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Transporting Real-World Evidence: Is it Possible to Transport OS Estimates in HER2+ mBC from US to UK?

Philani Mpofu[1], Per-Olof Thuresson[2], Thibaut Sanglier[2], Elsie Horne[3], Harlan Pittell[1], Amit Samani[3], Christoph Buhl[3], Arun Sujenthiran[3], Christophe Tchakoute[4], Caitlin Clunie-O'Connor[3], Blythe Adamson[1,5]

[1]Flatiron Health, New York, NY; [2]Roche, Basel, Switzerland; [3]Flatiron Health UK, London, UK; [4]Genentech, San Francisco, CA; [5]University of Washington, Seattle, WA

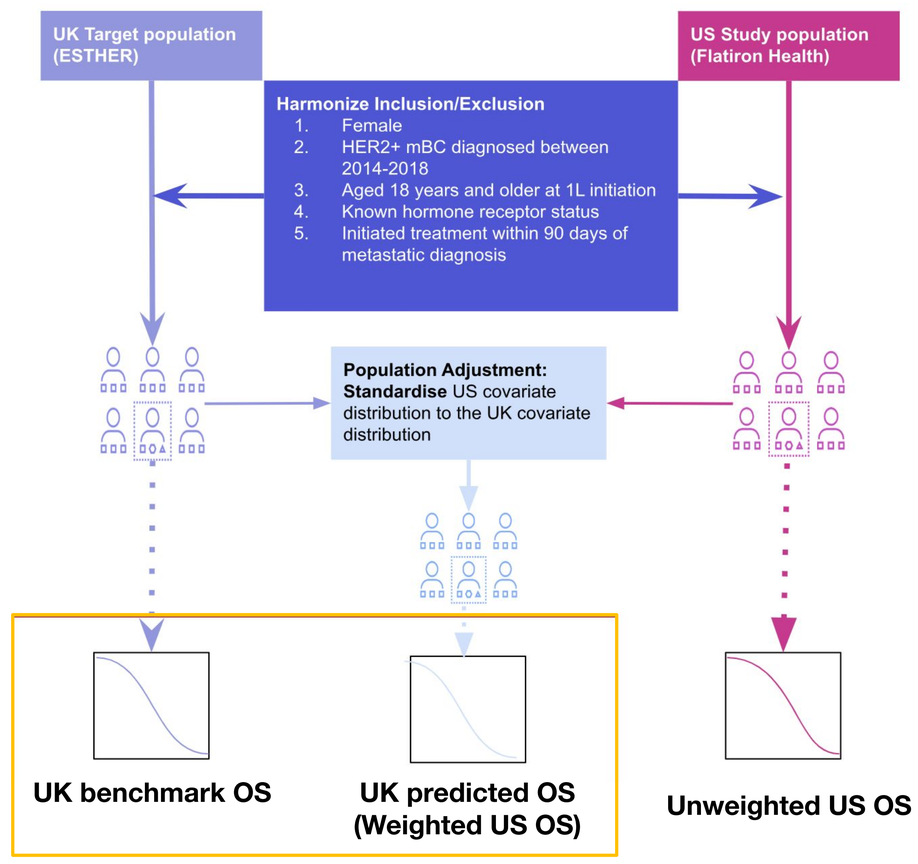
Background

- **Real-world Data (RWD) and real-world evidence (RWE)** can supplement clinical trial data to approximate treatment value in health technology assessment (HTA)
- **Local RWD** is preferred but may not be available in timely manner
- **Key question:** Can non-local data be used when local data is lacking? Is evidence generated using non-local data transportable or relevant to the local context?
- We explore these questions through a demonstration transportability study. Specifically, we studied **whether overall survival (OS) estimates from the United States (US) are transportable to the United Kingdom (UK) for a population of women with human epidermal growth factor receptor 2 positive (HER2+) metastatic breast cancer (mBC)**

