Improper Age Adjustment of Health State Utilities in Cost-Effectiveness Models: Assessing the Impact and Key Drivers

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Background

- A gradual decline in health-related quality of life (HRQoL) has been observed as individuals age, potentially due to an increasing number of comorbidities or a natural decline in mental and physical functioning.[1-3] While it is generally preferred that health-state utility values (HSUVs) are derived directly from the patient group of interest,[4] modeling the impact of age directly in the population of interest is often not feasible.
- In cost-effectiveness models (CEMs), crude adjustment of HSUVs over time to account for age-related decline has become standard practice,[5] with multiplicative age adjustment of utilities now formally recommended as part of current National Institute for Health and Care Excellence (NICE) guidance.[6]
- Correct implementation of age adjustment of utilities using a multiplicative approach relies on deriving an appropriate utility multiplier. This is done by dividing the HSUV by an age-matched general population utility norm, using the average age of the original utility study sample (hereafter referred to as the "reference" age). This multiplier is then applied to the general population norms to derive age-specific HSUVs for all relevant ages in the model, assuming the same proportional utility reduction holds true across all ages.[7]
- However, given the lack of detailed guidance from NICE on proper implementation of age adjustment of utilities, modelers may incorrectly use the model baseline age for deriving this multiplier instead of the reference age. As such, improper projection of HSUVs by age may occur when differences in the model baseline age and reference age are present.

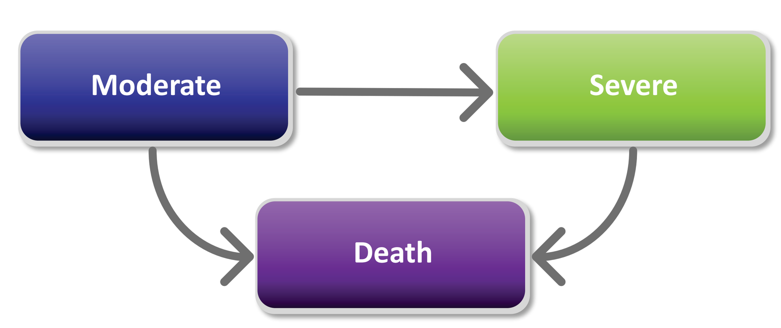
Objectives

- This study aimed to compare the potential impact of "improper" implementation of HSUV age adjustment of utilities (no accounting for age differences in model baseline and utility study sample ages) vs. "proper" implementation on CEM results as well as identify key drivers of differences in results.

