

# **High-dose steroids, treatment escalation and healthcare burden in myasthenia gravis: a US claims-based cohort study**

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## Supplementary Methods

### Algorithms for defining outcome variables

#### ***MG exacerbation***

An MG exacerbation was defined as administration of any acute IVIg treatment or PLEX cycle, or an MG-related hospitalization (any ward or specialist unit), including recording of an ICD-10 code for MG as a primary reason for hospitalization. MG exacerbation began on the date of starting a qualifying treatment or hospital admission, whichever occurred first. Claims for IVIg and/or PLEX that coincided with a hospital claim were not counted in addition to the hospital claim. For patients who had no prior claim for MG-specific treatment, the first claim for IVIg, PLEX cycle or MG-related hospitalization was not considered to define MG exacerbation.

Patients meeting the definition for MG crisis (see below) within 7 days before or after meeting the definition for MG exacerbation were classified as having a crisis, not as having an exacerbation. Claims for Ig that were classified as chronic Ig were not taken into account when defining MG exacerbation.

ICD codes and Current Procedural Terminology (CPT)/ Healthcare Common Procedure Coding System (HCPCS) codes used to define MG exacerbation are provided in **Table S1**.

#### ***MG crisis***

Together with an ICD-10 code for MG, an MG crisis was defined as the combination of:

- At least one primary diagnosis of acute respiratory failure with inpatient hospitalization; **or** at least one event of regulated mechanical ventilation (endotracheal intubation, continuous positive airway pressure, non-invasive mechanical ventilation) within 3 days following the hospital admission date, and at least one acute respiratory failure diagnosis (in any position, that is, recorded as primary or secondary diagnosis);

AND

- Acute IVIg treatment or PLEX cycle within 7 days of a hospital admission date.

An instance of MG crisis began on the date of the qualifying hospital admission. Additional events meeting the definition criteria for MG crisis within 7 days of another MG crisis were considered to be part of the same crisis event.

ICD codes and CPT/HCPCS codes used to define MG crisis are provided in **Table S1**.

### ***Chronic Ig treatment***

Chronic Ig was defined as follows: administration of three or more cycles of any combination of IVIg and SCIg in any 365-day rolling period. Therefore, any Ig cycle that was followed by two or more additional Ig cycles within the 365 days after starting Ig was classified as a chronic treatment. Any other recorded administration of Ig not meeting this criterion was classified as acute IVIg treatment.

### ***Classification of MG-TEs***

We classified MG-TEs by escalation type: single treatments that included HDCS (oral or intravenous steroids with a daily prednisolone-equivalent dose of at least 15 mg), NSIST, Ig, PLEX, eculizumab or rituximab; use of multiple treatments when claims for two types of treatment overlapped for under 28 days; and concomitant treatment for claims overlapping for at least 28 days. Fifteen different combinations were possible.

### ***Other algorithms (primary outcome measures)***

To account for unequal periods of follow-up in the analysis, Kaplan–Meier methods were used to describe time since diagnosis, duration of high-dose steroids, and duration of escalation. For high-dose steroid escalation and treatment escalation, the following study definitions were used:

- Number of patients with at least one event: number of patients with at least one event during the appropriate time period
- Total number of events (mean, median, P25–P75, min–max): sum of all the events during the appropriate time period, for all patients at risk during the year
- Number of patients at risk of having a new event: number of patients contributing follow-up data in the appropriate time period for the analysis
- Person-time at risk (time at risk of having an event): time from the study entry start index date (or the start of the year post-study entry index date, as appropriate) [0d], to the end of follow-up (or end of year post-study entry index date, as appropriate), [364d]
- Crude incidence rates per 100 person-years were calculated as the total number of events occurring during the appropriate time period multiplied by 100, and divided by the total number of person-time at risk of the event

- 95% CIs for the incidence rate were calculated using the formula:  $r = e^{\ln(IR) \pm 1.96(SE)}$ , where IR is the incidence rate; and SE is the standard error (SE). SE was calculated as:  $SE = \sqrt{(1-IR)/N}$ , where N=number of qualifying events.

### Treatment status

Patients could be in one of four different treatment statuses, defined as follows:

**Treatment break:** the first gap of at least 90 days between consecutive claims for all pharmacological treatments given for MG (excluding symptomatic treatment with AChEI), based on the assumption that a gap between prescriptions of more than 3 months is an indicator of a break in treatment. Patients in treatment break status could transition into treatment re-escalation.

**Treatment re-escalation:** the start of a new escalation of any type following the first MG treatment break.

**Treatment de-escalation:** a gap of more than 14 days between the end of the first escalation of any type and the start of a new escalation. A patient could transition from this state to rescue treatment.

**Rescue treatment:** the start of a new escalation of any type following the first recorded treatment de-escalation.

### Sensitivity analysis (SA)

#### SA1:

Restriction of the study population used for primary analyses to patients with a minimum of three years of continuous health plan membership with medical and pharmacy benefits ( $\geq 1$  year prior to the study entry index date and  $\geq 2$  years after the study entry index date).

#### SA2:

Exclusion of Ig escalation occurring within 28 days of thymectomy from the Ig escalation definition used for primary analysis. The rationale for this exclusion is that Ig may be provided as a prophylactic, preoperative therapy to prevent myasthenia crisis in patients undergoing thymectomy.

#### SA3:

Additional inclusion of all patients who had at least one claim with an MG diagnosis code recorded (as opposed to restriction to patients with two claims with an MG diagnosis code at least 90 days apart, which was an inclusion criterion for the primary analysis). This SA was conducted for the primary objectives.

**SA4:**

Restriction of the SA3 population to patients without a claim with a diagnosis code for another peripheral neural disorder recorded within 12 months after the study entry index date (**Table S14**). The rationale for this further exclusion is that some patients may be given an initial diagnosis of MG (differential diagnosis) but later receive a final/confirmed diagnosis for another peripheral neural disorder.

The key differences between the primary analyses and the four SAs are provided in **Table S3**.

Sensitivity analyses were carried out for the 30 study estimands:

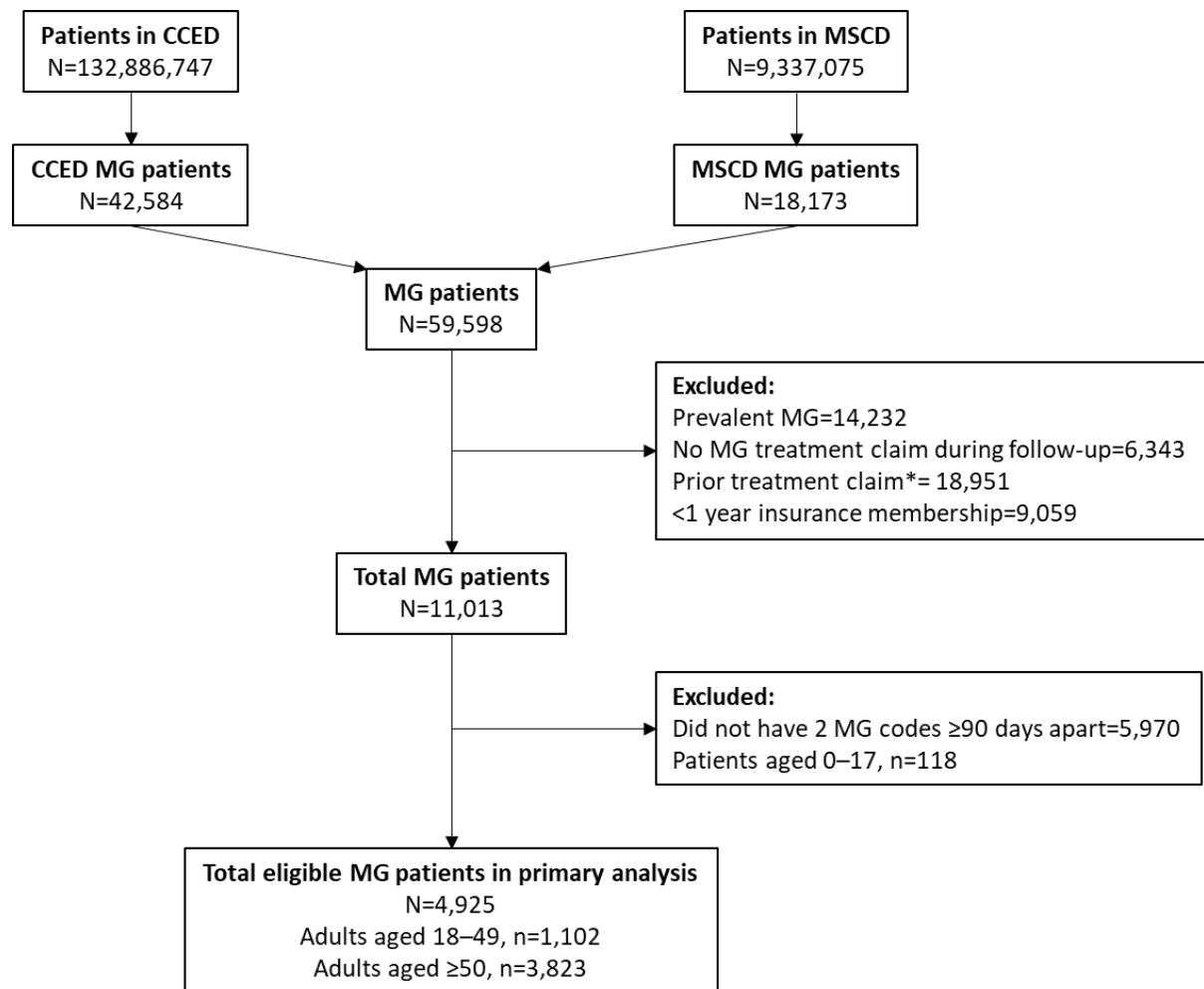
- Proportion of patients with the three most common baseline comorbidities
- Proportion of patients receiving NSISTs at baseline
- Proportion of patients with at least one MG-TE
- Median number of MG-TEs per patient
- Most common MG-TE type
- Incidence of MG-TEs over time
- Proportion of patients with
  - De-escalation
  - Rescue treatment
  - De-escalation, who subsequently required re-escalation
- Proportion of patients with an HDCS MG-TE following diagnosis
- HDCS incidence by age group
- Total duration of HDCS per person by age
- IR of HDCS MG-TE over time
- Duration of HDCS over time
- Mean maximal daily prednisolone-equivalent corticosteroid dose in the first year by age
- Mean maximal daily prednisolone-equivalent corticosteroid dose over time
- Proportion of patients prescribed AChEI by age
- Peak year of
  - Ig treatment
  - AChEI treatment
  - Thymectomy
- Incidence of comorbidities

- Incidence of
  - MG exacerbation
  - MG crisis
- MG-related HCRU over time
  - Neurologist visit
  - Hospitalization
  - ICU
  - ER
- MG-related hospitalizations by age
- MG-related costs
  - Total healthcare costs
  - Pharmacy costs

Estimations of peak year of Ig treatment, AChEI treatment, and thymectomy could not be interpreted for any of the four SAs, due to low numbers. SA results for the majority of estimands (82 out of the 108 analyses that could be interpreted) were similar to the primary analysis. Differences for the remaining 26 estimations are summarised and discussed in the main article and are presented in **Tables S9–S13**.

