Opportunities to use EHR-derived RWE to inform HTA decision-making

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Agenda

1. **AKSHAY SWAMINATHAN** — Enhanced Cost-Effectiveness Analysis using EHR Data for Real-World Value
2. **PÁLL JÓNSSON** — Can Early U.S. Adoption of Cancer Drugs Inform HTA Decision-Making?
3. **ALL SPEAKERS** — Panel discussion and audience Q&A

POLL

How frequently do you include RWE in your Global Value Dossiers for new oncology medicines?

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

Akshay Swaminathan, Chumeng Xu, Sharon Zhang, Kevin Du, Evelyn Siu, Laurynas Kalesinskas, Samuel Lite, Youna Song, Jeremy Snider, Scott Ramsey, Danielle Bargo, Blythe Adamson

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Motivation

- 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 can 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.

Approach

- 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 and survival times from clinical trials with RWE-derived hazard ratios for progression-free and overall survival (“RWE-enhanced”).

Figure 1.
Patient selection

*Patients who received pembrolizumab or atezolizumab were required to be positive for PDL1

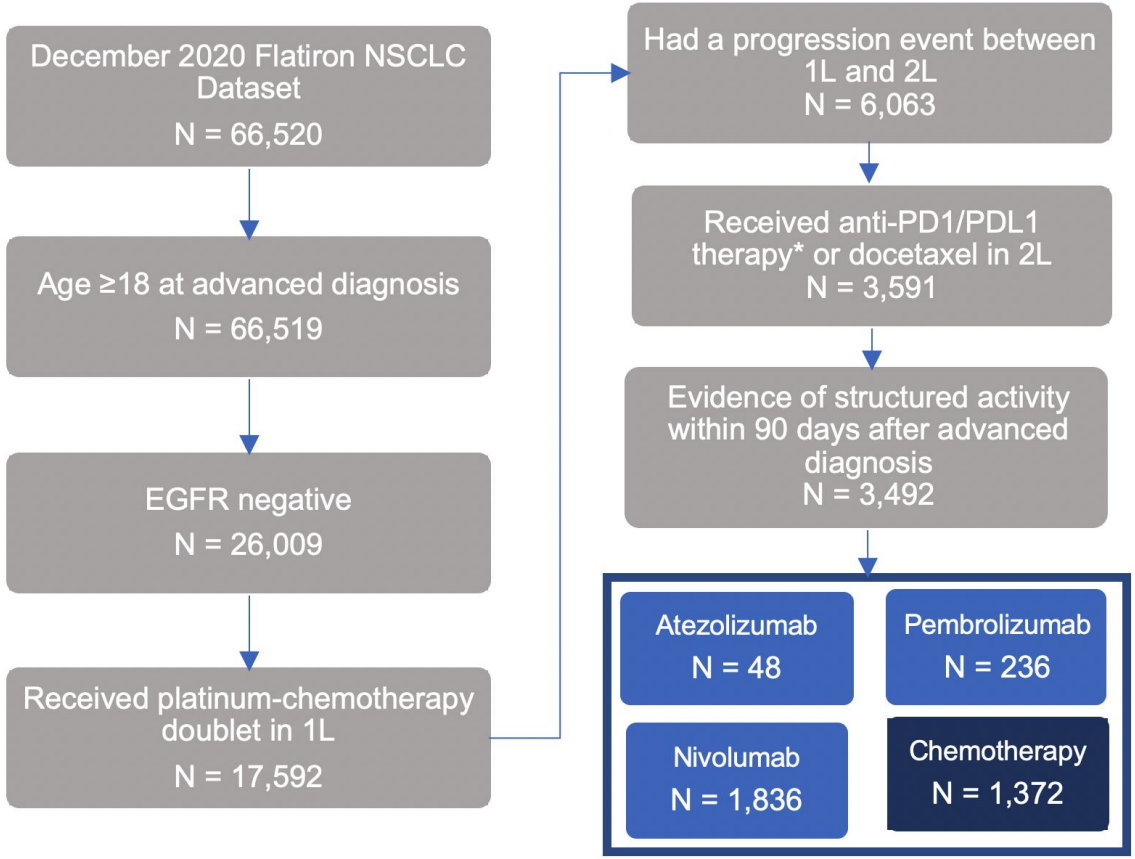

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Figure 2. Demographic and clinical characteristics of RWE cohorts vs clinical trial cohorts

Clinical trials: POPLAR for atezolizumab, CheckMate 017 for nivolumab, and KEYNOTE-010 for pembrolizumab.