Methods

- We analysed the transportability of OS in patients with HER2+ mBC from the US to the UK
- **Data sources:** US nationwide Flatiron Health electronic health record-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] and the ESTHER study (NCT02393924), a registry of UK patients with advanced HER2+ breast cancer
- **OS:** Defined as the time from initiating the first-line of therapy (1L) until death
- **Population adjustment methodology:** Used inverse odds of sampling weighting to standardize the US data to the UK target population[3-5]
- **Population adjustment factors:** Age, race, Eastern Cooperative Oncology Group (ECOG) performance status (PS), hormone receptor status, denovo/recurrent status, time from diagnosis to treatment initiation, brain metastases, and 1L treatment class

Figure 1. Study design schema



Results

Table 1: Demographics and clinical characteristics of patients included in the study

Characteristic	Overall (N = 1155)	UK (N = 248)	US (N = 907)
Median Age (IQR) at 1L start	60 (51-70)	57 (48-68)	61 (52-70)
Race/Ethnicity, No. (%)			
Non–Latinx-White	805 (69.7)	232 (93.5)	573 (63.2)
Non–Latinx-Black	101 (8.7)	3 (1.2)	98 (10.8)
Non–Latinx-Asian	36 (3.1)	6 (2.4)	30 (3.3)
Latinx	67 (5.8)	3 (1.2)	64 (7.1)
Unknown	75 (6.5)	4 (1.6)	71 (7.8)
Non–Latinx-Other	71 (6.1)	0 (0.0)	71 (7.8)
De novo disease, No. (%)	583 (50.5)	70 (28.2)	513 (56.6)
ECOG PS at 1L start No. (%)			
0-1	671 (58.1)	125 (50.4)	546 (60.2)
2+	136 (11.8)	18 (7.3)	118 (13.0)
Unknown	348 (30.1)	105 (42.3)	243 (26.8)
Hormonal receptor status, No. (%)	819 (70.9)	173 (69.8)	646 (71.2)
Brain/CNS Disease, No. (%)	295 (25.5)	85 (34.3)	210 (23.2)
Exposed to anti-HER2 therapy in 1L, No. (%)	950 (82.3)	233 (94.0)	717 (79.1)
Chemotherapy in 1L, No. (%)	841 (72.8)	206 (83.1)	635 (70.0)
Hormone therapy in 1L, No. (%)	415 (35.9)	96 (38.7)	319 (35.2)

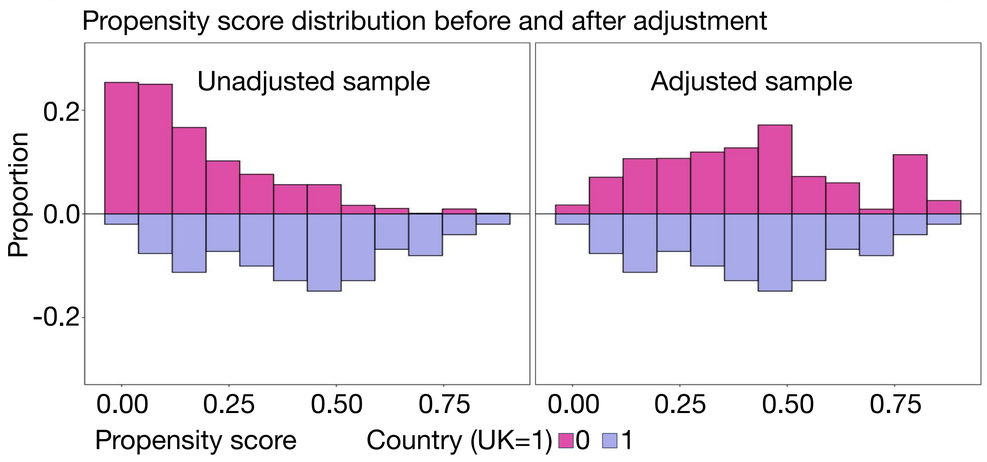
Abbreviations: CNS, central nervous system; IQR, interquartile range