## Supplementary Figures and Tables

Figure S1. STROBE flow diagram



\*Pharmacy claim for AChEI, IVIg, SClg or PLEX.

AChEI, acetylcholinesterase inhibitor; CCED, Commercial Claims and Encounters Database; IVIg, intravenous immunoglobulin; MG, myasthenia gravis; MSCD, Medicare Supplemental and Coordination of Benefits Database; PLEX, plasma exchange; SClg, subcutaneous immunoglobulin; STROBE, STrengthening the Reporting of OBservational studies in Epidemiology.

**Table S1. Codes used to define study variables**

| <b>MG exacerbation</b>                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Administration of acute IVIg treatment or PLEX cycle | <p>Inpatient claims with any of the following codes in the primary position:</p> <p>Acute IVIg treatment</p> <p>NDC:</p> <p>26064012, 26064020, 26064071, 26064512, 26064515, 26064520, 26064524, 26064571, 26064612, 26064620, 26064624, 26064625, 26064671, 26064812, 26064815, 26064820, 26064824, 26064871, 53748601, 53748602, 53748605, 53748606, 53748610, 53749001, 53749002, 53749005, 53749006, 53749010, 69101101, 69101102, 69110901, 69110902, 69122401, 69122402, 69131201, 69131202, 69141501, 69141502, 69155801, 69155802, 78012058, 78012094, 78012219, 78012259, 78012295, 78012419, 78012460, 78012496, 78024419, 78024493, 944047169, 944047172, 944047175, 944047180, 944262001, 944262002, 944262003, 944262004, 944265503, 944265504, 944265603, 944265804, 944280701, 944280702, 944280703, 944280704, 944295002, 944295004, 944295006, 944296701, 944296703, 944296705, 944296707, 944296709, 13533064512, 13533064515, 13533064520, 13533064524, 13533064571, 14362011901, 44206041501, 44206041603, 44206041706, 44206041812, 44206043605, 44206043710, 44206043820, 44206043940, 44206050653, 44206050756, 44206050862, 44206053211, 44206053290, 44206310101, 49669160001, 49669160200, 49669160201, 49669160300, 49669160301, 49669160401, 49669161201, 49669161301, 49669161401, 49669162201, 49669162301, 49669162401, 52769011902, 52769026866, 52769026972, 52769041706, 52769041712, 52769041812, 52769047070, 52769047072, 52769047075, 52769047080, 52769047172, 52769047175, 52769047180, 53270300001, 53270310001, 53270330001, 53270350001, 54129023310, 54129023325, 54129023350, 59730650201, 59730650301, 60492002101, 60492002301, 60492002401, 60492008101, 60492008201, 60492017302, 60492024902, 60574210101, 60574210201, 60574310101, 60574310201, 61953000301, 61953000302, 61953000303, 61953000304, 61953000401, 61953000402, 61953000403, 61953000404, 61953000405, 61953000501, 61953000502, 61953000503, 64193025050, 64208823401, 64208823402, 64208823403, 64208823404, 64208823405, 64208823406, 64208823407, 64208823408, 64208823501, 64208823502, 64208823503, 64208823505, 64208823506, 64208823507, 67467084301, 67467084302, 67467084303, 67467084304, 67467084305, 68209084301, 68209084302, 68209084303, 68209084304, 68403110007, 68516161201, 68516161301, 68516161401, 68516162201, 68516162301, 68516162401, 68982082001, 68982082002, 68982082003, 68982082004, 68982082005, 68982082006, 68982082081, 68982082082, 68982082083, 68982082084, 68982082085, 68982082086, 68982082201, 68982082202, 68982082203, 68982082204, 68982082205, 68982082206, 68982082281, 68982082282, 68982082283, 68982082284, 68982082285, 68982082286, 68982084001, 68982084002, 68982084003, 68982084004, 68982084005, 68982085001, 68982085002, 68982085003, 68982085004, 68982085005, 69800025001, 69800025002, 69800650201, 69800650202, 69800650301, 70257053251</p> <p>53759601, 53759603, 53759610, 53759615, 53759620, 53759625, 69106101, 69106102, 69147601, 69147602, 69150901, 69150902, 69180202, 69196002, 69196501, 69196502, 944251002, 944251102, 944251202, 944251302, 944251402, 944285001, 944285002, 944285003, 944285004, 944285005, 944285006, 944285007, 944285008, 944285009, 944285010, 13533081005, 13533081006, 13533081010, 13533081011, 13533081020, 13533081021, 13533081050, 13533081051,</p> |

|                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|--------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                              | <p>44206045101, 44206045202, 44206045404, 44206045510, 44206045621, 44206045722, 44206045824, 44206045896, 68982081001, 68982081002, 68982081003, 68982081004, 68982081005, 68982081006, 68982081081, 68982081082, 68982081083, 68982081084, 68982081085, 68982081086</p> <p>CPT/HCPCS:</p> <p>36530, 90283, C8950, C8951, C8957, C9270, G0332, J1459, J1557, J1566, J1568, J1569, J1572, J1599, Q4097, Q9941, Q9942, Q9943, 90284, G0069, G0089</p> <p>PLEX</p> <p><b>CPT/HCPCS:</b></p> <p>36514, 36516, 6A550Z3, 6A551Z3, 99.71</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| MG-related hospitalization (for MG exacerbation)                                                             | <p>Inpatient claims with an MG code (ICD-10: G70.0, G70.00, G70.01, ICD-9: 358.0, 358.00, 358.01) recorded in a primary position</p> <p>OR</p> <p>an MG code (ICD-10: G70.0, G70.00, G70.01, ICD-9: 358.0, 358.00, 358.01) in a secondary position AND one of the following codes in the primary position:</p> <p>ICD-9: 322.0, 335.22, 358.1, 368.2, 374.30, 378.51, 380, 381.1, 381.2, 381.9, 382, 383, 384.2, 384.9, 388, 389, 465.9, 466.11, 478, 482.0, 482.41, 482.42, 482.83, 482.9, 483.0, 486, 487.0, 487.1, 488.82, 490, 507.0, 516.36, 518.81, 518.82, 518.84, 519.09, 590.80, 728.87, 780.09, 784.51, 786.05, 786.09, 787.20, 787.22, 790.7, 793, 799.9, 997.39, 998.89, 999.31, 999.32, 999.33, V46.11</p> <p>ICD-10: A31.0, A40.0, A40.1, A41.01, A41.3, A41.4, A41.50, A41.51, A41.52, A41.59, A41.81, A41.89, A41.9, B25.8, B25.9, B34.9, G97.82, J02.0, J02.8, J04.10, J06.9, J10.00, J10.01, J10.08, J10.1, J15.1, J15.212, J15.6, J15.8, J15.9, J16.8, J18.1, J18.9, J20.6, J40, J44.0, J47.0, J69.0, J95.821, J96.00, J96.01, J96.02, J96.20, J96.21, J96.22, J96.90, J98.6, R06.02, R13.10, R13.12, R53.1, R65.20, R78.81, T80.211A, T80.219A, T80.29XA, T80.89XA, T81.4XXA</p> |
| <b>MG crisis</b>                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| Hospitalization with acute respiratory failure diagnosis, primary position                                   | <p>Inpatient claims with any of the following diagnoses in the primary position:</p> <p><b>ICD-9:</b> 518.51, 518.53, 518.81, 518.84</p> <p><b>ICD-10:</b> J96.0*</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Hospitalization with acute respiratory failure diagnosis, any position                                       | <p>Inpatient claims with any of the following diagnoses in any position:</p> <p><b>ICD-9:</b> 518.51, 518.53, 518.81, 518.84</p> <p><b>ICD-10:</b> J96.0*</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Regulated mechanical ventilation (endotracheal intubation, CPAP, BiPAP, non-invasive mechanical ventilation) | <p><b>CPT/HCPCS:</b> A4604, A7027, A7030, A7034, A7035, A7036, A7037, A7038, A7039, A7044, A7045, A7046, E0470, E0471, E0472, E0482, E0561, E0562, G8845, G8847, G8849, G8850, G8851, G8852, G8853, G8854, G8855, K0185, K0187, E0470, E0471, E0472, A4483, 94002, 94003, 94660, 31500</p> <p><b>ICD-9-PCS:</b> 87.31, 96.04, 93.90, 96.7, 96.70, 96.71, 96.72, 93.90, 96.7, 96.70, 96.71, 96.72</p> <p><b>ICD-10-PCS:</b> 0B21X*, 0BH13*, 0BH17*, 0BH18*, 5A09357, 5A09457, 5A09458, 5A09557, 5A09558, 5A193*, 5A194*, 5A195*, 5A093*, 5A094*, 5A095*, 0BH17EZ, 0BH18EZ</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |

Administration of acute IVIg treatment or PLEX See codes provided above for MG exacerbation cycle

# HCRU

MG-related neurologist visit (neurologist visit + outpatient MG-related visit) Provider type: 260 - Neurology (outpatient)

Outpatient MG-related non-neurologist visit Non-neurologist and non-GP visit — provider type in (1, 5, 6, 10, 15, 20, 21, 22, 23, 25, 30, 31, 32, 33, 34, 35, 36, 37, 38, 40, 41, 42, 100, 105, 130, 200, 220, 225, 240, 260, 265, 355, 805, 820, 840, 845, 870, 910, 915, 920, 935, 940, 945, 950, 955, 960)

MG-related emergency room visit Any emergency room event (see below) with codes: ICD9: 358.0\* ICD10: G70.0\*

All-cause emergency room visit For inpatient emergency room, the definition for MG-related hospitalization was used  
Inpatient event with **CPT/HCPCS codes:** 99281, 99282, 99288, 99283, 99284, 99285, 0450, 0451, 0452, 0456, 0459, 0981, 31500, 99058, 99140, D7990, ER, ET, G0257, G0380, G0381, G0382, G0383, G0384, G0425, G0426, G0427, G2213, G8353, G8354, G9752, G9850, J2, Q0490, Q0491, Q0492, Q0493, Q0494, T2007  
OR  
Outpatient event with **Procedure Group codes:** 111  
OR  
Outpatient event with **Revenue codes:** 0450, 0451, 0452, 0456, 0459, 0981  
OR  
Outpatient event with **Place of Service codes:** Emergency Room - Hospital  
OR  
Outpatient event with **Service Sub-Category codes:** 10220, 10320, 10420, 10520, 12220, 20120, 21120, 22120, 30120, 30320, 30420, 31220, 31320, 31620, 10120, 20220, 21220, 22320, 30220, 30520, 30620, 31120, 31420, 31520