*Data not reported in trial publication

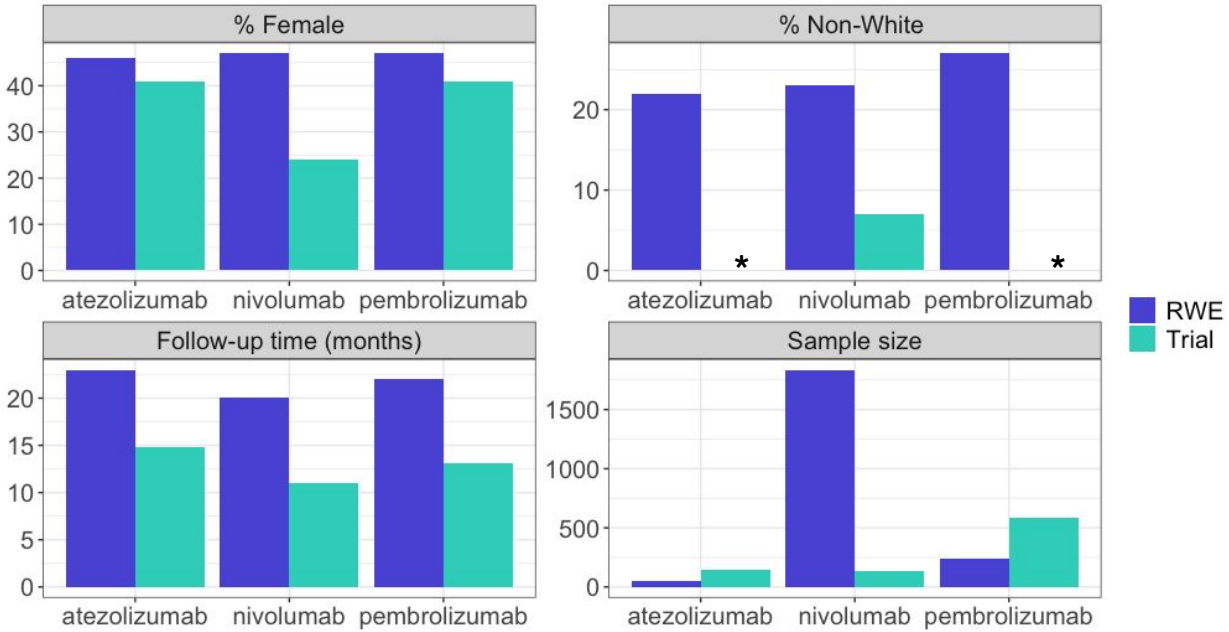

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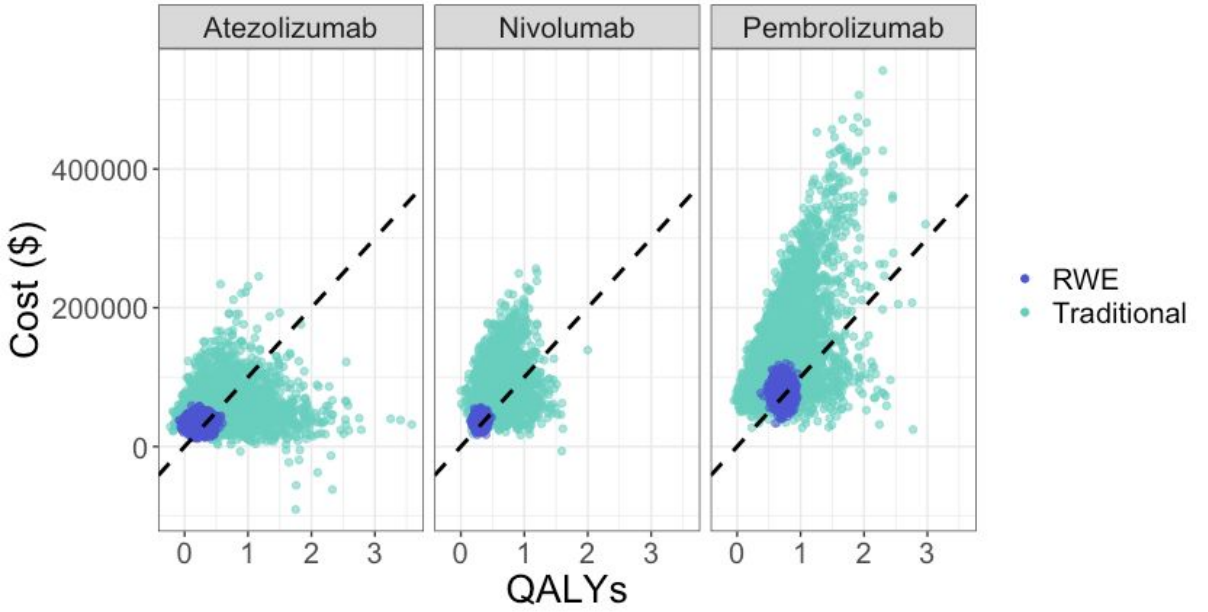
Figure 3. Results

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.

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.



Therapy	Traditional ICER ($/QALY) [95% CrI]	RWE-enhanced ICER ($/QALY) [95% CrI]
atezolizumab	84,000 [2,000-776,000]	138,000 [59,000-548,000]
nivolumab	136,000 [47,000-379,000]	123,000 [80,000-183,000]
pembrolizumab	181,000 [53,000-527,000]	110,890 [76,000-156,000]

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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 1 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.

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Which real world variables do you consider most important for HTA decision-making?

Research collaboration on the use of EHR-derived RWD for HTA decision-making

NICE National Institute for Health and Care Excellence

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Collaboration objectives:

- Conduct **high-quality research** using Flatiron data
- Develop and evaluate approaches to **reduce uncertainty in NICE Technology Appraisals** for oncology appraisals
- Support NICE in evaluating the ability of RWD to address evidence gaps and **inform HTA decision making**

NICE-Flatiron Health Research Collaboration: Aim 1 Results

Can Early U.S. Adoption of Cancer Drugs Inform HTA Decision-Making?

Páll Jónsson[1], Philani Mpofu[2], Amanda Copeland[2], Seamus Kent[1], Brad Groves[1], Danielle Bargo[2], Scott Ramsey[3,4], Shrujal Baxi[2], Blythe Adamson[2,4]

[1] NICE, Manchester, UK; [2]Flatiron Health, Inc, New York, NY; [3]Fred Hutchinson Cancer Research Center, Seattle, WA; [4]University of Washington, Seattle, WA

