Cost-Utility Analysis of Enhanced Physiotherapy for Motor Neuron Disease Using EQ-5D and SF-6D: A Missing Data and Perspective-Based Evaluation

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Introduction

Motor neuron disease (MND) is a rare but serious neurodegenerative condition that causes progressive loss of motor neuron function. This leads to physical disability, reduced quality of life (QoL), and shortened life expectancy. MND not only creates significant physical and emotional stress for patients and their families but also places a financial burden on public health systems, intensifying the challenges of resource allocation (Leigh and Ray-Chaudhuri, 1994; Moore et al., 2016). Developing interventions for MND is essential to improve health-related quality of life (HRQoL) and ease the strain on healthcare systems. (Morris et al., 2006; Cup et al., 2007).

Enhanced physical therapy has shown promise as an intervention, with evidence suggesting it can slow functional decline, improve mobility, and enhance HRQoL. Studies suggest it may reduce healthcare costs by lowering complications and extending independence (Morris et al., 2006; Cup et al., 2007). In health economic evaluations, tools like EQ-5D and SF-6D are frequently used to assess utility although their ability to capture disease impact and treatment outcomes differs significantly (Brazier et al., 2004; Obradovic et al., 2013). EQ-5D is often considered more sensitive to changes in severe health conditions, while SF-6D is better at distinguishing moderate health states (Brazier et al., 2004; Walters and Brazier, 2005). These differences support the use of cost-utility analysis (CUA) for enhanced physiotherapy, capturing both life length and quality.

This study aims to evaluate the cost-utility analysis (CUA) of enhanced physiotherapy for MND patients, using EQ-5D and SF-6D to capture utility measures and address the challenges of comparing quality-adjusted life years (QALYs) between treatments. It also investigates the impact of missing data imputation methods, including predictive mean matching (PMM) and random forest imputation, on analysis reliability. Furthermore, it introduces a societal perspective, accounting for travel costs, informal care, and productivity losses, to provide a broader evaluation of the intervention's value. These differences are critical when evaluating interventions for progressive diseases like MND.

Method

Data Description and Processing

This study uses data from a randomized controlled trial (RCT) of 90 participants, covering EQ5D, SF6D, costs, and QALYs. Within the dataset, the missing rates for EQ5D, SF6D, and total costs are approximately 38%, 15%, and 30%, respectively, posing challenges for subsequent analysis. To address these challenges, this study employed multiple imputation techniques, as recommended in health economics literature (Austin et al., 2021). Imputed data distributions were analyzed to confirm their validity, and different imputation methods were compared to ensure consistency and robustness in cost-effectiveness results. Special attention was given to the observed variability in SF6D outcomes, particularly its smaller incremental QALY differences, which were further investigated through sensitivity analyses.

Missing Data Imputation

The study primarily utilized the multiple imputation by chained equations (MICE) technique, employing predictive mean matching (PMM) to impute missing data.PMM selects values from similar observations, making it well-suited for both continuous and categorical data while enhancing the robustness of the model (Blankers et al., 2010; Austin et al., 2021). To evaluate the impact of different imputation methods on results, additional imputation strategies were implemented. Random Forest (RF) Imputation, which captures non-linear relationships using decision tree structures, was applied to explore its suitability for handling the dataset's complexity. Hot Deck Imputation, a non-parametric method based on sample similarity, was also tested. The comparison of these methods focused on their influence on QALYs, costs, and ICER outcomes, especially in the context of SF6D's observed instability.

Cost-Utility Analysis

Cost-utility analysis was conducted, including the evaluation of direct costs derived from the 2023 Unit Costs of Health and Social Care by PSSRU. GP visit costs were estimated at £39 per visit, while one-to-one adult physiotherapy sessions were assumed to last two hours, with a cost of £70 per hour (Jones et al., 2024).

To broaden the economic evaluation, a hypothetical societal perspective was introduced. Additional costs included travel expenses estimated at £15 per session (based on HMRC guidelines of £0.5/mile for a 30-mile round trip) (HMRC, n.d.), informal care costs were calculated using the 2023 average hourly market wage of

£15/hour (ONS, 2024), assuming average wages for caring are slightly higher than basic, with family or friends provide five hours of informal care per week. Productivity loss was estimated using the 2023 UK GDP per capita, equivalent to a daily productivity loss of £100 (World Bank, 2023), assuming 10 workdays lost per month due to illness. These societal costs aimed to provide a more comprehensive view of the intervention's economic impact.