MG-related hospitalization Inpatient claims with an MG code (ICD-10: G70.0, G70.00, G70.01, ICD-9: 358.0, 358.00, 358.01) recorded in a primary position  
OR  
an MG code (ICD-10: G70.0, G70.00, G70.01, ICD-9: 358.0, 358.00, 358.01) in a secondary position AND one of the following codes in the primary position:  
ICD-9: 164.0, 212.6, 254.0, 254.8, 322.0, 327.23, 335.22, 358.1, 368.2, 374.30, 378.51, 380, 381.1, 381.2, 381.9, 382, 383, 384.2, 384.9, 386.35, 388, 389, 463, 465.9, 466.11, 478, 482.0, 482.41, 482.42, 482.83, 482.9, 483.0, 486, 487.0, 487.1, 488.82, 490, 507.0, 516.36, 518.81, 518.82, 518.84, 519.09, 590.80, 595.2, 595.89, 595.9, 599.0, 682.0, 682.2, 682.3, 682.5, 682.6, 682.7, 682.9, 728.87, 730.27, 780.09, 780.60, 784.51, 786.05, 786.09, 787.20, 787.22, 790.7, 793, 799.9, 845, 997.39, 998.89, 999.31, 999.32, 999.33, V46.11  
ICD-10: A04.9, A08.4, A31.0, A40.0, A40.1, A41.01, A41.3, A41.4, A41.50, A41.51, A41.52, A41.59, A41.81, A41.89, A41.9, B25.8, B25.9, B34.9, B37.81, C37, D15.0, E32.0, E32.9, G03.1, G47.33, G70.80, G97.82, H05.011, J02.0, J02.8, J04.10, J06.9,

|                                     |                                                                                                                                                                                                                                                                                                                                                                                                                |
|-------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                     | J10.00, J10.01, J10.08, J10.1, J15.1, J15.212, J15.6, J15.8, J15.9, J16.8, J18.1, J18.9, J20.6, J40, J44.0, J47.0, J69.0, J95.821, J96.00, J96.01, J96.02, J96.20, J96.21, J96.22, J96.90, J98.59, J98.6, L02.212, L03.113, L03.114, L03.115, L03.116, L03.221, L03.311, N30.00, N30.01, N30.90, N39.0, N45.3, R06.02, R13.10, R13.12, R53.1, R65.20, R78.81, T80.211A, T80.219A, T80.29XA, T80.89XA, T81.4XXA |
| All-cause hospitalization           | Any event of hospitalization from the MarketScan inpatient table                                                                                                                                                                                                                                                                                                                                               |
| Thymectomy                          | Inpatient service or outpatient event with codes:<br><b>CPT/HCPCS:</b> 60520, 60521, 60522, 32673<br><b>ICD-9 Procedure code:</b> 07.8, 07.80, 07.81, 07.82, 07.83, 07.84<br><b>ICD-10 Procedure code:</b> 07BM0ZX, 07BM0ZZ, 07BM3ZX, 07BM3ZZ, 07BM4ZX, 07BM4ZZ, 07DM3ZX, 07DM4ZX                                                                                                                              |
| Intensive care unit hospitalization | Inpatient service event with revenue codes: 0200, 0201, 0202, 0203                                                                                                                                                                                                                                                                                                                                             |

\*Codes can be provided on request.

BiPAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure; CPT, Current Procedural Terminology; HCPCS, Healthcare Common Procedure Coding System; ICD, International Classification of Diseases; MG, myasthenia gravis; PCS, Procedure Coding System.

**Table S2. Prednisolone-equivalent dose conversion factors**

| Steroid            | Administration route* | Equivalent dose (mg) |
|--------------------|-----------------------|----------------------|
| Betamethasone      | IV                    | 1.5                  |
| Cortisone          | PO                    | 50                   |
| Deflacort          | PO                    | 12                   |
| Dexamethasone      | IV or PO              | 1.5                  |
| Hydrocortisone     | IV or PO              | 40                   |
| Methylprednisolone | IV or PO              | 8                    |
| Prednisolone       | PO                    | 10                   |
| Prednisone         | PO                    | 10                   |
| Triamcinolone      | IV                    | 8                    |

Source: British National Formulary.(25)

\*The same conversion factors were used for conversion of oral and IV steroids to prednisolone equivalent dose. E.g. 1 mg prednisolone is equivalent to 4 mg of oral or IV hydrocortisone.

IV, intravenous; PO, per os.

**Table S3. Study inclusion criteria in primary analysis and sensitivity analyses**

| Criterion                                                                                                                                                  | Primary analysis<br>N=4,925                          | SA1<br>N=2,736                                                           | SA2<br>N=4,925                                                                                              | SA3<br>N=10,788                                             | SA4<br>N=9,984                                              |
|------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------|-------------------------------------------------------------|
| Required length of healthcare coverage                                                                                                                     | ≥1 year before diagnosis                             | <b>≥3 years (≥1 year before diagnosis plus ≥2 years post-index data)</b> | ≥1 year before diagnosis                                                                                    | ≥1 year before diagnosis                                    | ≥1 year before diagnosis                                    |
| Chronic and acute Ig claim codes occurring within 28 days of thymectomy                                                                                    | Included                                             | Included                                                                 | <b>Excluded</b>                                                                                             | Included                                                    | Included                                                    |
| Number and timing of claims with MG diagnosis codes                                                                                                        | 2 MG diagnosis codes recorded at least 90 days apart | 2 MG diagnosis codes recorded at least 90 days apart                     | 2 MG diagnosis codes recorded at least 90 days apart                                                        | <b>At least 1 MG diagnosis code</b>                         | <b>At least 1 MG diagnosis code</b>                         |
| Claims with a diagnosis code for a non-MG peripheral neural disorder <b>up to 12 months after study index date (i.e. after date of first MG diagnosis)</b> | Included                                             | Included                                                                 | Included                                                                                                    | Included                                                    | <b>Excluded</b>                                             |
| Expected patient numbers compared with primary analysis                                                                                                    | -                                                    | Fewer patients included since diagnosis criteria are narrower            | Same number (this SA only impacts whether treatment claim codes are counted in a particular MG-TE category) | More patients included since diagnosis criteria are broader | More patients included since diagnosis criteria are broader |

Bold font indicates where the SA diverges from the primary analysis.

Ig, immunoglobulin; MG, myasthenia gravis; MG-TE, myasthenia gravis treatment escalation; SA, sensitivity analysis.

**Table S4. Baseline infections**

| Infection type                                      | Infections<br>(N=581) |
|-----------------------------------------------------|-----------------------|
| Acute infection resulting in hospitalization, n (%) |                       |
| Total                                               | 314 (100)             |
| Lower respiratory tract infection                   | 120 (38.2)            |
| Urinary tract infection                             | 87 (27.7)             |
| Septicaemia                                         | 62 (19.8)             |
| Other acute infection                               | 36 (11.5)             |
| Meningitis                                          | 8 (2.6)               |
| Hepatitis                                           | 1 (0.3)               |
| Chronic infection, n (%)                            |                       |
| Total                                               | 267 (100)             |
| Chronic cystitis                                    | 65 (24.3)             |
| Helicobacter                                        | 62 (23.2)             |
| Hepatitis                                           |                       |
| Other hepatitis (non C/B)                           | 59 (22.1)             |
| Hepatitis C                                         | 18 (6.7)              |
| Hepatitis B                                         | 10 (3.8)              |
| Infectious mononucleosis                            | 20 (7.5)              |
| Non-tuberculosis mycobacterial infections*          | 10 (3.8)              |
| Tuberculosis                                        | 10 (3.8)              |
| HIV                                                 | 6 (2.3)               |
| CMV                                                 | 3 (1.1)               |
| Parvovirus                                          | 3 (1.1)               |
| Other chronic infection                             | 1 (0.4)               |

\*Includes atypical and unspecified mycobacterial infections.

Infections are listed by acute or chronic, then in rank order of frequency. One type of infection is counted once per patient. Percentages of individual infection types are calculated using the total number of acute/chronic infections as the denominator.

HIV, human immunodeficiency virus; CMV, cytomegalovirus.

**Table S5. Baseline characteristics of MG patients with HDCS MG-TE and composite escalation (any MG-TE), by age group**

|                                             | HDCS MG-TE           |                      | Composite escalation |                      |
|---------------------------------------------|----------------------|----------------------|----------------------|----------------------|
|                                             | 18–49 years<br>N=714 | ≥50 years<br>N=2,237 | 18–49 years<br>N=811 | ≥50 years<br>N=2,710 |
| <b>Age at study entry index date, years</b> |                      |                      |                      |                      |
| Mean (SD)                                   | 38.9 (8.3)           | 65.8 (10.3)          | 38.9 (8.3)           | 66.1 (10.3)          |
| <b>Sex</b>                                  |                      |                      |                      |                      |
| Female (%)                                  | 496 (69.5)           | 994 (44.4)           | 570 (70.3)           | 1,185 (43.7)         |
| <b>Comorbidities, n (%)</b>                 |                      |                      |                      |                      |
| Anxiety                                     | 82 (11.5)            | 168 (7.5)            | 88 (10.9)            | 194 (7.2)            |
| Autoimmune thyroiditis                      | 4 (0.6)              | 19 (0.8)             | 4 (0.5)              | 20 (0.7)             |
| Depression                                  | 40 (5.6)             | 133 (5.9)            | 44 (5.4)             | 161 (5.9)            |
| Diabetes (any type)                         | 53 (7.4)             | 559 (25.0)           | 62 (7.6)             | 744 (27.5)           |
| Type 2 diabetes                             | 51 (7.1)             | 545 (24.4)           | 60 (7.4)             | 726 (26.8)           |
| Dyslipidaemia                               | 59 (8.3)             | 290 (13.0)           | 67 (8.3)             | 343 (12.7)           |
| Hypertension                                | 64 (9.0)             | 318 (14.2)           | 78 (9.6)             | 370 (13.7)           |
| Infection                                   | 52 (7.3)             | 242 (10.8)           | 60 (7.4)             | 286 (10.6)           |
| Other autoimmune diseases                   | 6 (0.8)              | 45 (2.0)             | 9 (1.1)              | 53 (2.0)             |
| Rheumatoid arthritis                        | 15 (2.1)             | 29 (1.3)             | 18 (2.2)             | 35 (1.3)             |
| Systemic lupus erythematosus                | 10 (1.4)             | 13 (0.6)             | 14 (1.7)             | 17 (0.6)             |
| <b>Treatment, n (%)</b>                     |                      |                      |                      |                      |
| Chronic use of corticosteroids*             | 20 (2.8)             | 99 (4.4)             | 26 (3.2)             | 130 (4.8)            |
| NSIST <sup>†</sup>                          | 30 (4.2)             | 109 (4.9)            | 45 (5.5)             | 197 (7.3)            |
| Eculizumab/rituximab                        | 2 (0.3)              | 6 (0.3)              | 5 (0.6)              | 10 (0.4)             |

Baseline was defined as the period of 12 months prior to MG diagnosis. Composite escalation includes: steroid escalation as monotherapy, NSIST escalation, NSIST combined with steroids, NSIST add-on with another NSIST, Ig escalation, eculizumab escalation, rituximab escalation, PLEX escalation, PLEX combined with steroids, PLEX combined with NSIST.