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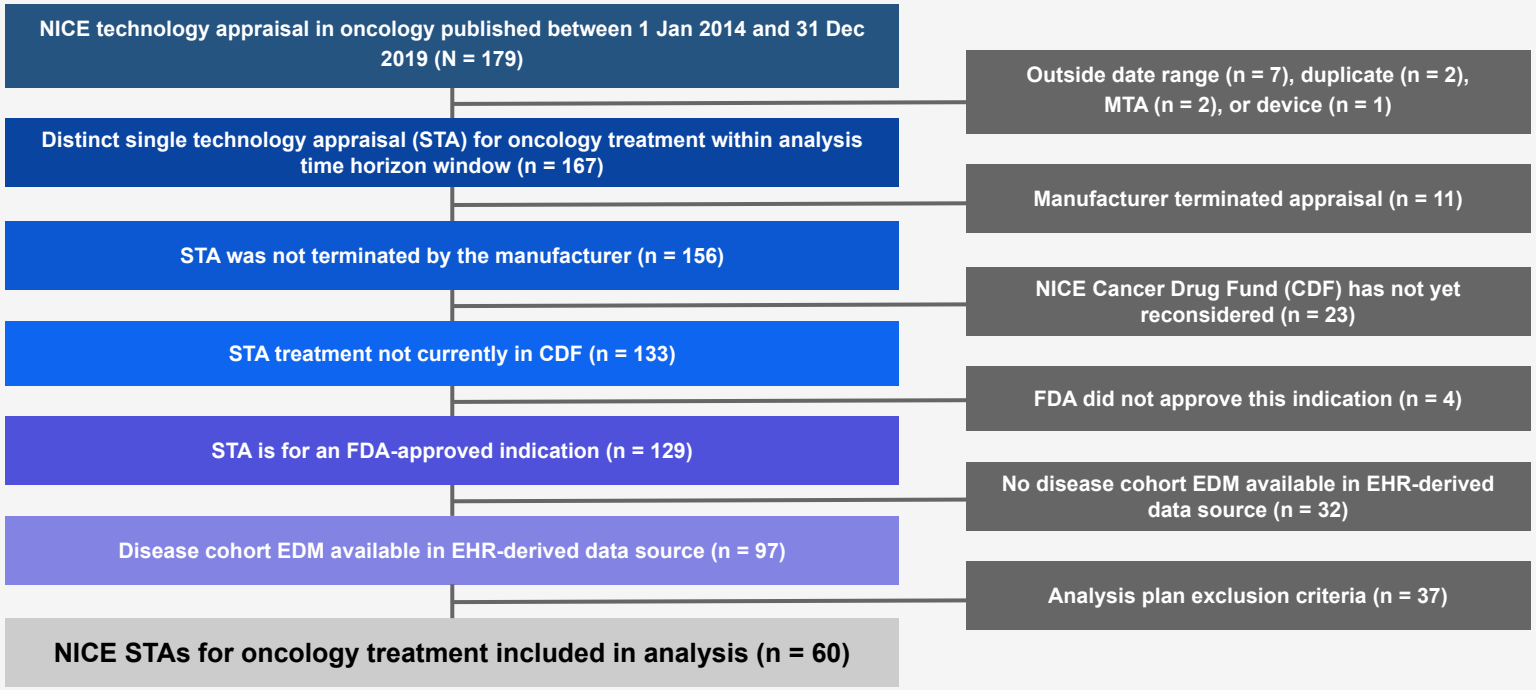
Methods

- **Study Design:** For each NICE TA in a selected set, we calculated the **time between FDA approval and EMA market authorization, NICE TA submission, and NICE TA publication.** The distributions of time were described using mean, median, range, and stratified by therapy class, cancer type, biomarker-driven indication, submission period (≤2016 or >2017), first-in- class, and NICE decision.

- **Data Sources:** This retrospective study used the Flatiron Health electronic health record (EHR)-derived de-identified data **representing approximately 280 cancer clinics in the United States (~800 sites of care)**. We used research-ready electronic data mart cohorts. We also used **publicly available publications of NICE single technology appraisals.**

- **Outcomes:** The primary outcome was **the mean total number of patients exposed to a new product over time that received both FDA and EMA initial approval or label extension.** We counted the number of patients in the EHR-derived RWD cohort who had started the drug before each milestone date (EMA market authorization, NICE TA submission, and NICE TA publication). We correspondingly calculated the possible follow-up time of each patient that would have been available at each milestone.

Selection of NICE Oncology Appraisals for Analysis



Includes one reappraisal. Analysis plan excluded disease cohort EDM if there was less than two years since the EDM was initiated or insufficient experience with disease specific data models.
Abbreviations: CDF, Cancer Drug Fund; FDA, US Food and Drug Administration; EDM, electronic data mart; MTA, multiple technology appraisal; STA, single technology appraisal.

