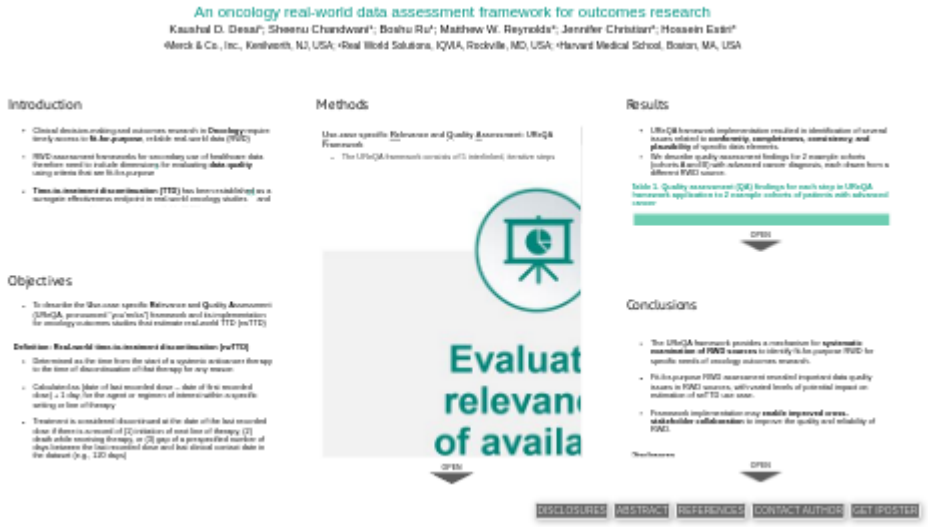
# An oncology real-world data assessment framework for outcomes research

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**PRESENTED AT:**

# INTRODUCTION

- Clinical decision-making and outcomes research in **Oncology** require timely access to **fit-for-purpose**, reliable real-world data (RWD)

- RWD assessment frameworks for secondary use of healthcare data therefore need to include dimensions for evaluating **data quality** using criteria that are fit-for-purpose[1]

- **Time-to-treatment discontinuation (TTD)** has been established as a surrogate effectiveness endpoint in real-world oncology studies[2,3] and can be measured in commercially available RWD sources, such as electronic medical records (EMR) and claims and billing records

# OBJECTIVES

- To describe the **U**se-case specific **Re**levance and **Q**uality **A**ssessment (UReQA, pronounced “you'reːka”) framework and its implementation for oncology outcomes studies that estimate real-world TTD (rwTTD)

**Definition: Real-world time-to-treatment discontinuation (rwTTD)**

- Determined as the time from the start of a systemic anticancer therapy to the time of discontinuation of that therapy for any reason

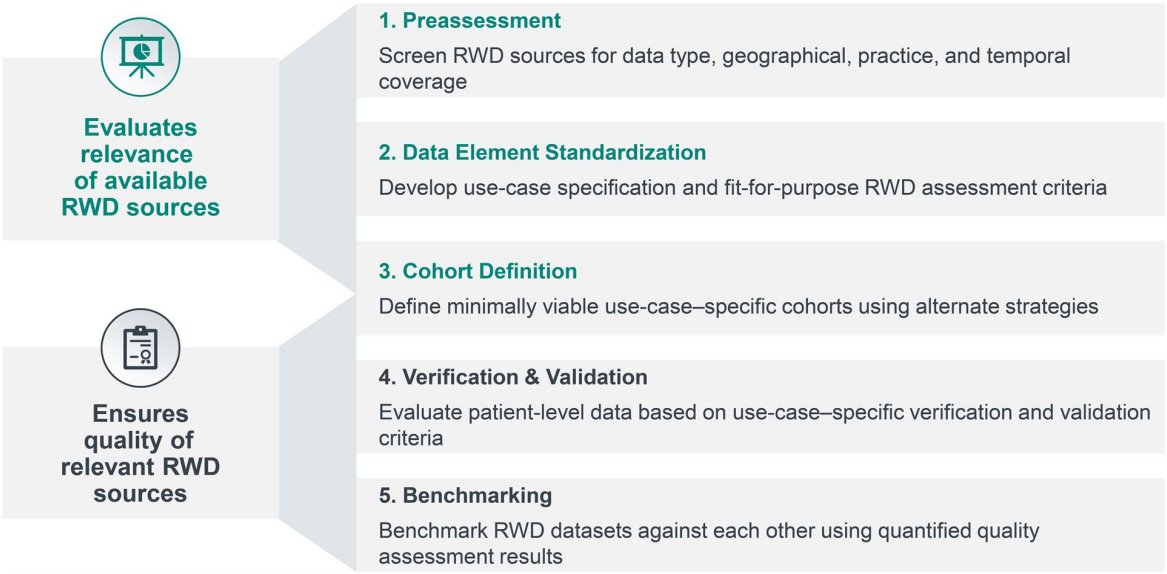
- Calculated as (date of last recorded dose – date of first recorded dose) + 1 day, for the agent or regimen of interest within a specific setting or line of therapy

