Digital data collection to measure the impact of Myasthenia Gravis on patients' utility values in the real world

Dewilde S[1], Kousoulakou H[2], Janssen MF[3], Claeys KG[4], Friconneau M[5], Jacob S[6], Meisel A[7], Day L[8], Quinn C[8], Larkin M[8], Leighton T[9], Phillips G[10], Paci S[11]

[1] SHE Bv, Brussels, Belgium, [2] Health Economist, Athens, Greece, [3] Erasmus MC, Rotterdam, the Netherlands, [4] UZ Leuven, Belgium, [5] AFM Téléthon, Paris, France, [6] Neurologist, University Hospitals; Institute of Immunology and Immunotherapy, Birmingham, United Kingdom, [7] Charité, Department of Neurology, Center for Stroke Research Berlin, Germany, [8] Vitaccess Ltd, Oxford, United Kingdom, [9] Former Argenx employee, [10] Senior Director HEOR, Argenx, Boston, USA, [11] Director Market Access & Patient Advocacy Europe, Argenx, Ghent, Belgium

Objective

- Myasthenia gravis (MG) is a neuromuscular disorder causing weakness in arms, legs, double vision, and problems with speech, eating and breathing.
- This study sets out to measure utility values in MG patients, in order to present the impact of the disease on patients' health-related quality-of-life (HRQoL) in relation to sociodemographic, disease classification and relevant (condition-specific) outcomes in a real-world setting.

Methods

- A digital, prospective, observational, longitudinal study collected data using a smartphone/tablet application among 840 MG patients in Belgium, Canada, Germany, Italy, Japan, Spain, UK and USA
- Adults suffering from MG use a smartphone application developed for the study, MyRealWorld-MG (Vitaccess Limited, London, UK) to enter monthly data about the impact of MG on their lives over a period of approximately 2 years.
- The study was designed in close collaboration with MG patients via patient advisory groups. The rationale and methods of the study MyRealWorld-MG have been published previously.
- This study reports measurements taken at enrollment. Patients filled HRQoL data (EQ-5D-5L and bolt-ons), simultaneously with their demographics, disease-related classification (MG Foundation of America class: MGFA), clinical outcomes (MG-Activities of Daily Living: MG-ADL, MG-Quality of life: MG-QoL, Hospital Anxiety and Depression: HADS) and whether they need a caregiver.
- Utility values were calculated using the UK algorithm for the whole MG patient sample and contrasted with utilities from the general population.
- In univariable analyses, the association between utility and the following determinants was examined: age and gender; MGFA; whether patients need help from a caregiver and how many hours of help they need; the presence and severity of anxiety or depression; and with the total scores of the MG-ADL and MG-QoL.

Outcomes

- **EQ-5D-5L:** a generic instrument to measure HRQoL (2) in five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, with five severity levels for each dimension. The responses can be converted into a utility score ranging from 0 for death to 1 for full health.
- **Bolt-on items**: additional dimensions to the EQ-5D-5L concerning vision, breathing, tiredness, sleep, social relationships, and self-confidence. Each bolt-on dimension has five severity levels (3-8)
- **MG-ADL**: is a frequently-used outcome in MG studies, assessing MG severity through the following symptoms: talking, chewing, swallowing, breathing, impairment of ability to brush teeth/comb hair, impairment of ability to rise from a chair, double vision, and eyelid droop. The total score ranges from 0: no impact to 24: severe impact on daily living (9, 10).
- **MG-QoL**: is an MG-specific HRQoL questionnaire with 5 domains spread over 15 questions: emotions, physical health, self-care, social life, and role (11, 12). The total score ranges from 0 to 30.
- **HADS**: is a generic instrument to assess psychological distress in non-psychiatric patients (13, 14). It consists of two subscales: anxiety and depression with seven items each. The total subscale score ranges from 0 to 21, with 0-7 no anxiety/depression; 8-10 mild; 11-14 moderate; scores ≥15 severe anxiety or depression.
- **Caregiver data**: whether patients need help from a caregiver (yes/no) and how many hours per week they need help.

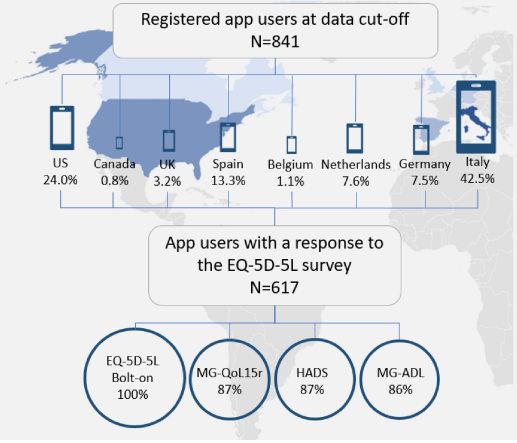
Ethical Considerations

- Ethics approval was granted by Salus IRB for all participating countries except Canada by Veritas IRB. At enrolment, all participants provided informed consent by reading and acknowledging their agreement with on-screen briefing and informed consent materials. The study was performed in accordance with the Declaration of Helsinki.