HDCS was defined as a daily prednisolone-equivalent dose of ≥15 mg

\*Oral steroid use (any dose) with a supply of  $\geq 90$  days, with up to 14 days' gap allowed between prescription refills.

<sup>†</sup>NSIST with or without concomitant treatment.

HDCS, high-dose corticosteroid; Ig, immunoglobulin; MG, myasthenia gravis; MG-TE, myasthenia gravis treatment escalation; NSIST, non-steroidal immunosuppressant therapy; PLEX, plasma exchange; SD, standard deviation.

**Table S6. Treatment status following the first MG-TE after MG diagnosis, by age group**

|                                                 | <b>18–49 years<br/>N=1,102</b> | <b>≥50 years<br/>N=3,823</b> |
|-------------------------------------------------|--------------------------------|------------------------------|
| <b>Treatment de-escalation, n (%)</b>           | 759 (68.9)                     | 2,456 (64.2)                 |
| Mean (SD) number per patient                    | 3.2 (3.0)                      | 2.8 (2.4)                    |
| Median (IQR) number per patient                 | 2.0 (1.0–4.0)                  | 2.0 (1.0–3.0)                |
| IR in PY during follow-up (95% CI)              | 0.73 (0.71–0.76)               | 0.65 (0.63–0.66)             |
| <b>Rescue treatment, n (%)</b>                  | 546 (49.5)                     | 1,752 (45.8)                 |
| Mean (SD) number per patient                    | 3.3 (3.1)                      | 2.9 (2.5)                    |
| Median (IQR) number per patient                 | 2.0 (1.0–4.0)                  | 2.0 (1.0–4.0)                |
| IR in PY during follow-up (95% CI)              | 0.55 (0.52–0.58)               | 0.48 (0.46–0.50)             |
| <b>Treatment break (excluding AChEI), n (%)</b> | 580 (52.6)                     | 1,716 (44.9)                 |
| Mean (SD) number per patient                    | 1.9 (1.5)                      | 1.7 (1.1)                    |
| Median (IQR) number per patient                 | 1.0 (1.0–2.0)                  | 1.0 (1.0–2.0)                |
| IR in PY during follow-up (95% CI)              | 0.34 (0.32–0.37)               | 0.28 (0.27–0.29)             |
| <b>Treatment re-escalation, n (%)</b>           | 330 (29.9)                     | 970 (25.4)                   |
| Mean (SD) number per patient                    | 2.0 (1.6)                      | 1.6 (1.1)                    |
| Median (IQR) number per patient                 | 1.0 (1.0–2.0)                  | 1.0 (1.0–2.0)                |
| IR in PY during follow-up (95% CI)              | 0.20 (0.18–0.22)               | 0.15 (0.14–0.16)             |

Treatment de-escalation was defined as a gap of >14 days between the end of the first escalation of any type and the start of a new escalation; rescue treatment was defined as the start of a new escalation of any type following the last treatment de-escalation; treatment break was defined as a gap of ≥90 days between consecutive claims of all MG-related treatments, defined as a gap between prescriptions of more than three months; treatment re-escalation was defined as the start of a new escalation of any type following the last MG treatment break.

AChEI, acetylcholinesterase inhibitor; CI, confidence interval; IQR, interquartile range; IR, incidence rate; MG, myasthenia gravis; MG-TE, myasthenia gravis treatment escalation; PY, patient years; SD, standard deviation.

**Table S7. Treatment pattern following the first MG-TE after MG diagnosis, by MG-TE sub-cohort and age group**

|                         |          | De-escalation<br>n (%) | Rescue treatment<br>n (%) | Treatment break*<br>n (%) | Re-escalation<br>n (%) |
|-------------------------|----------|------------------------|---------------------------|---------------------------|------------------------|
| <b>18–49 years</b>      |          |                        |                           |                           |                        |
| <b>MG-TE sub-cohort</b> | <b>N</b> |                        |                           |                           |                        |
| HDCS                    | 714      | 678 (95.0)             | 503 (70.4)                | 529 (74.1)                | 313 (43.8)             |
| NSIST                   | 194      | 181 (93.3)             | 161 (83.0)                | 109 (56.2)                | 82 (42.3)              |
| HDCS + NSIST            | 117      | 102 (87.2)             | 93 (79.5)                 | 48 (41.0)                 | 33 (28.2)              |
| PLEX                    | 107      | 102 (95.3)             | 88 (82.2)                 | 63 (58.9)                 | 43 (40.2)              |
| Ig                      | 72       | 68 (94.4)              | 54 (75.0)                 | 45 (62.5)                 | 29 (40.3)              |
| Rituximab               | 16       | 16 (100.0)             | 15 (93.8)                 | 9 (56.3)                  | 7 (43.8)               |
| HDCS + PLEX             | 16       | 14 (87.5)              | 13 (81.3)                 | 6 (37.5)                  | 4 (25.0)               |
| NSIST + NSIST           | 7        | 6 (85.7)               | 6 (85.7)                  | 5 (71.4)                  | 5 (71.4)               |
| PLEX + NSIST            | 9        | 8 (88.9)               | 7 (77.8)                  | 2 (22.2)                  | 1 (11.1)               |
| <b>≥50 years</b>        |          |                        |                           |                           |                        |
| <b>MG-TE sub-cohort</b> | <b>N</b> |                        |                           |                           |                        |
| HDCS                    | 2,237    | 2,085 (93.2)           | 1,499 (67.0)              | 1,544 (69.0)              | 891 (39.8)             |
| NSIST                   | 801      | 706 (88.1)             | 649 (81.0)                | 336 (41.9)                | 262 (32.7)             |
| HDCS + NSIST            | 457      | 391 (85.6)             | 360 (78.8)                | 161 (35.2)                | 119 (26.0)             |
| PLEX                    | 288      | 270 (93.8)             | 222 (77.1)                | 134 (46.5)                | 88 (30.6)              |
| Ig                      | 189      | 182 (96.3)             | 149 (78.8)                | 106 (56.1)                | 73 (38.6)              |
| Rituximab               | 43       | 43 (100.0)             | 41 (95.3)                 | 21 (48.8)                 | 15 (34.9)              |
| HDCS + PLEX             | 32       | 30 (93.8)              | 29 (90.6)                 | 11 (34.4)                 | 10 (31.3)              |
| NSIST + NSIST           | 30       | 25 (83.3)              | 24 (80.0)                 | 9 (30.0)                  | 6 (20.0)               |
| PLEX + NSIST            | 27       | 23 (85.2)              | 21 (77.8)                 | 7 (25.9)                  | 6 (22.2)               |

\*Excluding AChEI.

HDCS was defined as a daily prednisolone-equivalent dose of ≥15 mg

AChEI, acetylcholinesterase inhibitor; HDCS, high-dose corticosteroid; Ig, immunoglobulin; MG, myasthenia gravis; MG-TE, myasthenia gravis treatment escalation; NSIST, non-steroidal immunosuppressive therapy; PLEX, plasma exchange.

**Table S8. MG treatment after MG diagnosis, by follow-up year and age group**

|                       |              | Follow-up year from MG diagnosis |              |            |            |            |            |           |           |
|-----------------------|--------------|----------------------------------|--------------|------------|------------|------------|------------|-----------|-----------|
|                       | All years    | 1                                | 2            | 3          | 4          | 5          | 6          | 7         | 8         |
| 18–49 years           |              |                                  |              |            |            |            |            |           |           |
| N                     | 1,102        | 1,102                            | 884          | 636        | 433        | 304        | 199        | 125       | 84        |
| Maintenance Ig, n (%) | 86 (7.8)     | 65 (5.9)                         | 50 (5.7)     | 27 (4.2)   | 16 (3.7)   | 10 (3.3)   | 7 (3.5)    | 5 (4.0)   | 6 (7.1)   |
| AChEI, n (%)          | 844 (76.6)   | 797 (72.3)                       | 313 (35.4)   | 203 (31.9) | 132 (30.5) | 92 (30.3)  | 55 (27.6)  | 27 (21.6) | 18 (21.4) |
| Thymectomy, n (%)     | 186 (16.9)   | 151 (13.7)                       | 18 (2.0)     | 8 (1.3)    | 4 (0.9)    | 1 (0.3)    | 4 (2.0)    | 0 (0.0)   | 0 (0.0)   |
| ≥50 years             |              |                                  |              |            |            |            |            |           |           |
| N                     | 3,823        | 3,823                            | 3,064        | 2,100      | 1,421      | 914        | 552        | 304       | 124       |
| Maintenance Ig, n (%) | 242 (6.3)    | 178 (4.7)                        | 135 (4.4)    | 75 (3.6)   | 38 (2.7)   | 27 (3.0)   | 14 (2.5)   | 7 (2.3)   | 1 (0.8)   |
| AChEI, n (%)          | 3,107 (81.3) | 2,928 (76.6)                     | 1,261 (41.2) | 742 (35.3) | 438 (30.8) | 235 (25.7) | 132 (23.9) | 57 (18.8) | 26 (21.0) |
| Thymectomy, n (%)     | 193 (5.0)    | 167 (4.4)                        | 16 (0.5)     | 4 (0.2)    | 3 (0.2)    | 2 (0.2)    | 1 (0.2)    | 0 (0.0)   | 0 (0.0)   |

Patients may have been prescribed more than one type of treatment, or no treatment so percentages may add up to more or less than 100.

AChEI, acetylcholinesterase inhibitor; Ig, immunoglobulin; MG, myasthenia gravis.