Methods

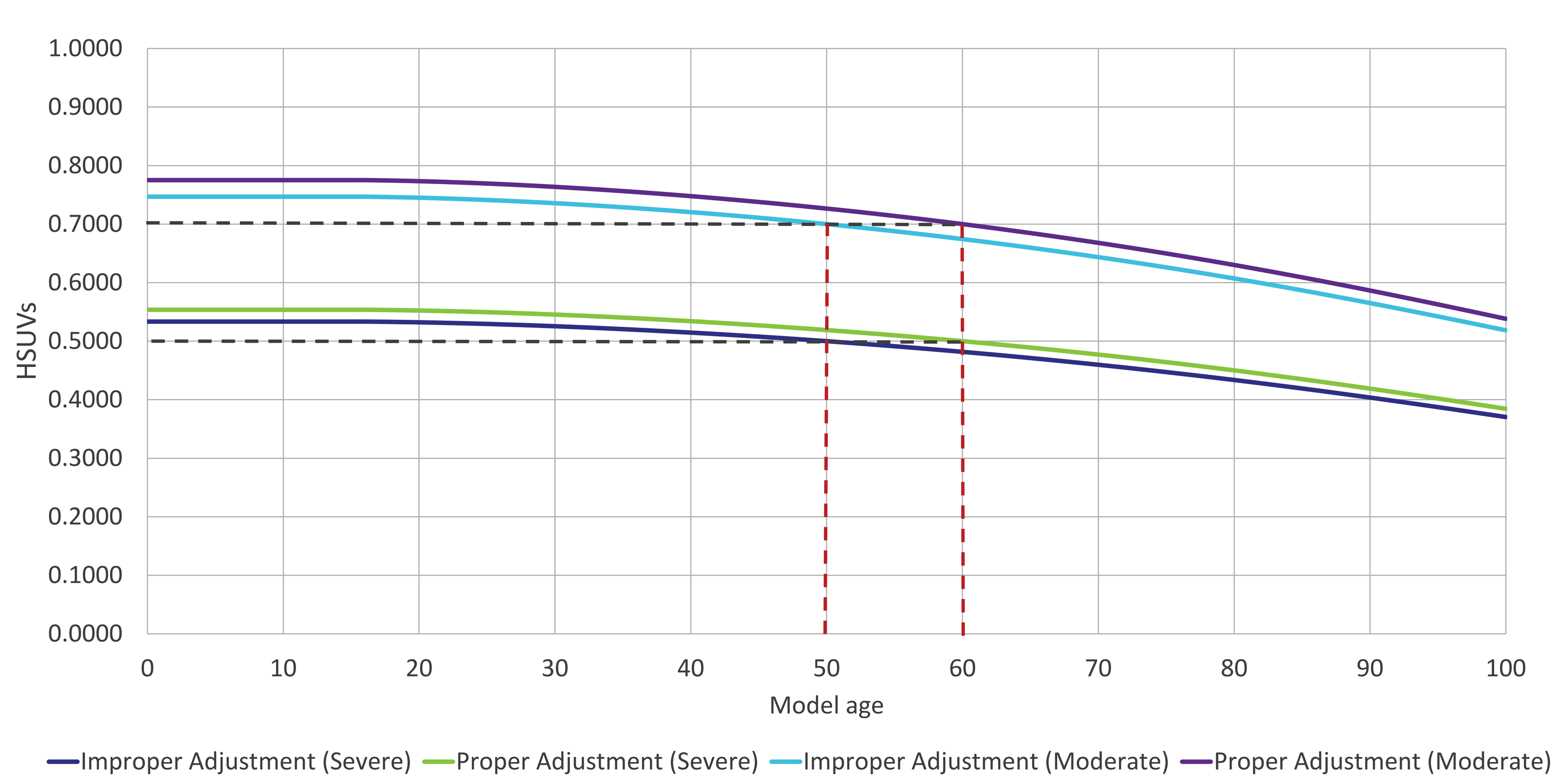
- A hypothetical three-state Markov model (Moderate, Severe, Dead) was developed from a UK payer perspective, with a lifetime horizon and 3.5% discount rates. All patients start in the "Moderate" health state, with no backward transitions permitted from the "Severe" health state for simplicity (**Figure 1**).

Figure 1. Model Diagram



- HSUV age adjustment was performed using UK general population norms[3] and a multiplicative approach. HSUVs of 0.7 and 0.5 were used for the moderate and severe health states, respectively.
- Baseline population age of the model was assumed to be 50 years, with a 10-year increase in the reference age (i.e., 60 years) compared with the baseline age for the base-case analysis. The resulting difference in age-adjusted HSUV projections between proper and improper adjustments for each health state are represented in **Figure 2**.

Figure 2. Change in HSUVs by Model Age (Proper vs. Improper Method)



Abbreviation: HSUV = health-state utility value.

- Mortality hazard ratios of 2 and 4 vs. the general population were used for moderate and severe health states, respectively, and applied to UK life table data.[8]
- Hypothetical treatment efficacy was applied as a 50% risk reduction for Severe health state transitions, applied to a 5% annual probability for standard of care (SoC).
- Annual theoretical treatment, moderate health state, and severe health state costs of £3,000, £1,500 and £9,000 were assumed, respectively.
- Key outcomes of the analysis were proportional and absolute differences in incremental cost-effectiveness ratios (ICERs) for hypothetical treatment vs. SoC between improper and proper age-adjustment methods. Deterministic sensitivity analyses (DSA) and univariate/bivariate analyses were conducted to identify and quantify key model drivers and their impact.

