Poster HTA234

How Long Is the Weight? A Framework for Linear Interpolation of the National Institute for Health and Care Excellence (NICE) Severity Weighting in the Context of Probabilistic Sensitivity Analysis (PSA): A Case Study

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Background

In February 2022, an update to the NICE methods guide was published.[1] As part of this update, NICE introduced a quality-adjusted life-year (QALY) weighting, which translates to a change in the decision-making threshold based on the severity of a condition.

This approach is based on the absolute and proportional QALY shortfall estimated with standard-of-care (SoC) treatment for a given condition relative to the general population.

If eligible, either a 1.2x or 1.7x weighting is applicable to the incremental QALYs of an intervention which alters the willingness-to-pay (WTP) threshold to £36,000 or £51,000 per QALY, respectively. Limited details were provided for how the 1.2x and the 1.7x weights and corresponding thresholds for the absolute or proportional shortfall were determined.

There is a large difference in the QALY shortfall required to meet each threshold, and therefore some conditions may fall short of the 1.7x weighting and only qualify for the 1.2x which may impact estimates of cost-effectiveness and decisions influencing patient access in England and Wales.

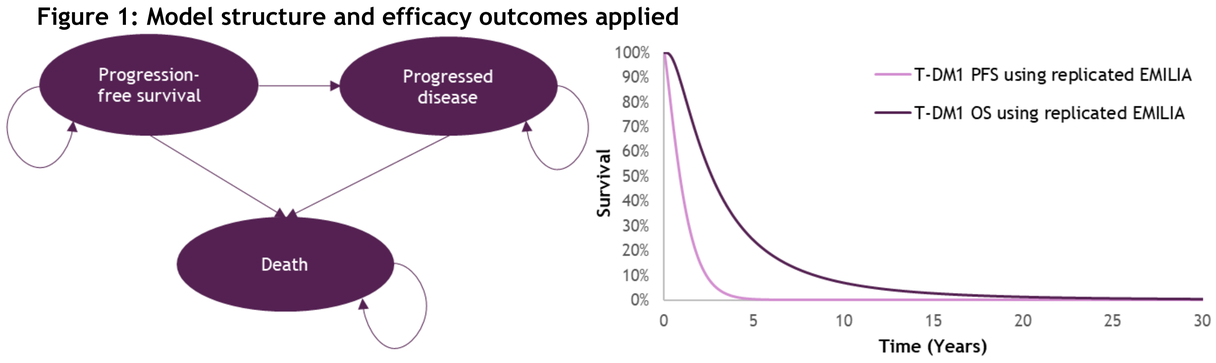
Objective

Using an example of trastuzumab emtansine (T-DM1) in metastatic breast cancer (mBC) to inform total QALY estimates for the SoC, this research looks at an alternative approach using the probabilistic framework for estimating additional severity weights (and corresponding thresholds) using linear interpolation between the 1.2x and 1.7x modifiers.

Methods

To estimate total T-DM1 QALYs (to inform the shortfall calculations) a partitioned-survival model was constructed containing three health states; '*progression-free*', '*progressed disease*' and '*death*'. Overall survival (OS) and progression-free survival (PFS) were informed by pseudo patient-level data created using publicly available information from the EMILIA study (NCT00829166).[2,3] The EMILIA trial was a phase 3, randomized controlled trial in HER2-positive advanced breast cancer which assessed T-DM1 versus lapatinib plus capecitabine.[2] Parametric survival curves were fitted to the replicated OS and PFS data to extrapolate outcomes and inform health state occupation within the partitioned-survival model. The model structure and a summary of survival is shown in Figure 1.

Figure 1: Model structure and efficacy outcomes applied



Abbreviations: OS, overall survival; PFS, progression-free survival; T-DM1, trastuzumab emtansine. Note: The log-normal curve was selected to inform OS and Weibull for PFS based on visual fit to the Kaplan-Meier.

Utility values of 0.809 and 0.575 were applied to PFS and PD health states respectively which are estimated using response rates for T-DM1 (from EMILIA) as part of a regression by Lloyd et al. 2006.[4] Utilities were age-adjusted using an algorithm from the literature.[5] Health outcomes were discounted at 3.5% in line with the NICE reference case.[1] Distributions and corresponding uncertainty information were assigned to parameters to create a probabilistic framework to estimate total T-DM1 QALYs.

A published QALY shortfall tool by Schneider et al, 2021, was used to estimate the total discounted QALYs which would be needed to meet the 1.2x and the 1.7x severity modifier based on the age and sex matched population from the EMILIA trial.[6] The reference case within the shortfall tool was used to inform thresholds. Using the age and sex matched population, a 1.2x QALY weighting was appropriate if the SoC remaining QALYs were between 0.75 and 3.11. Less than 0.75 QALYs for the SoC resulted in a QALY shortfall which met eligibility for the 1.7x weighting. Linear interpolation was used to create four scenarios which created additional thresholds between 1.2x and 1.7x (Table 1).