Table S9. MG-TEs after MG diagnosis in each sensitivity analysis, by age group

|                                         | SA1           | SA2           | SA3           | SA4           | Primary analysis |
|-----------------------------------------|---------------|---------------|---------------|---------------|------------------|
| 18–49 years                             |               |               |               |               |                  |
| N                                       | 636           | 1,102         | 2,870         | 2,651         | 1,102            |
| Pts with ≥1 MG-TE, n (%)                | 499 (78.5)    | 808 (73.3)    | 2,217 (77.2)  | 2,032 (76.7)  | 811 (73.6)       |
| No. of escalations per pt, median (IQR) | 3.0 (1.0–6.5) | 2.0 (0.0–5.0) | 1.0 (1.0–3.0) | 1.0 (1.0–3.0) | 2.0 (0.0–5.0)    |
| ≥50 years                               |               |               |               |               |                  |
| N                                       | 2,100         | 3,823         | 7,918         | 7,333         | 3,823            |
| Pts with ≥1 MG-TE, n (%)                | 1,623 (77.3)  | 2,710 (70.9)  | 5,700 (72.0)  | 5,240 (71.5)  | 2,710 (70.9)     |
| No. of escalations per pt, median (IQR) | 3.0 (1.0–6.0) | 2.0 (0.0–4.0) | 1.0 (0.0–3.0) | 1.0 (0.0–3.0) | 2.0 (0.0–4.0)    |

IQR, interquartile range; MG, myasthenia gravis; MG-TE, myasthenia gravis treatment escalation; pt(s), patient(s); SA, sensitivity analysis.

**Table S10. Incidence of MG-TEs in primary analysis and each sensitivity analysis, by follow-up year and age group**

|                               | Overall | Follow-up year from MG diagnosis    |                                     |                                     |                                     |                                     |                                     |                                     |                                     |
|-------------------------------|---------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
|                               |         | 1                                   | 2                                   | 3                                   | 4                                   | 5                                   | 6                                   | 7                                   | 8                                   |
| 18–49 years                   |         |                                     |                                     |                                     |                                     |                                     |                                     |                                     |                                     |
| SA1, N                        | 636     | 636                                 | 636                                 | 636                                 | 433                                 | 304                                 | 199                                 | 125                                 | 84                                  |
| IR, per 10,000 PY<br>(95% CI) |         | 5,723.27<br>(5,351.39–<br>6,120.99) | 4,700.14<br>(4,319.21–<br>5,114.68) | 4,510.68<br>(4,099.65–<br>4,962.92) | 4,640.83<br>(4,141.69–<br>5,200.13) | 4,794.97<br>(4,195.24–<br>5,480.43) | 4,950.81<br>(4,215.35–<br>5,814.59) | 5,323.68<br>(4,420.69–<br>6,411.12) | 5,438.29<br>(4,270.69–<br>6,925.12) |
| SA2, N                        | 1,102   | 1,102                               | 884                                 | 636                                 | 433                                 | 304                                 | 199                                 | 125                                 | 84                                  |
| IR, per 10,000 PY<br>(95% CI) |         | 6,483.96<br>(6,197.80–<br>6,783.33) | 5,076.46<br>(4,722.93–<br>5,456.45) | 4,510.68<br>(4,099.65–<br>4,962.92) | 4,640.83<br>(4,141.69–<br>5,200.13) | 4,794.97<br>(4,195.24–<br>5,480.43) | 4,950.81<br>(4,215.35–<br>5,814.59) | 5,323.68<br>(4,420.69–<br>6,411.12) | 5,438.29<br>(4,270.69–<br>6,925.12) |
| SA3, N                        | 2,870   | 2,870                               | 2,194                               | 1,561                               | 1,088                               | 757                                 | 509                                 | 331                                 | 204                                 |
| IR, per 10,000 PY<br>(95% CI) |         | 6,311.50<br>(6,127.68–<br>6,500.83) | 4,529.70<br>(4,306.89–<br>4,764.04) | 3,985.70<br>(3,726.75–<br>4,262.64) | 4,107.66<br>(3,797.41–<br>4,443.27) | 4,004.98<br>(3,632.00–<br>4,416.27) | 3,656.84<br>(3,216.47–<br>4,157.51) | 3,934.26<br>(3,384.86–<br>4,572.84) | 4,141.80<br>(3,401.28–<br>5,043.56) |
| SA4, N                        | 2,651   | 2,651                               | 2,037                               | 1,455                               | 1,015                               | 706                                 | 480                                 | 312                                 | 190                                 |
| IR, per 10,000 PY<br>(95% CI) |         | 6,134.47<br>(5,941.79–<br>6,333.41) | 4,504.24<br>(4,273.87–<br>4,747.03) | 3,976.16<br>(3,708.37–<br>4,263.29) | 4,063.65<br>(3,743.66–<br>4,411.00) | 3,891.01<br>(3,510.02–<br>4,313.37) | 3,462.92<br>(3,016.76–<br>3,975.08) | 3,742.05<br>(3,183.50–<br>4,398.59) | 4,084.15<br>(3,320.25–<br>5,023.81) |
| Primary analysis, N           | 1,102   | 1,102                               | 884                                 | 636                                 | 433                                 | 304                                 | 199                                 | 125                                 | 84                                  |
| IR, per 10,000 PY<br>(95% CI) |         | 6,503.52<br>(6,217.70–<br>6,802.47) | 5,102.37<br>(4,748.88–<br>5,482.18) | 4,510.68<br>(4,099.65–<br>4,962.92) | 4,640.83<br>(4,141.69–<br>5,200.13) | 4,794.97<br>(4,195.24–<br>5,480.43) | 4,950.81<br>(4,215.35–<br>5,814.59) | 5,323.68<br>(4,420.69–<br>6,411.12) | 5,438.29<br>(4,270.69–<br>6,925.12) |
| ≥50 years                     |         |                                     |                                     |                                     |                                     |                                     |                                     |                                     |                                     |
| SA1, N                        | 2,100   | 2,100                               | 2,100                               | 2,100                               | 1,421                               | 914                                 | 552                                 | 304                                 | 124                                 |
| IR, per 10,000 PY<br>(95% CI) |         | 5,552.38<br>(5,343.85–<br>5,769.05) | 4,796.50<br>(4,579.31–<br>5,023.98) | 4,868.32<br>(4,628.42–<br>5,120.66) | 4,686.42<br>(4,394.65–<br>4,997.56) | 4,773.14<br>(4,407.42–<br>5,169.20) | 4,545.62<br>(4,073.19–<br>5,072.84) | 4,624.20<br>(3,970.83–<br>5,385.08) | 5,086.55<br>(4,070.34–<br>6,356.47) |

|                     | Overall | Follow-up year from MG diagnosis |                         |                         |                         |                         |                         |                         |                         |
|---------------------|---------|----------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
|                     |         | 1                                | 2                       | 3                       | 4                       | 5                       | 6                       | 7                       | 8                       |
| SA2, N              | 3,823   | 3,823                            | 3,064                   | 2,100                   | 1,421                   | 914                     | 552                     | 304                     | 124                     |
| IR, per 10,000 PY   |         | 6,222.40                         | 5,094.38                | 4,870.12                | 4,686.42                | 4,773.14                | 4,545.62                | 4,624.20                | 5,086.55                |
| (95% CI)            |         | (6,064.90–<br>6,383.98)          | (4,896.52–<br>5,300.23) | (4,630.18–<br>5,122.51) | (4,394.65–<br>4,997.56) | (4,407.42–<br>5,169.20) | (4,073.19–<br>5,072.84) | (3,970.83–<br>5,385.08) | (4,070.34–<br>6,356.47) |
| SA3, N              | 7,918   | 7,918                            | 5,988                   | 4,194                   | 2,835                   | 1,856                   | 1,167                   | 637                     | 277                     |
| IR, per 10,000 PY   |         | 6,084.95                         | 4,538.24                | 4,299.63                | 4,214.83                | 4,169.41                | 3,997.95                | 3,966.10                | 4,152.69                |
| (95% CI)            |         | (5,971.81–<br>6,200.22)          | (4,399.89–<br>4,680.94) | (4,134.45–<br>4,471.40) | (4,013.43–<br>4,426.34) | (3,921.28–<br>4,433.24) | (3,681.01–<br>4,342.18) | (3,532.58–<br>4,452.81) | (3,504.52–<br>4,920.73) |
| SA4, N              | 7,333   | 7,333                            | 5,568                   | 3,905                   | 2,636                   | 1,738                   | 1,097                   | 597                     | 258                     |
| IR, per 10,000 PY   |         | 5,952.53                         | 4,498.54                | 4,286.32                | 4,187.49                | 4,159.16                | 3,949.08                | 3,961.09                | 4,121.36                |
| (95% CI)            |         | (5,834.42–<br>6,073.04)          | (4,355.43–<br>4,646.36) | (4,115.43–<br>4,464.31) | (3,979.22–<br>4,406.65) | (3,903.16–<br>4,431.95) | (3,623.01–<br>4,304.50) | (3,514.34–<br>4,464.64) | (3,456.64–<br>4,913.91) |
| Primary analysis, N | 3,823   | 3,823                            | 3,064                   | 2,100                   | 1,421                   | 914                     | 552                     | 304                     | 124                     |
| IR, per 10,000 PY   |         | 6,222.40                         | 5,092.22                | 4,868.32                | 4,686.42                | 4,773.14                | 4,545.62                | 4,624.20                | 5,086.55                |
| (95% CI)            |         | (6,064.90–<br>6,383.98)          | (4,894.40–<br>5,298.03) | (4,628.42–<br>5,120.66) | (4,394.65–<br>4,997.56) | (4,407.42–<br>5,169.20) | (4,073.19–<br>5,072.84) | (3,970.83–<br>5,385.08) | (4,070.34–<br>6,356.47) |

CI, confidence interval; IR, incidence rate; MG, myasthenia gravis; MG-TE, myasthenia gravis treatment escalation; PY, patient years; SA, sensitivity analysis.

