Pilot project data: Correlation of real-world endpoints to overall survival among immune checkpoint inhibitor-treated aNSCLC patients

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Establishing a Framework to Evaluate Real-World Endpoints

Project Goals: Explore potential endpoints that may be fit for regulatory purposes as well as assessing long term benefits of a product	
Project Focus	Evaluate the performance of real-world endpoints across multiple data sets by focusing on a common question: ***What outcomes can be evaluated for advanced NSCLC (aNSCLC) patients treated with immune checkpoint inhibitors?***
Research Objectives	Objective 1: Characterize the demographic and clinical characteristics of aNSCLC patients treated with immune checkpoint inhibitors Objective 2: Assess ability to generate real-world endpoints (OS, PFS, TTP, TTNT, TTD) in aNSCLC patients treated with immune checkpoint inhibitors, and segmented by clinical and demographic characteristics Objective 3: Assess performance of real-world endpoints (PFS, TTP, TTNT, TTD) as surrogate endpoints for overall survival (OS)
Study Design	This is a retrospective observational analysis of data derived from electronic health record (EHR) and claims based databases. The datasets generated for the study will include all relevant, retrospective patient-level data available for eligible individuals up to the data cutoff date, pending approval by a third-party de-identification.
Data Partners	**Cota, Flatiron Health, IQVIA, Kaiser Permanente/CRN, Mayo Clinic/OptumLabs®, and PCORnet/University of Iowa**

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Real-World Endpoint Assessment

Real-world derived endpoint definitions

Overall survival (OS)

- *Data definition / computation*: length of time from the date the patient initiates the PD-(L)1 regimen to the date of death. Patients without a date of death will be censored at their last known activity.

Time to Next Treatment (TTNT)

- *Data definition / computation*: length of time from the date the patient initiates the PD-(L)1 regimen to the date the patient initiates their next systemic treatment. When subsequent treatment is not received (e.g., continuing on current treatment), patients will be censored at their last known activity.

Time to Treatment Discontinuation (TTD)

- *Data definition / computation*: length of time from the date the patient initiates the PD-(L)1 regimen to the date the patient discontinues treatment. Patients still on treatment will be censored at their last known activity.

Definition of progression in aNSCLC as evident in the EHR

A **progression event** is a distinct episode in which the treating clinician concludes that there has been growth or worsening in the aNSCLC. The progression event (and date) is based on review of the patient chart.

Progression Free Survival (PFS)

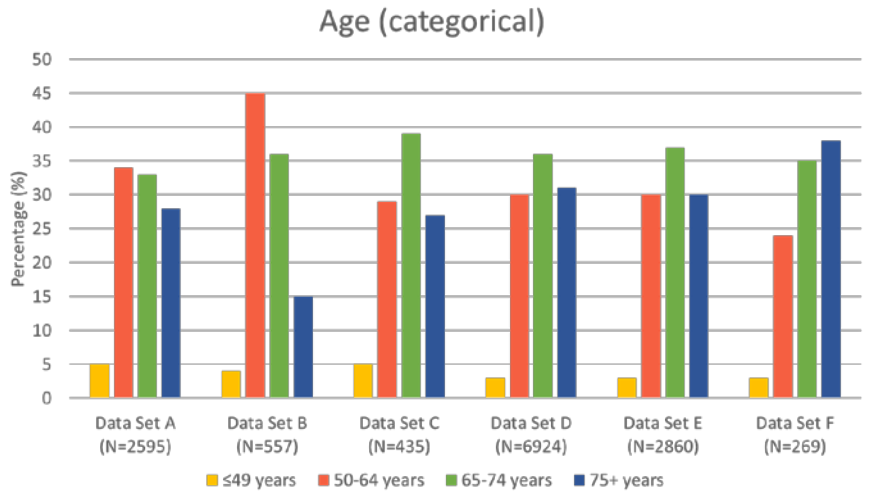
- *Data definition / computation*: length of time from the date the patient initiates the PD-(L)1 regimen to the date that a progression event as evident in the EHR is documented in the patient's chart or the patient passes away. Patients without a progression event or date of death will be censored at the end of the patient's chart.

