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Estimating the minimal clinically important difference for the Myasthenia Gravis Quality of Life revised scale (MG-QOL15R)

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Abstract

Purpose To estimate the minimal clinically important difference (MCID) for the MG-QOL15R.

Methods Data from two multi-country myasthenia gravis studies were used: the ADAPT RCT (n = 157) and the MyReal-World-MG (MRW-MG) survey (n = 92). MCIDs were estimated using four anchor-based methods: change difference (CD), receiver operating characteristic (ROC) curve with Area Under the Curve (AUC), linear regression, and equipercentile linking. MG-Activities of Daily Living (MG-ADL) was the anchor. MCIDs were applied to the ADAPT RCT to assess the impact of different thresholds. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to estimate the odds of achieving an MCID threshold at week 4 in the efgartigimod arm compared with placebo among patients positive for acetylcholine receptor antibodies.

Results Baseline mean age was 46.7 years old in ADAPT and 49.8 years old in MRW-MG; women comprised 71.3% and 71.7%, respectively. ADAPT included only generalized MG, while MRW-MG included 12.0% ocular and 88.0% generalized MG. Average disease severity (MG-ADL 9.0 vs. 6.3) and HRQoL impairment (MG-QOL15R 16.3 vs. 12.0) were greater in ADAPT. MCID estimates were: CD (ADAPT 1.6; MRW-MG 2.8), ROC (both 2.5, AUCs 0.66; 0.71), linear regression (2.1; 1.6), and equipercentile linking (2.0; 3.0). Applying MCIDs of ≥2.0 and≥3.0 resulted in ORs of 3.31 (95%CI 1.65–6.87) and 4.14 (95%CI 2.11–8.38).

Conclusions MCID estimates ranged between 1.6 and 3.0 across both studies. MCID thresholds of 2- and 3-points may indicate a minimal clinically meaningful change for monitoring progress and guiding treatment. Future research should use patient global impression of change anchors to improve interpretability and clinical relevance of MCID estimates.

Plain English summary

People with Myasthenia Gravis (MG), a rare disease that causes muscle weakness, often face problems that affect their daily lives and overall well-being. To better understand how MG impacts people and whether treatments are working, health professionals use a questionnaire called the MG-QOL15R. This tool captures key aspects of patients' experiences with MG. However, it is unclear how much a person's score needs to change for that change to be considered meaningful. This study looked at how much change in the MG-QOL15R score is needed to reflect a real difference in someone's health. We used data from two international studies involving people living with MG and tested different ways to determine what amount of change matters to patients. We found that a change between 2 and 3 points on the MG-QOL15R is likely to be minimally meaningful. Smaller changes may reflect early improvement, while larger changes are more reliable for guiding treatment decisions. These findings can help doctors, researchers, and policymakers understand whether a treatment is truly helping people with MG feel better.

Keywords Minimal clinically important difference · Myasthenia gravis · Quality of life

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Introduction

A minimal clinically important difference (MCID) is the smallest score change in a measure of interest (e.g. clinical or health-related quality-of-life [HRQoL]) that patients perceive as beneficial [1, 2]. The use of MCID has been increasingly adopted by clinicians, researchers, and policymakers to evaluate whether an observed change over time represents treatment benefit or a meaningful improvement from patients' perspective.

Myasthenia Gravis (MG) is a rare autoimmune neuromuscular condition characterized by fluctuating muscle weakness that affects the extraocular, bulbar, respiratory, and limb muscles. As a result, patients' physical functioning, energy levels, and mental health are often impacted. The disease is typically managed with immunosuppressants, acetylcholinesterase inhibitors, or surgical options such as thymectomy [3]. The revised version of the Myasthenia Gravis Quality of Life scale (MG-QOL15R) is a condition-specific, HRQoL measure that assesses important aspects of patients' experience [4]. Widely used in both routine clinical care to guide treatment decisions and in clinical trials to evaluate the effectiveness of treatments, it was designed to be interpreted as the simple sum of fifteen item responses [4]. Its refinement, from a five- to a three-level response format, was based on Rasch analysis, which improved the scale's measurement precision by ensuring that each item contributes meaningfully to the total score and that score differences reflect differences in HRQoL [4].

