Master; Dx: Professional Fee Claims Data; HE: Health Economics; OEMR: Oncology Electronic Medical Record; PMTX+: Pharmetrics Plus; RWE: Real-World Evidence; Rx: Prescription Claims

Figure 2. HE Modeling Inputs Data Availability across US-based Data Assets



AEMR: Ambulatory Electronic Medical Record; BMI: Body Mass Index; CDM: Charge Data Master; Dx: Professional Fee Claims Data; HE: Health Economics; OEMR: Oncology Electronic Medical Record; PMTX+: Pharmetrics Plus; RWE: Real-World Evidence; Rx: Prescription Claims

Conclusion

- Observational data needed for HE models in precision oncology may not be satisfied with a unique RWE data asset, but commonly requires linkage of databases
- Understanding both the research question and available data assets to rapidly query a dataset and identify patients should guide the choice of observational data to use in HE modeling
- The possibility of enriching RWE databases using patient/provider surveys should also be considered

Future trends and challenges

- **Increasing RWE data use and expanded information on biomarkers:** Future solutions can include platforms for data science to incorporate artificial intelligence, increasing the potential of existing data to serve as synthetic historical controls[4]
- **Understanding uncertainty on natural disease history due to novel or newly identified biomarkers:** The availability of predictive biomarkers and diagnostic tests can help bring a more precise course of treatment to an individual patient. However, the true causal effect of new treatments that target these markers needs to be understood
- **Bridging the gap between the unconventional, or limited, data for many of these new treatments and the current requirements of payers and HTA bodies:** Many of the HE modeling tools that payers and HTA bodies leverage to discern value when informing their decisions must keep pace with treatment innovation

Disclaimers

- This study was sponsored by IQVIA. Oscar Herrera-Restrepo, Vamshi Ruthwik Anupindi, Elizabeth Wehler, and Stacey Kowal are employees of IQVIA. The authors report no other conflicts of interest in this work

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