



Redefining the Scope: The Urgent Need for Holistic Multiple Sclerosis Modeling in Health Economics

Bergemann, R¹; Libanore, A²; Rudell, K³; Poirrier JE⁴

1: Parexel Intl, Basel, Switzerland; 2: Parexel Intl, Ontario, Canada; 3: Parexel Intl, London, UK; 4: Parexel Intl, Wavre, Belgium

Abstract:

Objective:

This study aims to critically analyze the development, limitations, and structures of health economic models for Multiple Sclerosis (MS), identifying the need for more comprehensive approaches in modeling to better capture the multifaceted nature of the disease.

Methods:

An exhaustive review of 163 health economic models and two overview articles was conducted, focusing on models published up to December 15, 2023. The methodology included a detailed search in PubMed and Google Scholar, supplemented with secondary sources. The analysis targeted parameters related to relapse/remission, EDSS (Expanded Disability Status Scale) progression, disability progression, quality of life (QoL), imaging parameters, cognitive function, fatigue, biomarkers, time to treatment continuation, and work productivity.

Results:

The majority of the 163 reviewed models (>90%) predominantly focused on relapse and remission, with a notable lack of incorporation of imaging parameters in long-term outcome modeling for Disease-Modifying Therapies (DMTs). The "gold standard" model from Tasman University emphasized EDSS progression, but does not take into account disability, fatigue, work productivity, health resources use during relapsing and remission cycles. Markov models emerged as the most common structure (>90%) featuring cycle lengths ranging from one month to three years. A key finding was the absence of models incorporating a holistic or multi-criteria perspective, highlighting a significant limitation in current approaches. Discretely Integrated Condition Event (DICE) simulation was suggested as an improvement compared to Markov models.

Conclusion:

The review highlights the necessity for the development of MS models that are a more accurate representation of the disease. Current models predominantly focus on singular dimensions of MS, failing to encompass the complex dynamics affecting patient outcomes. The establishment of comprehensive, multi-criteria models is essential to reflect the real-world impact of DMTs more realistically on patients' lives. A paradigm shift for accurately modelling patient experience with remitting relapsing conditions is needed.

Introduction:

Multiple Sclerosis (MS) is a chronic, neurodegenerative disease that affects millions of people worldwide, causing a wide range of physical, cognitive, and emotional impairments. The multifaceted nature of MS necessitates a comprehensive understanding of the disease to optimize patient care and inform healthcare decision-making. While health economic models are widely used to assess the cost-effectiveness of interventions, the current models used for MS often fall short in capturing the full complexity of the disease.

In the past, clinical trials for new therapies in MS have traditionally focused on the registration endpoints of relapse rates and disability progression measured by tools such as the Expanded Disability Status Scale (EDSS). These endpoints, although important for regulatory approval, provide only a limited view of the disease and its impact on patients' lives. The EDSS, which quantifies the level of disability based on neurological examinations, has been a valuable tool in measuring disease progression over time. However, it fails to account for important aspects such as quality of life, fatigue, cognitive function, work productivity, and the overall burden of the disease on patients.