Determining the MCID for the MG-QOL15R is relevant as it provides essential evidence for approval of health technologies and reimbursement decisions, supporting resource allocation based on HRQoL from the patients' perspective [5]. Although the MCID for the MG-QOL15R has not yet been established, the MCID for the MG-activities of daily living (MG-ADL) [6], a patient-reported outcome measure (PROM), is currently in use and is required for many US payers when approving, initiating, or continuing MG treatments [7].

While the MG-ADL is crucial for assessing functional status from a patient perspective (i.e., mobility or difficulty of daily tasks), the MG-QOL15R provides a complementary measure by helping to evaluate how patients feel about their overall health and disease burden, including physical, mental and social health [8]. This study, therefore, aimed to estimate the MCID for the MG-QOL15R using anchor-based methods, with MG-ADL as an anchor.

Methods

Study design

This is a cross-design comparative study to estimate the MCID for the MG-QOL15R using two different data sources: a randomized controlled trial (RCT) (ADAPT), and a longitudinal survey (MyRealWorld-MG [MRW-MG]). The two data sources focused on the MG population and included both the MG-QOL15R and MG-ADL at baseline and at follow-up.

Data sources

The ADAPT is a multicenter randomized, double-blind, placebo controlled, phase 3 trial of efgartigimod conducted in 15 countries (the United States [US], Canada, Italy, Germany, France, Belgium, Denmark, the Netherlands, Poland, Hungary, the Czech Republic, Georgia, Serbia, Russia, and Japan). In total, 167 adult patients with generalized MG were eligible to participate in the study according to the inclusion criteria: MG-ADL score ≥ 5 and on a stable dose of one or more treatments for generalized MG (acetylcholinesterase inhibitors, corticosteroids, or non-steroidal immunosuppressive therapies). Patients were randomized in a 1:1 ratio to efgartigimod (10 mg/kg) or matching placebo and followed up to 5 months between September 2018 and November 2019 [9].

The MRW-MG is a prospective, observational, digital, longitudinal survey conducted in 10 countries (US, Canada, Italy, Germany, France, Belgium, Denmark, Spain, UK, and Japan) in adults diagnosed with MG. Respondents were enrolled via patient advocacy groups, and were asked to enter data monthly using a mobile application, over a 3-year period. The only exclusion criterion was age (≤ 18 years). In total, 2,406 participants responded to the survey between January 2020 and January 2023 [10, 11].

Questionnaires

The MG-QOL15R [4] is a 15-item questionnaire designed to measure HRQoL domains in patients with MG, namely: emotions (3 items), physical health (4 items), self-care (4 items), social life (3 items), and impact on role (1 item). Each item has 3 response levels (i.e., not at all, somewhat, or very much) and the total score ranges from 0 to 30. A lower score indicates better HRQoL. In both studies, the MG-QOL15R was completed by patients after completing MG-ADL at baseline and follow-up.

The MG-ADL [6] is an 8-item questionnaire that assesses functional status, i.e., the ability to perform daily activities (talking, chewing, swallowing, breathing, ability to brush

teeth or comb hair, ability to rise from a chair, double vision and eyelid droop). Item scores range from 0 to 3 and the total score ranges from 0 to 24. A score of 0 indicates no difficulty in performing daily activities. A score of 24 indicates severe impairment. For descriptive analysis, MG-ADL score was categorized based on the literature into severity levels as follows: mild (0–4), moderate (5–9), and severe (≥10) [9, 11, 12].

Other variables

Both studies included data on age, sex, country of residence, and the Myasthenia Gravis Foundation of America (MGFA) Clinical Classification (I–V), reported at MG diagnosis by patients in MG-MRW and by investigators in ADAPT. MGFA classes range from I (eye muscle weakness only) to V (intubation, with or without ventilation), with classes II–IV indicating increasing severity of non-eye muscle weakness [12].

Statistical analysis

Descriptive analyses were conducted separately for each study. Continuous variables were summarized using mean (SD) or median (IQR), and categorical variables as counts and percentages. Countries were grouped as Europe, Russia, Japan, US, and Canada. The MRW-MG survey included additional comorbidities (yes/no), whereas this was not collected in ADAPT. MG type was defined using MGFA (ocular: class I; generalized: classes II–V), and treatment status (yes/no) was self-reported in MRW-MG. Details on treatment types are available elsewhere [11].