**Table S11. HDCS escalations in primary analysis and each sensitivity analysis, by follow-up year and age group**

|                                      | Overall | Follow-up year from MG diagnosis |                                     |                                     |                                     |                                     |                                     |                                     |                                     |
|--------------------------------------|---------|----------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
|                                      |         | 1                                | 2                                   | 3                                   | 4                                   | 5                                   | 6                                   | 7                                   | 8                                   |
| 18–49 years                          |         |                                  |                                     |                                     |                                     |                                     |                                     |                                     |                                     |
| HDCS incidence rate                  |         |                                  |                                     |                                     |                                     |                                     |                                     |                                     |                                     |
| SA1, N                               | 636     | 636                              | 636                                 | 636                                 | 433                                 | 304                                 | 199                                 | 125                                 | 84                                  |
| IR, per 10,000 PY<br>(95% CI)        |         | 12,814.47<br>(–)                 | 8,556.39<br>(8,153.17–<br>8,979.55) | 6,535.92<br>(6,007.17–<br>7,111.20) | 6,776.09<br>(6,157.18–<br>7,457.21) | 7,824.09<br>(7,077.02–<br>8,650.03) | 7,304.25<br>(6,397.90–<br>8,338.99) | 7,052.95<br>(5,973.15–<br>8,327.96) | 7,396.15<br>(6,030.35–<br>9,071.28) |
| SA2, N                               | 1,102   | 1,102                            | 884                                 | 636                                 | 433                                 | 304                                 | 199                                 | 125                                 | 84                                  |
| IR, per 10,000 PY<br>(95% CI)        |         | 14,014.35<br>(–)                 | 8,957.78<br>(8,637.49–<br>9,289.95) | 6,535.92<br>(6,007.17–<br>7,111.20) | 6,776.09<br>(6,157.18–<br>7,457.21) | 7,824.09<br>(7,077.02–<br>8,650.03) | 7,304.25<br>(6,397.90–<br>8,338.99) | 7,052.95<br>(5,973.15–<br>8,327.96) | 7,396.15<br>(6,030.35–<br>9,071.28) |
| SA3, N                               | 2,870   | 2,870                            | 2,194                               | 1,561                               | 1,088                               | 757                                 | 509                                 | 331                                 | 204                                 |
| IR, per 10,000 PY<br>(95% CI)        |         | 10,953.68<br>(–)                 | 6,938.37<br>(6,665.38–<br>7,222.54) | 5,564.04<br>(5,231.96–<br>5,917.19) | 5,650.54<br>(5,265.25–<br>6,064.04) | 5,876.34<br>(5,379.50–<br>6,419.06) | 5,620.74<br>(5,007.38–<br>6,309.23) | 5,353.11<br>(4,653.49–<br>6,157.92) | 5,632.72<br>(4,672.22–<br>6,790.66) |
| SA4, N                               | 2,651   | 2,651                            | 2,037                               | 1,455                               | 1,015                               | 706                                 | 480                                 | 312                                 | 190                                 |
| IR, per 10,000 PY<br>(95% CI)        |         | 10,750.06<br>(–)                 | 6,833.47<br>(6,550.47–<br>7,128.70) | 5,628.66<br>(5,285.73–<br>5,993.83) | 5,683.12<br>(5,283.53–<br>6,112.93) | 5,540.21<br>(5,033.21–<br>6,098.28) | 5,336.33<br>(4,704.99–<br>6,052.40) | 5,100.21<br>(4,387.19–<br>5,929.12) | 5,623.47<br>(4,624.99–<br>6,837.53) |
| Primary analysis, N                  | 1,102   | 1,102                            | 884                                 | 636                                 | 433                                 | 304                                 | 199                                 | 125                                 | 84                                  |
| IR, per 10,000 PY<br>(95% CI)        |         | 14,014.35<br>(–)                 | 8,957.78<br>(8,637.49–<br>9,289.95) | 6,535.92<br>(6,007.17–<br>7,111.20) | 6,776.09<br>(6,157.18–<br>7,457.21) | 7,824.09<br>(7,077.02–<br>8,650.03) | 7,304.25<br>(6,397.90–<br>8,338.99) | 7,052.95<br>(5,973.15–<br>8,327.96) | 7,396.15<br>(6,030.35–<br>9,071.28) |
| HDCS mean total duration per patient |         |                                  |                                     |                                     |                                     |                                     |                                     |                                     |                                     |
| SA1, N                               | 636     | 636                              | 636                                 | 636                                 | 433                                 | 304                                 | 199                                 | 125                                 | 84                                  |
| Mean duration,<br>months<br>(95% CI) |         | 2.1<br>(1.9–2.4)                 | 1.3<br>(1.1–1.5)                    | 0.9<br>(0.7–1.0)                    | 0.8<br>(0.6–1.0)                    | 0.7<br>(0.5–0.9)                    | 0.7<br>(0.4–1.0)                    | 0.5<br>(0.2–0.8)                    | 0.4<br>(0.2–0.7)                    |

|                                                        | Overall | Follow-up year from MG diagnosis |               |               |               |               |               |               |               |
|--------------------------------------------------------|---------|----------------------------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|
|                                                        |         | 1                                | 2             | 3             | 4             | 5             | 6             | 7             | 8             |
| SA2, N                                                 | 1,102   | 1,102                            | 884           | 636           | 433           | 304           | 199           | 125           | 84            |
| Mean duration, months (95% CI)                         |         | 2.4 (2.2–2.6)                    | 1.2 (1.0–1.4) | 0.9 (0.7–1.0) | 0.8 (0.6–1.0) | 0.7 (0.5–0.9) | 0.7 (0.4–1.0) | 0.5 (0.2–0.8) | 0.4 (0.2–0.7) |
| SA3, N                                                 | 2,870   | 2,870                            | 2,194         | 1,561         | 1,088         | 757           | 509           | 331           | 204           |
| Mean duration, months (95% CI)                         |         | 1.2 (1.1–1.3)                    | 0.6 (0.5–0.7) | 0.4 (0.4–0.5) | 0.4 (0.3–0.5) | 0.4 (0.3–0.5) | 0.4 (0.2–0.5) | 0.3 (0.1–0.4) | 0.2 (0.1–0.4) |
| SA4, N                                                 | 2,651   | 2,651                            | 2,037         | 1,455         | 1,015         | 706           | 480           | 312           | 190           |
| Mean duration, months (95% CI)                         |         | 1.1 (1.0–1.2)                    | 0.6 (0.5–0.6) | 0.4 (0.3–0.5) | 0.4 (0.3–0.5) | 0.3 (0.2–0.4) | 0.3 (0.2–0.4) | 0.2 (0.1–0.3) | 0.2 (0.1–0.3) |
| Primary analysis, N                                    | 1,102   | 1,102                            | 884           | 636           | 433           | 304           | 199           | 125           | 84            |
| Mean duration, months (95% CI)                         |         | 2.4 (2.2–2.6)                    | 1.2 (1.0–1.4) | 0.9 (0.7–1.0) | 0.8 (0.6–1.0) | 0.7 (0.5–0.9) | 0.7 (0.4–1.0) | 0.5 (0.2–0.8) | 0.4 (0.2–0.7) |
| <b>HDCS maximal daily prednisolone-equivalent dose</b> |         |                                  |               |               |               |               |               |               |               |
| SA1, N                                                 | 636     | 636                              | 636           | 636           | 433           | 304           | 199           | 125           | 84            |
| Mean maximal daily dose, mg (SD)                       |         | 73.2 (131.0)                     | 52.8 (85.2)   | 52.6 (107.5)  | 51.4 (98.1)   | 59.1 (146.9)  | 60.5 (124.5)  | 46.5 (45.5)   | 45.2 (40.2)   |
| SA2, N                                                 | 1,102   | 1,102                            | 884           | 636           | 433           | 304           | 199           | 125           | 84            |
| Mean maximal daily dose, mg (SD)                       |         | 71.1 (123.6)                     | 54.6 (97.4)   | 52.6 (107.5)  | 51.4 (98.1)   | 59.1 (146.9)  | 60.5 (124.5)  | 46.5 (45.5)   | 45.2 (40.2)   |
| SA3, N                                                 | 2,870   | 2,870                            | 2,194         | 1,561         | 1,088         | 757           | 509           | 331           | 204           |
| Mean maximal daily dose, mg (SD)                       |         | 63.8 (112.2)                     | 60.2 (116.5)  | 51.2 (92.6)   | 63.4 (140.4)  | 55.6 (125.7)  | 63.2 (126.4)  | 58.6 (118.0)  | 60.6 (137.6)  |

|                                  | Overall | Follow-up year from MG diagnosis |                              |                              |                              |                              |                              |                              |                              |
|----------------------------------|---------|----------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|
|                                  |         | 1                                | 2                            | 3                            | 4                            | 5                            | 6                            | 7                            | 8                            |
| SA4, N                           | 2,651   | 2,651                            | 2,037                        | 1,455                        | 1,015                        | 706                          | 480                          | 312                          | 190                          |
| Mean maximal daily dose, mg (SD) |         | 60.8 (107.6)                     | 61.0 (120.1)                 | 51.4 (95.3)                  | 62.5 (133.9)                 | 56.8 (131.0)                 | 59.6 (102.4)                 | 57.3 (121.1)                 | 46.4 (42.0)                  |
| Primary analysis, N              | 1,102   | 1,102                            | 884                          | 636                          | 433                          | 304                          | 199                          | 125                          | 84                           |
| Mean maximal daily dose, mg (SD) |         | 71.1 (123.6)                     | 54.6 (97.4)                  | 52.6 (107.5)                 | 51.4 (98.1)                  | 59.1 (146.9)                 | 60.5 (124.5)                 | 46.5 (45.5)                  | 45.2 (40.2)                  |
| <b>≥50 years</b>                 |         |                                  |                              |                              |                              |                              |                              |                              |                              |
| <b>HDGS incidence rate</b>       |         |                                  |                              |                              |                              |                              |                              |                              |                              |
| SA1, N                           | 2,100   | 2,100                            | 2,100                        | 2,100                        | 1,421                        | 914                          | 552                          | 304                          | 124                          |
| IR, per 10,000 PY (95% CI)       |         | 11,485.71 (–)                    | 7,463.98 (7,195.69–7,742.28) | 6,383.66 (6,078.24–6,704.43) | 5,771.33 (5,387.51–6,182.50) | 4,707.40 (4,264.25–5,196.60) | 3,736.41 (3,231.17–4,320.66) | 4,122.51 (3,372.53–5,039.26) | 5,747.83 (4,473.49–7,385.19) |
| SA2, N                           | 3,823   | 3,823                            | 3,064                        | 2,100                        | 1,421                        | 914                          | 552                          | 304                          | 124                          |
| IR, per 10,000 PY (95% CI)       |         | 12,501.16 (–)                    | 7,755.80 (7,527.41–7,991.12) | 6,383.66 (6,078.24–6,704.43) | 5,771.33 (5,387.51–6,182.50) | 4,707.40 (4,264.25–5,196.60) | 3,736.41 (3,231.17–4,320.66) | 4,122.51 (3,372.53–5,039.26) | 5,747.83 (4,473.49–7,385.19) |
| SA3, N                           | 7,918   | 7,918                            | 5,988                        | 4,194                        | 2,835                        | 1,856                        | 1,167                        | 637                          | 277                          |
| IR, per 10,000 PY (95% CI)       |         | 10,428.49 (–)                    | 6,637.00 (6,464.00–6,814.63) | 5,881.24 (5,667.99–6,102.51) | 5,589.36 (5,326.81–5,864.85) | 4,775.43 (4,469.21–5,102.62) | 4,473.62 (4,091.97–4,890.86) | 4,271.76 (3,750.62–4,865.32) | 4,898.42 (4,100.55–5,851.54) |
| SA4, N                           | 7,333   | 7,333                            | 5,568                        | 3,905                        | 2,636                        | 1,738                        | 1,097                        | 597                          | 258                          |
| IR, per 10,000 PY (95% CI)       |         | 10,190.51 (–)                    | 6,556.58 (6,376.68–6,741.56) | 5,784.88 (5,565.06–6,013.38) | 5,561.82 (5,289.99–5,847.62) | 4,678.10 (4,364.63–5,014.07) | 4,349.75 (3,959.76–4,778.14) | 4,270.71 (3,731.87–4,887.34) | 4,806.63 (3,999.25–5,777.00) |
| Primary analysis, N              | 3,823   | 3,823                            | 3,064                        | 2,100                        | 1,421                        | 914                          | 552                          | 304                          | 124                          |
| IR, per 10,000 PY (95% CI)       | 3,823   | 12,501.16 (–)                    | 7,755.80 (7,527.41–7,991.12) | 6,383.66 (6,078.24–6,704.43) | 5,771.33 (5,387.51–6,182.50) | 4,707.40 (4,264.25–5,196.60) | 3,736.41 (3,231.17–4,320.66) | 4,122.51 (3,372.53–5,039.26) | 5,747.83 (4,473.49–7,385.19) |