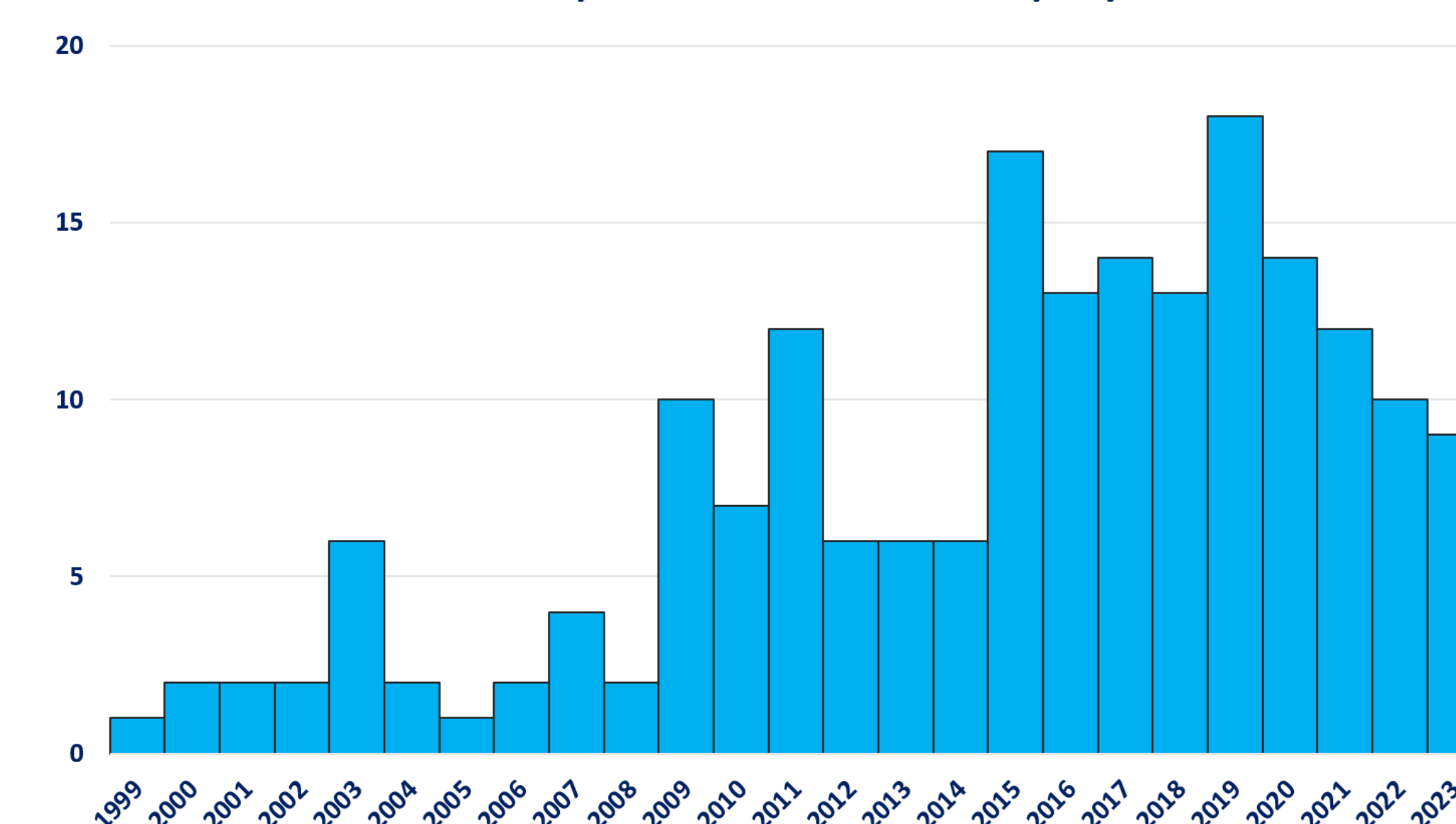
While it is crucial to consider these primary endpoints, it is equally important to incorporate a broader range of parameters that reflect the multifaceted nature of MS.

Therefore, this poster aims to critically analyze the development, limitations, and structures of existing health economic models for MS, with a specific focus on the incorporation of various parameters such as relapse/remission, EDSS progression, disability progression, quality of life, imaging parameters, cognitive function, fatigue, biomarkers, time to treatment continuation, and work productivity. By examining the extent to which these models incorporate these parameters, we can shed light on their limitations and advocate for a more comprehensive approach in modeling MS in health economics.

Methods:

To conduct the targeted literature review, a search strategy was implemented using PubMed and Google Scholar databases. The search encompassed relevant keywords related to EDSS progression, relapse, remission, cognitive function, fatigue, time to treatment continuation, and Work Productivity and Activity Impairment Score (WPAI). The cut-off date for the study was set at December 15th, 2023. Google Scholar search was limited to the first 100 results sorted by relevance. Exclusion criteria included studies not utilizing Health Economic models, studies involving non-human subjects, and studies primarily focused on pathological pathways. Deduplication was applied.

Number of published HE MS studies per year



Results:

163 health economic studies related to MS were identified. Among these studies, 114 explicitly specified the type of model structure employed.

•Model Structures: The majority of the identified studies (89%) utilized Markov Models as their primary modeling framework.

•Single Outcome Focus: All of the analyzed models presented data for single outcomes only, indicating a limited perspective on the economic impact of MS.

•Absence of Multi-Criteria Decision Analysis: Surprisingly, none of the reviewed studies employed multi-criteria decision analysis techniques, highlighting a potential gap in the existing research.

