

Predicting Outcome in Guillain-Barré Syndrome


International Validation of the Modified Erasmus GBS Outcome Score

Alex Y. Doets, MD, PhD candidate, Hester F. Lingsma, PhD, Christa Walgaard, MD, PhD candidate, Badrul Islam, MBBS, PhD, Nowshin Papri, MD, PhD candidate, Amy Davidson, MD, PhD candidate, Yuko Yamagishi, MD, PhD, Susumu Kusunoki, MD, PhD, Mazen M. Dimachkie, MD, Waqar Waheed, MD, Noah Kolb, MD, Zhahirul Islam, PhD, Quazi Deen Mohammad, MD, Thomas Harbo, MD, PhD, Soren H. Sindrup, MD, PhD, Govindsinh Chavada, MD, PhD, Hugh J. Willison, MD, PhD, Carlos Casanovas, MD, PhD, Kathleen Bateman, MBChB, James A.L. Miller, MD, PhD, Bianca van den Berg, MD, PhD candidate, Christine Verboon, MD, PhD candidate, Joyce Roodbol, MD, PhD candidate, Sonja E. Leonhard, MD, PhD candidate, Luana Benedetti, MD, PhD, Satoshi Kuwabara, MD, PhD, Peter Van den Bergh, MD, PhD, Soledad Monges, MD, Girolama A. Marfia, MD, Nortina Shahrizaila, FRCP, PhD, Giuliana Galassi, MD, Yann Péréon, MD, PhD, Jan Bürmann, MD, Krista Kuitwaard, MD, PhD, Ruud P. Kleyweg, MD, PhD, Cintia Marchesoni, MD, María J. Sedano Tous, MD, Luis Querol, MD, PhD, Isabel Illa, MD, PhD, Yuzhong Wang, MD, Eduardo Nobile-Orazio, MD, PhD, Simon Rinaldi, MBChB, PhD, Angelo Schenone, MD, Julio Pardo, MD, PhD, Frederique H. Vermeij, MD, Helmar C. Lehmann, MD, PhD, Volkan Granit, MD, Guido Cavaletti, MD, Gerardo Gutiérrez-Gutiérrez, MD, Fabio A. Barroso, MD, Leo H. Visser, MD, PhD, Hans D. Katzberg, MD, Efthimios Dardiotis, MD, Shahram Attarian, MD, PhD, Anneke J. van der Kooij, MD, PhD, Filip Eftimov, MD, PhD, Paul W. Wirtz, MD, PhD, Johnny P.A. Samijn, MD, H. Jacobus Gilhuis, MD, PhD, Robert D.M. Hadden, MD, PhD, James K.L. Holt, FRCP, PhD, Kazim A. Sheikh, MD, Summer Karafiath, MD, Michal Vytopil, MD, Giovanni Antonini, MD, Thomas E. Feasby, MD, Catharina G. Faber, MD, PhD, Cees J. Gijssbers, MD, Mark Busby, MD, Rhys C. Roberts, MB BChir PhD, Nicholas J. Silvestri, MD, Raffaella Fazio, MD, Gert W. van Dijk, MD, Marcel P.J. Garssen, MD, PhD, Chiara S.M. Straathof, MD, PhD, Kenneth C. Gorson, MD, and Bart C. Jacobs, MD, PhD, on behalf of the IGOS Consortium

Correspondence

Dr. Jacobs
b.jacobs@erasmusmc.nl

MORE ONLINE

 **Class of Evidence**
Criteria for rating
therapeutic and diagnostic
studies

[NPub.org/coe](https://npub.org/coe)

 **CME Course**
[NPub.org/cmelist](https://npub.org/cmelist)

 **Podcast**
[Npub.org/Podcast9805](https://npub.org/Podcast9805)

Neurology® 2022;98:e518-e532. doi:10.1212/WNL.0000000000013139

Abstract

Background and Objectives

The clinical course and outcome of the Guillain-Barré syndrome (GBS) are diverse and vary among regions. The modified Erasmus GBS Outcome Score (mEGOS), developed with data from Dutch patients, is a clinical model that predicts the risk of walking inability in patients with GBS. The study objective was to validate the mEGOS in the International GBS Outcome Study (IGOS) cohort and to improve its performance and region specificity.

From the Departments of Neurology (A.Y.D., C.W., B.v.d.B., C.V., J.R., S.E.L., K.K., B.C.J.), Public Health (H.F.L.), and Immunology (B.C.J.), Erasmus MC, University Medical Centre Rotterdam; Department of Neurology (C.W., J.P.A.S.), Maastricht Hospital, Rotterdam, the Netherlands; Laboratory of Gut-Brain Signaling (B.I., N.P., Z.I.), Laboratory Sciences and Services Division, Dhaka, Bangladesh; Department of Neurology (A.D., G. Chavada, H.J.W.), College of Medical, Veterinary and Life Sciences, University of Glasgow, UK; Department of Neurology (Y.Y., S. Kusunoki), Kindai University Faculty of Medicine, Osaka-Sayama City, Osaka, Japan; Department of Neurology (M.M.D.), University of Kansas Medical Center, Kansas City; Department of Neurology (W.W., N.K.), University of Vermont Medical Center, Burlington; National Institute of Neurosciences and Hospital (Q.D.M.), Agargaon, Bangladesh; Department of Neurology (T.H.), Aarhus University Hospital; Department of Neurology (S.H.S.), Odense University Hospital and University of Southern Denmark, Odense, Denmark; Department of Neurology, Neuromuscular Unit (C.C.), Bellvitge University Hospital-IDIBELL, CIBERER, Barcelona, Spain; Department of Neurology (K.B.), Groote Schuur Hospital, University of Cape Town, South Africa; Department of Neurology (J.A.L.M.), Royal Victoria Infirmary, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle, UK; Department of Neurology (B.v.d.B., C.J.G.), Franciscus Vlietland Hospital, Schiedam, the Netherlands; Department of Neurology (L.B.), IRCCS Ospedale Policlinico San Martino, Genova, Italy; Department of Neurology (S. Kuwabara), Chiba University, Japan; Department of Neurology (P.V.d.B.), Neuromuscular Reference Centre, University Hospital Saint-Luc, University of Louvain, Brussels, Belgium; Department of Neurology (S.M.), Hospital de Pediatría J.P. Garrahan, Buenos Aires, Argentina; Dysimmune Neuropathies Unit, Department of Systems Medicine (G.A.M.), Tor Vergata University Hospital, Rome, Italy; Department of Medicine (N.S.), University of Malaya, Kuala Lumpur; Department of Neurology (G.G.), University Hospital of Modena, Italy; Department of Clinical Neurophysiology, Reference Centre for NMD (Y.P.), CHU Nantes, France; Department of Neurology (J.B.), Saarland University Medical School, Homburg-Saarland (previous affiliation); MVZ Palztklinikum (J.B.), Kusel, Germany (current affiliation); Department of Neurology (K.K., R.P.K.), Albert Schweitzer Hospital, Dordrecht, the Netherlands; Department of Neurology (C.M.), Hospital Británico, Buenos Aires, Argentina; Department of Neurology (M.J.S.T.), Hospital Marques de Valdeilla, Santander; Department of Neurology (L.Q., I.I.), Hospital de la Santa Creu i Santa Pau, U.A.B. CIBERER and ERN-NMD, Barcelona, Spain; Department of Neurology (Y.W.), Affiliated Hospital of Jining Medical University, Shandong Province, China; Neuromuscular and Neuroimmunology Service (E.N.-O.), IRCCS Humanitas Clinical and Research Institute, Milan University, Rozzano, Italy; Nuffield Department of Clinical Neurosciences (S.R.), University of Oxford and Oxford University Hospitals NHS Foundation Trust, UK; Department of Neurosciences, Ophthalmology, Rehabilitation, Genetics and Maternal Sciences (A.S.), University of Genova; IRCCS San Martino Hospital (A.S.), Genova, Italy; Department of Neurology (J.P.), Hospital Clínico de Santiago, Santiago de Compostela (A. Coruña), Spain; Department of Neurology (F.H.V.), Franciscus Vlietland Hospital (location: Franciscus Gasthuis), Rotterdam, the Netherlands; Department of Neurology (H.C.L.), University Hospital of Cologne, Germany; Department of Neurology (V.G.), Montefiore Medical Centre, Bronx, NY; Department of Neurology (G. Cavaletti), University Milano-Bicocca, Monza, Italy; Department of Neurology (G.G.-G.), Hospital Universitario Infanta Sofía, San Sebastián de los Reyes, Spain; Department of Neurology (F.A.B.), Instituto de Investigaciones Neurológicas Raúl Carrea, Buenos Aires, Argentina; Department of Neurology (L.H.V.), St. Elisabeth-TweeSteden Hospital, Tilburg, the Netherlands; Department of Neurology (H.D.K.), University Health Network, University of Toronto, Canada; Department of Neurology (E.D.), University Hospital of Larissa, Greece; Department of Neurology, Reference Centre for NMD (S.A.), CHU Timone, Marseille, France; Department of Neurology (A.J.v.d.K., F.E.), Amsterdam University Medical Centre, University of Amsterdam, Neuroscience Institute, Netherlands Neuromuscular Centre, Euro-NMD; Department of Neurology (P.W.W.), Haga Hospital, Den Haag; Department of Neurology (H.J.G.), Reinier de Graaf Hospital, Delft, the Netherlands; Department of Neurology (R.D.M.H.), King's College Hospital, London; Department of Neurology (J.K.L.H.), The Walton Centre, Liverpool, UK; Department of Neurology (K.A.S.), University of Texas Health Science Centre at Houston; Department of Neurology (S. Karafiath), University of Utah School of Medicine, Salt Lake City; Department of Neurology (M.V.), Lahey Hospital and Medical Center, Tufts University School of Medicine, Burlington, MA; Department of Neurology (G.A.), Mental Health and Sensory Organs (NESMOS), University of Rome "Sapienza," Sant'Andrea Hospital, Rome, Italy; Department of Clinical Neurosciences (T.E.F.), University of Calgary, Canada; Department of Neurology (C.G.F.), Maastricht University Medical Centre, the Netherlands; Department of Neurology (M.B.), Leeds Teaching Hospitals; Department of Neurology (R.C.R.), Addenbrooke's Hospital, Cambridge, UK; Department of Neurology (N.J.S.), University at Buffalo Jacobs School of Medicine and Biomedical Sciences, NY; Department of Neurology (R.F.), Scientific Institute San Raffaele, Milan, Italy; Department of Neurology (G.W.v.D.), Canisius Wilhelmina Hospital, Nijmegen; Department of Neurology (M.P.J.G.), Jeroen Bosch Hospital, 's-Hertogenbosch; Department of Neurology (C.S.M.S.), Leiden University Medical Centre, the Netherlands; and Department of Neurology (K.C.G.), St. Elizabeth's Medical Centre, Tufts University, School of Medicine, Boston, MA.

Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

IGOS Consortium coinvestigators are listed at links.lww.com/WNL/B728.

Glossary

AUC = area under the receiver operating characteristic curve; **CI** = confidence interval; **Eu/NA** = Europe/North America; **GBS** = Guillain-Barré syndrome; **IGOS** = International GBS Outcome Study; **IVIg** = IV immunoglobulin; **mEGOS** = modified Erasmus GBS Outcome Score; **MFS** = Miller Fisher syndrome; **MRC** = Medical Research Council; **OR** = odds ratio; **RCT** = randomized controlled trial; **ROC** = receiver operating characteristic.

Methods

We used prospective data from the first 1,500 patients included in IGOS, aged ≥ 6 years and unable to walk independently. We evaluated whether the mEGOS at entry and week 1 could predict the inability to walk unaided at 4 and 26 weeks in the full cohort and in regional subgroups, using 2 measures for model performance: (1) discrimination: area under the receiver operating characteristic curve (AUC) and (2) calibration: observed vs predicted probability of being unable to walk independently. To improve the model predictions, we recalibrated the model containing the overall mEGOS score, without changing the individual predictive factors. Finally, we assessed the predictive ability of the individual factors.

Results

For validation of mEGOS at entry, 809 patients were eligible (Europe/North America [n = 677], Asia [n = 76], other [n = 56]), and 671 for validation of mEGOS at week 1 (Europe/North America [n = 563], Asia [n = 65], other [n = 43]). AUC values were >0.7 in all regional subgroups. In the Europe/North America subgroup, observed outcomes were worse than predicted; in Asia, observed outcomes were better than predicted. Recalibration improved model accuracy and enabled the development of a region-specific version for Europe/North America (mEGOS-Eu/NA). Similar to the original mEGOS, severe limb weakness and higher age were the predominant predictors of poor outcome in the IGOS cohort.

Discussion

mEGOS is a validated tool to predict the inability to walk unaided at 4 and 26 weeks in patients with GBS, also in countries outside the Netherlands. We developed a region-specific version of mEGOS for patients from Europe/North America.

Classification of Evidence

This study provides Class II evidence that the mEGOS accurately predicts the inability to walk unaided at 4 and 26 weeks in patients with GBS.

Trial Registration Information

NCT01582763.

The clinical course and outcome of Guillain-Barré syndrome (GBS) are highly variable, which complicates the management and evaluation of treatment effects in individual patients.¹ In the past, several prediction models based on sets of prognostic factors have been developed for GBS.²⁻⁴ Such models could help to personalize disease management and conduct treatment studies in selected groups of patients. The modified Erasmus GBS Outcome Score (mEGOS) predicts the risk of being unable to walk independently within the first 6 months of disease based on age, muscle strength, and preceding diarrhea.^{4,5} With this model, a patient >60 years of age with a severe tetraparesis and preceding diarrhea will have the worst predicted outcome (Table 1). The mEGOS was developed with data from Dutch patients with GBS, and until now has been validated in a Dutch cohort and 2 Asian cohorts.^{6,7} In our previous study, based on the first 1,000 patients included in the International GBS Outcome Study (IGOS), we found marked regional differences in the clinical presentation, disease course, subtypes, and outcome of GBS.⁸ Western patients with GBS

most frequently showed the demyelinating subtype of GBS, with involvement of both sensory and motor nerves. In Asia, Miller Fisher syndrome (MFS) was more frequent, and the overall outcome was better.⁸

The first aim of our study was to validate the mEGOS in the IGOS cohort and to define its performance in various regions. The second aim was to determine whether we could improve the mEGOS predictions by applying region-specific adjustments.

Methods

Modified Erasmus GBS Outcome Score

Details of the development of the mEGOS model have been published previously⁴ (see Table 1 for a summary). The model was developed using multivariable logistic regression analysis and was based on data from 394 severely affected patients with GBS who were unable to walk independently and were enrolled in 2 randomized controlled trials (RCTs)

Table 1 mEGOS Scoring System⁴

Prognostic factors	mEGOS at hospital admission, score	mEGOS at day 7 of admission, score
Age at onset, y		
≤40	0	0
41–60	1	1
>60	2	2
Preceding diarrhea^a		
Absent	0	0
Present	1	1
MRC sum score at hospital admission		
51–60	0	0
41–50	2	3
31–40	4	6
0–30	6	9
mEGOS total score	0–9	0–12

Abbreviations: mEGOS = modified Erasmus GBS Outcome Score; MRC = Medical Research Council.

^a Diarrhea in the 4 weeks preceding onset of weakness.

and one pilot study.^{9–11} Patients in the development cohort were mainly enrolled in Dutch centers, but some were enrolled in Belgian or German centers. The model was validated in an independent prospective cohort of 191 patients with GBS who were enrolled in 2 Dutch studies, one open-label pilot study, and one observational study.^{12,13} The observational study also included patients with GBS who were able to walk throughout the disease course, but these patients were excluded for validation.⁴ Table 1 provides the scoring system for the mEGOS.

The model can be used at hospital admission as a 9-point scale and at day 7 of admission as a 12-point scale.

Dataset for External Validation

For external validation of the mEGOS, we used data from the first 1,500 patients included in IGOS, an ongoing prospective multicenter cohort study on GBS in which all severities, variants, and subtypes of GBS are represented.¹⁴ Patients were enrolled between May 2012 and April 2017 in 155 hospitals from 19 countries: Argentina, Australia, Bangladesh, Belgium, Canada, China, Denmark, France, Germany, Greece, Italy, Japan, Malaysia, the Netherlands, South Africa, Spain, Taiwan, United Kingdom, and United States.