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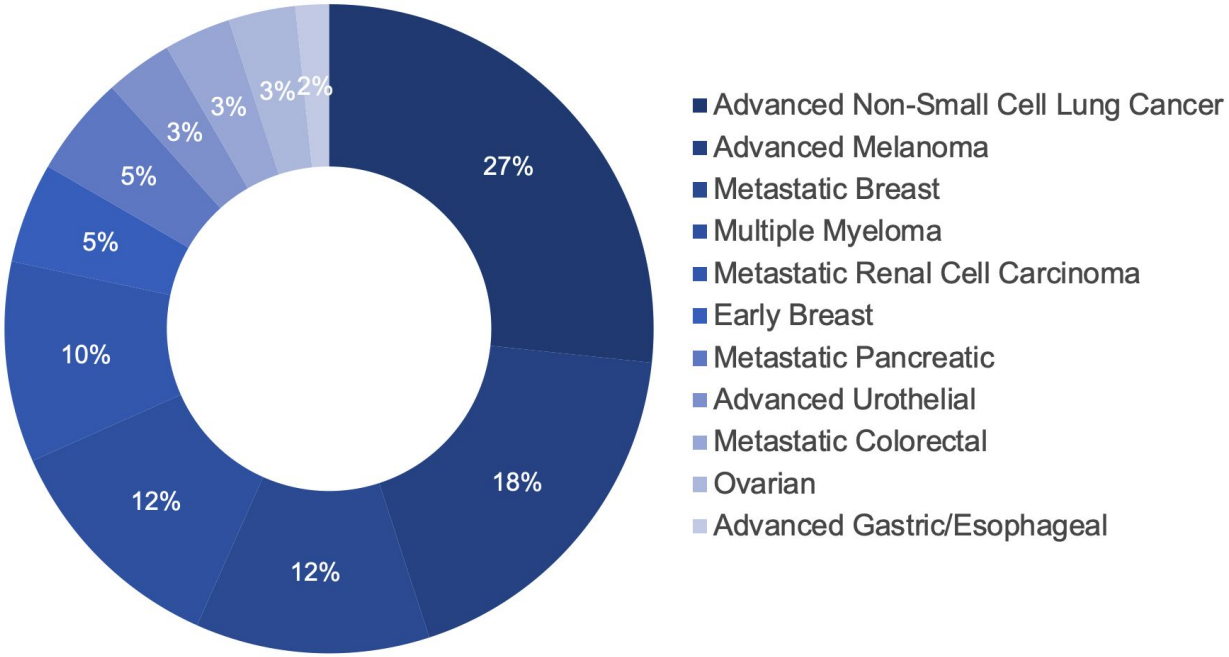
NICE Technology Appraisals (N = 60)



Timeline with median months between FDA approval and HTA milestones

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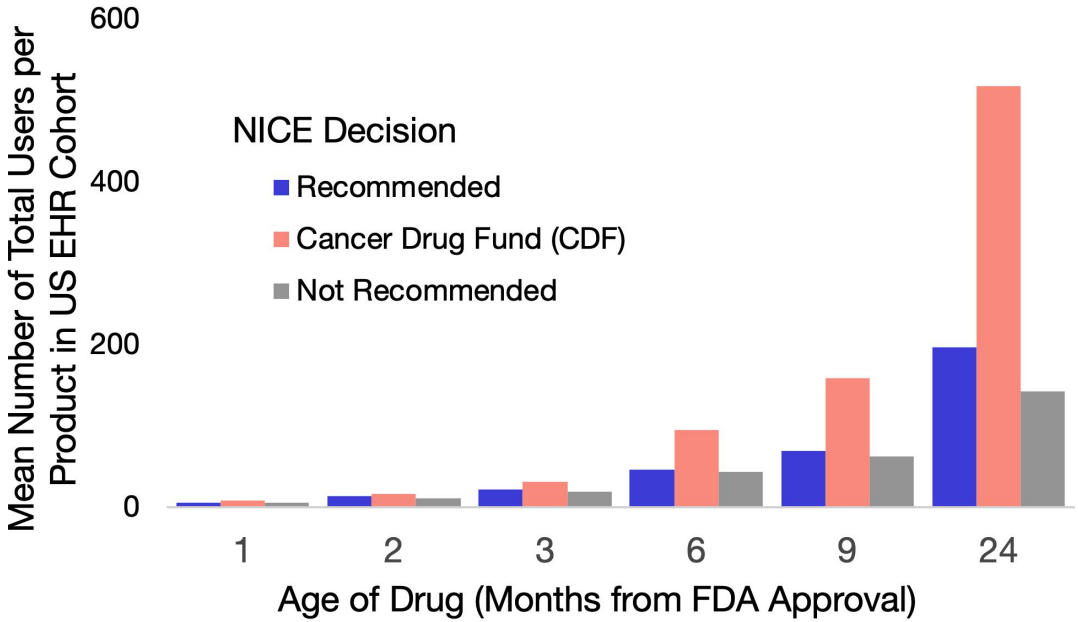
Uptake of new drugs after FDA approval