The analysis used baseline to 4-week changes in ADAPT and baseline to 4-month changes in MRW-MG. ADAPT's shorter follow-up reflected its active intervention, while MRW-MG participants, mostly on stable treatment, required a longer period to capture meaningful change. Participants with missing MG-ADL or MG-QOL15R data were excluded. Spearman's rank correlation assessed the association between changes in MG-QOL15R and MG-ADL. Correlation strength was interpreted as follows: none (<0.10), weak (0.10–0.29), moderate (0.30–0.49), and strong (≥0.50) [13].

Given the absence of a gold standard for MCID estimation and the variety of available methods [14]—each with its own strengths and limitations—we opted to apply four anchor-based methods. Anchor-based methods were employed as they aim to reflect changes in scores perceived as meaningful by patients. The following anchor-based approaches were applied: change difference, Receiver Operating Characteristic (ROC) curve, linear regression, and equipercentile linking—using the MG-ADL score as an anchor for patients' perceived improvement [14, 18, 19]. Bias-corrected and accelerated 95% confidence intervals (CIs) for the MCID estimates were derived using bootstrapping with 10,000 resamples [20].

The MG-ADL was used as an anchor, as it is widely employed by clinicians to monitor disease progression, demonstrates strong correlation with patients' perceived functional status [21], and served as a proxy in the absence of patient-reported global ratings of change in the available data sources. We categorized change from baseline in groups as follows: i) great improvement: a≥3-point decrease in MG-ADL scores from baseline; ii) minimal improvement: a 2-point decrease in MG-ADL scores from baseline, considered minimally clinically meaningful; iii) no change or stable: a maximum of 1-point decrease, no change, or 1-point increase in MG-ADL scores from baseline, indicating no meaningful change; iv) deterioration: a 2-point increase in MG-ADL scores from baseline, indicating clinical deterioration [9–11]. For the MCID estimation using change difference and ROC methods, we compared the minimal improvement group to the stable group to ensure that observed changes reflected meaningful improvements and not symptom deterioration.

MCID estimation methods

Change difference was used to estimate the MCID by comparing the average change in MG-QOL15R scores between participants with minimal improvement in MG-ADL scores and those with no change [9–11]. The MCID was then estimated as the difference between the mean change $(\overline{x})$ in both groups, as shown in the formula below.

$$MCID_{CD} = \overline{x}_{minimalimprovement} - \overline{x}_{stable}$$

The ROC curve was used to identify the optimal threshold in the MG-QOL15R score that best discriminates between participants with minimal improvement in MG-ADL scores and those with no change [14]. Cases with great improvement (≥3-point decrease in MG-ADL) or deterioration (≥2-point increase in MG-ADL) were excluded to ensure that the analysis focused specifically on detecting minimal but meaningful change. The optimal threshold for the MCID is the point that maximizes both sensitivity and specificity, correctly identifying those with a meaningful change in MG-QOL15R. The discriminative ability (or accuracy) of this threshold was evaluated using the area under the ROC curve (AUC) and its respective 95% confidence interval (95%CI). An AUC between 0.50 and 0.59 indicates no discrimination (i.e., performance no better than chance), values between 0.60 and 0.69 are considered to reflect poor discrimination, 0.70 to 0.79 indicate acceptable discrimination,

0.80 to 0.89 are considered very good, and values of 0.90 or higher reflect excellent discrimination [22].

A univariable linear regression analysis was used to estimate the change in MG-QOL15R score associated with a change in the MG-ADL score [18]. A 2-point improvement from baseline in the MG-ADL score was used as a clinically meaningful anchor, thus MCID = $\beta_1 \times 2$.

The model was specified as:

$$MGQOL15r_{change} = \beta_0 + \beta_1 \times MGADL_{change} + \varepsilon$$

where $MGQOL15r_{change}$ and $MGADL_{change}$ represent the change between the last scores and the baseline scores; β_0 is the intercept; β_1 is the estimated change in MG-QOL15R per 1-point change in MG-ADL. ε represents the residual error, i.e., the part of MG-QOL15R change not explained by the MG-ADL change. A multivariable linear regression analysis was also conducted to evaluate the influence of age, sex, and country on the estimated MCID.