- Treatment is considered discontinued at the date of the last recorded dose if there is a record of (1) initiation of next line of therapy, (2) death while receiving therapy, or (3) gap of a prespecified number of days between the last recorded dose and last clinical contact date in the dataset (e.g., 120 days)

# METHODS

**Use-case specific Relevance and Quality Assessment: UReQA Framework**

- The UReQA framework consists of 5 interlinked, iterative steps




**UReQA Framework Application**

- For the rwTTD, core components of the use-case specification were as follows:
  - A **core list of data elements** required to estimate rwTTD
  - **Variable definitions, constraints, and formats** (collectively termed "business rules") for each core data element
  - A list of checks to **ascertain internal validity** (alignment with business rules) for core data elements
  - A list of checks to **ascertain external validity** (alignment with published literature, reference data sources, or expert input) for core data elements
- **Data element standardization** involved a manual review of vendor-provided data element definitions to ensure alignment with use-case specification
- **Cohort definition** was carried out through exploration of alternate cohort build strategies to identify advanced disease cohorts.
  - For cohort definitions that involved stratification using biomarker test results, temporal trends in biomarker testing results were plotted.
- To check for **completeness of treatment records**, the annual counts of patients who initiated treatment (year of first dose) and ended treatment (year of last dose) were plotted as bar charts.
- Density of treatment records was also evaluated using **average gap in treatment visits** as a measure
  - The average number of days between consecutive treatment visits was estimated and plotted as a histogram for each cohort
- Gaps identified in each step were documented and communicated with the data providers as recommendations for data quality enrichment.

# RESULTS

- UReQA framework implementation resulted in identification of several issues related to **conformity, completeness, consistency, and plausibility** of specific data elements.
- We describe quality assessment findings for 2 example cohorts (cohorts A and B) with advanced cancer diagnosis, each drawn from a different RWD source.

**Table 1. Quality assessment (QA) findings for each step in UReQA framework application to 2 example cohorts of patients with advanced cancer**

| QA step | QA results at each step (illustrative examples) |
|---|---|
| 1. Verification (plausibility check) | Biomarker-stratified cohort definition for rwTTD estimation requires unambiguous determination of biomarker status at a specific time point:<br>• Unresolved, conflicting biomarker results identified for 2 patients (Figure 1) |
| 2. Validation (completeness check) | rwTTD estimation requires complete treatment records:<br>• Unexpected reduction found in annual frequency of treatment initiation and treatment discontinuation, highlighting possible incompleteness of treatment records (Figure 2) |
| 3. Validation (completeness check) | rwTTD estimation requires complete treatment records:<br>• Differences in average gap identified between visits as compared with reference benchmark (Figure 3) |
| 4. Validation (plausibility check) | rwTTD estimation requires complete mortality event records:<br>• Decreasing trend identified in percentage mortality with increasing age group (Table 2) |

