Transportability of Overall Survival Estimates from the US to England in Metastatic Breast Cancer Using Nationally Representative Data Sources

HTA359

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Background

- Real-world data (RWD) from other countries are often used to address uncertainty in health technology assessments
- This approach assumes, outcomes are **transportable**, ie, by performing population adjustments, RWD in a source population can be used to predict real-world outcomes in a target population
- It is unclear if these predicted outcomes align with true outcomes in the target population

Objective

- Test the validity of transporting real-world overall survival (rwOS) estimates in de novo metastatic breast cancer (mBC) from the United States (US) to England, based on the conceptual framework presented in **Figure 1**

Methods

Data Sources

- US data from the Flatiron Health electronic health record (EHR)-derived, deidentified database, comprising patient-level data originated from ~280 US cancer clinics (~800 sites of care; primarily community oncology settings) and curated via technology-enabled abstraction[1,2]
- England data from the National Cancer Registration and Analysis Service, a nationwide cancer registry,[3] and the Systemic Anti-Cancer Therapy dataset[4]

Cohort

- Patients diagnosed with de novo mBC between 2015 and 2021 and treated with systemic therapy, with follow-up through January 5, 2024

Table 1. Patient Attrition

Patients, No.	Eng	US
Diagnosed with de novo mBC in 2015-2021	14 700	6720
Did not receive a drug on the Cancer Drugs Fund*	14 460	N/A
Received systemic therapy**	7860	6100
Did not receive a clinical study drug in the 1L, 2L, or 3L setting	7770	5840
Had known breast cancer molecular subtype***	**4240**	**5580**

Table notes: Counts rounded to the nearest 10 due to reporting restrictions. *The Cancer Drugs Fund is a program in England that provides access to certain cancer treatments not routinely available through the National Health Service. **Systemic therapy is defined as treatment with at least 1 oncology drug within 14 days or any time after mBC diagnosis. Differences in treatment rates between England and the US may be due to variations in data sources, with England data coming from a cancer registry and the US data from an EHR-derived dataset. ***The lower capture of breast cancer subtype in the England data reflects the voluntary nature of molecular testing reporting. Abbreviations: 1L, first-line; 2L, second-line; 3L, third-line; Eng, England; mBC, metastatic breast cancer; N/A, not applicable; US, United States.