QALYs were calculated using the trapezium rule, incorporating utility scores from EQ-5D and SF-6D measured at baseline 0, 3, 12, and 24 months to reflect both the quality and length of life gained. Cumulative QALYs were computed for each patient, and costs and utilities were discounted at a rate of 3.5% as per NICE guidelines.

Sensitivity Analysis

To explore the stability and reliability of the results, sensitivity analyses were conducted. These included comparisons of imputation methods (MICE, RF, and Hot Deck) to assess their impact on QALYs, costs, and ICERs. Additionally, the relationship between willingness-to-pay (WTP) thresholds and cost-effectiveness probabilities was analyzed using cost-effectiveness acceptability curves (CEACs). Particular attention was paid to the variability of SF6D results, as its incremental QALY differences between treatments were small, potentially influencing ICER stability and leading to negative values in some scenarios.

Model Integration

This study integrated NHS and societal perspectives into the analysis framework to compare the incremental costs and QALYs under these perspectives. The societal perspective incorporated additional hypothetical costs, enabling an examination of their influence on cost-effectiveness outcomes. Cost-effectiveness planes and CEACs were generated to visualize the results, highlighting the differences in cost-effectiveness conclusions between EQ5D and SF6D under the two perspectives. These analyses provided a comprehensive basis for policy recommendations.

Results

Missing rates for EQ5D (38%), SF6D (15%), and costs (30%) prompted the use of multiple imputation by chained equations (MICE), a reliable method for missing data (Austin et al., 2021). However, upon completing the analysis, the ICER results for SF6D showed negative values, raising concerns about the stability of SF6D

outcomes. Exploratory analyses were conducted to investigate this.

Primary Analysis Results

The initial analysis of treatment groups revealed that for the standard care group, the mean cost was £768, with mean QALYs of 1.36 (EQ5D) and 1.42 (SF6D). For the enhanced physiotherapy group, the mean cost was £1,310, with mean QALYs of 1.49 (EQ5D) and 1.41 (SF6D). The calculated incremental cost (delta cost) was £542, while the delta QALYs were 0.13 for EQ5D and -0.01 for SF6D. The resulting ICER for EQ-5D was £4,349, which falls significantly below the thresholds of £20,000–£30,000 per QALY on the CEAC, indicating a high probability of cost-effectiveness for enhanced physiotherapy. In contrast, the ICER for SF6D was -£42,790. These results suggested potential cost savings but also reflecting instability in SF6D results. Figures A-C illustrate the analysis results of the primary imputation methods, specifically for QALYs (Figure A), the cost-effectiveness plane (Figure B), and the CEAC (Figure C).