**Figure 1. Verification (plausibility check) for biomarker status of 2 patients: (A) multiple measurements were recorded on the same day for the same biomarker, with conflicting/unresolved results for patient 1, and (B) progesterone marker status was negative for three measurements, followed by a positive result several days after the third measurement for patient 2**

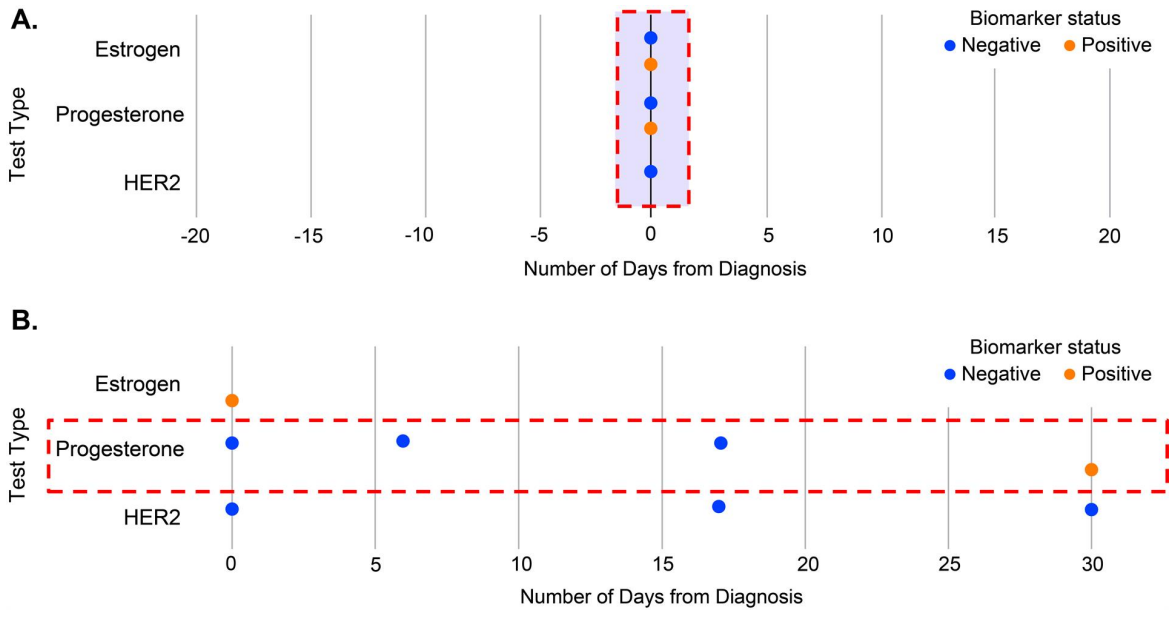



**Figure 2. Validation (completeness check) for treatment records: unexpected reduction found in annual frequency of treatment initiation and treatment discontinuation for cohort A, highlighting possible incompleteness of treatment records**

