Theoretical Exploration of the Inclusion of Non-Traditional Multiple Sclerosis Measurement Variables on the Cost-Effectiveness of Future Treatments

POSTER #EE460

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Background

Multiple Sclerosis (MS) underwent a paradigm shift with the advent of Disease-Modifying Treatments (DMTs) at the beginning of the new century [1]. To some extent, the cost-effectiveness of these new treatments was demonstrated [2] using traditional outcomes like Annualized Relapse Rate (ARR) and Confirmed Disability Progression (CDP). However, the continuously improving understanding of MS from a clinical perspective tends to show that ARR and CDP only partially cover MS patients' experience of the disease. For instance, fatigue [3] is the most prevalent and one of the most disabling symptoms among MS patients, leading to lower quality of life. Although multiple definitions of Progression Independent of Relapse Activity (PIRA) exist, PIRA begins to be considered as another important disabling factor for MS patients [4]. Brain Volume Loss (BVL) is emerging as a major contributor to disability progression and a critical biomarker of neurodegeneration, independent of MS activity [5].

However, these variables are rarely collected in clinical trials, and their impacts are seldom studied in health economics models.

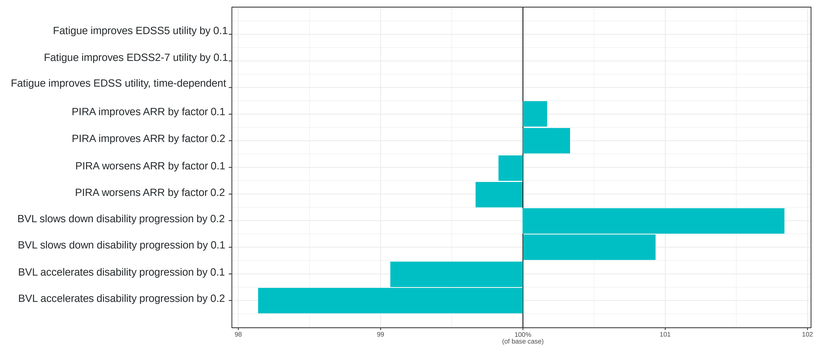

Figure 1. Relative variation of total costs of the intervention with additional parameters (compared to base case)

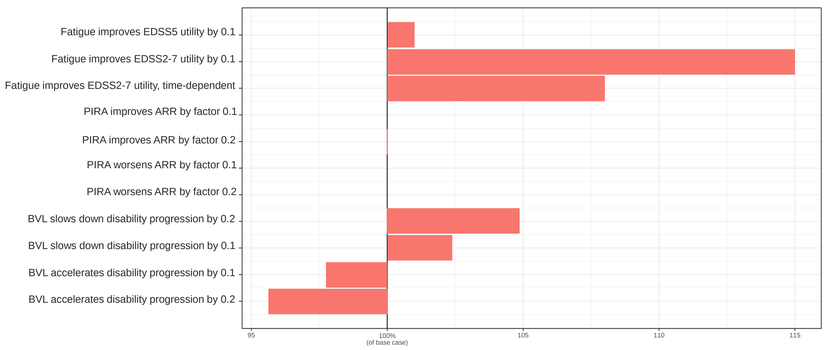

Figure 2. Relative variation of total QALY of the intervention with additional parameters (compared to base case)

Methods

A cohort-based Markov model with 11 health states (10 Expanded Disability Status Scale (EDSS) plus death) was developed in R, based on a previously published cost-effectiveness model (CEM) [6]. This model specifically studies relapse-remitting MS (RRMS) patients (and does not consider secondary progressive MS patients).

The analysis followed the NICE reference case. Traditional parameters were derived from trials, past submissions, NHS, and literature. The intervention used in the model was one of the latest DMTs with its publicly available price.