Figure A

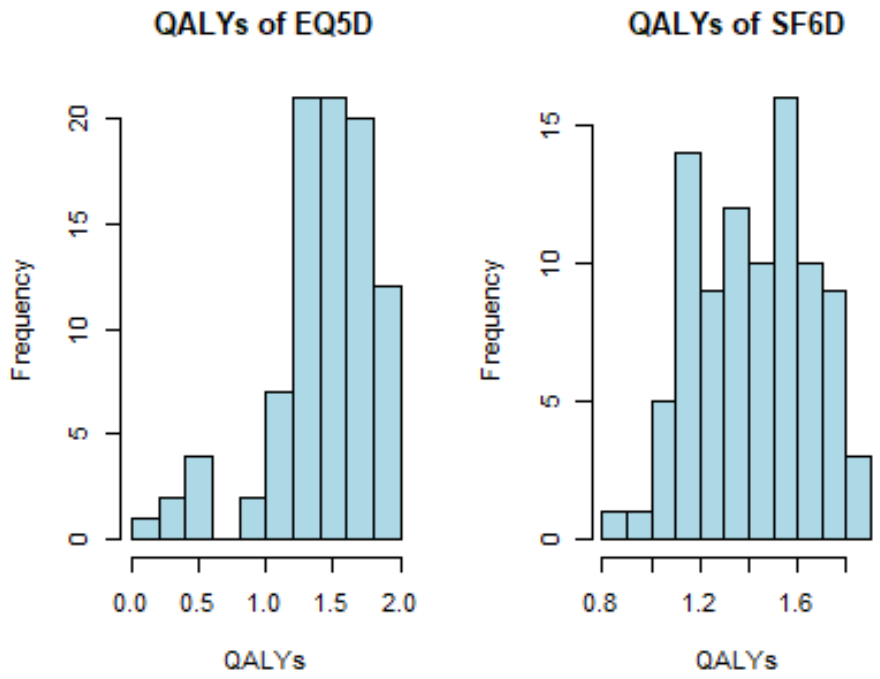
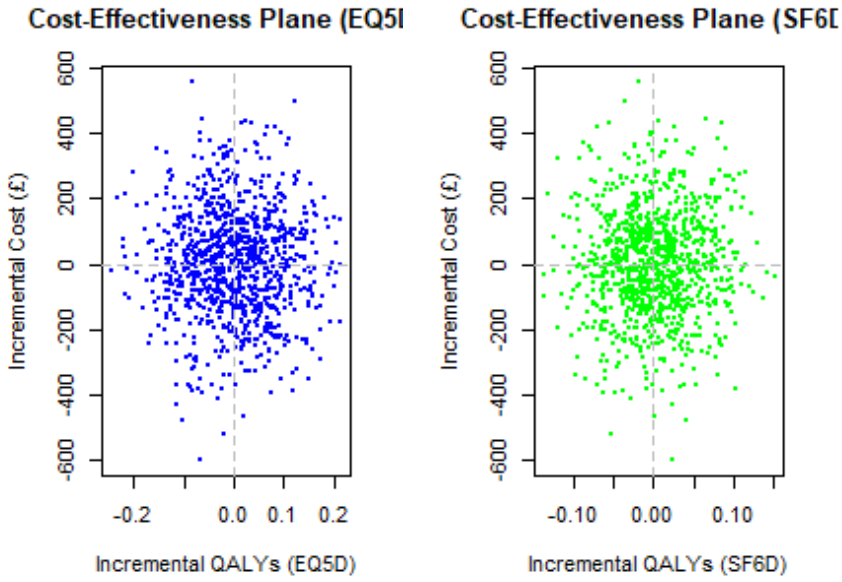
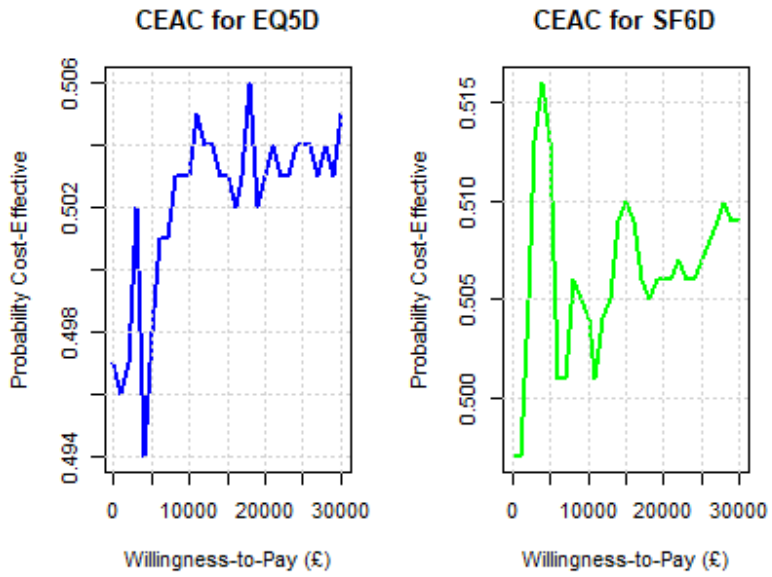


Figure B



FigureC



Data Analysis Before and After Imputation

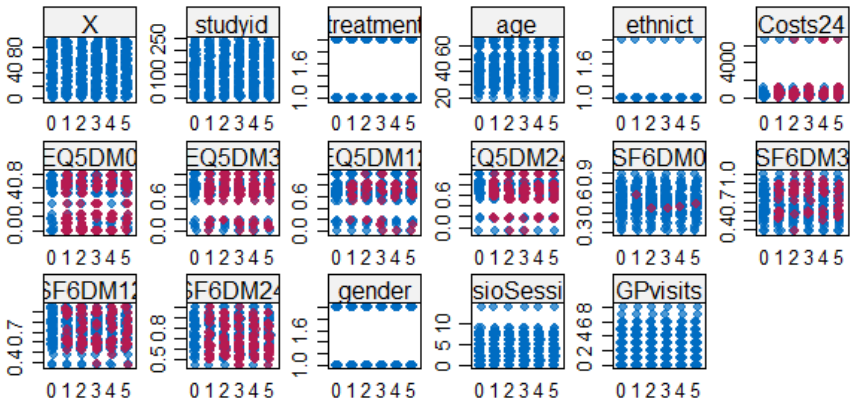
Further inspection of the data showed clear differences in distributions before and after imputation. For EQ5D, the imputed values filled significant gaps, especially in the lower utility ranges, resulting in a smoother and more balanced pattern. On the other hand, SF6D had fewer missing values, so its distribution changed less. However, the imputed SF6D data showed more variability than EQ5D, with smaller