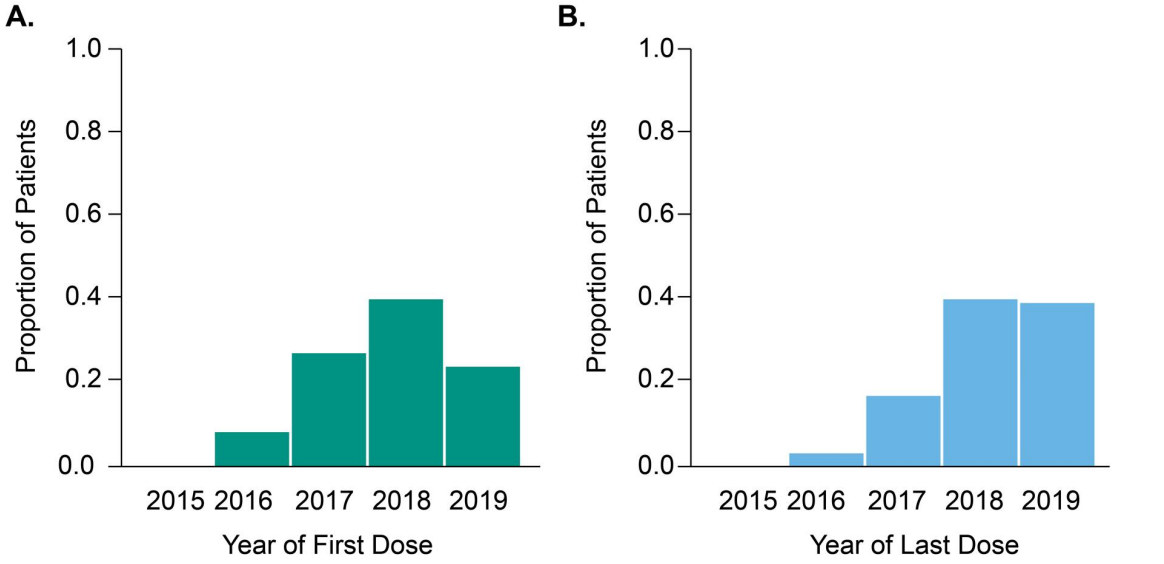
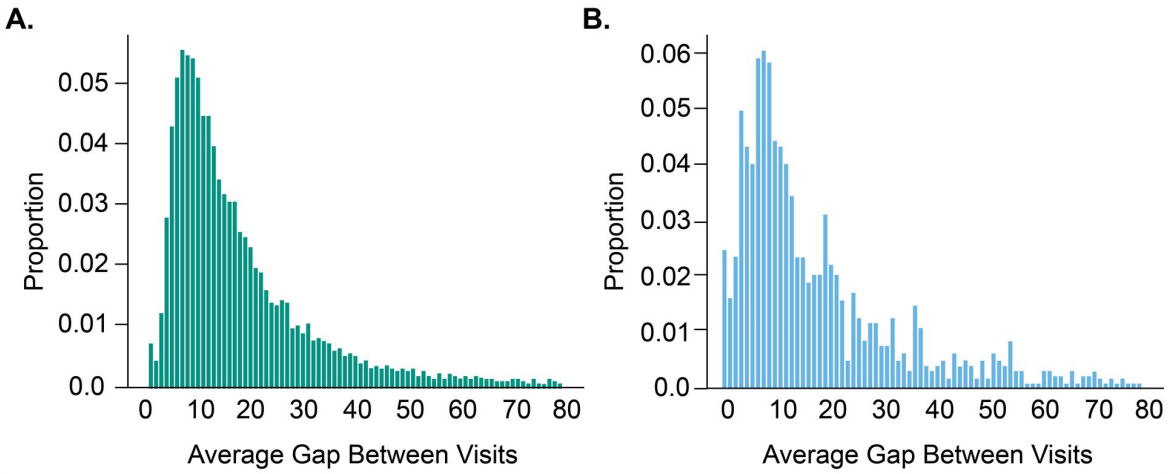



**Figure 3. Validation (completeness check): differences in average gap identified between visits in (A) cohort A and (B) cohort B as compared with reference benchmark. The check was implemented using the same criteria for the two different RWD sources**




| | Days between visits | | |
|---|---|---|---|
| | Mean (SD) | Median (IQR) | Range |
| Cohort A (structured EMR); N=16,406 | 26 (52) | 14 (8–26) | 0–2,436 |
| Cohort B (structured EMR); N=982 | 27 (51) | 13 (7–27) | 0–945 |
| Benchmark (structured + unstructured EMR) | 13 (17) | 10 (6–15) | 0–733 |