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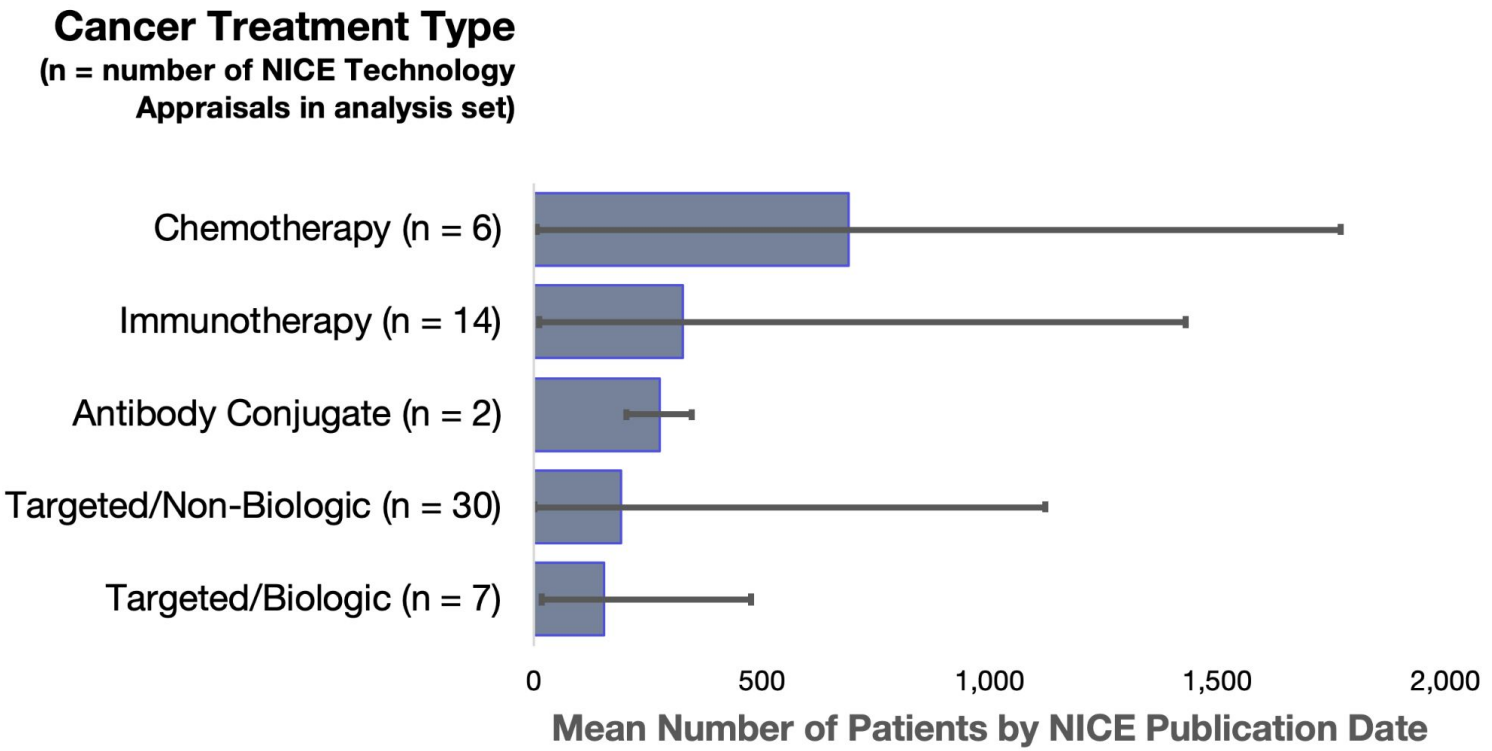
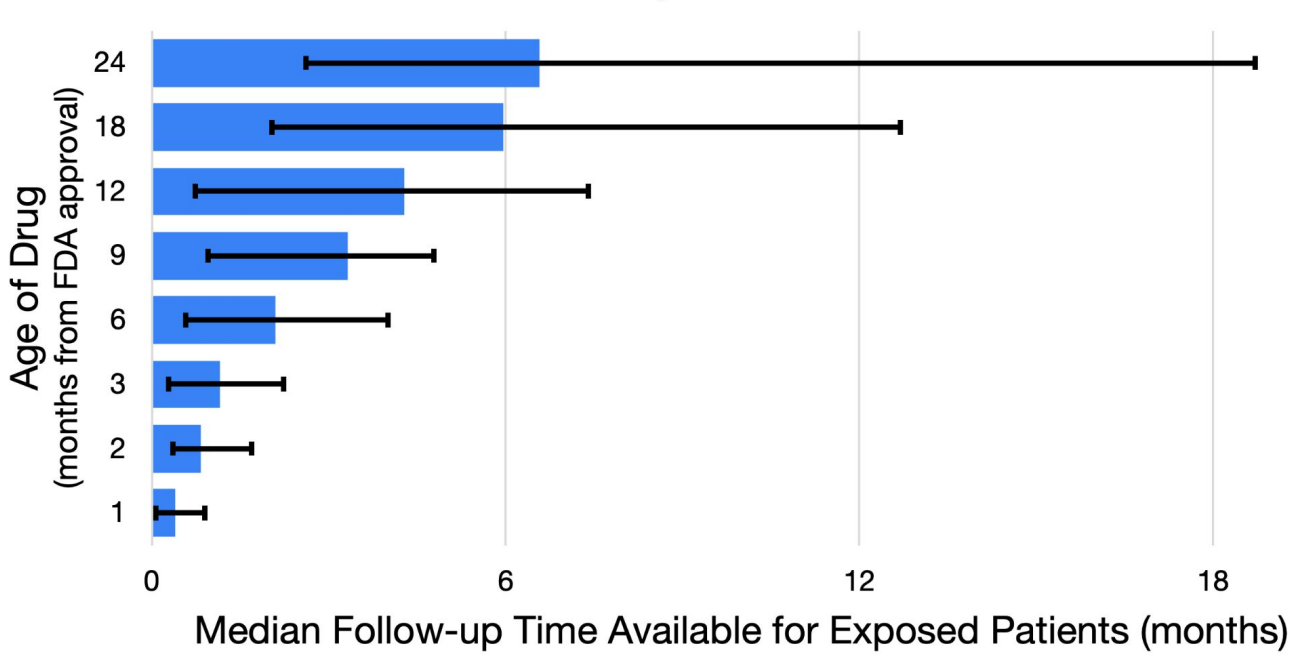