Because we aimed to validate the mEGOS in an international GBS cohort that reflects the diversity as is seen in usual clinical practice, we included all patients with GBS who had lost the ability to walk (GBS disability score >2) at

entry and at day 7 after study entry, including variants such as MFS and pure sensory GBS.^{15,16} We used the GBS clinical variants as classified by the treating physician at week 2, or if unavailable, at week 1 or study entry. We excluded patients in whom the diagnosis was altered during the 1–3 years follow-up (n = 85, of whom 53 had chronic inflammatory demyelinating polyradiculoneuropathy). We also excluded children under 6 years, because the Medical Research Council (MRC) scores cannot be assessed in young children, and patients from Bangladesh because the majority received no specific treatment and the facilities for supportive care and rehabilitation are limited in Bangladesh, which could influence the clinical course and outcome.^{8,17} Validation and recalibration of the mEGOS will be performed in Bangladesh separately.

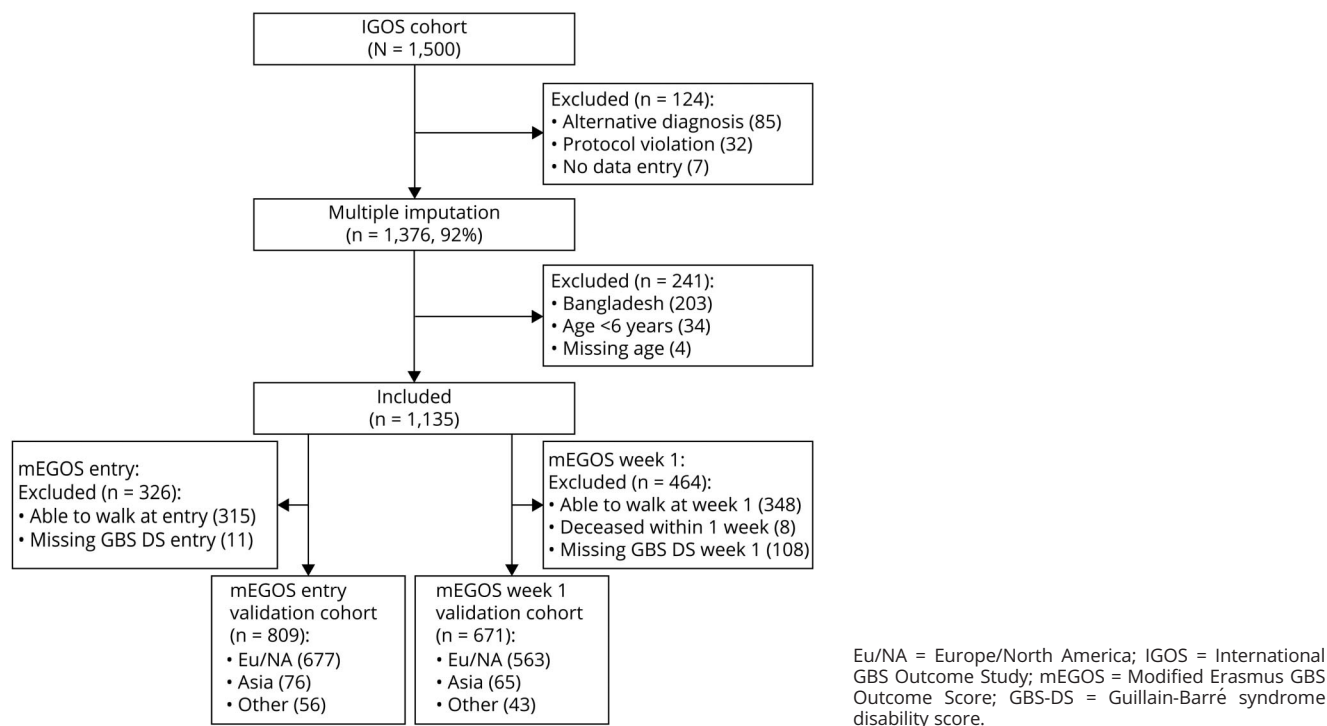
Statistical Analysis

Predictive Performance

For validation of the mEGOS, we looked at outcome at 4 weeks and 6 months. We chose the 4-week time point because this time point is often used in RCT to assess treatment efficacy, and the 6-month time point because it reflects long-term outcome. We assessed model performance by determining the discrimination and calibration. Discrimination represents the ability of the model to distinguish between patients with a good and a poor outcome and is quantified by the area under the receiver operating characteristic (ROC) curve. The ROC curve provides the sensitivity (i.e., true positive rate) of a model at different probability thresholds plotted against (1 – specificity) (i.e., false positive rate). The area under the ROC curve (AUC) ranges from 0.5 (discriminative ability equal to flipping a coin) to 1 (perfect discrimination), and represents the probability that in a random pair of patients, one with a good outcome and one with a poor outcome, the mEGOS is higher in the patient with the poor outcome. We also calculated the refitted AUC value, which is obtained by refitting the model in the validation sample, and thus reestimating the coefficients for age, diarrhea, and the MRC sum score. The refitted AUC value provides the optimum for model discriminative ability in the validation sample for the model with these 3 clinical factors. Calibration defines the accuracy of model predictions by comparing predicted probabilities with observed frequencies of poor outcome. We compared mean predicted and observed probabilities, and also plotted calibration curves to graphically delineate the correspondence between the observed and predicted risks. In case of perfect calibration, observed frequencies of poor outcome are equal to predicted risks; i.e., in a group of patients who all have a predicted probability of 0.6, the event should occur in 60% of patients.^{18,19}

We assessed model performance in the total group and in regional subgroups: Europe/North America (Eu/NA) (including the United Kingdom) and Asia. This subdivision was based on previously identified differences in clinical presentation, disease course, and subtypes of GBS

Figure 1 Study Population



between different regions.⁸ For external validation, we used the original regression formulas with the mEGOS as a single predictor. We also assessed the predictive ability of the individual factors included in the mEGOS model, and compared these between the development and regional validation cohorts.

Model Recalibration

To improve the accuracy of the model predictions (i.e., the correspondence between the predicted values and those observed in the validation cohorts), we recalibrated the mEGOS model. With recalibration, systematic errors in model predictions can be corrected. For example, if predicted probabilities are systematically too low in the validation cohort, then recalibration increases all predicted probabilities. This is done by applying correction factors to the original regression formula (intercept and coefficients), which is used to calculate the predicted probabilities. For recalibration of the mEGOS in this study, we corrected the regression formula that contained the mEGOS total score as single predictor. We did not separately correct the coefficients of the individual factors included in the mEGOS total score, so their relative contribution to the score has remained the same. Therefore, this recalibration method only corrects the overall predicted probabilities, but does not change the discriminative ability. Average correction factors from the 10 imputation sets were used to recalibrate the model.^{18,20} We used bootstrapping to internally validate the recalibrated mEGOS model.

Missing Values

We used multiple imputation ($n = 10$) to impute missing values for the mEGOS predictors and GBS disability scores at 4 weeks and 6 months (R function: *aregImpute*). In the imputation model, we included demographic data (e.g., age, sex, region), data on preceding events, disease progression rate, involvement of cranial nerves, sensory deficits, pain, ataxia, autonomic dysfunction, treatment and supportive care, the clinical GBS variant and the nerve conduction study subtype, and longitudinal data (entry, week 1, 2, 4, 8, 13, 26, and 52) for the individual MRC scores and the GBS disability scores. We performed a separate analysis comparing cases with a complete dataset to those with imputed values. We used SPSS Statistics version 24 and R Studio version 3.6.1. for data analysis (R packages: *Hmisc*, *rms*, *devtools*, *CalibrationCurves*).

Standard Protocol Approvals, Registrations, and Patient Consents

IGOS was approved by the review board of the Erasmus University Medical Centre, Rotterdam, the Netherlands, and the local institutional review boards of participating hospitals or universities. Written informed consent was obtained from all patients or their legal representatives.