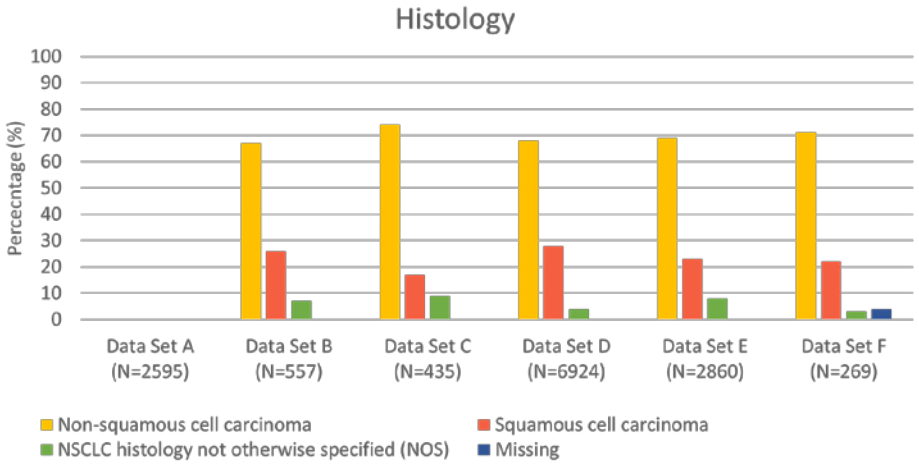
Time to Progression (TTP)

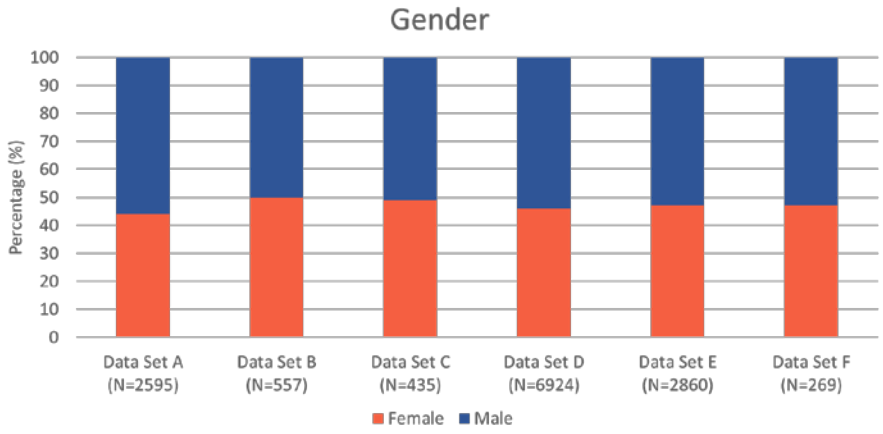
- *Data definition / computation*: length of time from the date the patient initiated the PD-(L)1 regimen to the date that a progression event as evident in the EHR is documented in the patient's chart (excludes death as an event). Patients without a progression event will be censored at the end of the patient's chart.

