HTA 177

Health-state utilities for hormone receptor-positive (HR+) / human epidermal growth factor receptor 2-negative (HER2-) breast cancer

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OBJECTIVE

- Trial-based health-related quality-of-life data for HR+/HER2- breast cancer (BC) are often limited to the progression-free health state (~30 days post-disease progression for advanced disease) or the invasive disease-free survival (IDFS) health state with widening of the assessment intervals for early BC over time, leading to reliance on alternative sources for determining long-term health-state utilities in economic evaluations.
- In the absence of longer-term and more comprehensive utility data from BC trial-based measures, manufacturers of HR+/HER2- BC medicines have used utility values from Lloyd et al. (2006)[1] and/or Mitra et al. (2016)[2] as an assumption of post-progression utility in National Institute for Health and Care Excellence (NICE) Health Technology Assessment dossiers, but the use of these data sources in economic analyses has been criticised.
- Although EQ-5D data reported by patients and/or care partners are the ideal data source according to NICE hierarchical preferences, data from the general population using a vignette approach are acceptable where patient-reported data are not available from a relevant study or the literature.[3]
- The aim of this study was to estimate HR+/HER2- BC health-state utilities across different stages of the disease pathway using United Kingdom (UK) general population participants.

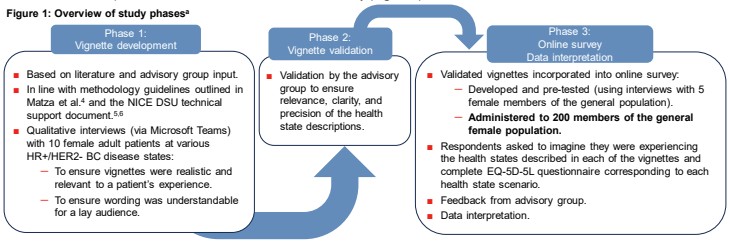
CONCLUSION

- This study provides new **UK health utility estimates across a broad spectrum of HR+/HER2- BC disease states aligned with NICE guidance**[3] for use in economic evaluations.
- While a logical decrease in estimated health-state utility was observed with increasing disease severity, our values were much lower than those reported from clinical trials and alternative general population-based studies.
- These data are valuable in the absence of patient-reported data. However, they highlight the **challenges associated with the vignette-based approach** and obtaining disease-specific values from the general population using the EQ-5D.
- Underestimation of utilities by the general public relative to a patient population may skew ICERs.
- To address these limitations, scenario and sensitivity analyses are recommended when these estimates are used in cost-effectiveness modelling to help assess the robustness of the results to methodological differences.
- **We recommend using these utility values for health states that do not have available patient-reported data** (e.g. metastatic progressive disease).
  - All health states were considered for consistency and understanding; we do not recommend using these utility values in place of trial data.
  - **Further research is needed** to obtain **health-state utility values from patients**, that have greater reliability, for use in decision-making.

STUDY DESIGN

- This was a three-phase non-interventional UK observational study (**Figure 1**).

Figure 1: Overview of study phases[a]



[a]During each study phase, the research team collaborated with an advisory group composed of two UK oncologists and one UK patient expert.
BC, breast cancer; DSU, Decision Support Unit; EQ-5D-5L, 5-level EQ-5D; HER2-, human epidermal growth factor receptor 2-negative; HR+, hormone receptor-positive; NICE, National Institute for Health and Care Excellence; UK, United Kingdom.

METHODS

Table 2: Overview of the current approach for HR+/HER2- BC EQ-5D utility estimation using the NICE-preferred value set vs. previous value sets by Lloyd et al. (2006)[1] and Mitra et al. (2016)[2]

Lloyd et al. 2006[1]	Mitra et al. 2016[2]	Current approach (NICE-preferred value set[7])
▪ UK general population (N=100) estimates generated using standard gamble method using vignettes (making no explicit reference to cancer) validated by HCPs but not patients.	▪ Patient-reported data (N=739 EU and US patients with advanced / metastatic HR+/HER2- BC); 83% of patients had metastatic BC.	▪ **UK general population (N=200) estimates using vignettes validated by oncologists and a patient expert.**
▪ Utilities estimated for patients (male or female) with metastatic BC.	▪ Post-progression utility estimated using the EQ-5D-3L.	▪ **Estimated utilities for 5 HR+/HER2- BC disease states using the EQ-5D-5L.**
▪ Standard gamble method requires participants to comprehend complex probabilities.	▪ Study published in abstract form only and considered unlikely to represent UK tariffs.[11]	▪ **Base case dataset used NICE-preferred value set, mapping to EQ-5D-3L.**[7]
– The underlying assumption of expected utility theory (where participants choose a treatment/management option believed to optimise utility, but without knowing the outcome) has been shown to be violated in real populations.[5,10]		– **Scenario analyses compared the base case dataset with the previous NICE-preferred value set (mapping to EQ-5D-3L[8]) and an approach not accepted by NICE (EQ-5D-5L direct valuation set for England[9]).**

BC, breast cancer; EQ-5D-3L, 3-level EQ-5D; EQ-5D-5L, 5-level EQ-5D; EU, European Union; HCP, healthcare professional; HER2-, human epidermal growth factor receptor 2-negative; HR+ hormone receptor-positive; NICE, National Institute for Health and Care Excellence; UK, United Kingdom; US, United States.