Data Availability

Data collected in IGOS will be used initially for planned research projects conducted by the IGOS Consortium. Data can be made available by the IGOS Steering Committee upon reasonable request for specific research projects. The data are

Table 2 Clinical Characteristics of mEGOS Development and Validation Cohorts

Characteristics	Validation cohort		Development cohort ⁴ (n = 394)
	Patients unable to walk unaided at entry (n = 809)	Patients unable to walk unaided at week 1 (n = 671)	
Years	2012–2017	2012–2017	1985–2000
Data source	Cohort study	Cohort study	2 RCTs, 1 pilot study
Study country	Argentina, Australia, Belgium, Canada, China, Denmark, France, Germany, Greece, Italy, Japan, Malaysia, the Netherlands, South Africa, Spain, Taiwan, UK, US	Argentina, Australia, Belgium, Canada, China, Denmark, France, Germany, Greece, Italy, Japan, Malaysia, the Netherlands, South Africa, Spain, Taiwan, UK, US	The Netherlands, Belgium, Germany
Age, y	57 (43–69)	58 (45–69)	52 (33–66)
≤40	181 (22)	132 (20)	138 (35)
41–60	276 (34)	234 (35)	114 (29)
>60	352 (44)	305 (46)	142 (36)
Range	7–90	7–90	5–89
Male	459 (57)	388 (58)	215 (55)
Preceding diarrhea^a	194/797 (24)	162/660 (25)	89/392 (23)
Onset^b to admission, d	2 (1–4)	2 (1–4)	NA
Onset^b to entry, d	5 (3–8)	5 (3–8)	5 (3–8)
MRC sum score at entry	45 (35–52)	44 (34–51)	43 (33–48)
51–60	228/803 (28)	169/663 (26)	47/393 (12)
41–50	278/803 (35)	239/663 (36)	180/393 (46)
31–40	138/803 (17)	113/663 (17)	82/393 (21)
0–30	159/803 (20)	142/663 (21)	84/393 (21)
Range	0–60	0–60	0–58
Sensory deficits at entry	536/782 (69)	439/645 (68)	255/388 (66)
CNI at entry	399/806 (50)	323/667 (48)	152 (39)
Autonomic dysfunction^c at entry	229/808 (28)	193/667 (29)	NA
MRC sum score at week 1	46 (33–54)	45 (30–52)	43 (30–50)
51–60	275/730 (38)	205/664 (31)	95/385 (25)
41–50	192/730 (26)	188/664 (28)	116/385 (30)
31–40	95/730 (13)	98/664 (15)	75/385 (20)
0–30	168/730 (23)	173/664 (26)	99/385 (26)
Range	0–60	0–60	0–60
GBS variant^d sensorimotor	519/765 (68)	447/636 (70)	NA
Pure motor	117/765 (15)	99/636 (16)	NA
MFS	45/765 (6)	24/636 (4)	0 (0)
MFS/GBS overlap	52/765 (7)	39/636 (6)	NA
Other^d	32/765 (4)	27/636 (4)	NA
Mechanical ventilation	170 (21)	164 (24)	118 (30)
ICU admission	257 (32)	241 (36)	NA
IVIg/PE^e	775 (96)	658 (98)	394 (100)

Continued

Table 2 Clinical Characteristics of mEGOS Development and Validation Cohorts (continued)

Characteristics	Validation cohort		Development cohort ^d (n = 394)
	Patients unable to walk unaided at entry (n = 809)	Patients unable to walk unaided at week 1 (n = 671)	
Onset ^b to start IVIg/PE, d	4 (2–7)	4 (2–6)	NA
GBS-DS >2 at week 4 ^f	379/671 (57)	373/579 (64)	217/394 (55)
GBS-DS >2 at 3 months ^f	182/595 (31)	177/513 (35)	111/389 (29)
GBS-DS >2 at 6 months ^f	125/599 (21)	118/512 (23)	74/388 (19)

Abbreviations: CNI = cranial nerve involvement; GBS = Guillain-Barré syndrome; GBS-DS = Guillain-Barré syndrome disability score; ICU = intensive care unit; IVIg = IV immunoglobulin; mEGOS = modified Erasmus GBS Outcome Score; MRC = Medical Research Council; NA = not available/applicable; PE = plasma exchange; RCT = randomized controlled trial.

Overview of the characteristics of the (nonimputed) development and validation cohorts. Numbers are provided as median (interquartile range) or n (%), unless stated otherwise.

^a Symptoms of a gastrointestinal infection within the 4 weeks preceding onset of weakness.

^b Onset of weakness.

^c Autonomic dysfunction includes cardiac (arrhythmia, tachycardia, bradycardia), blood pressure (fluctuations, hypertension, hypotension), gastro-enteric, bladder, pupil dysfunction, excessive sweating, hyponatremia, et cetera.

^d GBS variants represent the classification as reported by the local researchers at week 2 (and if missing at week 1 or study entry). Other variants include pharyngeal-cervical-brachial variant, pure sensory GBS, ataxic variant, Bickerstaff brainstem encephalitis, et cetera.

^e Treated with IV immunoglobulin or plasma exchange. This variable was based on the first 2 treatment episodes reported in the International GBS Outcome Study.

^f Proportion of patients unable to walk independently.

not publicly available because they contain information that could compromise the privacy of the patients.

Classification of Evidence

This study provides Class II evidence that the mEGOS accurately predicts the inability to walk unaided at 4 and 26 weeks in patients with GBS.

Results

From the IGOS-1500 cohort, we excluded 85 patients (6%) because of an alternative diagnosis, 32 (2%) because of a protocol violation, and 7 (0.5%) because of insufficient data. In addition, we excluded patients from Bangladesh (n = 203), patients under 6 years or with missing age (n = 38), patients who were still able to walk independently at study entry (n = 315) or at 1 week after study entry (n = 348), patients who had died within the first week after study entry (n = 8), and those with missing values for the GBS disability score at entry (n = 11) or week 1 (n = 108). The remaining validation cohorts consisted of 809 patients with GBS for the mEGOS at entry and 671 patients for the mEGOS at week 1 (Figure 1). For validation of the mEGOS at entry in the full IGOS cohort, patients were included in the following countries: Argentina (n = 25), Australia (n = 6), Belgium (n = 15), Canada (n = 22), China (n = 9), Denmark (n = 83), France (n = 25), Germany (n = 36), Greece (n = 9), Italy (n = 75), Japan (n = 40), Malaysia (n = 25), the Netherlands (n = 81), South Africa (n = 25), Spain (n = 70), Taiwan (n = 2), United Kingdom (n = 129), and United States (n = 132). In total, 6% of the data points (2,624/41,280) were missing for the mEGOS predictors (age, preceding diarrhea, MRC scores at entry and 1 week) and outcome variables (GBS disability scores at 4 weeks and 6 months), and were imputed using multiple imputation.

Characteristics of the Development and Validation Cohorts

Patients in the validation cohorts were slightly older and more often had mild muscle weakness (MRC sum score 51–60) than patients in the development cohort. Patients with MFS were excluded from the mEGOS development cohort, but were included in the IGOS validation cohorts (Table 2 and eTable 1, links.lww.com/WNL/B684).

Discriminative Ability

For mEGOS at entry, AUC values ranged from 0.74 to 0.79 for predicting outcome at 4 weeks and from 0.73 to 0.82 for predicting outcome at 6 months. For mEGOS at week 1, AUC values ranged from 0.79 to 0.82 for outcome at 4 weeks and from 0.74 to 0.89 for outcome at 6 months (Table 3). Compared to the AUC values in the development cohort, AUC values for the full cohort and Eu/NA subgroup were lower upon external validation (except for the week 4 AUC values for the mEGOS at entry, which were similar to the development AUCs). In Asia, all AUC values were higher than the development AUCs (except for the week 4 AUC value for mEGOS at week 1), but 95% confidence intervals (CIs) were wide. When we refitted the model in the validation cohorts, discriminative ability in the full IGOS cohort and Eu/NA subgroup was similar to the discriminative ability of the externally validated original model for both the mEGOS at entry and week 1. In Asia, refitted AUC values were higher than AUC values derived upon external validation of the original model (Table 3).

