Burden of remaining symptoms and fluctuations of generalized myasthenia gravis on patients' daily lives – BEYOND study

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Background

- Generalised myasthenia gravis (gMG) is a rare autoimmune disorder affecting the neuromuscular junction with varying clinical manifestations that disrupt patients' daily lives.
- An estimated 30% of patients with gMG experience remaining symptoms despite treatment; very little is known about the specific burden of **remaining** gMG symptoms and **changes in their intensity and unpredictability** on the day-to-day lives of those living with gMG.[1-5]

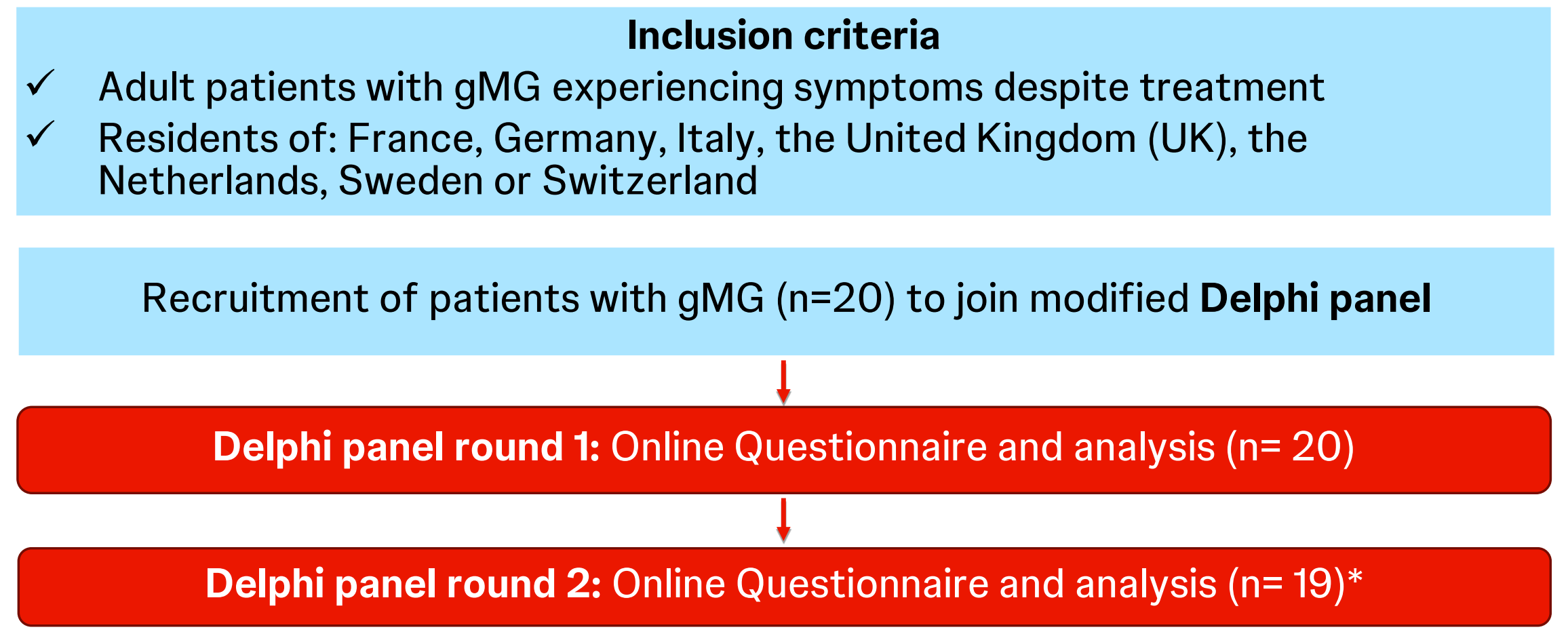
Objective

To describe how remaining symptoms despite gMG treatment, and their fluctuations, may affect a person's daily life while living with gMG.

Methods

- An initial phase of 1:1 qualitative interviews with patients confirmed the domains that are most impacted by gMG on patients' daily lives, which were then explored in a subsequent Delphi panel. The domains identified were daily activities, social life, mental and personal wellbeing, work and education, future plans.
- A modified Delphi panel comprising two survey rounds was conducted with patients with gMG who were experiencing symptoms despite treatment.

FIGURE 1: Modified Delphi panel process



Inclusion criteria
- ✓ Adult patients with gMG experiencing symptoms despite treatment
- ✓ Residents of: France, Germany, Italy, the United Kingdom (UK), the Netherlands, Sweden or Switzerland

Recruitment of patients with gMG (n=20) to join modified **Delphi panel**

Delphi panel round 1: Online Questionnaire and analysis (n= 20)

Delphi panel round 2: Online Questionnaire and analysis (n= 19)*

* One participant did not complete the round 2 questionnaire

- A nine-point Likert scale (from 1 [strongly disagree] to 9 [strongly agree]) was used to rate consensus.
- A statement had to be agreed, or disagreed, by ≥80% of patients in order to be reported as having achieved a consensus.[6]
- Statements were also analyzed to see if they were nearing consensus, defined as agreed or disagreed by ≥60% participants.