Results continued

The treatments used were fairly similar in both countries. The most common regimen in 1L was a combination of **pertuzumab + trastuzumab + chemotherapy +/- hormonal therapy** (61.9% in UK vs. 57.5% in US). In second line, **trastuzumab emtansine** (25.4% in UK vs 21.5% in US) monotherapy was the most common in both settings

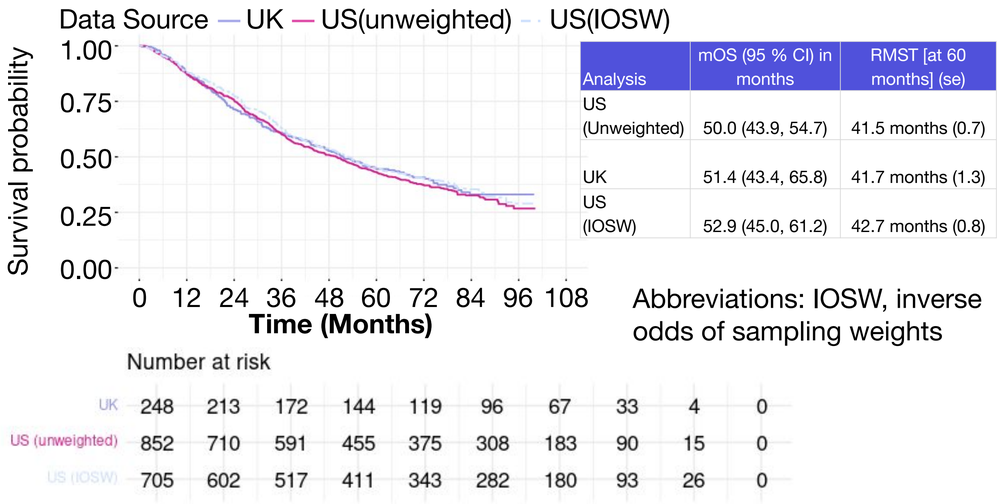
Inverse-odds of sampling weighting (IOSW) improved the covariate balance across the the settings

Figure 2. Propensity score distribution before and after weighting



The OS estimates between the two settings were fairly similar, with or without population adjustment

Figure 3. UK vs US OS (with and without weighting)



Analysis	mOS (95 % CI) in months	RMST [at 60 months] (se)
US (Unweighted)	50.0 (43.9, 54.7)	41.5 months (0.7)
UK	51.4 (43.4, 65.8)	41.7 months (1.3)
US (IOSW)	52.9 (45.0, 61.2)	42.7 months (0.8)

Abbreviations: IOSW, inverse odds of sampling weights

Conclusions:

- US OS estimates are a reasonable proxy for UK OS estimates in the HER2+ mBC population
- The OS estimates were fairly similar, with or without population adjustment to balance baseline characteristics
- The treatment landscapes were fairly similar, as evidenced by the similarity in available treatments and the most prescribed regimens within lines of therapy

Future Directions

- Evidence transportability will likely need to be demonstrated on an indication basis
- We plan to conduct more demonstration studies for specific drug exposure groups with HER2+ mBC; other mBC molecular subtypes, and other cancer types. The goal will be understand where and when transportability of evidence is plausible.
- The study did not fully consider the implications of missing data assumptions—future work will explore the implications in depth

References

1. Ma X et al. *MedRxiv*. 2023. doi:10.1101/2020.03.16.20037143
2. Birnbaum B et al. *arXiv*. 2020. doi:10.48550/arxiv.2001.09765
3. Ling AY et al. *arXiv*. 2022. doi:10.48550/arXiv.2202.00820
4. Westreich D et al. *Am J Epidemiol*. 2017. doi:10.1093/aje/kwx164
5. Dahabreh et al. *Eur J Epidemiol.* 2019. doi: 10.1002/sim.8426

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Author contact: flatiron.forum@flatiron.com
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