When we compared the individual predictor effects for predicting outcome after 4 weeks between the development cohort and the full IGOS cohort and Eu/NA subgroup, we found similar effects for age and MRC sum score, and a

Table 3 Discriminative Ability

	mEGOS entry		mEGOS week 1	
AUC values	Development ⁴		Development ⁴	
4 weeks	0.73		0.87	
6 months	0.77		0.84	
AUC values	Ext. validation	Refitted	Ext. validation	Refitted
4 weeks				
IGOS full	0.74 (0.71; 0.78)	0.75 (0.71; 0.78)	0.79 (0.75; 0.83)	0.80 (0.76; 0.83)
IGOS Eu/NA	0.74 (0.70; 0.78)	0.74 (0.71; 0.78)	0.79 (0.75; 0.83)	0.80 (0.76; 0.84)
IGOS Asia	0.79 (0.68; 0.89)	0.83 (0.73; 0.94)	0.82 (0.71; 0.93)	0.89 (0.79; 0.98)
6 months				
IGOS full	0.74 (0.69; 0.79)	0.74 (0.69; 0.79)	0.75 (0.70; 0.80)	0.76 (0.71; 0.81)
IGOS Eu/NA	0.73 (0.67; 0.78)	0.73 (0.68; 0.79)	0.74 (0.69; 0.80)	0.75 (0.70; 0.80)
IGOS Asia	0.82 (0.68; 0.96)	0.84 (0.71; 0.97)	0.89 (0.79; 0.99)	0.93 (0.84; 1.00)

Abbreviations: AUC = area under the receiver operating characteristic curve; Eu/NA = Europe/North America; IGOS = International GBS Outcome Study; mEGOS = modified Erasmus GBS Outcome Score. Values in parentheses are 95% confidence intervals.

smaller, nonsignificant effect for diarrhea upon external validation (diarrhea odds ratio [OR] [95% CI]): mEGOS entry, full IGOS cohort 1.1 (0.8–1.6), Eu/NA 1.1 (0.7–1.6); mEGOS week 1, full IGOS cohort 1.0 (0.6–1.6), Eu/NA 1.0 (0.6–1.7).⁴ For outcome after 6 months, diarrhea was a significant predictor in both the full IGOS cohort and the Eu/NA subgroup (diarrhea OR [95% CI]): mEGOS entry, full IGOS cohort 1.9 (1.3–2.9), Eu/NA 1.7 (1.1–2.7); mEGOS week 1, full IGOS cohort 1.8 (1.2–2.9), Eu/NA 1.8 (1.1–2.9), although its predictive effect was smaller than the predictive

effects for age and the MRC sum score. The Asian sample was too small to estimate the individual predictor effects reliably.

Calibration

In the full cohort and Eu/NA subgroup, the observed frequencies of poor outcome exceeded the predicted risks of poor outcome based on the mEGOS model (Figure 2). For example, in the full IGOS cohort 67% of the patients with an mEGOS entry score of 4 had a poor outcome after 4 weeks, while the predicted risk of poor outcome for patients with an

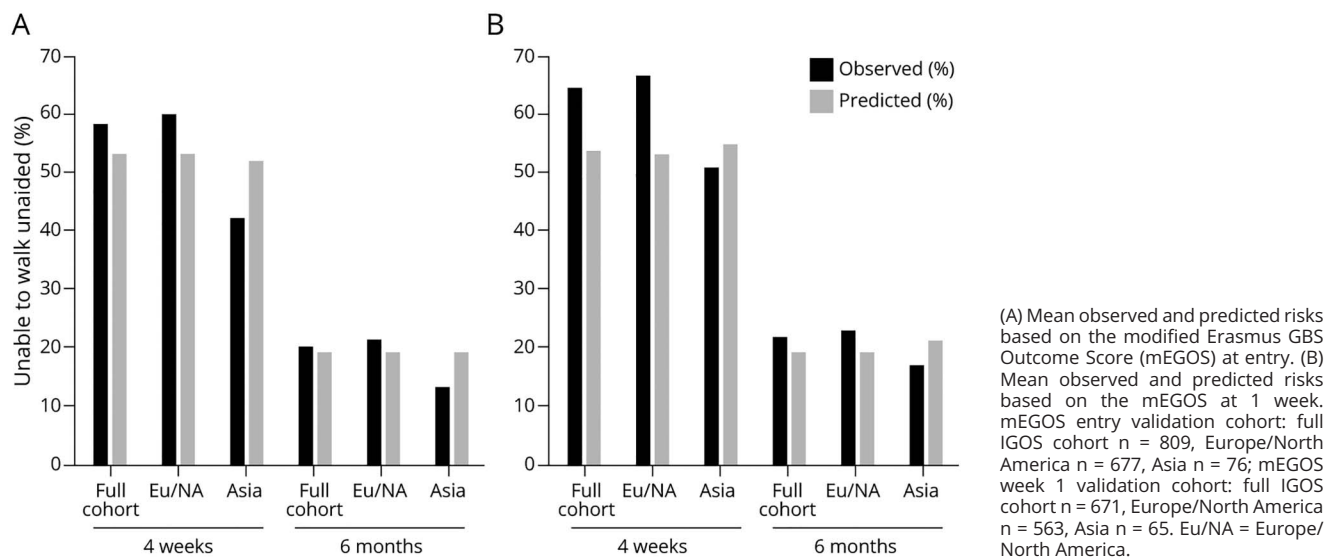
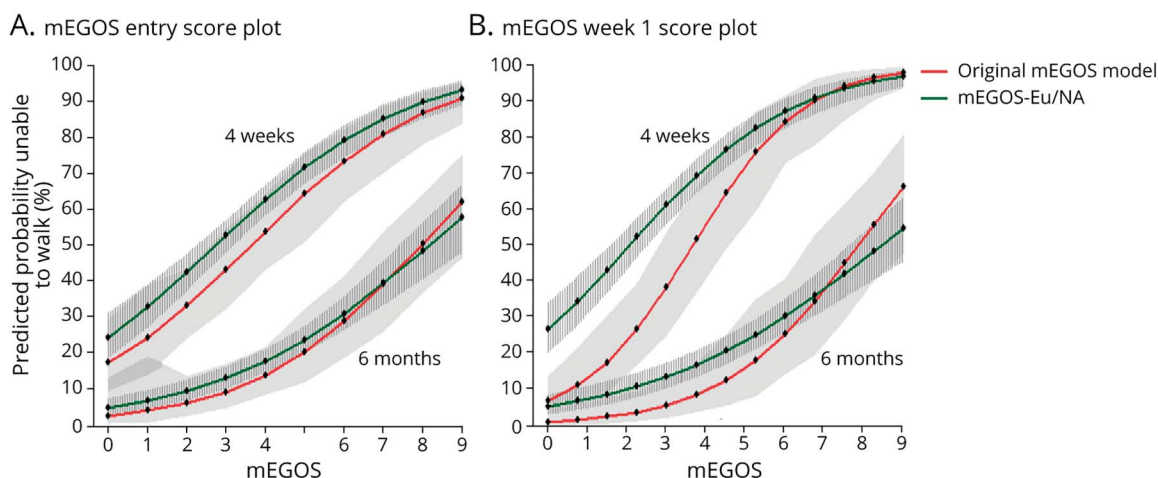
Figure 2 Mean Observed Probabilities of Poor Outcome vs Mean Predicted Risks Based on the Original mEGOS Model

Figure 3 Predicted Proportion of Patients Unable to Walk Independently Based on Original and Recalibrated mEGOS



Predicted probabilities of not being able to walk independently at 4 weeks and 6 months based on the modified Erasmus GBS Outcome Score (mEGOS) at entry (A) and mEGOS at week 1 (B). Probability graphs are based on the original mEGOS model (red) and the recalibrated model for the Europe/North America subgroup (green). Dashed and gray areas around the curves represent the 95% confidence intervals. The top (red and green) graphs provide the probabilities of not being able to walk independently at 4 weeks, and the bottom (red and green) graphs provide probabilities at 6 months. The mEGOS model can be used in all patients with Guillain-Barré syndrome (GBS) and variants of GBS who have lost the ability to walk. The mEGOS score can be calculated based on the scoring system provided in Table 1. Based on the mEGOS score and Figure 3, the probability of being unable to walk independently at 4 weeks or 6 months can be deduced for an individual patient. For predictions with the mEGOS in European and North American patients with GBS, the probability of poor outcome can be determined using the probability graphs based on the recalibrated model (green lines). For predictions in patients with GBS from countries outside Europe and North America, the probability graphs based on the original mEGOS model can be used (red lines).