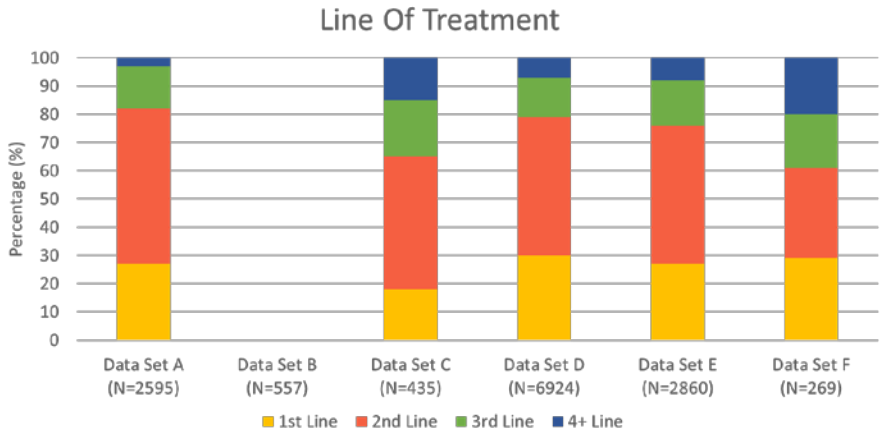
Shared demographic and clinical characteristics among data sets

Table 1









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Real-world Overall Survival (OS), Time to Discontinuation (TTD) & Time to Next Treatment (TTNT)

Table 2

Data Set	rwOS	rwTTD	rwTTNT
Data Set A	13.50 [12.80, 14.50] #	7.03 [6.27, 9.97]	22.50 [NA]
Data Set B	15.78 [12.2, 24.59]; 8.58 [7.56, 10.26] *	3.25 [2.76, 3.75]	
Data Set C	8.67 [6.83, 10.02]	4.70 [3.68, 5.52]	11.60 [8.80, 16.10]
Data Set D	9.15 [8.82, 9.51]	3.21 [3.21, 3.44]	14.03 [12.89, 15.15]
Data Set E	12.69 [11.7, 13.87]	3.63 [3.40, 3.87]	12.07 [11.24, 13.48]
Data Set F	12.30 [9.61, 16.94]	4.60 [3.71, 6.32]	12.50 [9.29, NA]

OS was calculated as days between I/O initiation and disenrollment.

* Sites with social security or state death data, censored at estimated earliest date such data should be available if no death was observed