incremental QALY differences (-0.01 for SF6D vs. 0.13 for EQ5D), which may explain the negative ICERs observed.

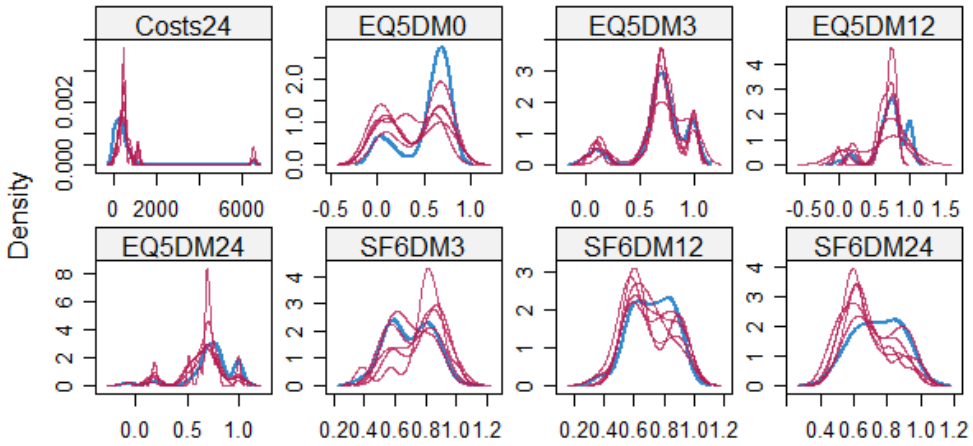
Before imputation, the ICERs were £152.62 for EQ5D and £229.74 for SF6D, based on incremental QALYs of 0.038 (EQ5D) and 0.026 (SF6D) with a delta cost of £5.87. After imputation, the ICER for EQ5D increased to £4,349, showing more stable cost-effectiveness results. In contrast, the ICER for SF6D became -£42,790, highlighting its instability due to the smaller QALY differences. This suggests that SF6D may not be as sensitive as EQ5D in capturing changes in health outcomes.

Figures D and E show the data distributions before and after imputation. The EQ5D results became smoother and more consistent, while the SF6D results showed more variation.