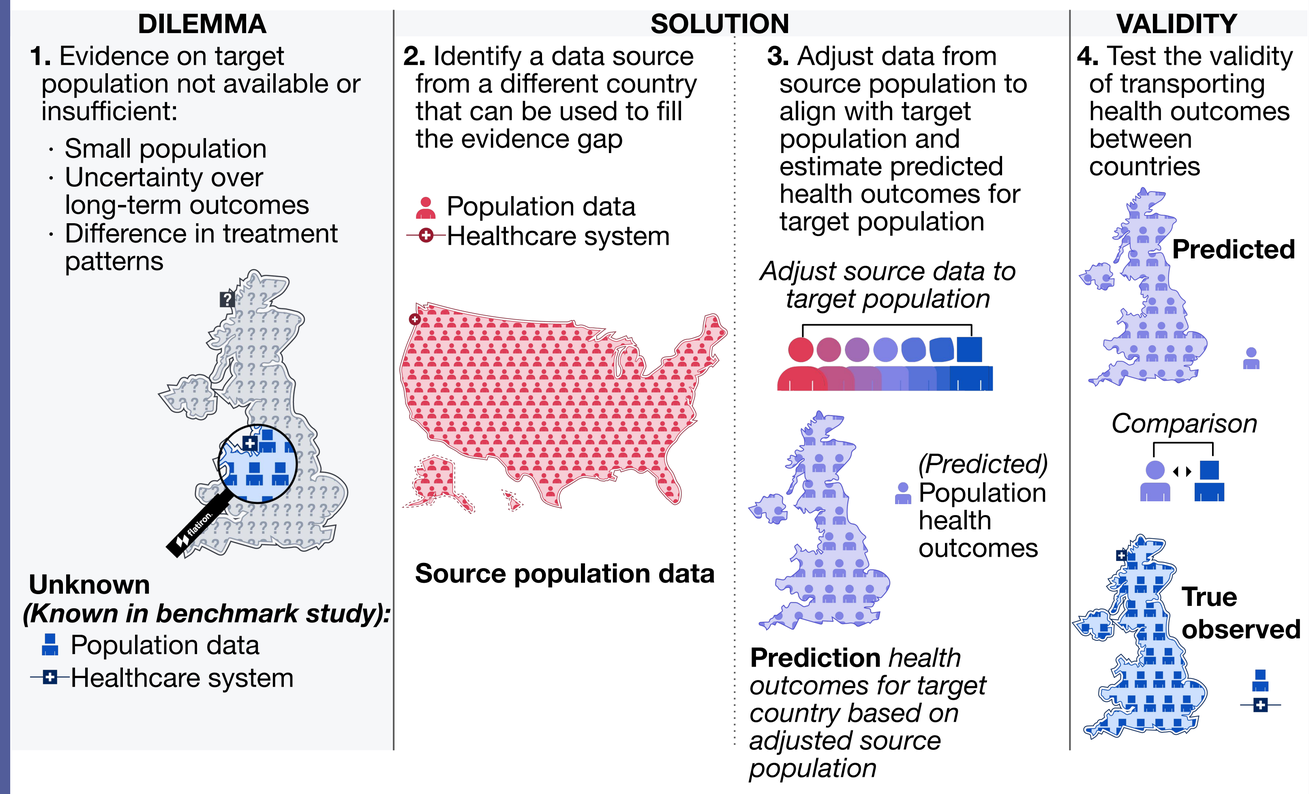
Outcomes

- **rwOS**: time from start of first-line (1L) systemic therapy to death with patients censored at last activity (US) or vital status date (England)

Statistical methods

- **Matching-adjusted indirect comparison** (MAIC) was used to adjust US data to the distribution of age (median, interquartile range [IQR]), sex, race, Eastern Cooperative Oncology Group (ECOG) performance status, year of mBC diagnosis, socioeconomic status, and 1L treatment class in the England data
- Kaplan-Meier methods used to examine crude rwOS in the US and England cohorts and predicted rwOS in the England cohort
- Models were stratified by molecular subtype to reflect their influence on treatments and outcomes