IQR, interquartile range

**Table 2. Plausibility/completeness check of mortality records: Decreasing trend identified in percentage mortality with increasing age group in cohorts A and B. The check was implemented using the same criteria for the two different RWD sources**

| Age, years | Cohort A | | Cohort B | |
|---|---|---|---|---|
| | N | Died, n (%) | N | Died, n (%) |
| ≤64 | 8,132 | 3,842 (47) | 473 | 318 (67) |
| 65–74 | 5,369 | 2,432 (45) | 326 | 195 (60) |
| 75–84 | 2,397 | 1,047 (44) | 143 | 77 (54) |
| ≥85 | 192 | 72 (38) | 8 | 2 (25) |
| Missing | 330 | 164 (50) | 38 | 17 (45) |
| Total | 16,420 | 7,557 (46) | 988 | 609 (62) |

# CONCLUSIONS

- The UReQA framework provides a mechanism for **systematic examination of RWD sources** to identify fit-for-purpose RWD for specific needs of oncology outcomes research.
- Fit-for-purpose RWD assessment revealed important data quality issues in RWD sources, with varied levels of potential impact on estimation of rwTTD use case.
- Framework implementation may **enable improved cross-stakeholder collaboration** to improve the quality and reliability of RWD.

### Disclosures

KD Desai, S Chandwani, and B Ru are employees of Merck & Co., Inc., Kenilworth, NJ, USA; MW Reynolds and J Christian are employees of IQVIA; H Estiri has no conflicts of interest to declare.

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### References

1. Determining real-world data's fitness for use and the role of reliability: Duke-Margolis Center for Health Policy. 2019. Available at: https://healthpolicy.duke.edu/publications/determining-real-world-datas-fitness-use-and-role-reliability. Accessed May 6, 2021.
2. Stewart M, et al. *JCO Clin Cancer Inform.* 2019;3:1-15.
3. Blumenthal GM, et al. *Ann Oncol.* 2019;30(5):830-838.

# DISCLOSURES

KD Desai, S Chandwani, and B Ru are employees of Merck & Co., Inc., Kenilworth, NJ, USA; MW Reynolds and J Christian are employees of IQVIA; H Estiri has no conflicts of interest to declare.

# ABSTRACT

Objectives

Clinical decision-making and outcome research in Oncology requires timely access to fit-for-purpose, real-world data (RWD). RWD assessment frameworks for secondary use of healthcare data therefore need to include dimensions that evaluate data quality using fit-for-purpose evaluation criteria. This conceptual paper describes the Use-case specific Relevance and Quality Assessment ('UReQA', pronounced as 'Eureka') framework and its implementation for outcomes studies that estimate real-world Time to Treatment Discontinuation (TTD).

Methods

The UReQA framework consists of five interlinked, iterative process steps –

1. Pre-assessment to screen commercialized RWD sources on population coverage, timeliness, and use case experience

2. Data Elements Evaluation based on study-specific data elements and review of business rules specification

3. Cohort Identification to ensure a reasonably sized, viable cohort for the specific study

4. Verification to ensure internal validity of patient-level data elements of interest

5. Validation to examine external validity using metrics for longitudinality, conformity, plausibility and completeness

Various steps in the UReQA framework were applied to 10 large, commercial Oncology EHR cohorts in the US.

Results

UReQA framework implementation revealed important quality issues in RWD sources, with varied levels of potential impact on estimation of TTD. Data element evaluation revealed ambiguous coding of medication date for oral therapies. Internal validity checks revealed ambiguous biomarker results and testing dates. External validity checks revealed lower than expected drug exposure rates and mortality events.

Conclusion

The UReQA framework provides a mechanism for systematic examination of RWD sources to identify fit-for-purpose RWD for specific outcomes research needs. Framework implementation may enable improved cross-stakeholder collaboration to improve the quality and reliability of real-world data.

# REFERENCES

1. Determining real-world data's fitness for use and the role of reliability: Duke-Margolis Center for Health Policy. 2019; https://healthpolicy.duke.edu/publications/determining-real-world-datas-fitness-use-and-role-reliability
2. Stewart M, et al. *JCO Clin Cancer Inform.* 2019;3:1–15.
3. Blumenthal GM, et al. *Ann Oncol.* 2019;30(5):830–838.