|                                                 |         | Follow-up year from MG diagnosis |               |               |               |               |               |               |               |
|-------------------------------------------------|---------|----------------------------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|
|                                                 | Overall | 1                                | 2             | 3             | 4             | 5             | 6             | 7             | 8             |
| HDCS mean total duration per patient            |         |                                  |               |               |               |               |               |               |               |
| SA1, N                                          | 2,100   | 2,100                            | 2,100         | 2,100         | 1,421         | 914           | 552           | 304           | 124           |
| Mean duration, months (95% CI)                  |         | 2.4 (2.3–2.6)                    | 1.6 (1.4–1.7) | 1.1 (1.0–1.2) | 0.9 (0.8–1.0) | 0.7 (0.5–0.8) | 0.6 (0.4–0.7) | 0.5 (0.3–0.7) | 0.8 (0.4–1.2) |
| SA2, N                                          | 3,823   | 3,823                            | 3,064         | 2,100         | 1,421         | 914           | 552           | 304           | 124           |
| Mean duration, months (95% CI)                  |         | 2.7 (2.6–2.9)                    | 1.4 (1.3–1.5) | 1.1 (1.0–1.2) | 0.9 (0.8–1.0) | 0.7 (0.5–0.8) | 0.6 (0.4–0.7) | 0.5 (0.3–0.7) | 0.8 (0.4–1.2) |
| SA3, N                                          | 7,918   | 7,918                            | 5,988         | 4,194         | 2,835         | 1,856         | 1,167         | 637           | 277           |
| Mean duration, months (95% CI)                  |         | 1.6 (1.5–1.7)                    | 0.8 (0.8–0.9) | 0.6 (0.6–0.7) | 0.5 (0.5–0.6) | 0.4 (0.3–0.5) | 0.4 (0.3–0.4) | 0.3 (0.2–0.4) | 0.4 (0.2–0.6) |
| SA4, N                                          | 7,333   | 7,333                            | 5,568         | 3,905         | 2,636         | 1,738         | 1,097         | 597           | 258           |
| Mean duration, months (95% CI)                  |         | 1.5 (1.5–1.6)                    | 0.8 (0.8–0.9) | 0.6 (0.5–0.7) | 0.5 (0.5–0.6) | 0.4 (0.3–0.5) | 0.3 (0.2–0.4) | 0.2 (0.2–0.3) | 0.3 (0.2–0.5) |
| Primary analysis, N                             | 3,823   | 3,823                            | 3,064         | 2,100         | 1,421         | 914           | 552           | 304           | 124           |
| Mean duration, months (95% CI)                  |         | 2.7 (2.6–2.9)                    | 1.4 (1.3–1.5) | 1.1 (1.0–1.2) | 0.9 (0.8–1.0) | 0.7 (0.5–0.8) | 0.6 (0.4–0.7) | 0.5 (0.3–0.7) | 0.8 (0.4–1.2) |
| HDCS maximal daily prednisolone-equivalent dose |         |                                  |               |               |               |               |               |               |               |
| SA1, N                                          | 2,100   | 2,100                            | 2,100         | 2,100         | 1,421         | 914           | 552           | 304           | 124           |
| Mean maximal daily dose, mg (SD)                |         | 68.9 (130.1)                     | 63.2 (132.1)  | 56.5 (116.5)  | 51.8 (94.8)   | 51.6 (90.3)   | 45.0 (90.3)   | 47.1 (56.1)   | 41.3 (39.8)   |
| SA2, N                                          | 3,823   | 3,823                            | 3,064         | 2,100         | 1,421         | 914           | 552           | 304           | 124           |
| Mean maximal daily dose, mg (SD)                |         | 72.3 (138.1)                     | 62.7 (134.2)  | 56.5 (116.5)  | 51.8 (94.8)   | 51.6 (90.3)   | 45.0 (90.3)   | 47.1 (56.1)   | 41.3 (39.8)   |

|                                  | Overall | Follow-up year from MG diagnosis |              |              |              |              |             |             |             |
|----------------------------------|---------|----------------------------------|--------------|--------------|--------------|--------------|-------------|-------------|-------------|
|                                  |         | 1                                | 2            | 3            | 4            | 5            | 6           | 7           | 8           |
| SA3, N                           | 7,918   | 7,918                            | 5,988        | 4,194        | 2,835        | 1,856        | 1,167       | 637         | 277         |
| Mean maximal daily dose, mg (SD) |         | 69.4 (137.6)                     | 61.8 (130.6) | 60.2 (127.6) | 54.7 (108.6) | 56.9 (110.8) | 48.8 (89.7) | 47.7 (52.8) | 43.6 (42.2) |
| SA4, N                           | 7,333   | 7,333                            | 5,568        | 3,905        | 2,636        | 1,738        | 1,097       | 597         | 258         |
| Mean maximal daily dose, mg (SD) |         | 67.7 (132.8)                     | 60.5 (127.0) | 60.1 (128.7) | 54.8 (111.8) | 56.8 (113.9) | 49.7 (92.2) | 47.4 (52.8) | 45.2 (43.3) |
| Primary analysis, N              | 3,823   | 3,823                            | 3,064        | 2,100        | 1,421        | 914          | 552         | 304         | 124         |
| Mean maximal daily dose, mg (SD) |         | 72.3 (138.1)                     | 62.7 (134.2) | 56.5 (116.5) | 51.8 (94.8)  | 51.6 (90.3)  | 45.0 (90.3) | 47.1 (56.1) | 41.3 (39.8) |

HDGS was defined as a daily prednisolone-equivalent dose of  $\geq 15$ mg.

CI, confidence interval; HDGS, high-dose corticosteroids; IR, incidence rate; MG, myasthenia gravis; PY, patient years; SA, sensitivity analysis; SD, standard deviation.

**Table S12. Direct MG healthcare costs in primary analysis and each sensitivity analysis, by follow-up year and age group, USD (SD)**

|                     |         | Follow-up year from MG diagnosis |                     |                     |                     |                     |                     |                    |                    |
|---------------------|---------|----------------------------------|---------------------|---------------------|---------------------|---------------------|---------------------|--------------------|--------------------|
|                     | Overall | 1                                | 2                   | 3                   | 4                   | 5                   | 6                   | 7                  | 8                  |
| 18–49 years         |         |                                  |                     |                     |                     |                     |                     |                    |                    |
| SA1, N              | 636     | 636                              | 636                 | 636                 | 433                 | 304                 | 199                 | 125                | 84                 |
| Mean cost, USD (SD) |         | 27,828.8 (81,442.8)              | 12,873.0 (40,396.3) | 11,407.8 (44,530.8) | 13,606.4 (54,978.1) | 10,090.4 (38,453.4) | 12,496.9 (47,236.4) | 8,747.3 (30,361.7) | 5,929.3 (20,340.8) |
| SA2, N              | 1,102   | 1,102                            | 884                 | 636                 | 433                 | 304                 | 199                 | 125                | 84                 |
| Mean cost, USD (SD) |         | 33,022.7 (85,747.5)              | 13,187.5 (42,317.3) | 11,407.8 (44,530.8) | 13,606.4 (54,978.1) | 10,090.4 (38,453.4) | 12,496.9 (47,236.4) | 8,747.3 (30,361.7) | 5,929.3 (20,340.8) |
| SA3, N              | 2,870   | 2,870                            | 2,194               | 1,561               | 1,088               | 757                 | 509                 | 331                | 204                |
| Mean cost, USD (SD) |         | 13,791.8 (55,752.1)              | 5,408.8 (27,631.0)  | 4,732.0 (28,964.0)  | 5,489.1 (35,293.6)  | 4,122.5 (24,843.7)  | 4,979.8 (30,118.1)  | 3,337.7 (19,086.2) | 2,472.0 (13,329.3) |
| SA4, N              | 2,651   | 2,651                            | 2,037               | 1,455               | 1,015               | 706                 | 480                 | 312                | 190                |
| Mean cost, USD (SD) |         | 11,855.3 (50,397.0)              | 4,631.3 (24,654.5)  | 3,738.9 (22,899.3)  | 4,073.1 (25,717.5)  | 3,838.6 (24,446.5)  | 4,346.3 (29,162.0)  | 2,736.7 (17,087.9) | 2,410.6 (13,741.8) |
| Primary analysis, N | 1,102   | 1,102                            | 884                 | 636                 | 433                 | 304                 | 199                 | 125                | 84                 |
| Mean cost, USD (SD) |         | 33,022.7 (85,747.5)              | 13,187.5 (42,317.3) | 11,407.8 (44,530.8) | 13,606.4 (54,978.1) | 10,090.4 (38,453.4) | 12,496.9 (47,236.4) | 8,747.3 (30,361.7) | 5,929.3 (20,340.8) |
| ≥50 years           |         |                                  |                     |                     |                     |                     |                     |                    |                    |
| SA1, N              | 2,100   | 2,100                            | 2,100               | 2,100               | 1,421               | 914                 | 552                 | 304                | 124                |
| Mean cost, USD (SD) |         | 21,341.0 (63,657.0)              | 12,946.3 (56,318.3) | 10,599.0 (49,590.6) | 9,622.6 (54,126.7)  | 11,185.8 (83,519.5) | 8,936.0 (37,873.2)  | 6,531.9 (37,863.9) | 3,022.2 (11,528.0) |
| SA2, N              | 3,823   | 3,823                            | 3,064               | 2,100               | 1,421               | 914                 | 552                 | 304                | 124                |
| Mean cost, USD (SD) |         | 24,982.4 (76,666.6)              | 11,036.3 (48,810.6) | 10,599.0 (49,590.6) | 9,622.6 (54,126.7)  | 11,185.8 (83,519.5) | 8,936.0 (37,873.2)  | 6,531.9 (37,863.9) | 3,022.2 (11,528.0) |
|                     |         |                                  |                     |                     |                     |                     |                     |                    |                    |
| SA3, N              | 7,918   | 7,918                            | 5,988               | 4,194               | 2,835               | 1,856               | 1,167               | 637                | 277                |