METHODS CONT…

- Five BC health states were detailed in the vignettes (**Table 1**).

Table 1: Five health states developed and validated for HR+/HER2- BC

Health states
IDFS on treatment
IDFS off treatment and/or remission
Locally advanced (following disease recurrence, curable)
Advanced (locally advanced non-curable or metastatic, on treatment/stable disease)
Metastatic (palliative/off active treatment OR progressive disease)

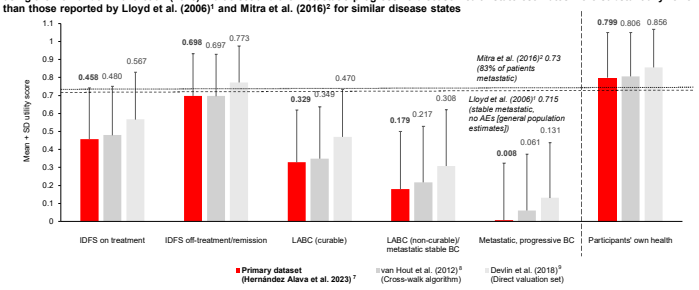
BC, breast cancer; IDFS, invasive disease-free survival; HER2-, human epidermal growth factor receptor 2-negative; HR+ hormone receptor-positive.

Statistical methods

- Data were summarised descriptively.
- For the base case, 5-level EQ-5D (EQ-5D-5L) data were converted into 3-level EQ-5D (EQ-5D-3L) utility data using the NICE-preferred cross-walk algorithm from Hernández Alava et al (2023).[7]
- For comparison, scenario analyses derived data by mapping to EQ-5D-3L utility values using the van Hout et al. (2012) cross-walk algorithm that was previously recommended by NICE[8] and by using the Devlin et al. (2018) EQ-5D-5L direct valuation set for England (that has not been accepted by NICE).[9]
- An overview of the current approach vs. previous approaches by Lloyd et al. (2006)[1] and Mitra et al. (2016)[2] is presented in **Table 2**.

KEY RESULT

Figure 2: Estimated health state utility values decreased with increasing HR+/HER2- BC severity – overall values were numerically lowest using the Hernández Alava et al. (2023)[7] value set and the metastatic progressive disease health state estimates were substantially lower than those reported by Lloyd et al. (2006)[1] and Mitra et al. (2016)[2] for similar disease states



Possible utility scores range from 0 to 1; higher scores indicate better health status.
AE, adverse event; BC, breast cancer; IDFS, invasive disease-free survival; LABC, locally advanced breast cancer; HER2-, human epidermal growth factor receptor 2-negative; HR+ hormone receptor-positive; SD, standard deviation.

Results

Phase 3 survey participants

- Overall, 200 females from the UK general population completed the Phase 3 survey (**Table 3**).

HR+/HER2- BC-related utility values

- Estimated health state utility values for the vignettes followed a logical order, decreasing as BC severity increased (**Figure 2**).
- This general trend was observed for all value sets used. However, numerically higher utility values were reported when estimates were not cross-walked and the Devlin et al. (2018)[9] value set was used (EQ-5D-5L). This was observed to a lesser extent using the van Hout et al. (2012)[8] value set (mapping to EQ-5D-3L).

Table 3: Characteristics of UK general population survey participants

Characteristic	N=200
Female	200 (100.0)
Age (years), mean ± SD	49.9 ± **16.3**
Race	
White	157 (78.5)
Black	20 (10.0)
Asian	18 (9.0)
Highest level of education	
College or vocational qualification (e.g. BTEC, T-levels, etc.)	54 (27.0)
Secondary school (GCSEs, O-levels or equivalent)	53 (26.5)
University degree (Bachelor's)	49 (24.5)
Postgraduate degree (Master's, PhD, etc.)	42 (21.0)
Primary school	2 (1.0)
Employment status	
Employed full time (≥35 hours/week)	82 (41.0)
Retired	48 (24.0)
Employed part time (<35 hours/week)	38 (19.0)
Homemaker	14 (7.0)
Disabled (on a disability benefit or leave of absence)	6 (3.0)
Student (full- or part-time)	8 (4.0)
Unemployed	4 (2.0)
Other	1 (0.5)
UK nation of residence	
England	173 (86.5)
Scotland	11 (5.5)
Wales	10 (5.0)
Northern Ireland	6 (3.0)
Personal experience with BC	
No	127 (63.5)
Yes, I have cared for or assisted a relative or friend with BC	59 (29.5)
Yes, I have/have had BC myself	9 (4.5)
Prefer not to answer	5 (2.5)