•Prominence of EDSS and EDSS Progression: The most frequently used parameters for health economic outcomes were the Expanded Disability Status Scale (EDSS) and its progression. These parameters were consistently favored over other parameters like Fatigue, Quality of Life (QoL), Utility, Depression, Cognitive Function, Biomarkers, and Imaging.

•Independent Presentation of Additional Outcomes: Although some studies delved into various aspects of MS beyond EDSS and EDSS progression, such as Fatigue, QoL, Utility, Depression, Cognitive Function, Biomarkers, and Imaging, these outcomes were described independently without considering their broader economic implications.

•The patient perspective was not considered in any model / discussed in any model.

•Lack of a Holistic Perspective: None of the studies described the health economics of MS based on a comprehensive understanding of the disease, thus demonstrating a limitation in capturing the multifaceted nature of MS.

Discussion:

Our comprehensive analysis of the available literature on health economic models for Multiple Sclerosis (MS) has revealed several significant shortcomings and limitations. These findings shed light on the need for more comprehensive modeling approaches that better capture the complex nature of MS and provide a holistic understanding of its economic implications.

Firstly, the overwhelming reliance on Markov Models among the reviewed studies limits the ability to create a truly holistic model. Markov Models, by their design, assume independence of events and transitions between health states over time. This assumption may not adequately represent the intricacies and interdependencies within the MS disease trajectory, resulting in an oversimplified view of its economic impact. A more versatile modeling technique, such as differential equation modeling, would allow for a more nuanced representation of the disease's multifaceted nature. However, it is surprising to note that no published MS health economic models utilizing differential equation techniques were identified, despite their potential suitability for capturing the dynamic nature of the disease.

Additionally, we respectfully disagree with the conclusion of the Tasman EDSS model that considers the Expanded Disability Status Scale (EDSS) as the gold standard for MS modeling. While EDSS is indeed a widely accepted measure of disability in MS, it fails to capture the full spectrum of disease manifestations and does not adequately account for the various outcomes, such as fatigue, quality of life, utility, depression, cognitive function, biomarkers, and imaging, which were described independently in the reviewed studies. EDSS is used in clinical trials for market authorization as primary outcomes parameter, but relying solely on EDSS lead to an incomplete understanding of the economic consequences of MS. Therefore, a broader set of outcome measures should be considered to ensure a more comprehensive assessment of the disease's economic burden.

Furthermore, the absence of multi-criteria decision analysis techniques in the identified studies is a notable gap. Multi-criteria decision analysis provides a framework for considering multiple dimensions simultaneously and incorporating stakeholder preferences, thereby enhancing the comprehensiveness of economic modeling. By neglecting this approach, the reviewed studies missed an opportunity to capture the holistic impact of MS on various domains and to incorporate the perspectives and preferences of different stakeholders in the decision-making process.