|                     |         | Follow-up year from MG diagnosis |            |            |            |            |            |            |            |
|---------------------|---------|----------------------------------|------------|------------|------------|------------|------------|------------|------------|
|                     | Overall | 1                                | 2          | 3          | 4          | 5          | 6          | 7          | 8          |
| Mean cost, USD      |         | 13,439.3                         | 5,757.2    | 5,394.6    | 4,898.6    | 5,563.5    | 4,269.4    | 3,171.0    | 1,397.9    |
| (SD)                |         | (55,947.3)                       | (35,370.1) | (35,487.5) | (38,616.8) | (58,856.0) | (26,409.5) | (26,334.4) | (7,838.2)  |
| SA4, N              | 7,333   | 7,333                            | 5,568      | 3,905      | 2,636      | 1,738      | 1,097      | 597        | 258        |
| Mean cost, USD      |         | 12,495.5                         | 5,454.3    | 5,363.2    | 4,958.5    | 5,441.4    | 4,176.9    | 3,242.0    | 1,440.5    |
| (SD)                |         | (53,577.8)                       | (35,338.2) | (36,204.9) | (39,780.1) | (60,315.6) | (26,662.3) | (27,078.4) | (8,107.6)  |
| Primary analysis, N | 3,823   | 3,823                            | 3,064      | 2,100      | 1,421      | 914        | 552        | 304        | 124        |
| Mean cost, USD      |         | 24,982.4                         | 11,036.3   | 10,599.0   | 9,622.6    | 11,185.8   | 8,936.0    | 6,531.9    | 3,022.2    |
| (SD)                |         | (76,666.6)                       | (48,810.6) | (49,590.6) | (54,126.7) | (83,519.5) | (37,873.2) | (37,863.9) | (11,528.0) |

All costs were adjusted for inflation values from 2019, obtained from <https://www.bls.gov/cpi/tables/supplemental-files/home.htm>. Accessed April 2024.

MG, myasthenia gravis; SA, sensitivity analysis; SD, standard deviation; USD, United States dollars.

**Table S13. MG pharmacy costs in primary analysis and each sensitivity analysis, by follow-up year and age group, USD (SD)**

|                     |         | Follow-up year from MG diagnosis |           |            |            |           |            |           |           |
|---------------------|---------|----------------------------------|-----------|------------|------------|-----------|------------|-----------|-----------|
|                     | Overall | 1                                | 2         | 3          | 4          | 5         | 6          | 7         | 8         |
| 18–49 years         |         |                                  |           |            |            |           |            |           |           |
| SA1, N              | 636     | 636                              | 636       | 636        | 433        | 304       | 199        | 125       | 84        |
| Mean cost, USD      |         | 680.3                            | 923.2     | 1,703.3    | 1,604.1    | 837.0     | 651.0      | 490.8     | 363.4     |
| (SD)                |         | (1,925.6)                        | (4,882.3) | (19,284.3) | (16,573.9) | (3,608.9) | (2,493.1)  | (1,421.4) | (921.9)   |
| SA2, N              | 1,102   | 1,102                            | 884       | 636        | 433        | 304       | 199        | 125       | 84        |
| Mean cost, USD      |         | 693.6                            | 811.1     | 1,703.3    | 1,604.1    | 837.0     | 651.0      | 490.8     | 363.4     |
| (SD)                |         | (1,965.2)                        | (4,289.1) | (19,284.3) | (16,573.9) | (3,608.9) | (2,493.1)  | (1,421.4) | (921.9)   |
| SA3, N              | 2,870   | 2,870                            | 2,194     | 1,561      | 1,088      | 757       | 509        | 331       | 204       |
| Mean cost, USD      |         | 415.8                            | 422.1     | 778.1      | 712.4      | 406.4     | 348.5      | 219.7     | 180.1     |
| (SD)                |         | (2,735.2)                        | (3,015.6) | (12,370.9) | (10,511.2) | (2,445.3) | (1,888.8)  | (944.3)   | (681.4)   |
| SA4, N              | 2,651   | 2,651                            | 2,037     | 1,455      | 1,015      | 706       | 480        | 312       | 190       |
| Mean cost, USD      |         | 416.8                            | 430.6     | 802.6      | 723.7      | 400.3     | 327.1      | 180.6     | 142.1     |
| (SD)                |         | (2,831.8)                        | (3,122.8) | (12,801.2) | (10,858.7) | (2,491.4) | (1,866.4)  | (731.1)   | (518.3)   |
| Primary analysis, N | 1,102   | 1,102                            | 884       | 636        | 433        | 304       | 199        | 125       | 84        |
| Mean cost, USD      |         | 693.6                            | 811.1     | 1,703.3    | 1,604.1    | 837.0     | 651.0      | 490.8     | 363.4     |
| (SD)                |         | (1,965.2)                        | (4,289.1) | (19,284.3) | (16,573.9) | (3,608.9) | (2,493.1)  | (1,421.4) | (921.9)   |
| ≥50 years           |         |                                  |           |            |            |           |            |           |           |
| SA1, N              | 2,100   | 2,100                            | 2,100     | 2,100      | 1,421      | 914       | 552        | 304       | 124       |
| Mean cost, USD      |         | 1,091.8                          | 1,192.0   | 962.5      | 1,321.7    | 1,192.0   | 1,546.8    | 971.6     | 607.8     |
| (SD)                |         | (6,673.9)                        | (9,605.3) | (5,349.4)  | (20,320.9) | (6,318.0) | (10,588.1) | (3,770.4) | (1,833.3) |
| SA2, N              | 3,823   | 3,823                            | 3,064     | 2,100      | 1,421      | 914       | 552        | 304       | 124       |
| Mean cost, USD      |         | 1,111.6                          | 1,017.8   | 962.5      | 1,321.7    | 1,192.0   | 1,546.8    | 971.6     | 607.8     |
| (SD)                |         | (6,799.4)                        | (8,281.3) | (5,349.4)  | (20,320.9) | (6,318.0) | (10,588.1) | (3,770.4) | (1,833.3) |
| SA3, N              | 7,918   | 7,918                            | 5,988     | 4,194      | 2,835      | 1,856     | 1,167      | 637       | 277       |
| Mean cost, USD      |         | 645.7                            | 630.8     | 563.5      | 737.9      | 642.0     | 774.2      | 517.4     | 317.1     |
| (SD)                |         | (4,816.1)                        | (6,179.4) | (3,930.8)  | (14,426.3) | (4,478.6) | (7,320.3)  | (2,666.6) | (1,278.0) |
| SA4, N              | 7,333   | 7,333                            | 5,568     | 3,905      | 2,636      | 1,738     | 1,097      | 597       | 258       |
| Mean cost, USD      |         | 657.3                            | 615.6     | 549.4      | 731.2      | 598.9     | 800.7      | 532.3     | 318.9     |
| (SD)                |         | (4,993.1)                        | (6,204.9) | (3,943.8)  | (14,922.6) | (4,329.2) | (7,546.5)  | (2,745.5) | (1,312.9) |

|                     |         | Follow-up year from MG diagnosis |           |           |            |           |            |           |           |
|---------------------|---------|----------------------------------|-----------|-----------|------------|-----------|------------|-----------|-----------|
|                     | Overall | 1                                | 2         | 3         | 4          | 5         | 6          | 7         | 8         |
| Primary analysis, N | 3,823   | 3,823                            | 3,064     | 2,100     | 1,421      | 914       | 552        | 304       | 124       |
| Mean cost, USD      |         | 1,111.6                          | 1,017.8   | 962.5     | 1,321.7    | 1,192.0   | 1,546.8    | 971.6     | 607.8     |
| (SD)                |         | (6,799.4)                        | (8,281.3) | (5,349.4) | (20,320.9) | (6,318.0) | (10,588.1) | (3,770.4) | (1,833.3) |

All costs were adjusted for inflation values from 2019, obtained from <https://www.bls.gov/cpi/tables/supplemental-files/home.htm>. Accessed April 2024.

MG, myasthenia gravis; SA, sensitivity analysis; SD, standard deviation; USD, United States dollars.

**Table S14. Definition of non-MG peripheral neural disorders considered for exclusion in sensitivity analyses**

| <b>Disease</b>                                            | <b>ICD-9 codes</b>               | <b>ICD-10 codes</b>                                       |
|-----------------------------------------------------------|----------------------------------|-----------------------------------------------------------|
| Lambert-Eaton myasthenic syndrome                         | 358.3 (30, 31, 39)               | G70.80<br>G70.81<br>G73.1                                 |
| Neonatal MG                                               | 775.2                            | P94.0                                                     |
| Myasthenic syndromes in diseases classified elsewhere     | 358.1                            | G73.3                                                     |
| Guillain-Barré syndrome                                   | 357.0                            | G61.0                                                     |
| Chronic inflammatory demyelinating polyneuritis           | 357.81                           | G61.81                                                    |
| Critical illness polyneuropathy                           | 357.82                           | G61.82                                                    |
| Polyneuropathy due to other diseases classified elsewhere | 357.4                            | G63                                                       |
| Acute poliomyelitis with/without paralysis                | 045.0<br>045.1<br>045.2<br>045.9 | A80.39<br>A80.4<br>A80.9                                  |
| Acute transverse myelitis                                 | 323                              | G04.0<br>G04.3<br>G04.8<br>G04.9<br>G05.3<br>G05.4<br>G92 |
| Acute alcohol intoxication                                | 303.0                            | F10.229                                                   |
| Poisoning by drug and biologic substances                 | 960<br>979                       | T36<br>T49                                                |
| Botulism                                                  | 005.1                            | A05.1                                                     |

ICD, International Classification of Diseases; MG, myasthenia gravis.