Equipercentile linking was used to estimate the MCID on an outcome scale (i.e., MG-QOL15R) by identifying the percentile rank of a known meaningful change on an anchor scale (i.e.,≥2-point decrease in MG-ADL), and then finding the value on the outcome scale that corresponds to the same percentile [19]. This approach assumes that scores on different scales can be meaningfully compared based on their relative positions within their respective distributions [19].

Table 1 Baseline characteristic of the study populations

Baseline characteristics	ADAPT, n = 157	MRW-MG, N = 92
Age (years), mean (SD)	46.7 (14.7), n = 157	49.8 (13.9), n = 85
Sex: Female, n (%)	112 (71.3), n = 157	66 (71.7), n = 92
Europe, n (%)	99 (63.1), n = 157	61 (66.3), n = 92
Russia, n (%)	6 (3.8), n = 157	x
Japan, n (%)	14 (8.9), n = 157	6 (3.5), n = 92
United States, n (%)	35 (23.3), n = 157	24 (26.1), n = 92
Canada, n (%)	3 (1.9), n = 157	1 (1.1), n = 92
Comorbidities, n (%)	x	58 (63.0), n = 90
MGFA, n (%)		
Not known	0 (0.0), n = 157	1 (1.1), n = 90
Class I	0 (0.0), n = 157	13 (14.4), n = 90
Class II	60 (38.5), n = 157	19 (21.1), n = 90
Class III	91 (58.3), n = 157	42 (46.7), n = 90
Class IV	5 (3.2), n = 157	14 (15.6), n = 90
Class V	0 (0.0), n = 157	1 (1.1), n = 90
Ocular MG, n (%)	0	11 (12.0), n = 90
Generalized MG, n (%)	157 (100.0)	81 (88.0), n = 90
MG-ADL categories, n (%)		
Mild (0–4)	0	38 (41.3%), n = 92
Moderate (5–9)	100 (63.7), n = 157	34 (34.0%), n = 92
Severe (>= 10)	57 (36.3), n = 157	20 (21.7%), n = 92
MG-ADL, mean (SD)	9.0 (2.4), n = 157	6.3 (4.5), n = 92
MG-QOL15R, mean (SD)	16.3 (6.1), n = 157	12.0 (7.1), n = 92

SD, standard deviation; n, number of participants with complete data; %, proportions; x, information not collected; MGFA, Myasthenia Gravis Foundation of America Clinical Classification

Empirical application

The obtained MCID estimates were applied to the ADAPT RCT [9] to assess the impact of using different thresholds. The outcome of this study was the proportion of acetylcholine receptor antibody positive patients who achieved the estimated MCID thresholds at week 4. The outcome was tested by means of a two-sided exact test using a logistic regression model adjusted by MG-QOL15R baseline score and three pre-specified stratification factors in ADAPT: acetylcholine receptor antibody status (positive vs. negative), non-steroidal immunosuppressive therapies (taking vs. not taking), and Japanese nationality (yes vs. no). These factors were used in ADAPT's stratified randomization to support balance and consistency of effect across antibody status, background therapy, and ethnicity; adjusting for them aligns with the trial design and improves precision of the treatment-effect estimate [9]. The treatment effect based on each MCID threshold was presented as an odds ratio (OR) with 95% CI and two-sided p value. ORs represent the odds of achieving an MCID threshold at week 4 in the efgartigimod arm compared with placebo among patients positive for acetylcholine receptor antibodies.