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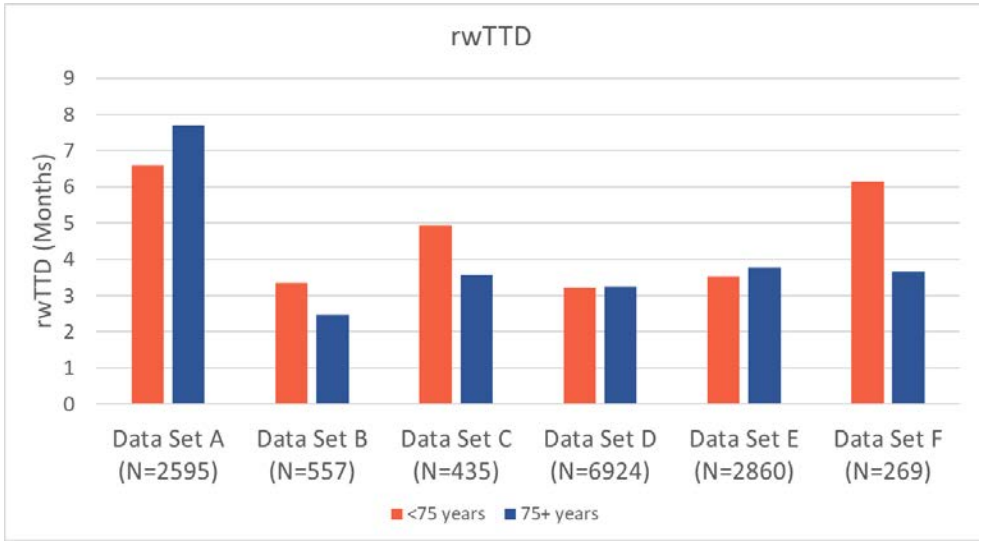
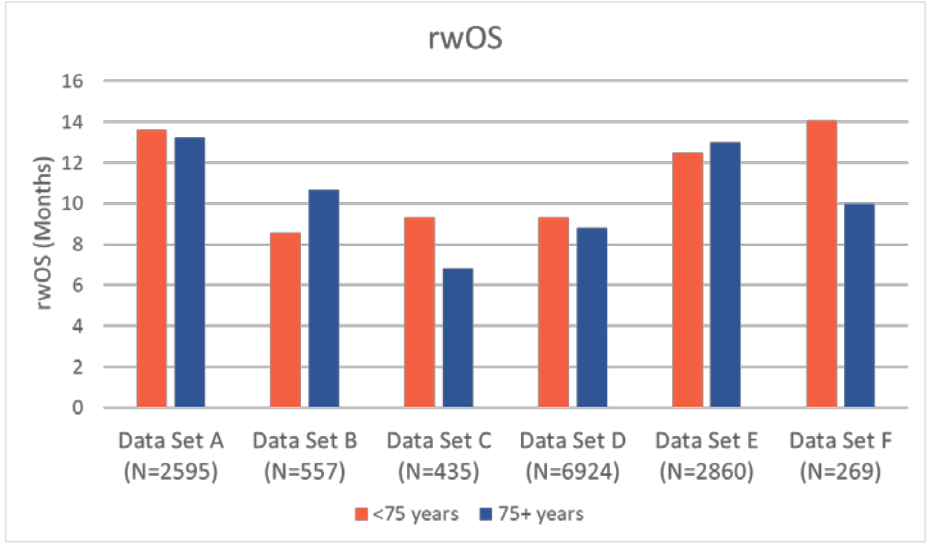
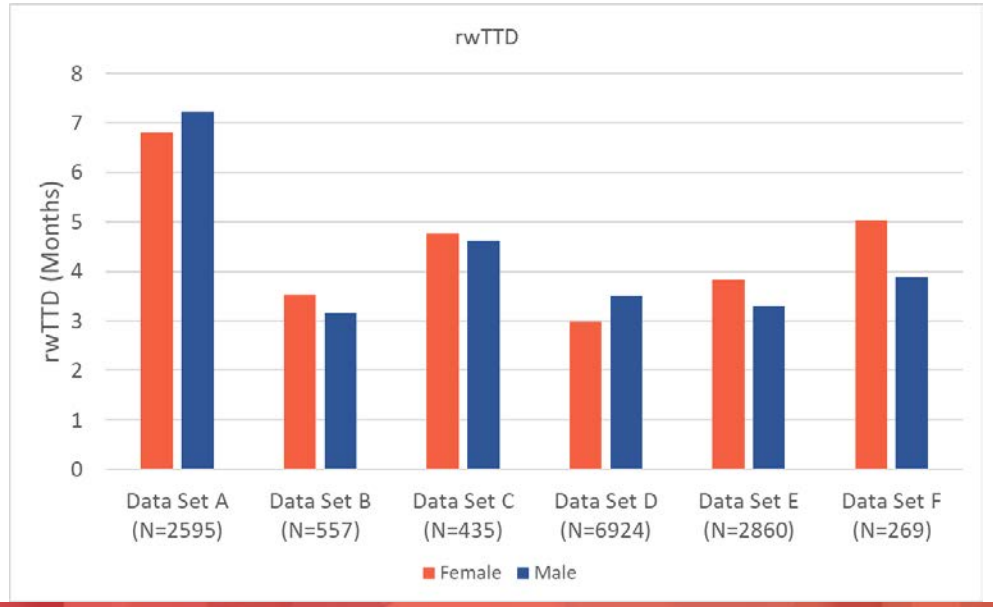
Table 2

Age (Binary)