Patient follow-up time available



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Discussion

The time from FDA approval to NICE guidance may provide **an opportunity to inform reimbursement decisions with real-world US patients.**

Time for real world evidence. Median time from FDA to NICE submission and final guidance publication was **5.6 and 18.5 months**, respectively, for a set of **60 oncology assessments between 2014–2019.**

Cancer Drug Fund data. Use of products recommended for the Cancer Drug Fund contributed more US patients per month by the time of NICE appraisal publication than products recommended and not recommended by NICE, especially after the drug has been approved in the US for at least six months. **EHR-derived RWD could provide a meaningful contribution in this area to better understand treatment effectiveness.**

Transportability of RWE. Opportunities to use international EHR-derived oncology data will vary by cancer type, the nature of uncertainties identified—most frequently cited for cancer products are longer term measures such as overall survival, progression-free survival, as well as quality of life—and will depend on whether the data is reflective of UK patient characteristics, treatment settings, and clinical pathways.

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Thank you

NICE-Flatiron Health Research Collaboration: Aim 1 Results
Can Early U.S. Adoption of Cancer Drugs Inform HTA Decision-Making?

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Which HTA bodies do you consider most accepting of RWD for HTA decision-making?

Q&A

Please submit questions through the Q&A feature at the bottom of your screen

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Thank you

Email additional questions to rwe@flatiron.com

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