Results

Participants

A total of 157 out of 167 participants in the ADAPT RCT and 92 out of 2,406 respondents to the MRW-MG survey had completed MG-ADL and MG-QOL15R data at both baseline and pre-defined follow-up. Baseline characteristics of participants included in the analysis were relatively similar to those of the full cohorts (Online Resource 1). At baseline, the MRW-MG population was slightly older, with similar proportions of women compared to ADAPT (Table 1). Most participants from both studies were from Europe. The MRW-MG cohort included both ocular MG (MGFA class I, n = 13, 14.4%) and generalized MG (MGFA classes II-V), n = 76, 84.4%). Most participants of the MRW-MG survey reported to be on some type of MG treatment (n = 86, 95.6%). Due to inclusion criteria, ADAPT participants presented higher MG-ADL and MG-QOL15R scores, indicating more severe condition and worse HRQoL, compared to MRW-MG participants at baseline. No significant differences in MG-ADL and MG-QOL scores were found between patients with complete and missing data at baseline (Online Resource 2),

Table 2 MG-QOL15R mean and median change by MG-ADL groups

MG-QOL15R	ADAPT, n = 157				MRW-MG, n = 92			
	MG-ADL groups				MG-ADL groups			
	Great n = 87	Min n = 16	Stable n = 49	Det n = 5	Great n = 6	Min n = 7	Stable n = 67	Det n = 12
Mean change (SD)	−7.2 (5.5)	−2.8 (2.7)	−1.2 (3.4)	−3.4 (4.3)	−2.3 (2.8)	−2.6 (4.1)	0.2 (2.6)	2.1 (4.3)
Median change (IQR)	−7.0 (−10.5; −3.0)	−3.0 (−4.2; −0.7)	−1.0 (−3.0; 1.0)	−2.0 (−8.0; 0.0)	−2.5 (−4.7; −1.0)	−3.0 (−4.0; −0.5)	0.0 (0.0; 0.0)	0.5 (−1.0; 2.7)

Great improvement: a ≥ 3-point decrease in MG-ADL scores from baseline, considered a substantial improvement. Minimal improvement (Min): a 2-point decrease in MG-ADL scores from baseline, considered minimally clinically meaningful. Stable: a maximum of 1-point decrease, no change or a 1-point increase in MG-ADL scores from baseline, considered no meaningful change. Deterioration (Det): a ≥ 2-point increase in MG-ADL scores from baseline, indicating clinical deterioration

Table 3 MCID results

MCID methods	ADAPT, MCID (95% CI)	MRW-MG, MCID (95% CI)
Anchor-based		
Change difference	1.6 (0.1; 3.3)	2.8 (0.3; 5.9)
ROC curve threshold	2.5 (2.5; 4.5)	2.5 (2.0; 4.5)
Linear regression analysis (univariable)	2.3 (1.8; 2.7)	1.6 (0.6; 2.7)
Linear regression analysis (multivariable)	2.1 (1.7; 2.6)	1.6 (0.6; 2.7)
Equipercentile linking	2.0 (2.0; 4.0)	3.0 (3.0; 5.0)

MCID, minimal clinically important difference. Multivariable regression analysis adjusted for age, sex, and country. CI: confidence interval

suggesting data are unlikely to be missing at random; therefore, no imputation of missing values was performed.

In the ADAPT cohort, 10.2% (n = 16) participants were classified as having minimal improvement from baseline, 31.2% (n = 49) as stable, and most participants had great improvement (55.4%, n = 87) (Table 2). In the MRW-MG cohort, 7 (7.6%) were classified as having minimal improvement from baseline and most (72.8%, n = 67) were stable.

The correlations between changes in MG-ADL and MG-QOL15R scores were strong in the ADAPT RCT while moderate in the MG-MRW survey (ADAPT r = 0.64; MRW-MG r = 0.46, Online Resource 3). Online Resource 4 shows the distribution of changes in MG-QOL15R scores in the full population and in the minimal improvement group. In ADAPT, both groups were left-skewed and peaked near –5, indicating improvement, with the minimal improvement group more concentrated in the negative range. In MRW-MG, both groups peaked near 0, with slight right skew and a flatter shape, suggesting overall stability and mild deterioration. Due to differences in MG-QOL15R score distributions across MG-ADL groups, distinct baseline characteristics, varying follow-up periods, and differing associations between changes in MG-ADL and MG-QOL15R, pooling data from the two studies was deemed inappropriate.