Gender



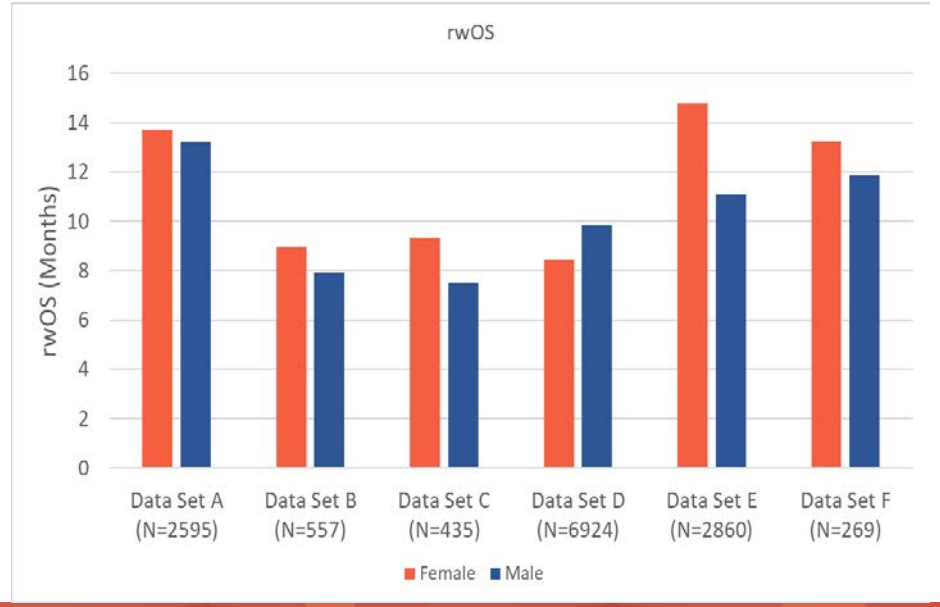


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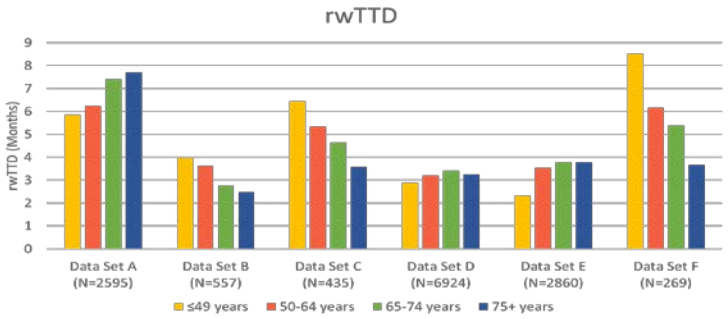
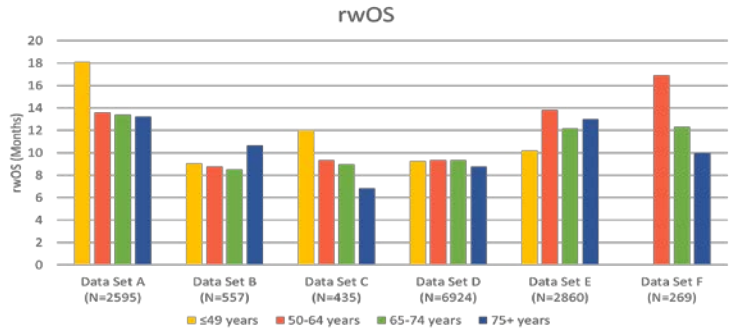
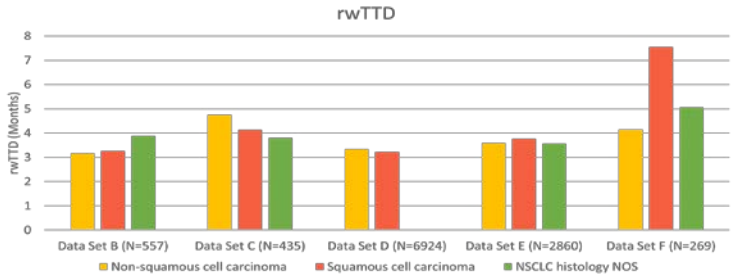
Table 2

Age (Categorical)