Definitions

- Remaining gMG symptoms: symptoms that occur despite treatment for gMG.
- Fluctuating symptoms: defined by a "sudden onset/ worsening of symptoms," and refers to variations in the intensity and predictability of symptoms.

Results

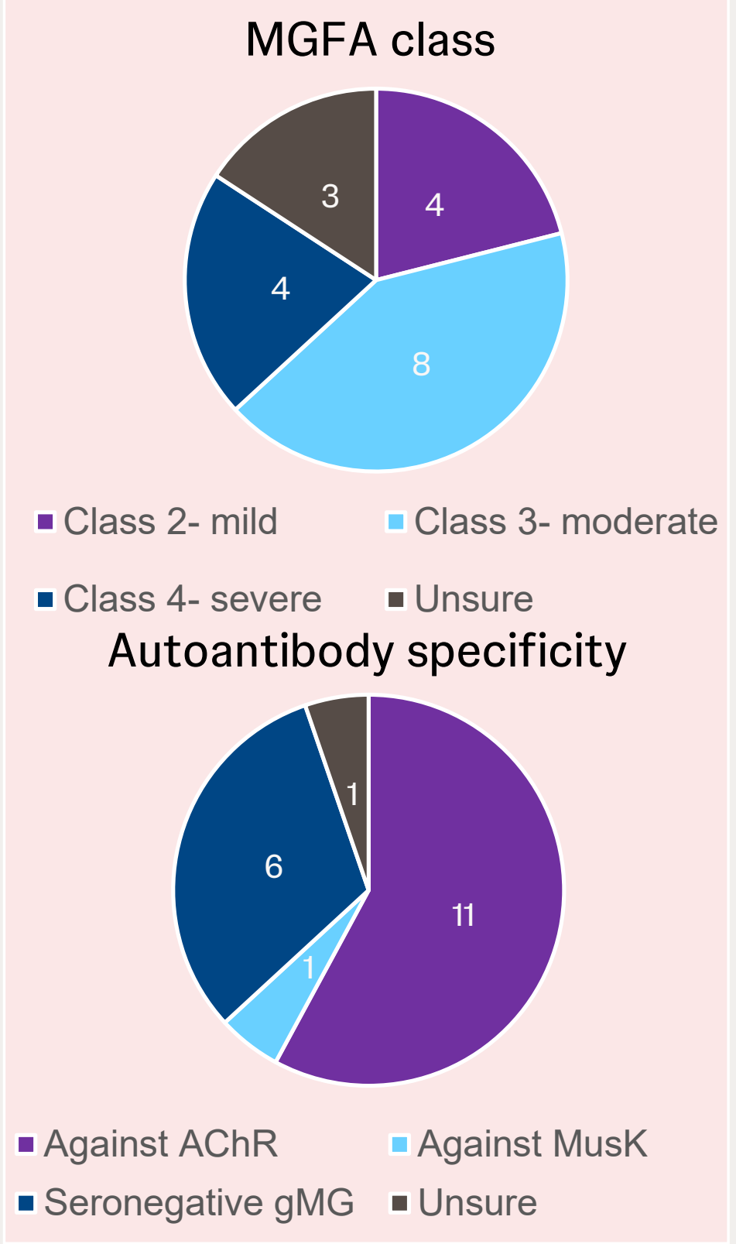
Panelist characteristics

Participants were recruited to ensure a real-world representative sample of the population of patients experiencing remaining symptoms despite being on MG therapy.

The sample included 14 female, and 5 male patients and patients had been diagnosed with gMG 1-5 years ago (n=9); 5-10 years ago (n=3); and >10 years ago (n=7).