Discussion

- This study provides **new alternative UK health utility estimates for HR+/HER2- BC disease states aligned with NICE hierarchical guidance** for use in economic evaluations, given the absence of trial-generated utility data and the limitations associated with previous value sets.[3]
- These data are not generalisable to non-UK populations due to country-specific differences and cultural preferences; valuation methods and health system context also limit direct applicability.
  - However, in the absence of country-specific utility value sets, UK estimates can be applied with justification.
- As expected, **estimated utilities decreased with disease severity**, with utility being highest for the IDFS off-treatment/remission state and lowest for the metastatic, progressive disease state.
- Our study used the **NICE-preferred cross-walk algorithm from Hernández Alava et al. (2023)**[7] for the base case analysis, although this resulted in utility values lower than those obtained using the previously recommended van Hout et al. (2012)[8] algorithm or the Devlin et al. (2018)[9] EQ-5D-5L English value set, particularly at more advanced stages of disease.
- Although all three value sets in our study reflected a decrease in utility with increasing disease severity, these **estimates are much lower than those collected through clinical trials and alternative health-state utility elicitation studies**, as summarised in **Table 4**.
- Accurate utility data are important as numerical underestimation of patient utilities (i.e., lower utility values) using the vignette approach (and influences of the EQ-5D scoring methods used) could result in overestimation of incremental cost-effectiveness ratios (ICERs) in cost-effectiveness analyses of new medicines.

Study strengths

- Robust development of the vignettes in collaboration with oncologists and patients with BC.
  - This combination of stakeholder insights helped ensure that the study vignettes provided a sufficient approximation of reality, while remaining generalisable to a typical patient experience.

Discussion cont…

Study limitations and challenges with using the vignette approach:

- The lower utility scores reported by the UK general population in the current study, compared with patient reports, highlight the challenges and limitations associated with the vignette-based approach and obtaining disease-specific values from the general population:
  - The general public may underestimate the ability of a patient living with the disease to adapt and develop resilience to BC symptoms and their effects; this may lead to overestimation of the impact of BC being reflected in low utility scores.
  - Most participants (63.5%) had no personal (direct or indirect) experience with BC and results may be different if based on scoring by those with experience of caring for someone with BC.
  - Since the vignettes were expected to include descriptions of symptoms and disease impact, it was decided not to target patients with BC for this unassisted survey.
- As the vignettes were assessed as a cross-sectional activity, it is possible that participants were not considering the time spent in each given health state, where there is potential for change over time, although this limitation also applies to other studies.

Table 4: Health state utilities from the current study and published literature

Source	IDFS	Locally advanced (curable)	Advanced / stable metastatic	Metastatic (progressive disease)
Current study	0.458–0.773	0.329–0.470	0.179–0.308	0.008–0.131
Literature	0.85 Early-stage BC[12] ▪ In Chinese women. ▪ Meta-analysis data using mainly the Chinese 5L time trade off value set. 0.78 IDFS[13] ▪ Estimated by women with high-risk early HR+/HER2− BC.	0.76 Non-metastatic recurrence[13] ▪ Estimated by women with high-risk early HR+/HER2− BC.	0.715 Stable metastatic[1] ▪ General population estimate. 0.78 Metastatic remission[13] ▪ In women with metastatic BC. ▪ Derived from the literature. 0.85 PFS[14] ▪ In women with HR+/HER2+ BC. ▪ Estimated from published economic study. 0.685 PFS[15] ▪ Estimated by patients with metastatic BC. ▪ Using the EQ-5D and direct time trade off. 0.73 (83% with metastatic disease)[2] ▪ Estimated by patients with HR+/HER2− BC. 0.62 Bone and visceral metastases[2] ▪ Estimated by patients with HR+/HER2− BC. 0.71 Metastatic BC[12] ▪ In Chinese women. ▪ Meta-analysis data using mainly the Chinese 5L time trade off value set.	0.443 Progressive metastatic[1] ▪ General population estimate. 0.52 Progressive[14] ▪ Estimated from repository of HRQoL estimates from various sources. 0.55 Progressive metastatic[15] ▪ Estimated by patients with metastatic HER2+ BC.

5L, 5-level; BC, breast cancer; HER2-, human epidermal growth factor receptor 2-negative; HER2+, human epidermal growth factor receptor 2-positive; HR+ hormone receptor-positive; HRQoL, health-related quality of life; IDFS, invasive disease-free survival.

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