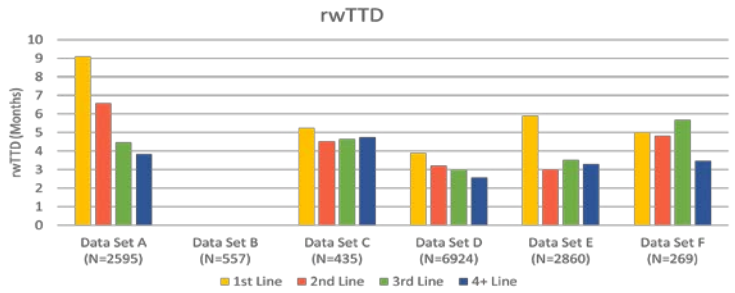


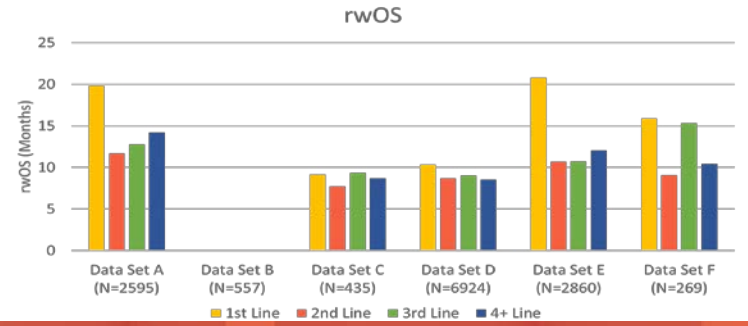


Histology



Line of therapy





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Correlation between real-world overall survival and real-world extracted endpoints

	rwOS vs rwTTNT		rwOS vs rwTTD	
Data Set	**N**	**Correlation [95% CI]**	**N**	**Correlation [95% CI]**
Data Set A	83	0.36	254	0.63
Data Set B			225	0.62 [0.54, 0.69]
Data Set C	96	0.70 [0.58, 0.79]	295	0.89 [0.86, 0.91]
Data Set D	1203	0.61 [0.57, 0.64]	4337	0.80 [0.79, 0.81]
Data Set E	358	0.62 [0.54, 0.68]	1456	0.77 [0.75, 0.79]
Data Set F	39	0.46 [0.33, 0.81]	142	0.80 [0.66, 0.85]

	rwOS vs rwPFS		rwOS vs rwTTP	
Data Set	**N**	**Correlation [95% CI]**	**N**	**Correlation [95% CI]**
Data Set D	4337	0.75 [0.74, 0.76]	2286	0.60 [0.57, 0.63]
Data Set F	142	0.84 [0.62, 0.86]	55	0.56 [0.21, 0.71]