Results

- For the base-case analysis with a 10-year higher reference age compared with the model baseline age, £1,109 absolute and 3.79% proportional ICER differences between approaches were observed, with ICERs of £29,249 and £30,358 for proper and improper age adjustment of utilities, respectively (**Table 1**).
- The DSA results for the absolute differences (**Figure 3**) highlighted that this outcome was most sensitive to disease-specific utility values, population starting age, cost of intervention, intervention efficacy, progression probability, cost of severe disease, and differences between baseline and reference ages. For the proportional differences in ICER results (**Figure 4**), the DSA indicated that differences between baseline and reference ages, as well as changes in the baseline age itself, were key drivers. Additionally, variations in the proportion of gender split had a minor impact, while other model inputs had no impact on the proportional ICER difference.

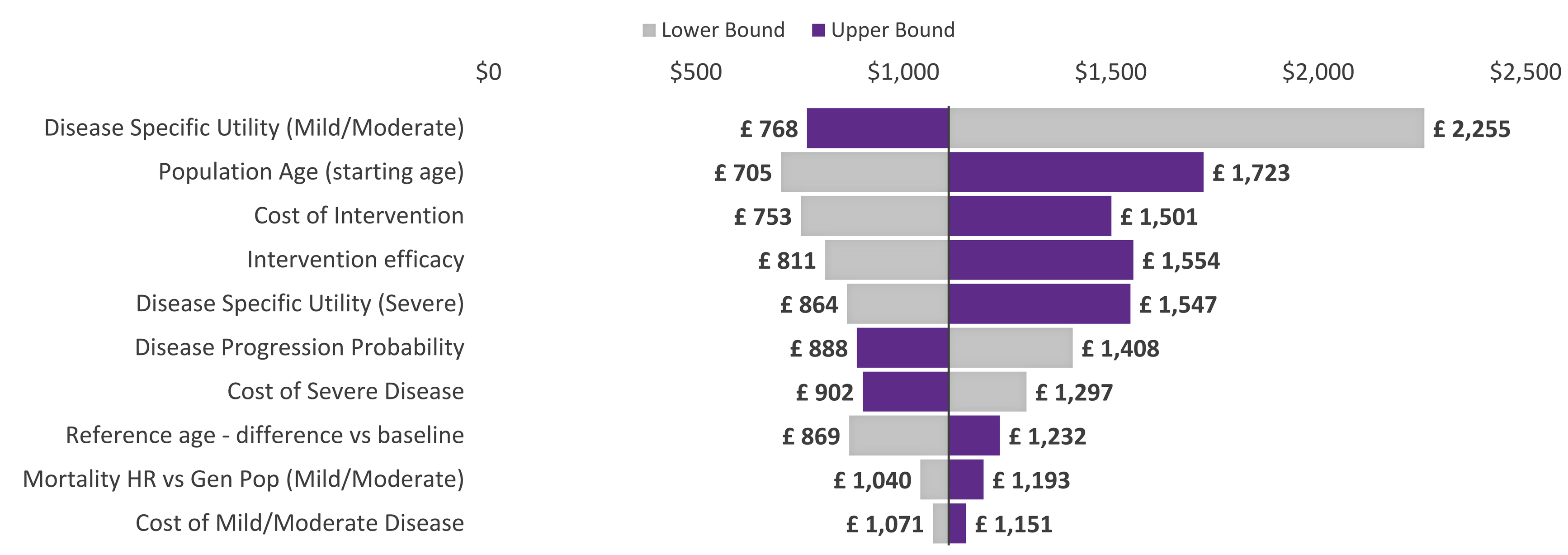
Results (Cont'd)