FIGURE 2. Participant characteristics

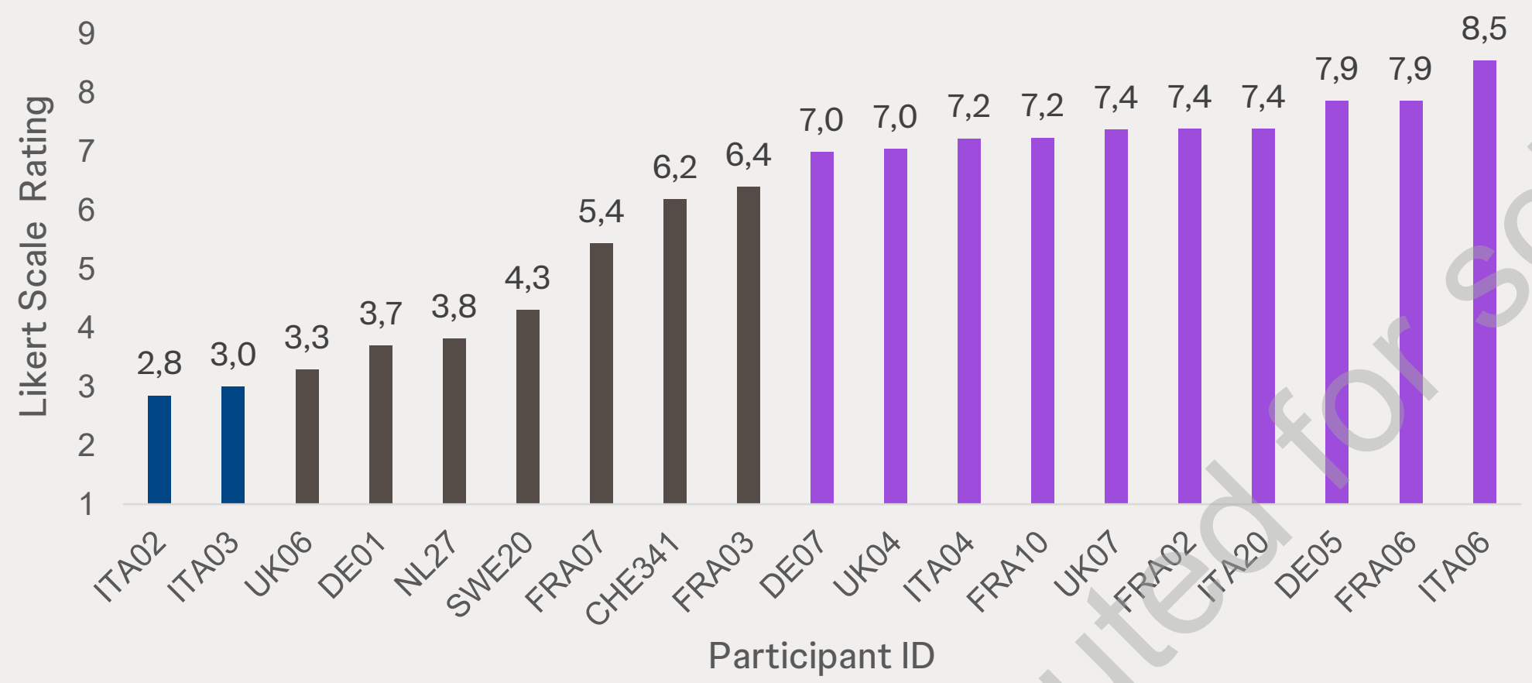
Characteristics (N=19)		
Country of residence		
France		5
Italy		5
Germany		3
United Kingdom		3
Sweden		1
Netherlands		1
Switzerland		1
Current treatment(s) at time of recruitment, by class		
Corticosteroids		12
Immunosuppressants		9
Cholinesterase inhibitors		12
Plasmapheresis/ Intravenous Immunoglobulin		4
Biologics	FcRn	1
	C5-inhibitor	1
	Anti-CD20	2



Overall impact on daily life

Many participants (n=10; 53%) reported a high impact across domains (rated ≥7 on Likert scale, Figure 3); however, some participants reported low-medium impact (rated ≤6) on average, highlighting the variability in the impact of gMG to participants.

FIGURE 3. Average (mean) rating across statements across domains per participant



Dark blue average rating ≤3; grey rating between 4-6; purple average rating ≥7

Impact on daily activities

Statement that neared consensus (>60%) related to the impact on household chores:

I sometimes need to stop, ask for help with, or adjust plans to complete household chores when my gMG symptoms suddenly worsen.

> *"Challenges also can involve needing to space out chores, take breaks etc which is frustrating."* UK

> *"Planning is often more difficult."* DE

Thematic findings from qualitative questions:
- **Other impacted daily activities:** participants were often impacted in their personal hygiene and ability to chew and swallow food, and some require adaptations
- **Transportation:** participants noted using public transport can be difficult, but sudden symptoms may make driving unsafe; leading to limited travel options.