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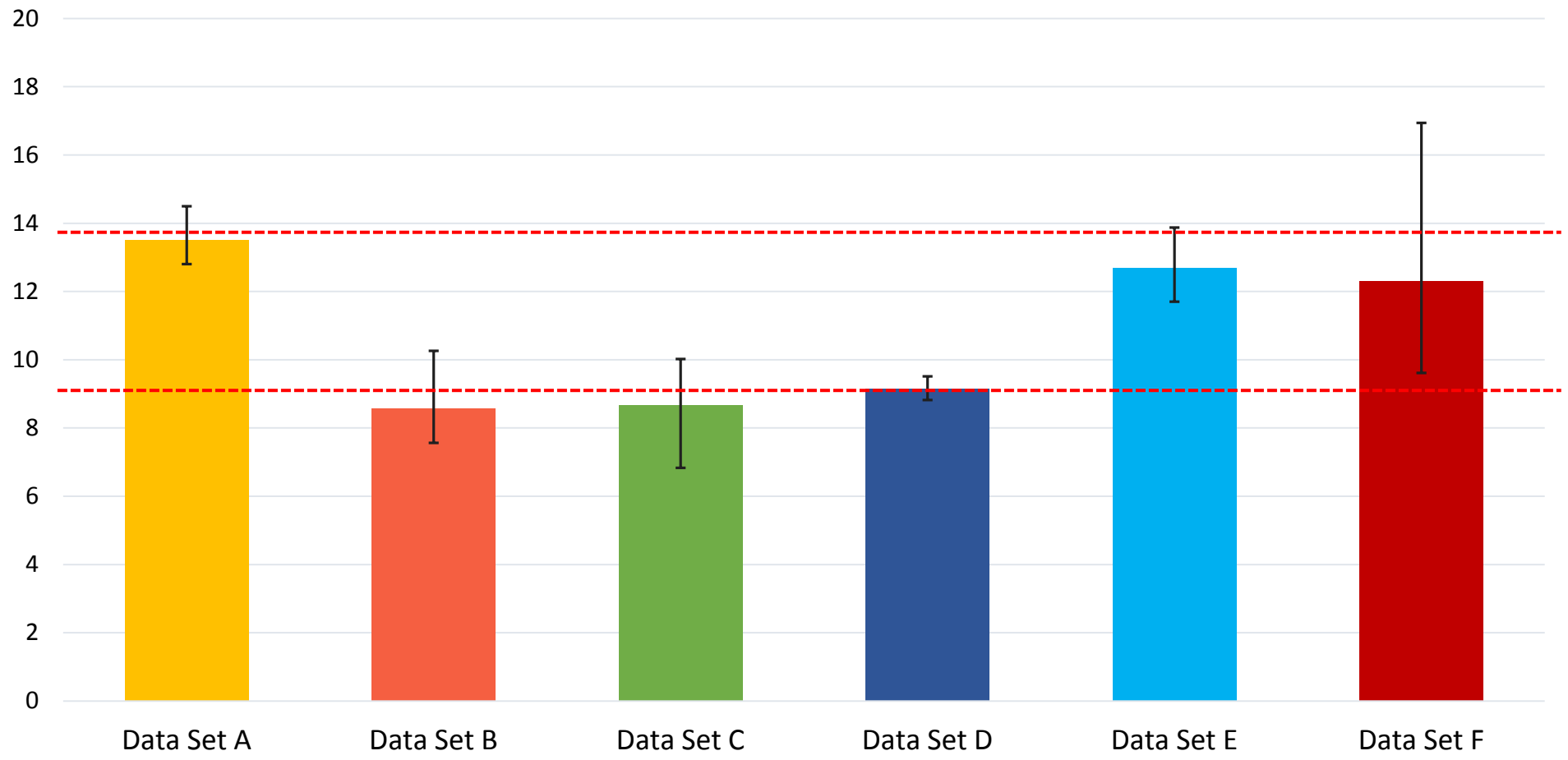
Real-world Overall Survival