Table 1. Results Table

Outcome	SoC	Treatment	Incremental
Total QALYs (Improper Adjustment)	9.2456	9.9635	0.7179
Total QALYs (Proper Adjustment)	9.5961	10.3413	0.7452
Total QALY Difference by Method	0.3506	0.3778	0.0272
Total Costs	£ 64,090.18	£ 85,885.15	£ 21,794.96
Age Adjustment Method	**ICER (Cost per QALY)**	**Absolute Difference**	**Proportional Difference**
Improper Adjustment	£ 30,357.86	£ 1,109.06	3.79%
Proper Adjustment	£ 29,248.80		

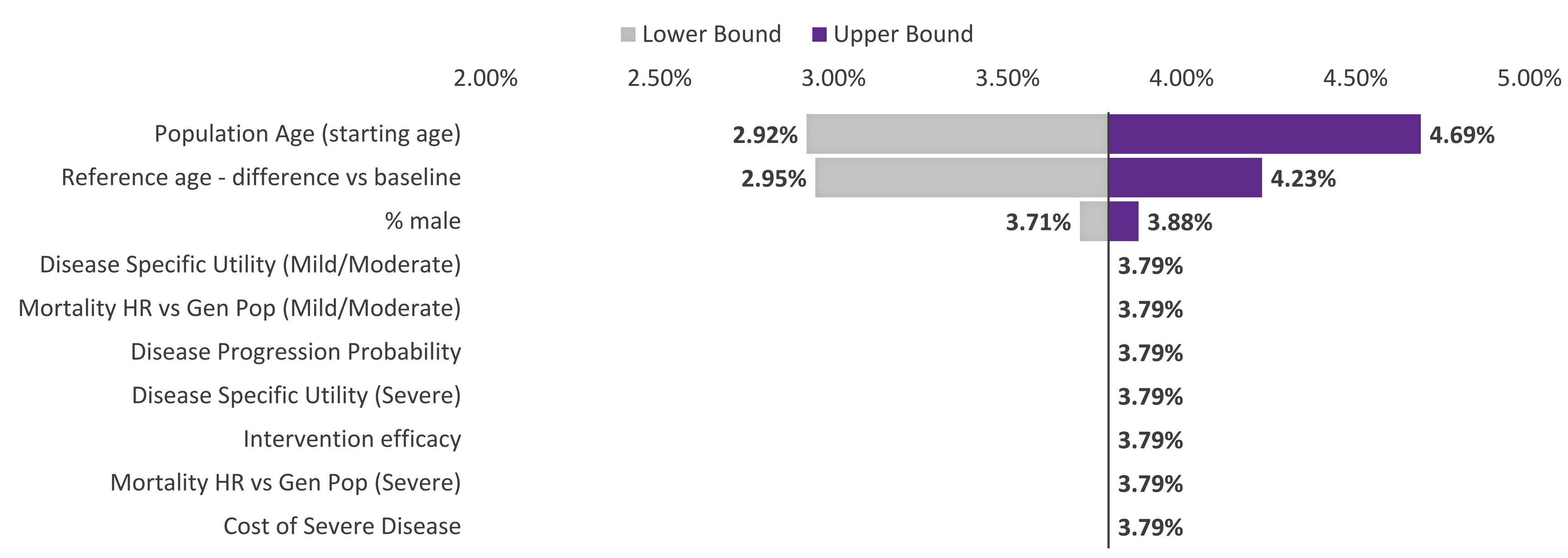
Abbreviations: ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year; SoC = standard of care

Figure 3. DSA Outcome: Absolute Difference in ICERs between Proper and Improper Age Adjustment of HSUVs



Abbreviations: HR = hazard ratio; ICER = incremental cost-effectiveness ratio.