Statements that neared consensus (>60%) related to the impact on hobbies

I need to take breaks or rely on accommodations for my hobbies to mitigate the impact of my remaining gMG symptoms, as my hobbies can cause physical/muscle weakness

I try to avoid strenuous physical activities that may leave me feeling fatigued and unable to do anything else due to my remaining gMG symptoms

I have not been able to do or resume my hobbies that I used to be able to do before my diagnosis, due to my remaining gMG symptoms

> IT *"I love painting, but I have to take breaks all the time to rest my arm and hand."*

> DE *"I love going to the gym and on bad days I can't go."*

Impact on social life and relationships

Statements that neared consensus (>60%) related to the impact on social life and the need to plan around remaining symptoms

Due to my remaining gMG symptoms, I have to plan my schedule and make sure I conserve my energy for the most important parts of my day

Due to unexpected worsening of my symptoms, I often have to allow myself to rest, which makes it difficult to plan my week or even my day

I find it necessary to rest so that I am able to attend a social event to mitigate the fatigue I may experience due to the sudden worsening of my gMG symptom*

***this statement neared consensus >70%**

> *"Over the last year my social life has shrunk to my husband and daughters. I don't really have any more energy to spend on anything else. I don't even have enough for my family."* IT

> *"On bad days I have to rest more and make sure that I have nothing planned or urgent that I need to do."* UK

Impact on work and education

Statement that neared consensus (>60%) related to the impact on patients' ability to learn/study

I have had to make adjustments to my work or career plans due to the potential unexpected worsening of my symptoms.*

*n=3 did not rank this statement as it was not applicable to them, resulting in n=16 responses

> *"I do not work, unfortunately I cannot find a job that suits my needs."* IT

> *"I had to retire at a young age."* DE

> *"Screen work is limited, speaking is difficult to sustain for a longer time, people don't understand, that's one of the biggest problems, they think you're pretending."* NL

Thematic findings from qualitative questions:
- **Education:** participants highlighted symptoms, such as diplopia and cramping in the hands, can hinder their focus when completing their studies and they often require adaptations.
- **Employment:** Decisions on jobs accepted were found to depend on hours, physical demands, proximity to home, and employer benefits.
- **Finances:** Extreme fatigue can limit full-time work, leading to reliance on external financial support.

Impact on mental and personal wellbeing

Although no statements on the impact of patients' remaining symptoms on their mental wellbeing were close to consensus, 63% of participants had median scores of ≥7 on the Likert scale across statements for mental wellbeing, highlighting the clear but variable impact. Some participants also reported having come to terms with their condition (rating ≥7 on the statement: *"I have come to terms with, and accepted, my remaining gMG symptoms and the impact this has on my life"*)

Emotional Impact: potential for anxiety caused by sudden worsening of symptoms, poor self-esteem due to physical changes, and frustration over reduced autonomy.

Coping strategies: some participants noted having made efforts to accept their disease (47%) and may see psychologists or be part of support groups.

Impact on future plans

Statements that neared consensus (>60%) related to the impact on future plans

I find it difficult to be (more) ambitious in my career, as I worry that the impact of my remaining symptoms will prevent me from taking on additional responsibilities within my job role*

My remaining symptoms have influenced my decision to have or continue having more children*

*n=5 did not rank this statement as it was not applicable to them resulting in n=14 responses

> *"Future planning is entirely focused on my monthly outpatient treatments. (...) I feel the unpredictability of MG makes me less ambitious about career progression."* UK

> IT *"[Due to symptoms] being unpredictable, I try to take it day by day."*

- Participants expressed **aspirations surrounding their work, family, and exercise if remaining symptoms were less severe and more predictable.**

Statement that <u>reached consensus</u> (≥80% in agreement)

If my symptoms were better controlled, I would have greater freedom to do the things I enjoy and lead a more satisfying life.

> *"The fatigue after exercise is the key challenge, as my hobbies are mostly outdoors and require effort. If my fatigue [were] lessened, my quality of live would improve."* UK

> DE *"Being able to predict symptoms would be a dream."*

> *"[With better controlled symptoms] I wouldn't just have one child. I'd continue my education and be very active in sports."* DE

Key takeaway

Remaining symptoms and their fluctuations in gMG significantly impact multiple aspects of patients' daily lives, highlighting the need for treatments or interventions that minimise these residual symptoms to improve overall quality of life.

Conclusions

Remaining symptoms despite gMG treatment impact various aspects of patients' daily lives. Statements that were close to consensus highlighted patients' need for support carrying out household chores, adjusting their hobbies and social plans to prevent excessive fatigue, and ensuring their work/study responsibilities fit their needs. Fluctuations further exacerbate the burden, requiring frequent adjustments to daily activities and future plans.

The variety in the impacts on each domain underscores the importance of considering patients' individual experiences in the management of gMG as many factors (such as patient clinical characteristics but also patients' attitude/ acceptance of their disease) influence how patients are impacted by their gMG.

Minimizing remaining gMG symptoms and their fluctuations could significantly improve patient satisfaction due to improved wellbeing and daily functioning in patients' lives as demonstrated by the one statement that reached consensus: **If my symptoms were better controlled, I would have greater freedom to do the things I enjoy and lead a more satisfying life.**

This research goes beyond clinicians' understanding from their consultations, providing a more comprehensive picture of the remaining burden of gMG patient's daily lives despite treatment and the need for sustained disease control.

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Conflicts of interest

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Myasthenia Gravis

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