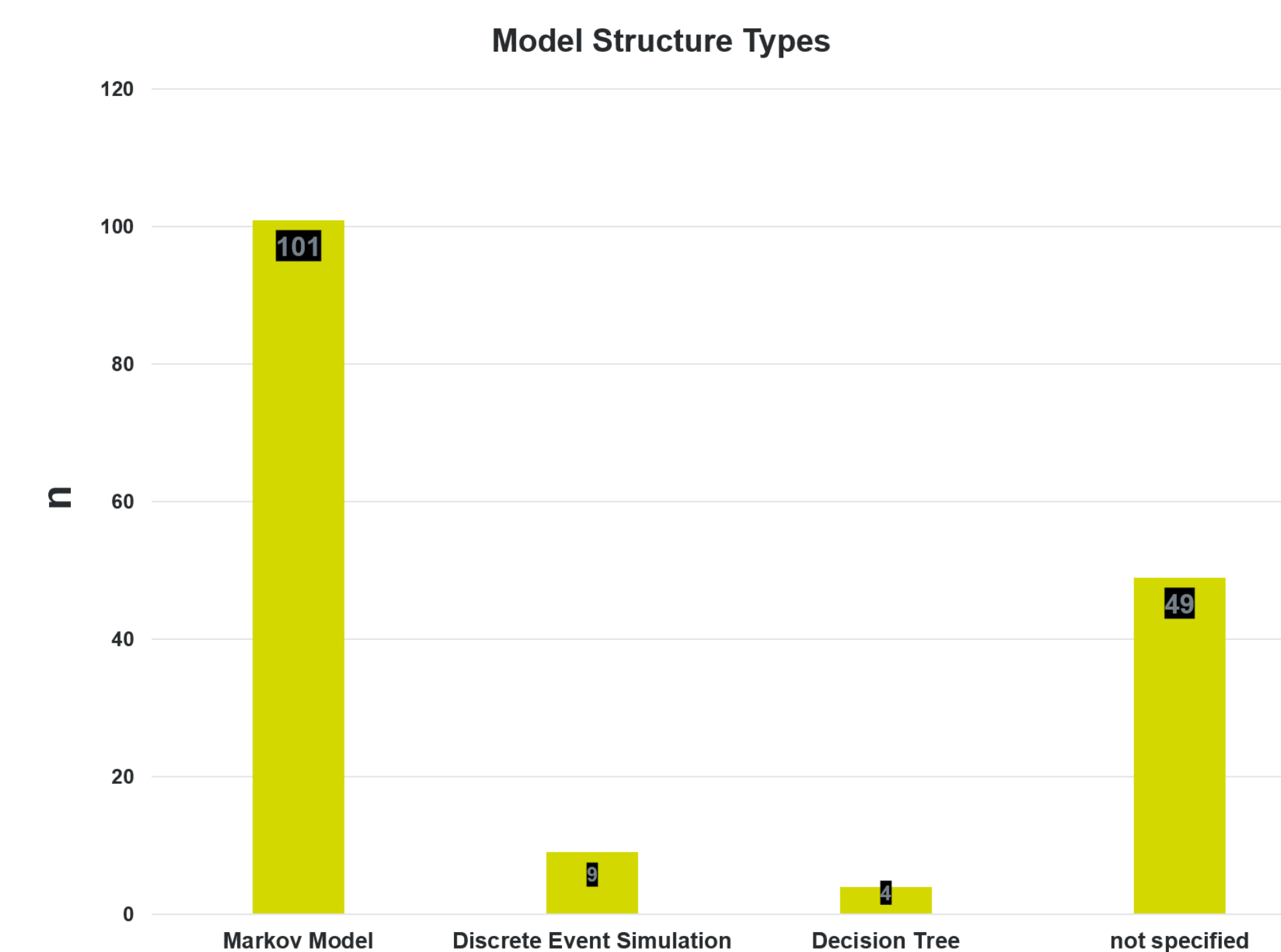
It is evident from our findings that the existing health economic models for MS lack a comprehensive perspective on the disease and its economic implications. While the identified studies provided valuable insights into specific aspects of MS, the absence of a holistic approach impedes a complete understanding of the economic burden and impacts the accuracy of policy recommendations and resource allocation decisions.

Future research endeavors should aim to bridge these gaps by incorporating differential equation techniques and multi-criteria decision analysis into health economic modeling for MS. By considering the interconnectedness of various outcomes and incorporating stakeholder preferences, a more comprehensive and robust model can be developed. In doing so, researchers can provide policymakers, healthcare providers, and patients with more accurate and informative insights into the economic aspects of MS, ultimately contributing to improved decision-making and resource allocation in the field of MS management.