Table 1: QALY weights explored through linear interpolation

Scenario	Number of weights	Corresponding QALY weights
Base case (current NICE methods)	3	1x, 1.2x, 1.7x
Scenario 1	4	1x, 1.2x, 1.45x, 1.7x
Scenario 2	7	1x, 1.2x, 1.3x, 1.4x, 1.5x, 1.6x, 1.7x
Scenario 3	12	1x, 1.2x, 1.25x, 1.30x, 1.35x, 1.40x, 1.45x, 1.50x, 1.55x, 1.60x, 1.65x, 1.70x

Abbreviations: QALY, quality-adjusted life-year

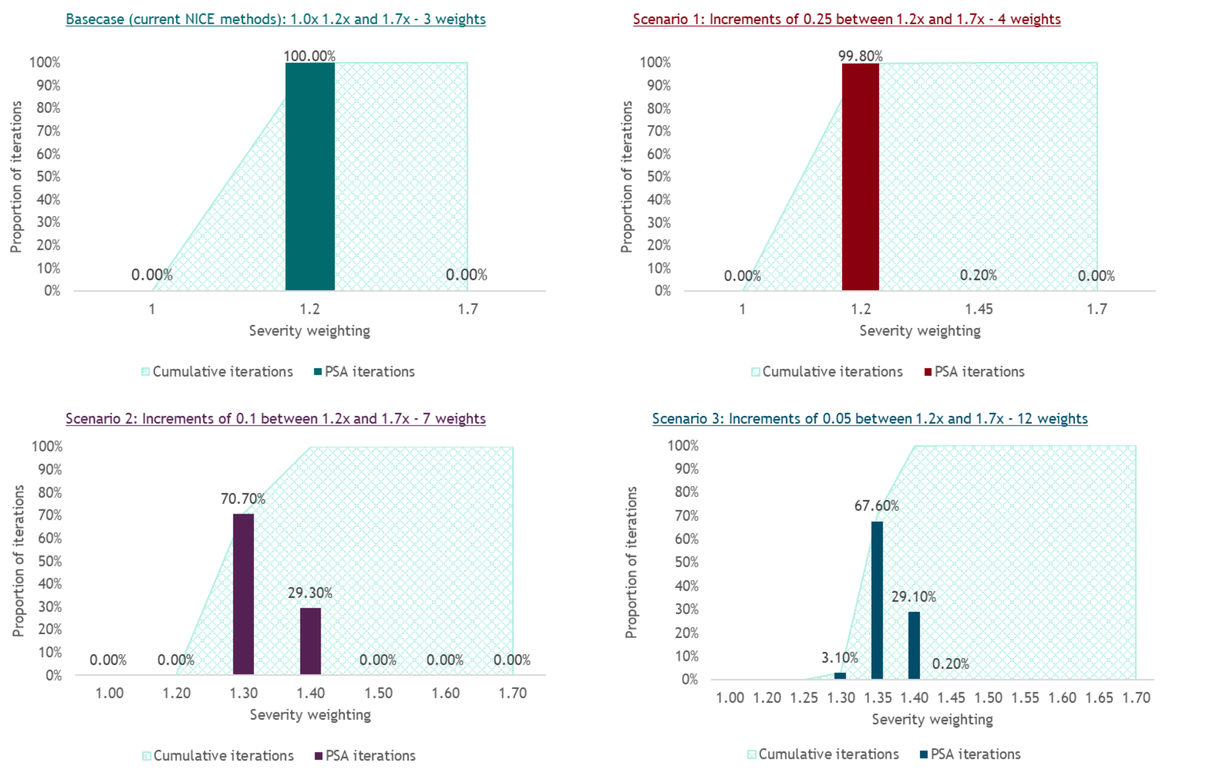
One thousand probabilistic iterations were then performed which recorded the total T-DM1 QALYs to reflect SoC in mBC. The outcomes were then compared to each individual threshold (ranging from 1.2x to 1.7x) to understand what proportion of probabilistic iterations fell into which weighting category across each of the four scenarios explored.

Results

With a deterministic result of 2.21 QALYs, in calculating the QALY shortfall, a 1.2x severity modifier weighting may be considered appropriate by NICE for this example based on the current methods guide and corresponding thresholds. In a probabilistic framework under the current NICE methods (i.e., base case), the 1.2x QALY modifier would be applicable in 100% of iterations. A summary of results across the probabilistic iterations and weightings are provided in Figure 2.

When considering scenario 1 (with the addition of the 1.45x weight), 99.80% of iterations corresponded with the 1.2x range and 0.20% with the 1.45x category. In scenario 2 (which considered increments of 0.1 between the 1.2x and the 1.7x weighting), no iterations fell within the 1.2x range, but instead 70.70% were considered appropriate for a 1.3x weighting and 29.30% relevant for a 1.4x severity weighting. This was further supported when exploring increments of 0.05 between 1.2x and 1.7x, in which all iterations fell between the 1.3x and 1.45x severity range.

Figure 2: Probabilistic outcomes versus sliding scale weights (1.2x - 1.7x): proportion of iterations within each weight across 4 different scenarios



Abbreviations: PSA. probabilistic sensitivity analysis

As indicated by the case study presented, based on current NICE methods, a severity weighting of 1.2x is considered appropriate versus the 1.0x and 1.7x severity weights. However, on further assessment, it is likely that the true severity of mBC when using T-DM1 as the SoC translates to a severity weighting somewhere above £36,000, between the 1.2x and 1.7x range. Based on the analysis conducted, a more appropriate range could be between 1.3x and 1.45x severity weightings which would translate to a WTP threshold between £39,000 and £43,500.

Conclusions

- This analysis presents an alternative novel approach to estimating severity weighting by combining the QALY shortfall calculations with an increased number of thresholds in a probabilistic framework.
- A sliding scale approach, with shorter increments between weights may offer a solution to quantifying disease severity more appropriately by increasing sensitivity and aligning this with parameter uncertainty. In this example, it is possible that the 1.2x severity weighting may underestimate the severity of the condition under consideration (mBC). This limitation would be further emphasized where technologies just miss out on the 1.7x modifier, having implications for cost-effectiveness estimates and subsequently patient access to new medicines.
- The framework, whilst informative, does not account for structural uncertainty within the model e.g., the choice of parametric curve, which should not be ignored. More research and case studies are needed to understand the impact of the new methods on cost-effectiveness and decision-making on access to new medicines in the NHS.

References

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