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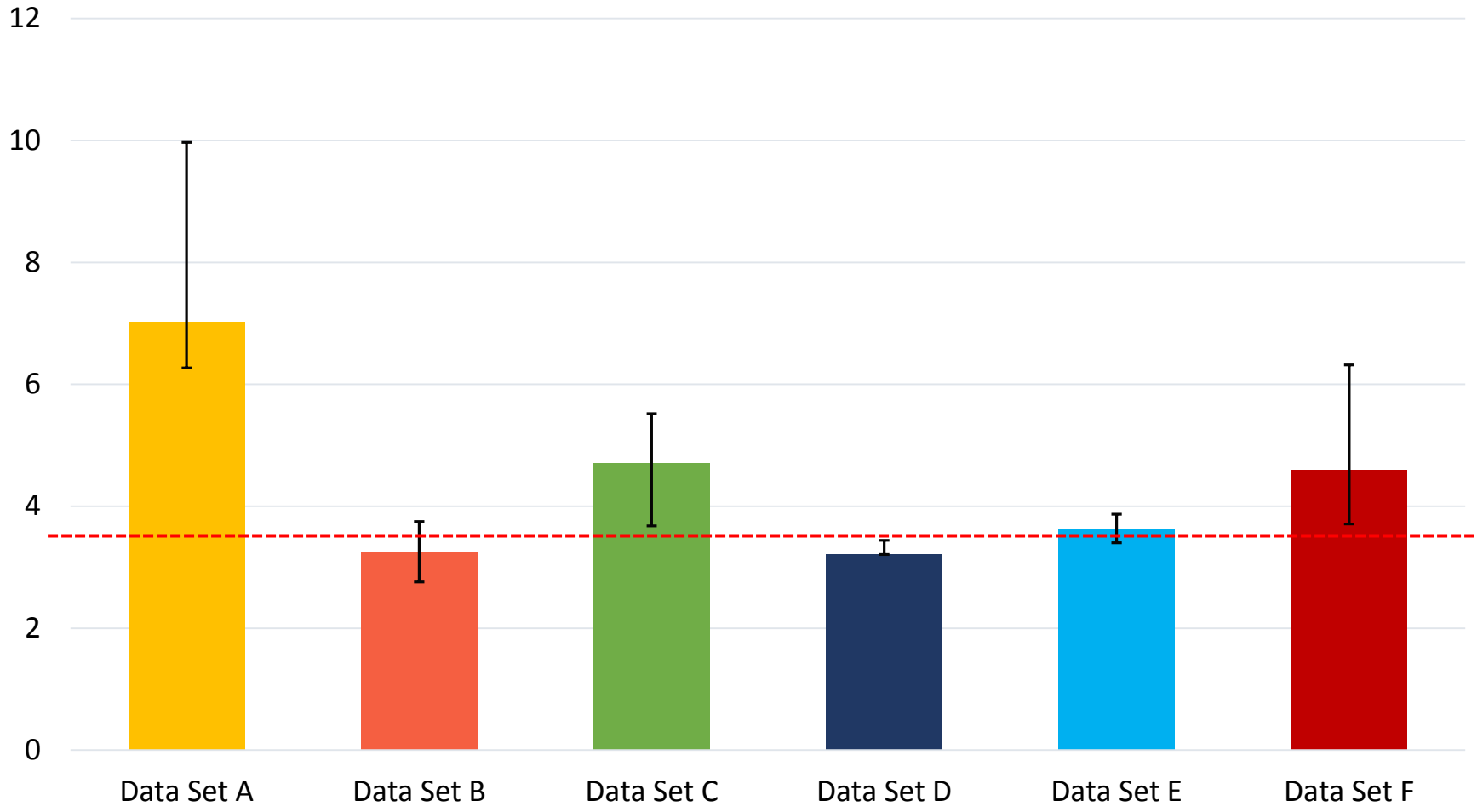
G Huang, et al. Oncotarget. (2018) 9(3) 4239-4248.

Real-world Time to Treatment Discontinuation



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Y Gong, et al. JCO. (2018) 36 suppl; abstract 9064.

Conclusions

1. There is a high level of shared characteristics among the varying data sets despite varying sample sizes, data capture processes, and data sources demonstrating the feasibility of identifying aNSCLC patients treated with immune checkpoint inhibitors from diverse RWD sources.

2. The pilot project demonstrated that several extractable endpoints from EHR and claims data correlate with OS. Further validation is required to determine whether these endpoints are reliable surrogates for OS outside of a traditional clinical trial and whether they can support regulatory and payer decision-making.

3. Survival among patients as assessed through EHR and claims data fall within the range of median OS values observed in several immune checkpoint inhibitor trials.

4. Assessment of extracted endpoints from EHR and claims data demonstrate that efficacy of immune checkpoint inhibitors is relatively consistent across a variety of patient characteristics, such as age and sex.

Acknowledgements

Participating Data Partners

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- University of Iowa/ PCORnet

Project Team

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- NCI

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