Results

- Recruitment started on December 12, 2019. At the time of data cut-off for this analysis (1 April 2020), a total of 812 participants downloaded the app and responded to at least one item in any of the questionnaires. Of those, a total of 617 MG patients completed the EQ-5D-5L at baseline and are included in the calculations. The participant flow is presented in Figure 1. The distribution of the total sample in terms of age and gender is presented in Fig 2, as well as the patient's classification on MGFA.

Figure 1. Participant flow



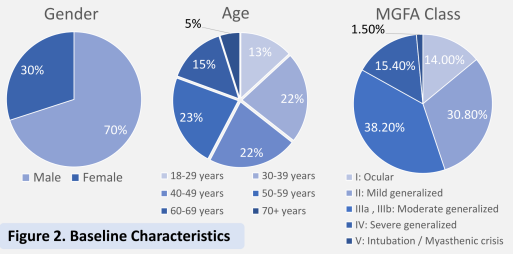


Figure 2. Baseline Characteristics

- The mean utility of all MG patients was 0.688 (IQR 0.599-0.837), compared to 0.855 in the general population of the same age and gender.
- Age (p=0.10) and gender (p=0.10) had no noteworthy impact on utilities.
- In univariable analyses, utility was significantly associated with disease classification MGFA (p=<.0001, Table 1).
- A highly significant association between utility values and the presence of mental health was found. The impact of mild, moderate and severe depression was associated with dis-utilities of -0.121, -0.230 and -0.408 compared to no depression among MG patients (p=<.0001), and for mild, moderate and severe anxiety dis-utilities were -0.078, -0.147 and -0.252 compared to no anxiety among MG patients (p=<.0001, Table 2).
- Needing help from a caregiver generated a disutility of -0.236, and this was significantly associated with the number of hours of help received (p=<0.0001, Fig 3A).
- A significant worsening in utility values was also found for patients with additional co-morbidities (-0.105, p=<0.0001, Fig 3B).

Table 1

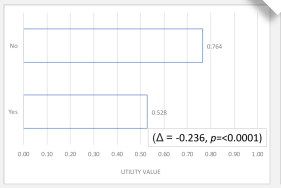
Utility values	Depression			Anxiety		
	Mean	Std	N	Mean	Std	N
1. None	0.764	0.168	308	0.755	0.189	262
2. Mild	0.643	0.171	135	0.677	0.169	116
3. Moderate	0.534	0.260	67	0.608	0.243	111
4. Severe	0.356	0.293	24	0.503	0.250	45

Table 2

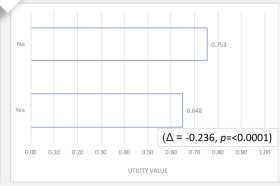
	Utility value (UK)		
MGFA	**Mean**	**Std**	**N**
Class I: Eye muscle weakness	0.811	0.175	85
Class II: Mild weakness affecting non-eye muscles	0.766	0.146	162
Class III: Moderate weakness affecting non-eye muscles	0.648	0.201	230
Class IV: Severe weakness affecting non-eye muscles	0.527	0.272	86
Class V: Intubation	0.360	0.508	6

Figure 3

A. Needing help from a caregiver



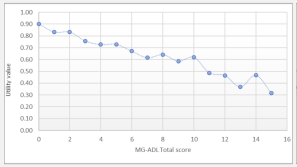
B. Having co-morbidities



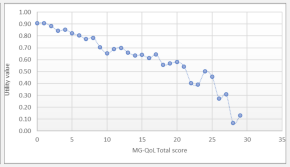
- Finally, highly significant negative associations were found with MG-ADL and MG-QoL total scores (Fig 4A and B). A 1-point worsening in the MG-ADL corresponded with a utility decline of 0.0375 (p=0.0001). Similarly, a 1-point increase (worsening) in the MG-QoL total score lead to a reduction of 0.0207 in utility value (*p*=<.0001).

Figure 4

A. Utility values by MG-ADL total score



B. Utility values by MG-QoL total score



Conclusion

- MG patients have impaired HRQoL compared to members of the general population of the same age and gender, with a mean difference in utility of 0.167
- Many factors significantly impacted the utility of MG patients in univariable analyses . The severity classification of the disease, as represented by the MGFA, confirmed that more severe patients have significantly worse HRQoL.
- Patients experience a continuing deterioration of HRQoL with increasing limitations in their activities of daily living, as measured with the MG-ADL. Utility values were not surprisingly also significantly associated with MG-QoL, which measures HRQoL on different domains than the EQ-5D.
- Furthermore, patients' mental health also impacted utility values of MG patients. The presence of anxiety, but even more so the presence of depression, lowered utility values considerably.
- Finally, the necessity for a caregiver and the number of hours that patients need help from a caregiver has a negative impact on their HRQoL.

Sarah Dewilde, PhD sd@she-consulting.be