mEGOS at entry of 4 was 54%. In contrast, in Asia, the observed frequencies of poor outcome were lower than the predicted risks (Figure 2). Differences between observed and predicted risks were more pronounced for outcome at 4 weeks than for outcome at 6 months (Figure 2). Calibration plots showed similar patterns of miscalibration, with underestimation of the risk of poor outcome in the full cohort and Eu/NA subgroup, and overestimation of the risk of poor outcome in the Asian subgroup (data not shown). Recalibration of the mEGOS model improved the accuracy of the model predictions for the full cohort and Eu/NA subgroup and enabled us to create a region-specific version (mEGOS-Eu/NA) (Figure 3). We also compared observed and (pre- and postrecalibration) predicted risks per score value of the mEGOS for the Eu/NA subgroup, which showed that for the majority of score values the predictions improved (i.e., predictions better corresponded to the observed outcomes) after recalibration (Figure 4). Due to the small sample sizes and wide 95% CIs around the calibration curves, it was not possible to recalibrate the model for the Asian cohort. Internal validation of the recalibrated mEGOS for European and North American patients (mEGOS-Eu/NA) by bootstrapping showed AUC values similar to the AUC values of the recalibrated mEGOS, indicating that the model was properly recalibrated and that there was no overfitting.

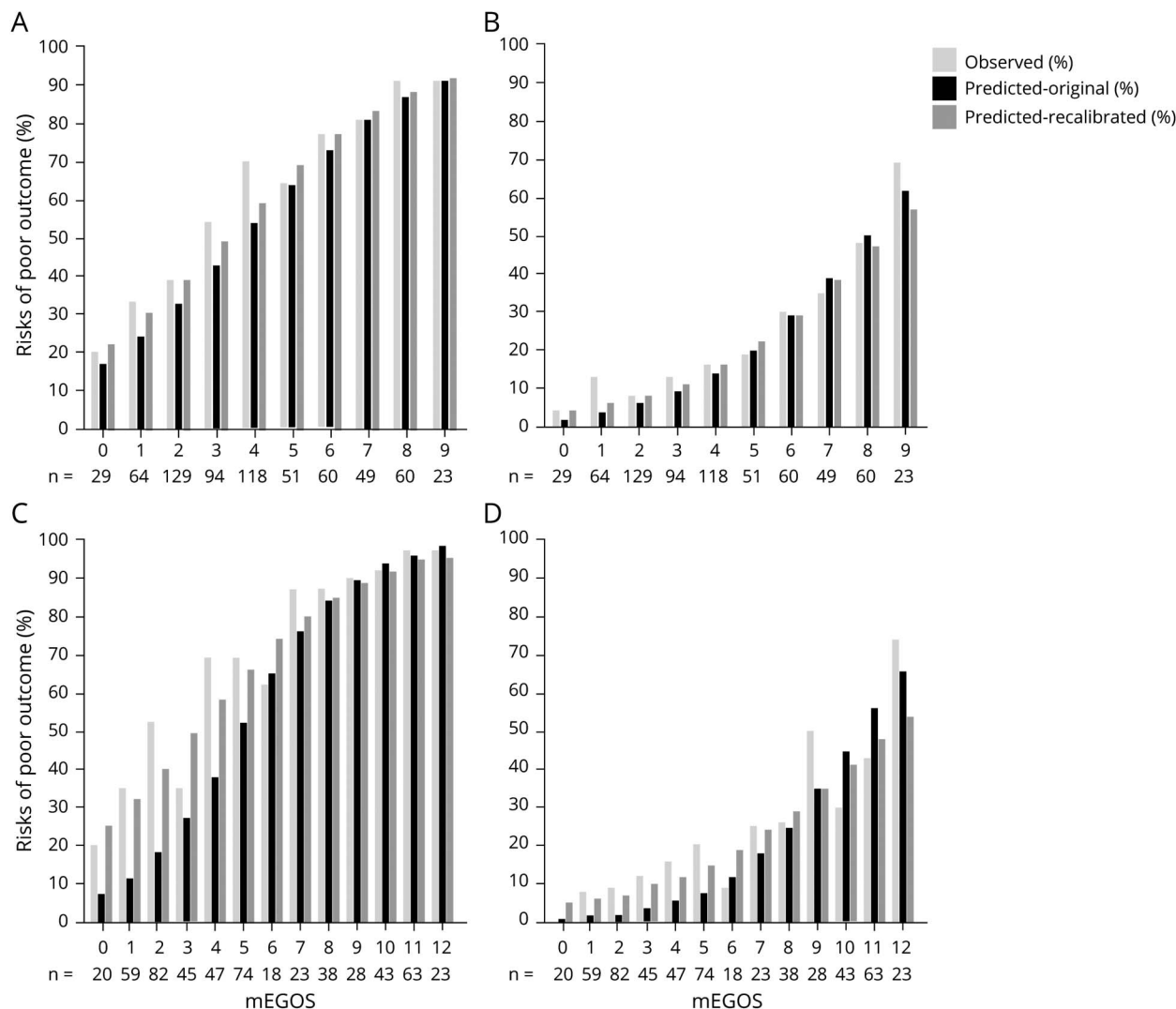
Complete Case Analysis

External validation of mEGOS performed in a subgroup of patients with complete data showed similar results to the analysis that used the imputed dataset (data not shown).

Discussion

This study showed that the mEGOS is a useful tool to predict the inability to walk unaided in individual patients with GBS. In the IGOS-1500 cohort, the model was able to distinguish between patients with a good and a poor outcome, as defined by the inability to walk at 4 weeks or 6 months. In all validation subgroups the AUC value was above 0.7. The accuracy of the model, as indicated by the comparison of the predicted and observed risks of poor outcome, varied between regions. In patients from Europe and North America, the mEGOS underestimated the risk of poor outcome, while this risk was overestimated in patients from Asia. By recalibration of the original mEGOS model, we were able to improve the accuracy of the predictions and to create a region-specific version of the model for patients from Europe and North America (mEGOS-Eu/NA). Recalibration of the model for patients from other regions was not possible, because of the smaller sample size. The mEGOS also was recently validated in 2 studies conducted in Japan and Malaysia.^{6,7} Both studies showed a significant correlation between the mEGOS at hospital admission and at day 7 and the GBS disability score at 6 months (and also at 4 weeks and 3 months for the Malaysian study). In patients with a poor outcome at 6 months, the mEGOS at admission and at day 7 were significantly higher than in patients with a good outcome.^{6,7} In our IGOS validation study, AUC values for the mEGOS at entry and 1 week in Asia ranged from 0.79 to 0.89. This indicates that in 79%–89% of the random comparisons of one patient with a good outcome and one patient with a poor outcome, the mEGOS was higher in the patient with the poor outcome.

Figure 4 Observed vs Predicted (Pre- and Postrecalibration) Risks (%) of Poor Outcome per mEGOS Score Value for European and North American Patients With Guillain-Barré Syndrome



Observed and predicted (pre- and postrecalibration) risks (%) of poor outcome per modified Erasmus GBS Outcome Score (mEGOS) score value for the Europe/North America subgroup. (A) Observed and predicted risks for the mEGOS at entry, predicting outcome at 4 weeks; (B) for the mEGOS at entry, predicting outcome at 6 months; (C) for the mEGOS at week 1, for predicting outcome at 4 weeks; and (D), for the mEGOS at week 1, predicting outcome at 6 months.