Figures D



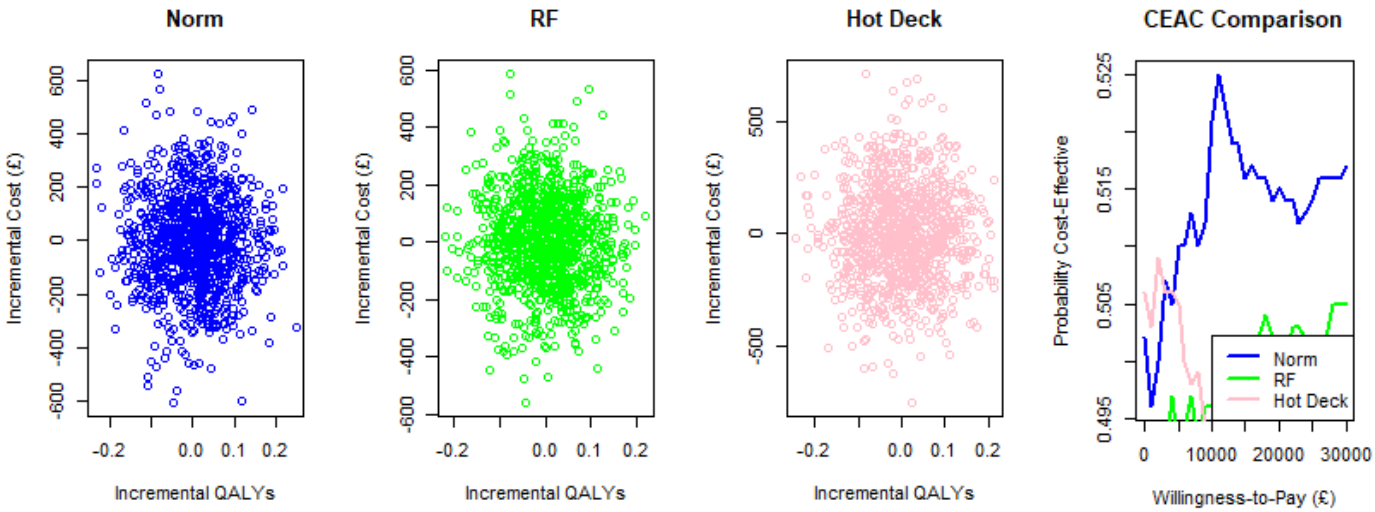
Figures E



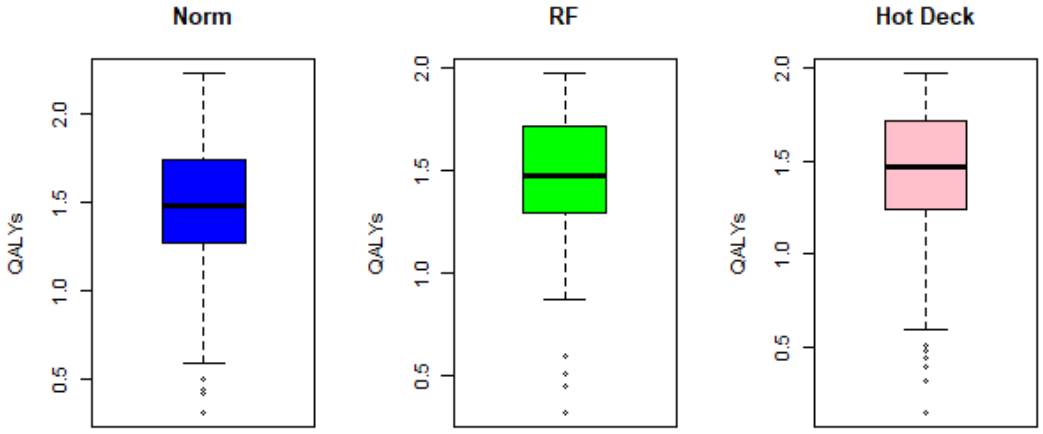
Comparison of Imputation Methods

A sensitivity analysis comparing three imputation methods—MICE (Norm), Random Forest (RF), and Hot Deck—was conducted. The results indicated that MICE provided the most consistent estimates, with mean QALYs of 1.46 (EQ5D) and mean total costs of £947.49. In contrast, RF yielded slightly lower mean QALYs (1.44) and total costs (£944.67), while Hot Deck produced the highest total costs (£1,048.88) but lower mean QALYs (1.42). Figures F and G present the cost-effectiveness results under different imputation methods. Despite these differences, the overall trends in ICERs were similar across methods, suggesting that the choice of imputation method did not substantially alter the conclusions.

