Introducing the Four Dimensions 4D Migraine Scale: A Composite Score Proposal Evaluating Migraine Severity and Treatment Efficacy

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INTRODUCTION

Different measures are currently used to evaluate migraine frequency and disability, but a single measure may only partially represent the burden of migraine. A composite measure that includes the most relevant parameters, obtained through a statistically weighted approach, would better assess migraine severity and treatment efficacy.

OBJECTIVES

This study aimed to develop a composite "four dimensions (4D) migraine scale" by selecting four commonly used endpoints: monthly migraine days (MMDs), number of monthly acute medications (MAMs), attack pain intensity (Numerical Rating Score, NRS), and Migraine Disability Assessment (MIDAS) Score.

METHODS

For each parameter, specific levels were chosen to cover the entire empirical range of each scale.

To estimate utilities and develop the 4D migraine scale, a series of pairwise choice tasks were generated using Lighthouse Studio, a Conjoint Analysis platform. In these tasks, respondents (patients and clinicians) were presented with two hypothetical migraine patient profiles, described by scale parameters, and asked to identify the patient in better health.

The design of the Discrete Choice Experiment (DCE) aimed for orthogonality and balance, meaning attribute levels should vary independently and occur equally often. However, a perfectly orthogonal and balanced design was not feasible due to the generation of unrealistic combinations, such as a patient with one monthly migraine day (MMD=1) taking more than 14 symptomatic medications or having a MIDAS score ≥ 16 points. To address this, expert clinicians identified and prohibited certain implausible combinations. Although prohibitions hinder a perfectly orthogonal and balanced design, statistical procedures were applied to adjust for these discrepancies.

The sample size was determined using Orme's formula, $n \geq 500b/(ac)$. With two alternatives ($a=2$), the largest attribute having seven levels (MAMs, $b=7$), and 12 choice tasks ($c=12$), a minimum sample size of 146 was calculated. Furthermore, simulations using Lighthouse Studio software estimated that the standard errors of the effects for each level, with 300 respondents, were consistently below the recommended threshold of 0.05.

For statistical analysis, discrete choices from patients and clinicians were used to estimate the utilities attributed to each attribute level. This estimation was performed using the Hierarchical Bayes algorithm within Lighthouse Studio. Positive utility values were indicated by values above a reference line of 0, while negative utility (disutility) was indicated by values less than 0. These utility measures were then regressed against the levels of each scale to identify polynomial models that best interpolated the relationship between scores and utility. A log-transformation was applied to MIDAS utilities to account for its lognormal distribution and mitigate outlier bias. Polynomial models were ap-

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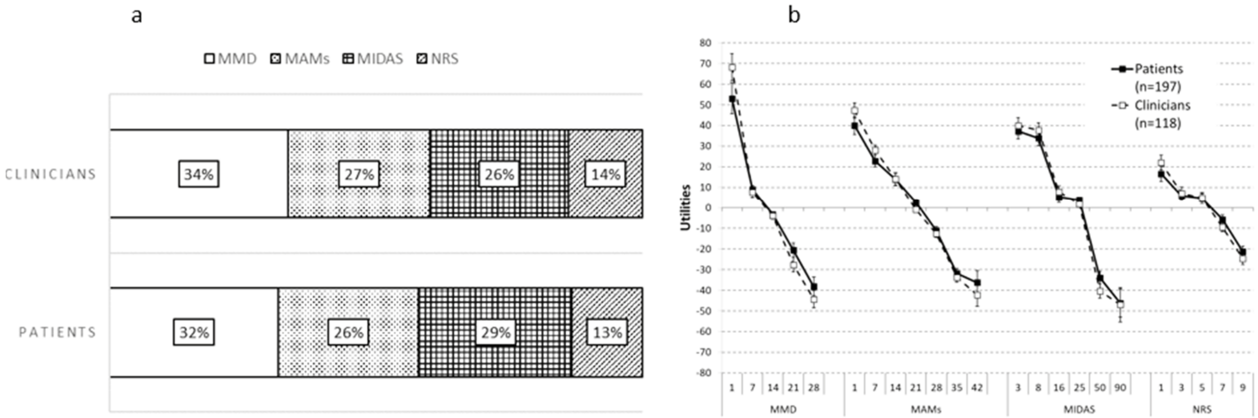
plied within a General Estimating Equations framework, treating each respondent as a "cluster" with an "unstructured" working correlation matrix. Finally, an overall composite score, weighted by utility, was computed and standardized to a 0-100 scale, representing a range from a patient without migraine to a patient with the most severe migraine condition.

RESULTS

The relative weight of each level per parameter was rated by 197 migraine patients and 118 headache experts using Conjoint Analysis. A substantial agreement was found between clinicians and patients regarding the relative importance (RI) of each parameter. MMDs was identified as the most important attribute for both categories (RI: 34% for clinicians, 32% for patients), while PAIN-NRS was the least important (RI: 14% for clinicians, 13% for patients). MIDAS was marginally more important than MAMs for patients (29% vs. 26%), while for clinicians, their relevance was almost equal (26% and 27%). The strong agreement between clinicians and patients was also confirmed in terms of the utility assigned to each level.



Polynomial models were developed to estimate the utilities for each scale:

- Utility_MMD = 68.48 - 11.52 MMD + 0.582 MMD2 - 0.011 MMD3
- Utility_MAMs = 43.57 - 1.96 MAMs
- Utility_MIDAS = 51.43 - 4.836 (loge(MIDAS + 1))
- Utility_NRS = 28.85 - 11.33 NRS + 1.916 NRS2 - 0.144 NRS3

A composite raw 4D score was calculated as: 4D score raw = -(Utility_MMD + Utility_MAMs + Utility_MIDAS + Utility_NRS) / 4 and finally a more intuitive and clinically relevant score ranging from 0 to 100 (0 = no migraine, 100 = most severe migraine) was derived using: 4D score = 100 (4D score raw + 48.1) / 110.7

The 4D score was applied to a sample of 205 migraine patients treated with galcanezumab. It demonstrated sensitivity to changes, effectively summarizing the treatment's effect with a larger effect size compared to single parameters (eta-squared = 0.685). The 4D score also showed concurrent validity with the Head Impact Test HIT-6, an external patient-reported outcome measure.

CONCLUSION

This composite score, based on the preference weights of both clinicians and patients, can serve as a valuable Patient-Reported Outcome to comprehensively quantify migraine burden and treatment efficacy. The study highlights the importance of a multi-dimensional approach to migraine assessment, as single measures often fail to capture the full complexity of the condition and treatment response.

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