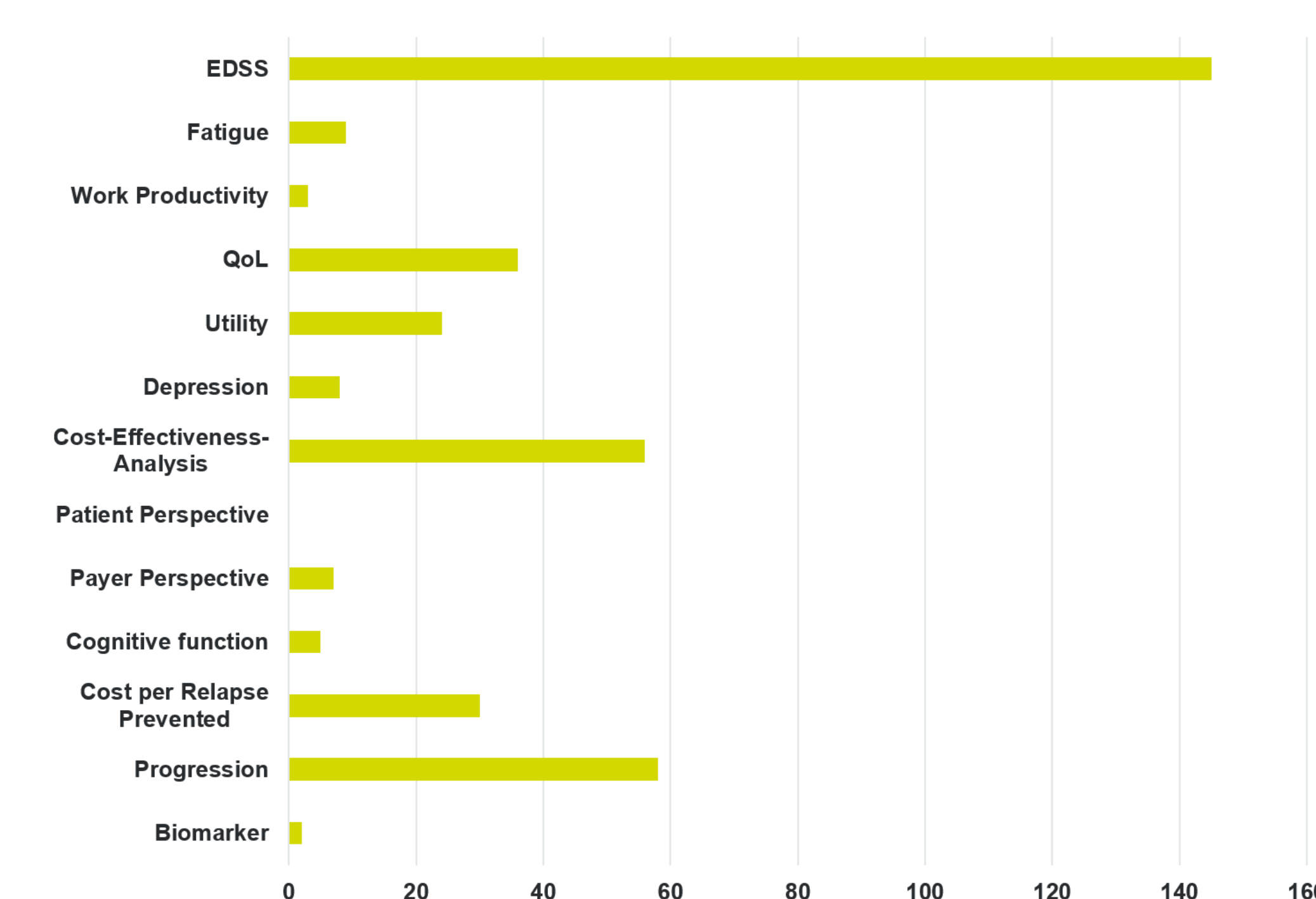
In conclusion, while the reviewed health economic models for MS have made valuable contributions, they fall short in capturing the multifaceted nature of the disease. The exclusive reliance on Markov Models restricts the ability to create comprehensive models, and the lack of differential equation techniques limits dynamic representation. Additionally, the emphasis on EDSS as the gold standard for modeling disregards the broader spectrum of MS outcomes. Incorporating multi-criteria decision analysis would enhance the comprehensiveness of modeling efforts. Future research endeavors should focus on addressing these limitations to develop more comprehensive and accurate health economic models for MS.

References:

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Outcomes assessed in health economic MS studies



Conclusion:

This literature review highlights several key findings regarding health economic models for MS. The predominant use of Markov Models suggests their widespread acceptance, but the exclusive focus on single outcomes limits the understanding of the overall economic burden of MS. The absence of multi-criteria decision analysis techniques further underscores the need for more comprehensive approaches. The prominent use of EDSS indicates a certain level of tunnel vision in modeling, disregarding other vital aspects of MS. The independent presentation of various outcomes, without considering their interconnectedness, hinders a holistic understanding of the economic impact of MS. Consequently, there is a clear need for more sophisticated modeling approaches that capture the complex and multidimensional nature of MS to provide comprehensive insights into its economic implications. In addition to addressing the limitations mentioned above, it is crucial to emphasize that any comprehensive health economic modeling for MS should include the patient perspective. Incorporating patient preferences, values, and quality of life measures into the modeling framework will provide a comprehensive understanding of the economic impact of MS from the patient's point of view, ultimately enhancing the relevance and applicability of the models in real-world decision-making processes.