These results need to be interpreted with caution as CIs for the AUC values were relatively wide. The Malaysian study also provided AUC values that ranged from 0.69 to 0.86 for the mEGOS at entry and from 0.78 to 0.92 for the mEGOS at day 7. These results show that the mEGOS can distinguish between patients with GBS with a good and a poor outcome in Asia, and therefore support the use of the original, validated model in Asia. In external validation studies, discrepancies between observed and predicted risks are usually explained by differences between the development and validation cohort, especially regarding factors that influence outcome but are not included in the prognostic model. The mEGOS was developed and validated in cohorts that largely contained patients with severe and typical forms of GBS from the Netherlands. In the IGOS-1500 cohort, there was a more

diverse population of patients, especially with respect to the GBS variants, which could have influenced clinical recovery. For example, the IGOS-1500 cohort also included patients with the MFS, who usually have a more favorable outcome and may not require treatment. Furthermore, the mEGOS may perform differently in patients with the axonal subtype of GBS, as this subtype is commonly associated with a poor outcome, but may also show a rapid clinical recovery due to resolution of conduction blocks.²¹ The differences between the observed and predicted risks, and also the differences in performance of the mEGOS between Eu/NA and Asia, may in part be explained by the regional variation in the prevalence of these clinical variants and subtypes. In this validation study, we included patients with all variants of GBS considering that the distinction between typical and variant forms of GBS is

complex and an inclusive model is most useful for clinical practice. Other factors that could have influenced the performance of the mEGOS are differences in treatment and health care facilities (including physiotherapy and rehabilitation) between hospitals and countries. Severity of limb weakness and age are the 2 predominant predictors of poor outcome in the mEGOS model, and constitute 8 out of 9 points for the score at entry and 11 out of 12 for the score at 1 week. Preceding diarrhea has a relatively small prognostic effect and in the current study was not a significant predictor of poor outcome after 4 weeks in the full IGOS cohort and Eu/NA subgroup. This may be explained by the fact that preceding diarrhea in GBS may have several causes. The strongest association with poor outcome is after an infection with *Campylobacter jejuni*, which is frequently followed by an axonal variant of GBS, with severe limb weakness and without sensory nerve involvement. Other causes of preceding diarrhea may have less impact on prognosis and their frequency may differ between countries. Refitting of the mEGOS model in the full IGOS cohort and Eu/NA subgroup showed that reestimation of the ORs for age, preceding diarrhea, and MRC sum score based on the IGOS data only resulted in minor improvement of the AUC values. This finding indicates that additional prognostic factors are required to further improve the discriminative ability of the mEGOS. Potential prognostic (bio)markers are electrophysiologic subtypes, preceding infections, antiganglioside antibodies, CSF protein, and serum Δ IgG levels and neurofilament light chain. Examples of previous studies reporting on serum biomarkers that could improve the mEGOS include a study from the Netherlands that found that low serum Δ IgG levels 2 weeks after standard IV immunoglobulin (IVIg) treatment were independently associated with a worse outcome at 6 months. In this study, the effect of serum Δ IgG on outcome was corrected for the age of the patient, preceding diarrhea, and the GBS disability score at study entry.²² A recent retrospective study from Japan showed that patients with serum IgG anti-GD1a antiganglioside antibodies more often had a poor outcome at 6 months than patients without these antibodies, and that the addition of information about the presence of serum anti-GD1a IgG antibodies could improve the performance of the mEGOS.²³ Finally, a recent study from Spain showed that higher baseline serum levels of neurofilament light chain were associated with a worse clinical outcome, also when corrected for the individual factors included in the mEGOS.²⁴

The mEGOS model can be applied to all patients diagnosed with GBS or a variant of GBS who are unable to walk independently in the acute stage of disease. The model can be used either at hospital admission or at day 7 of admission. To calculate the mEGOS score, no other information is required than the MRC sum score, age of the patient, and the presence of preceding diarrhea. Based on this information and the mEGOS scoring system (provided in Table 1),⁴ one can calculate the mEGOS. The corresponding risk of being unable to walk independently at 4 weeks and 6 months can be deduced from the mEGOS and the probability graphs in Figure 3. For patients from Europe and North America, we recommend using the

recalibrated mEGOS-Eu/NA model. For patients from other geographical regions, we recommend using the validated original mEGOS (Figure 3).⁴ The mEGOS can also be used via an online tool.²⁵ This tool provides the predicted probability of poor outcome based on the original mEGOS model, but this version will be updated to also incorporate the mEGOS-Eu/NA. The calculated risks for the inability to walk can be used to inform patients and their relatives about the expected clinical course and to plan further rehabilitation and care.

Aside from the standard course of IVIg or plasma exchange, no additional treatment is available for patients with a poor expected outcome.²⁶⁻²⁹ Several trials with new treatments for GBS are ongoing or planned, which may be reserved for patients with poor expected outcome, who may be identified in the earliest stage of the disease by the mEGOS (-Eu/NA). This clinical prognostic model can also be used in research to evaluate the independent contribution of other prognostic factors, including biomarkers, to select patients for treatment trials and to compare study cohorts by matching for the mEGOS. The stratification of patients by prognostic models provides a basis for the development of a more personalized treatment for GBS.

There are several limitations of this study. First, GBS disability scores were missing in about one-fifth of the patients, which were imputed using multiple imputation. To minimize the uncertainty induced by imputation, we imputed 10 times and took the average of the 10 imputed data sets. In addition, we used longitudinal data for the GBS disability score (and MRC scores) in our imputation model; that is, in case the GBS disability score at week 4 was missing, scores at week 2 or 8 could be used to impute this value. Second, because the mEGOS focuses on walking ability, the model can only be applied to severely affected patients who have lost the ability to walk. New prediction models are required that focus on different outcome measures and can be applied to the full GBS spectrum. Nevertheless, it will also remain important to use the GBS disability score as an outcome measure for comparison with previous studies. Finally, model validation is a continuous process. Given the varying patient populations and clinical settings to which the mEGOS will be applied, it will remain important to pay attention to differences in predicted and observed outcomes, especially in situations where clinical decision-making is primarily driven by specific cutoff values for the predicted outcome.

This study validated the mEGOS in an international GBS cohort and showed that the model, in its original form, can also be used in individual patients with GBS or its variants to predict the risk of poor outcome. A more accurate mEGOS-Eu/NA was developed for predicting poor outcome in patients from European countries and North America.

Acknowledgement

We thank the patients who participated in this long term follow up study. We thank K. Duong for her extensive work in the data management of the IGOS clinical database.

Study Funding

The IGOS is funded by the GBS-CIDP Foundation International, gain, Erasmus University Medical Centre, Glasgow University, CSL Behring, Grifols, Annexon and Hansa Biopharma.

Disclosure

A.J. van der Kooi received financial support from CSL Behring for the Immediate Myositis study, outside the submitted work. B.C. Jacobs received grants from Grifols, CSL-Behring, Annexon, Prinses Beatrix Spierfonds, Hansa Biopharma, and GBS-CIDP Foundation International and is on the Global Medical Advisory Board of the GBS CIDP Foundation International. C.G. Faber reports grants from European Union's Horizon 2020 research and innovation programme Marie Skłodowska-Curie grant for PAIN-Net, Molecule-to-man pain network (grant no. 721841); European Union 7th Framework Programme (grant n°602273) for the PROPANE study; the Prinses Beatrix Spierfonds; Grifols and Lamepro for a trial on IVIg in small fibre neuropathy; and from steering committees for studies in small fibre neuropathy/neuropathic pain of Biogen, Vertex and Lilly. E. Nobile-Orazio received personal fees for advisory or scientific boards from Kedrion Biopharma, Italy; Baxter/Baxalta/Shire/Takeda, USA/Japan; CSL-Behring, Italy; LFB Biomedicaments and Biotechnologies, France; Astellas, the Netherlands; UCB Biopharma srl, Belgium; Argenx BVBA, Belgium; Sanofi US Services, inc., USA, outside the submitted work, and travel grants to attend scientific meetings from Baxter, Grifols, Kedrion, and Novartis, Italy. H.C. Lehmann has received personal compensations and/or grant support in the last three years from Akcea, Alnylam, Biogen, Celgene, CSL Behring, Grifols, Novartis, and Takeda. J.K.L. Holt has received reimbursement for traveling and accommodation for foreign conference attendance and payment for Advisory Boards from CSL Behring, and has received a research grant from Grifols. K.C. Gorson provides consulting services for Annexon, Argenx, and UCB Pharma. L. Querol is funded by the Fondo de Investigaciones Sanitarias (FIS), Instituto de Salud Carlos III, Spain and FEDER FIS19/1407 and a personal grant SLT006/17/00131 of the Pla estratègic de recerca i innovació en salut (PERIS), Departament de Salut, Generalitat de Catalunya. L. Querol received speaker honoraria from Merck, Sanofi-Genzyme, Roche, Biogen, Grifols, CSL Behring, provided expert testimony for Grifols, Johnson and Johnson, Annexon Pharmaceuticals, Alexion, Sanofi-Genzyme, Novartis and CSL Behring and received research funds from Roche and Grifols. N. Kolb serves as a consultant for Abalone Bio and is on the Advisory Board for Alexion. R.D.M. Hadden received payments from CSL Behring, Grifols, Alnylam and Argenx. S. Kusunoki reports grants from Nihon Pharmaceutical, Teijin and Japan Blood Product Organization, and personal fees from Nihon Pharmaceutical, Teijin, Japan Blood Product Organization and CSL Behring, outside the submitted work. Z. Islam reports grants from the Fogarty International Center, National Institute of Neurological Disorders and Stroke of the National Institutes of Health, USA, under Award Number K43 TW011447 and Annexon Biosciences (South San Francisco, CA 94080, USA). A.Y. Doets, H.F.