Table 4 MCID estimates applied to the ADAPT RCT at Week 4

MCID estimates	Efgartigimod group	Placebo group	OR (95% CI)	*p* value
≥2.0	61/78 (78.2%)	42/79 (53.2%)	3.31 (1.65; 6.87)	< 0.0001
≥3.0	56/78 (71.8%)	31/79 (39.2%)	4.14 (2.11; 8.38)	< 0.0001

MCID, minimal clinically important difference; OR, odd ratio; CI, confidence interval

MCID results

MCID estimates ranged between 1.6 and 3.0 (Table 3). Methods produced different MCID point estimates across approaches and between studies, except for the ROC-based thresholds were identical (2.5 in both studies); however, these differences were not statistically significant, as indicated by overlapping 95% confidence intervals. ROC-based MCID thresholds yielded an AUC of 0.66 (95% CI 0.51–0.81) in ADAPT and 0.71 (95% CI 0.42–1.00) in MRW-MG, indicating poor to acceptable discrimination and greater uncertainty in the MRW-MG survey, as reflected by the wider confidence interval.

Empirical application

We applied integer values of 2 and 3 as MCID thresholds because the MG-QOL15R scale uses whole numbers, making decimal values impractical and clinically meaningless. Using an MCID estimate ≥ 2.0, 78.2% (61/78) of acetylcholine receptor antibody-positive patients receiving efgartigimod achieved this threshold at week 4, compared to 53.2% (42/79) in the placebo group (Table 4). With stricter MCID threshold ≥ 3.0, 71.8% (56/78) of patients in the efgartigimod arm achieved this threshold, vs. 39.2% (31/79) in the placebo arm. The odds of efgartigimod being effective compared to placebo were significant for all MCID estimated thresholds and modestly increased with higher MCID (from 3.31 to 4.14, ~ 25% increase).

Discussion

Main findings

This study estimated the MCID for the MG-QOL15R using four different anchor-based methods—change difference, ROC curve, linear regression, and equipercentile linking—across the ADAPT RCT and the MRW-MG survey. Overall, MCID estimates ranged from 1.6 to 3.0 across both studies. Empirical application results showed that a 2- or 3-point change in MG-QOL15R may be considered a minimally meaningful change.

Explanation of findings

The higher MCID point estimates for the change difference and equipercentile linking methods in MRW-MG suggest that, outside clinical trials, larger MG-QOL15R changes may be required to be perceived as meaningful. In contrast, the lower regression-based MCID estimates in MRW-MG compared with ADAPT suggest the opposite. The observed variation in MCID estimates may be attributable to the limited sample size employed in their estimation. Despite identical ROC-based MCID estimates, the wide confidence interval in MRW-MG likely reflects fewer patients with minimal improvement, greater response variability, and a moderate anchor-outcome correlation, all of which would reduce AUC precision and the robustness of the threshold. In contrast, ADAPT's more homogeneous sample and stronger correlation produced a more stable estimate. However, both studies showed poor to acceptable classification accuracy, suggesting that the ROC-derived thresholds should be interpreted with caution and complemented by other methods when defining meaningful change. As the MG-QOL15R scoring captures change in 1-point increments, the empirical finding of 2- or 3-point change may be considered a minimally meaningful change.

Comparison with the literature

Comparison with existing literature is limited by the lack of established MCID estimates for the MG-QOL15R, as acknowledged by MG experts [5, 12, 23]. To the best of our knowledge, only two studies have compared changes in MG-QOL15 scores with other clinical anchors, albeit it for the version with five-level of responses. These anchors were the Myasthenia Gravis Composite (MGC) and the Quantitative Myasthenia Gravis Score (QMGS), both clinician-rated measures of disease severity. Burns et al. reported that MG-QOL15 scores changed more in patients who improved, as defined by a $\geq$3-point improvement in MGC, and found a moderate correlation between MG-QOL15 and MGC score changes (r = 0.53) [8]. In another study, a RCT comparing intravenous immunoglobulin and plasma exchange, suggested that a 7-point or greater decrease in MG-QOL15 (score range between 0 and 60) was associated with meaningful improvement in patients with moderate to severe MG (QMGS $\leq$ 11) [24]. No similar analyses were found for the MG-QOL15R version. In addition, the lack of test–retest reliability data for MG-QOL15R, assessed via intraclass correlation, limited calculation of the minimal detectable change, an auxiliary distribution-based metric reflecting instrument measurement error and often used to set a lower bound for interpreting MCID, despite not incorporating patients perspective.