Three variables were incorporated into this traditional model:

- Fatigue was implemented as a discrete change of +0.1 utility value to reflect a potential positive effect of reducing fatigue. This was done in 3 ways: one-shot change of EDSS 5 utility, change in a range of EDSS states (2 to 7) utilities, and time-dependent change impacting the same range of EDSS states.
- PIRA was implemented as an additional variable amplifying the annualized relapse rate independently of the EDSS state.
- BVL was implemented as a modifier of the disability progression rate (modifying the CDP hazard ratio independently of the EDSS state).

The base case was reproduced to ensure a stable foundation for further explorations. Each parameter was investigated individually to understand its impact on the base case.

The outcomes of interest were the relative changes in total costs and total quality-adjusted life years (QALYs) with these three variables, which were compared to the same DMT without additional parameters (incremental cost-effectiveness ratio, "ICER").

Objectives

This research aims to measure the theoretical gain that could be seen by incorporating these additional variables into a cost-effectiveness model from the perspective of England's National Health Service (NHS).

Results

Compared to the initial base case, including fatigue improvements has the most significant impact on QALY (+8% to +15%). Demonstrating a benefit in fatigue reduction would drastically reduce the ICER and make this theoretical drug more cost-effective.

Reducing brain volume loss (leading to a slowdown of disability progression) also increases QALY (up to +5%) but does so while also increasing costs (up to 2%). If brain volume loss is demonstrated to be substantial, the cost-effectiveness benefit would be limited.

Finally, when PIRA worsens the annualized relapse rate, it slightly increases costs and has virtually no impact on QALY. Thus, the benefits of a lower PIRA would not significantly impact the ICER.

Discussion

Our research has provided a significant extension to traditional health economic models in multiple sclerosis (MS), which have predominantly focused on the Expanded Disability Status Scale (EDSS) and Annualized Relapse Rate (ARR) as primary outcomes derived from randomized controlled trials (RCTs). By incorporating three additional parameters: PIRA, fatigue, and BV our model highlights the potential shortcomings of restricting analyses to EDSS and ARR alone.

The inclusion of fatigue, PIRA, and BVL is predicated on their relevance to the long-term outcomes of MS, aspects that are often overshadowed in conventional models. Our findings indicate that the inclusion of these variables significantly alters the cost-effectiveness landscape of disease-modifying treatments (DMTs). Notably, the assumed influence of fatigue showed the most substantial impact on outcomes, followed by BVL, with PIRA having the least effect. This prioritization underscores the importance of fatigue as a significant outcome affecting patient quality of life and consequently, its economic evaluation in MS management.

The implications of our findings are profound. Incorporating these factors into future health economic models could radically change the decisions regarding the cost-effectiveness of new DMTs. Traditional models may underestimate the benefits of treatments that significantly impact fatigue and BVL, potentially leading to suboptimal treatment choices. Our results advocate for a more nuanced approach that captures a broader spectrum of MS impacts, thus offering a more comprehensive assessment of treatment value.

However, our analysis is not without limitations. The current model evaluates the impact of each variable in isolation, which may not accurately reflect their interdependent effects in real-world scenarios. Multi-variable sensitivity analyses are crucial to understand the synergistic or antagonistic effects of these parameters when combined. Probabilistic sensitivity analysis could further provide insights into the variability and uncertainty inherent in these estimates.

Additionally, multi-criteria decision analysis (MCDA) should be considered to integrate these variables more holistically, addressing potential issues such as double counting. Double counting occurs when effects captured by one variable are inadvertently included again under another measure, potentially exaggerating the benefits or costs associated with treatment.

Conclusions

In conclusion, while our study expands the scope of variables considered in the economic evaluation of MS treatments, it also underscores the complexity of accurately assessing treatment efficacy. Future models should aim to include these non-traditional parameters while developing robust methodologies to handle their interdependencies and the inherent uncertainties in their measurement. Such advancements will likely lead to more informed and effective healthcare decisions, ultimately improving outcomes for patients with MS. Further research is necessary to allow more robust and evidence-based conclusions on the cost-effectiveness of new DMTs for MS.

References

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