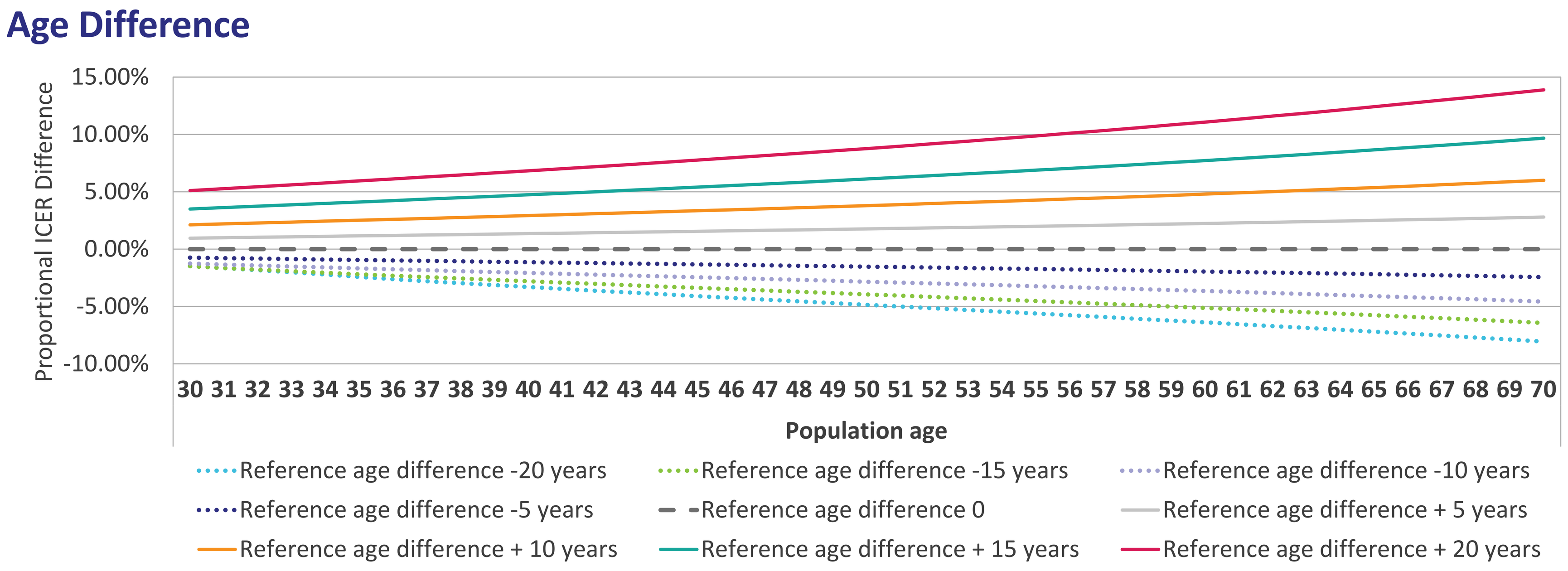
Figure 4. DSA Outcome: Proportional Difference in ICERs between Proper and Improper Age Adjustment of HSUVs



Abbreviations: HR = hazard ratio; ICER = incremental cost-effectiveness ratio.

- Univariate analysis indicated increasing proportional ICER differences with increasing baseline age as well as increasing differences in baseline and reference ages (results not shown), with no differences in the ICERs when the baseline and reference ages were equal. Bivariate analysis (**Figure 5**) showed ICER results deviating between −8.06% and 13.88% when simultaneously varying baseline age (30 to 70) and reference age differences (±20).

Figure 5. Change in Proportional ICER Differences by Population Baseline Age and Reference Age Difference



Abbreviation: ICER = incremental cost-effectiveness ratio.

Conclusions

- Improper age adjustment of HSUVs may produce non-trivial errors in CEM results, with the magnitude of error increasing with increasing differences in baseline and utility reference ages, and further compounded for higher model baseline ages.
- Further assessment of the impact of improper age adjustment of HSUVs should be explored, and clearer guidance developed on best practices for implementing age adjustment of HSUVs in cost-effectiveness analyses.

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