The empirical application produced results consistent with those observed in the ADAPT trial [9]. In ADAPT, for a $\geq$2-point MG-ADL improvement at week 4, 77.8% of patients in the efgartigimod group achieved this threshold (MG-QOL15R: 78.2%) compared to 48.3% in the placebo group (MG-QOL15R: 53.2%). For a $\geq$3-point improvement, the corresponding rates were 73.0% (MG-QOL15R: 71.8%) and 36.7% (MG-QOL15R: 39.2%).

Strengths and limitations

This study estimated MCID using two distinct multi-country data sources: a clinical trial, which offers estimates for more severe cases of MG, and a survey encompassing a broader and more diverse MG population. This dual-source approach strengthens the findings by enhancing their potential generalizability across different disease severities, countries, and healthcare settings.

This study has limitations. First, the MG-ADL, as our anchor, may not fully capture patients' subjective perceptions of improvement, despite being a PROM. This lack of sensitivity may be related to the fact that its items focus on specific daily activities rather than a global perception of wellbeing. Furthermore, the MG-ADL uses a 0–3 response scale, which can reduce discrimination as scores tend to cluster between 1 and 3. However, MG-ADL scores are strongly correlated with patient-reported functional status [21], and in the context of a progressive disease such as MG, even an unchanged score over time may reflect clinically meaningful stability or prevention of further decline [21]. Second, as this study involved a secondary analysis of existing data, direct patient and public involvement was not undertaken for this specific analysis. Nonetheless, patients were involved in the development of the MRW-MG survey. Third, the MCID estimate for the MG-ADL was partly based on changes in MG-QOL15 scores and physician impression [25]. Using the MG-ADL to anchor the MG-QOL15R MCID introduces circularity, as the former version of the MG-QOL15R influenced the anchor. This

lack of independence may artificially inflate the observed agreement between instruments or bias the estimated MG-QOL15R MCID thresholds. Future research should incorporate anchors that directly capture patient perspectives, such as the patient global impression of change (PGIC) scale [26] and ensure that anchors are independent of the MG-QOL15R.

Implications for clinical practice and decision making

Since patients can only have 1-point changes, clinicians may use MCID thresholds of 2- or 3-points minimal change to monitor patient progress and guide treatment adjustments, identifying individuals who may benefit from intensified management or further evaluation. For decision-makers, these MCID estimates offer context for interpreting the clinical relevance in trials and real-world studies, informing value-based care and reimbursement decisions. Incorporating PGIC anchors in future studies may strengthen the interpretability and external validity of MCID estimates, supporting their generalizability to broader clinical contexts.

Conclusions

MCID estimates for the MG-QOL15R ranged between 1.6 and 3.0 across both studies. MCID thresholds of 2- and 3-points may indicate a minimal clinically meaningful change to monitor clinical progress and adjust treatment. Future research should use patient global impression of change anchors to improve the relevance and interpretability of MCID estimates.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11136-026-04214-y.

Author contributions AJB was responsible for data analysis. All authors contributed to interpretation of the results, preparation, writing and/or review of the manuscript.

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Declarations

Competing interests SD, FB and AJB are employed by Services in Health Economics (SHE). SHE received fees from argenx in relation to this study. GP and CQ are employees of argenx.

Ethical approval Both studies included in this secondary analysis received ethical approval and were conducted in accordance with the principles of the Declaration of Helsinki. The ADAPT randomized clinical trial was approved by independent ethics committees and institutional review boards, covering the study protocol and all amendments. It is registered on ClinicalTrials.gov (NCT03669588). The MyRealWorld-MG study protocol was reviewed and approved by Salus institutional review board for participants residing in Germany, the United Kingdom, and the United States. Local ethics approval is being sought for additional study countries, including Belgium, Canada, France, Italy, Japan, and Spain. This study is registered on ClinicalTrials.gov (NCT04176211).

Consent to participate Informed consent was obtained from all participants in both studies used for this secondary analysis.

Consent for publication not applicable.

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