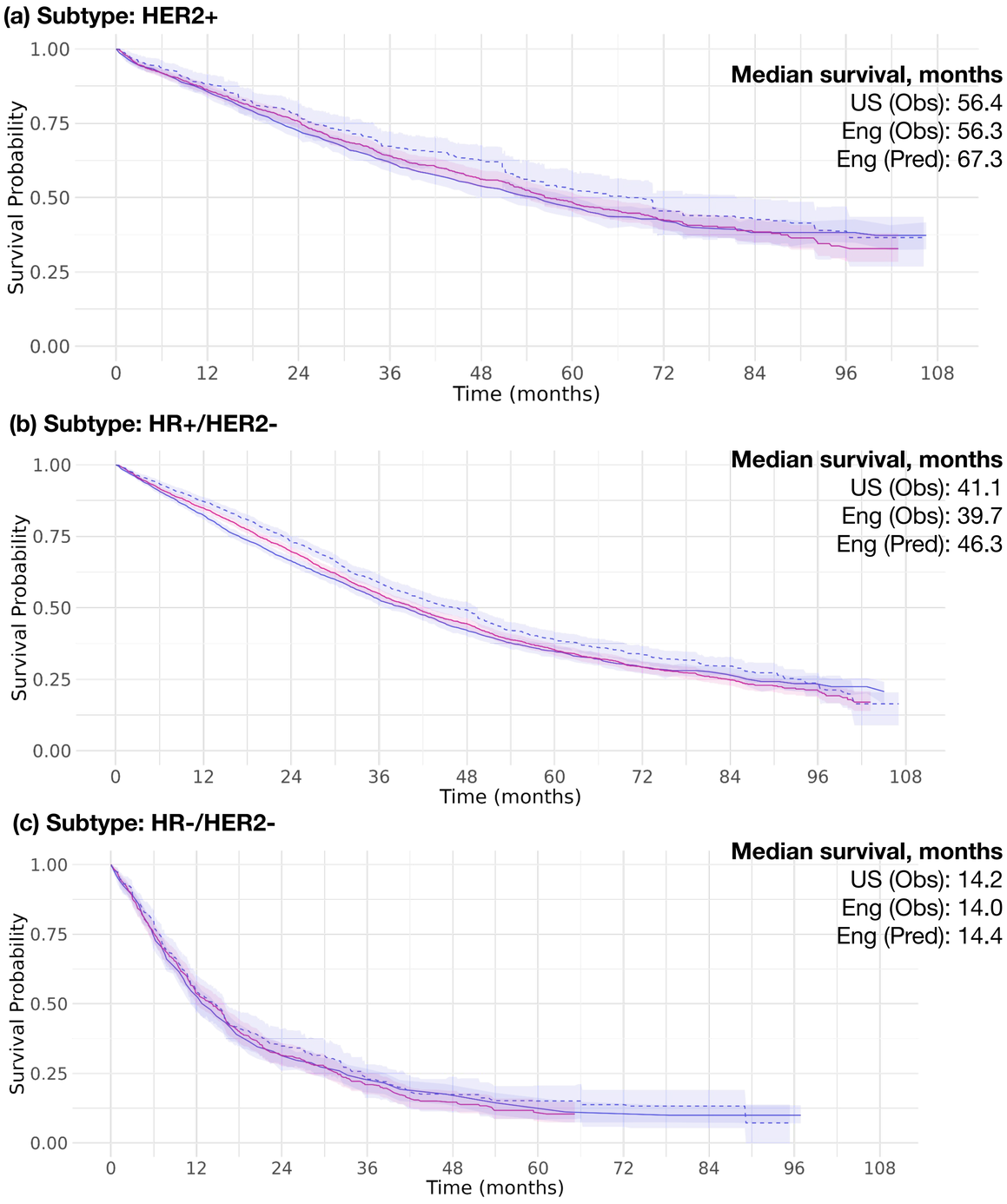
Figure 1. Illustrative Conceptual Framework for Transportability Benchmarking



Results

- Of the patients diagnosed with de novo mBC, 53% and 91% received systemic therapy in the US and England, respectively. Of these treated patients, 54% and 91% had known molecular subtype, respectively (**Table 1**)
- The median age (IQR) was 63 (53-72) years in the US cohort and 60 (50-71) years in the England cohort. Other baseline characteristics were similar in the 2 cohorts, with the exception of race/ethnicity: 70% of the US cohort was White compared with 89% of the England cohort
- Observed rwOS was similar between countries, whereas MAIC adjustments overpredicted rwOS in England (**Figure 2**)

Figure 2. Comparison of US Observed (—), England Observed (—), and England Predicted (- -) Survival Curves Across Molecular Subtypes



Abbreviations: Eng, England; HER2-, human epidermal growth factor receptor 2 negative; HER2+, HER2 positive; HR+, hormone receptor positive; HR-, hormone receptor negative; Obs, observed; Pred, predicted; US, United States.

Conclusions

We found evidence suggesting that observed rwOS in de novo mBC may be transportable from the US to England

Limitations

The need to harmonize variables across countries resulted in consolidation of **race/ethnic** groups into "White," "non-White," and "unknown" categories, with "non-White" representing a diverse mix of ethnicities that differs across countries. In addition, the England data had the following limitations:

- mBC diagnosis dates could not be identified for recurrent patients, so our analysis was limited to patients with de novo disease
- Incomplete information on molecular subtypes and certain oral therapies may have introduced selection bias and limited population adjustments
- Certain variables that are predictive of rwOS were missing (eg, brain metastasis)

These limitations highlight the need for more complete RWD outside the US

Future Directions

- Conduct sensitivity analyses for the race/ethnicity categorization
- Investigate explanations for the overprediction of rwOS
- Extend analysis to include patients with recurrent mBC (we have already done this in patients with HER2+ disease[5])

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