Figures F



Figures G

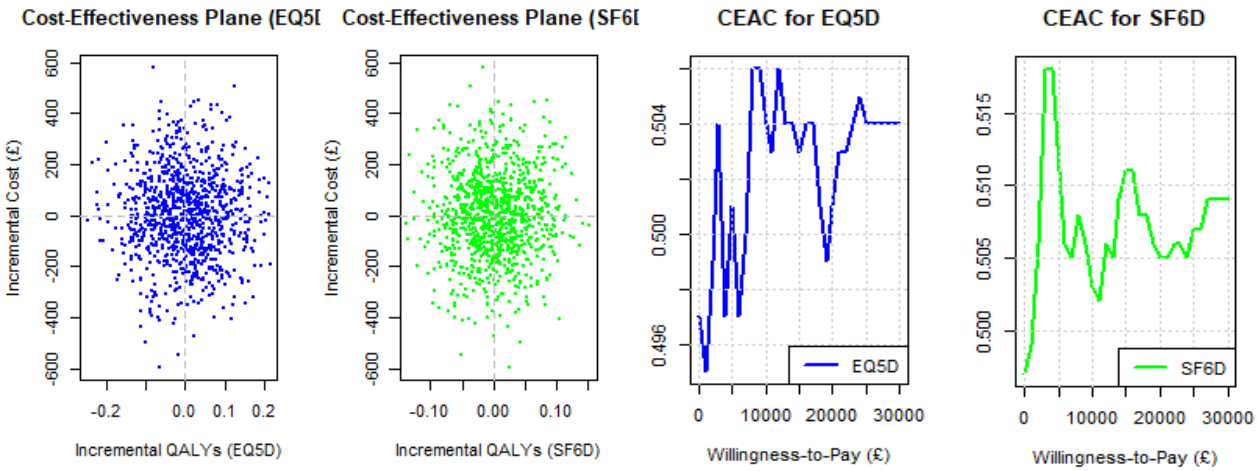


Societal Perspective Analysis

To account for broader economic implications, a societal perspective was introduced. This included additional costs such as travel (£15 per session), informal care (£30 per session), and productivity loss (£50 per workday). Under this perspective, the mean societal costs for the enhanced physiotherapy group rose to £7,846, compared to £7,233 for standard care. The mean QALYs remained consistent, with EQ5D at 1.49 for enhanced physiotherapy and 1.36 for standard care, while SF6D values slightly diverged, with 1.41 for enhanced physiotherapy and 1.42 for standard care. The resulting ICERs for EQ5D increased to £4,913, reflecting the added societal costs, while the ICER for SF6D remained negative (-£48,333), further highlighting its instability.

The cost-effectiveness acceptability curves (CEACs) under the societal perspective indicated a higher probability of cost-effectiveness for EQ5D compared to SF6D at various willingness-to-pay thresholds. Figure H presents the utility results after incorporating costs from a societal perspective. This reinforced the conclusion that SF6D may lack sensitivity to small health outcome differences and is more prone to variability when additional costs are considered.

Figure H



Discussion

The comparison of EQ-5D and SF-6D utility measures in this study highlights critical differences that influence their application in cost-effectiveness analysis. EQ-5D is often regarded as more sensitive to detecting changes in severe health conditions, such as motor neuron disease (MND), whereas SF-6D tends to perform better in capturing moderate health states (Brazier et al., 2004). This sensitivity difference may explain why the results for EQ-5D were more stable across imputation methods, while SF-6D produced negative ICER values in certain scenarios. The smaller incremental QALY differences for SF-6D between treatment groups (e.g., 0.703 vs. 0.678) suggest that it may lack precision in reflecting the benefits of enhanced physiotherapy, leading to unstable or counterintuitive cost-effectiveness results.

From a practical standpoint, the calculated QALY values have significant implications for assessing the economic viability of high-intensity physiotherapy for MND patients. Using EQ-5D results, the ICER of £4,913 (under the societal perspective) is significantly lower than the willingness-to-pay thresholds of £20,000–£30,000 per QALY observed on the CEAC. This suggests a high probability that enhanced physiotherapy is a cost-effective intervention from an NHS perspective, supporting its potential implementation. The findings align with evidence suggesting that such interventions improve patients' quality of life and reduce healthcare costs by delaying complications and prolonging independence (Moore et al., 2016). However, the societal perspective introduces broader costs, such as travel and informal care, which policymakers must consider when planning resource allocation.

Despite these positive findings, the observed variability and smaller QALY differences in SF-6D (-0.01) highlight its limitations in capturing the full benefits of enhanced physiotherapy for MND. While EQ-5D appears more reliable for this context, the choice of utility measure still depends on the specific research objectives. The inherent differences in sensitivity between EQ-5D and SF-6D mean that neither fully captures the multifaceted impact of MND on patients’ lives, particularly in domains such as mental health or caregiver burden. This limitation raises questions about whether existing QALY tools adequately reflect the unique challenges of evaluating interventions for rare and progressive diseases like MND.

Future research should address these gaps by exploring more tailored utility measures or combining multiple approaches to capture a comprehensive picture of health outcomes. Policymakers should consider the variability in ICERs, particularly for SF-6D, when using these results to guide resource allocation decisions for MND interventions. Incorporating real-world evidence and conducting longer-term studies could enhance the robustness of economic evaluations and strengthen the case for supporting enhanced physiotherapy. Overall, while this study supports the economic and clinical value of enhanced physiotherapy, further methodological improvements and broader perspectives are needed to ensure that health economic evaluations effectively inform NHS policy and resource allocation.

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