Lingsma, C. Walgaard, B. Islam, N. Papri, A. Davidson, Y. Yamagishi, M.M. Dimachkie, W. Waheed, Q.D. Mohammad, T. Harbo, S.H. Sindrup, G. Chavada, H.J. Willison, C. Casasnovas, K. Bateman, J.A.L. Miller, B. van den Berg, C. Verboon, J. Roodbol, S.E. Leonhard, L. Benedetti, S. Kuwabara, P. van den Bergh, S. Monges, G.A. Marfia, N. Shahrizaila, G. Galassi, Y. Péréon, J. Bürmann, K. Kuitwaard, R.P. Kleyweg, C. Marchesoni, M.J. Sedano Tous, I. Illa, Y. Wang, S. Rinaldi, A. Schenone, J. Pardo, F.H. Vermeij, V. Granit, G. Cavaletti, G. Gutiérrez-Gutiérrez, F.A. Barroso, L.H. Visser, H.D. Katzberg, E. Dardiotis, S. Attarian, F. Eftimov, P.W. Wirtz, J.P.A. Samijn, H.J. Gilhuis, K.A. Sheikh, S. Karafiath, M. Vytopil, G. Antonini, T.E. Feasby, C.J. Gijsbers, M. Busby, R.C. Roberts, N.J. Silvestri, R. Fazio, G.W. van Dijk, M.P.J. Garssen and C.S.M. Straathof declare no disclosures relevant to the manuscript. Go to [Neurology.org/N](#) for full disclosures.

Publication History

Received by *Neurology* February 10, 2021. Accepted in final form November 16, 2021.

Appendix 1 Authors

Name	Location	Contribution
Alex Y. Doets, MD, PhD candidate	Erasmus MC, University Medical Centre Rotterdam, the Netherlands	Design and conceptualization of the study; major role in data acquisition; analysis and interpretation of the data; drafting the manuscript; member of IGOS Coordinating Centre at Erasmus University MC Rotterdam; IGOS Country Coordinator
Hester F. Lingsma, PhD	Erasmus MC, University Medical Centre Rotterdam, the Netherlands	Design and conceptualization of the study; interpretation of the data; drafting the manuscript
Christa Walgaard, MD, PhD candidate	Erasmus MC, University Medical Centre Rotterdam; Maastricht Hospital, Rotterdam, the Netherlands	Design and conceptualization of the study; major role in data acquisition; interpretation of the data; drafting the manuscript
Badrul Islam, MBBS, PhD	icddr,b, Dhaka, Bangladesh	Design and conceptualization of the study; major role in data acquisition; interpretation of the data; drafting the manuscript
Nowshin Papri, MD, PhD candidate	icddr,b, Dhaka, Bangladesh	Design and conceptualization of the study; interpretation of the data; drafting the manuscript
Amy Davidson, MD, PhD candidate	College of Medical, Veterinary and Life Sciences, University of Glasgow, UK	Design and conceptualization of the study; major role in data acquisition; interpretation of the data; drafting the manuscript; IGOS Country Coordinator

Appendix 1 (continued)

Name	Location	Contribution
Yuko Yamagishi, MD, PhD	Kindai University Faculty of Medicine, Osaka-Sayama City, Japan	Design and conceptualization of the study; major role in data acquisition; interpretation of the data; drafting the manuscript
Susumu Kusunoki, MD, PhD	Kindai University Faculty of Medicine, Osaka-Sayama City, Japan	Design and conceptualization of the study; major role in data acquisition; interpretation of the data; drafting the manuscript; member of IGOS Steering Committee; IGOS Country Coordinator
Mazen M. Dimachkie, MD	University of Kansas Medical Center, Kansas City	Design and conceptualization of the study; interpretation of the data; drafting the manuscript
Waqar Waheed, MD	University of Vermont Medical Centre, Burlington	Design and conceptualization of the study; major role in data acquisition; interpretation of the data; drafting the manuscript
Noah Kolb, MD	University of Vermont Medical Centre, Burlington	Design and conceptualization of the study; major role in data acquisition; interpretation of the data; drafting the manuscript
Zhahirul Islam, PhD	icddr,b, Dhaka, Bangladesh	Major role in data acquisition; revising the manuscript for intellectual content; IGOS Country Coordinator
Quazi Deen Mohammad, MD	National Institute of Neurosciences and Hospital, Dhaka, Bangladesh	Major role in data acquisition; revising the manuscript for intellectual content; IGOS Country Coordinator
Thomas Harbo, MD, PhD	Aarhus University Hospital, Denmark	Major role in data acquisition; revising the manuscript for intellectual content; IGOS Country Coordinator
Soren H. Sindrup, MD, PhD	Odense University Hospital and University of Southern Denmark	Major role in data acquisition; revising the manuscript for intellectual content
Govindsinh Chavada, MD, PhD	College of Medical, Veterinary and Life Sciences, University of Glasgow, UK	Major role in data acquisition; revising the manuscript for intellectual content; IGOS Country Coordinator
Hugh J. Willison, MD, PhD	College of Medical, Veterinary and Life Sciences, University of Glasgow, UK	Major role in data acquisition; revising the manuscript for intellectual content; member of IGOS Steering Committee; IGOS Country Coordinator
Carlos Casasnovas, MD, PhD	Bellvitge University Hospital-IDIBELL Neurometabolic Diseases Group, CIBERER, Barcelona, Spain	Major role in data acquisition; revising the manuscript for intellectual content

Appendix 1 (continued)

Name	Location	Contribution
Kathleen Bateman, MBChB	Groote Schuur Hospital, University of Cape Town, South Africa	Major role in data acquisition; revising the manuscript for intellectual content; IGOS Country Coordinator
James A.L. Miller, MD, PhD	Royal Victoria Infirmary, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle, UK	Major role in data acquisition; revising the manuscript for intellectual content
Bianca van den Berg, MD, PhD candidate	Erasmus MC, University Medical Centre Rotterdam; Franciscus Gasthuis & Vlietland, Rotterdam, the Netherlands	Major role in data acquisition; revising the manuscript for intellectual content; member of IGOS Coordinating Centre at Erasmus University MC Rotterdam; IGOS Country Coordinator
Christine Verboon, MD, PhD candidate	Erasmus MC, University Medical Centre Rotterdam, the Netherlands	Major role in data acquisition; revising the manuscript for intellectual content; member of IGOS Coordinating Centre at Erasmus University MC Rotterdam; IGOS Country Coordinator
Joyce Roodbol, MD, PhD candidate	Erasmus MC, University Medical Centre Rotterdam, the Netherlands	Major role in data acquisition; revising the manuscript for intellectual content; member of IGOS Coordinating Centre at Erasmus University MC Rotterdam; IGOS Country Coordinator
Sonja E. Leonhard, MD, PhD candidate	Erasmus MC, University Medical Centre Rotterdam, the Netherlands	Major role in data acquisition; revising the manuscript for intellectual content; member of IGOS Coordinating Centre at Erasmus University MC Rotterdam; IGOS Country Coordinator
Luana Benedetti, MD, PhD	IRCCS Ospedale Policlinico San Martino, Genova, Italy	Major role in data acquisition; revising the manuscript for intellectual content
Satoshi Kuwabara, MD, PhD	Chiba University, Chiba, Japan	Major role in data acquisition; revising the manuscript for intellectual content
Peter Van den Bergh, MD, PhD	University Hospital Saint-Luc, University of Louvain, Brussels, Belgium	Major role in data acquisition; revising the manuscript for intellectual content; IGOS Country Coordinator
Soledad Monges, MD	Hospital de Pediatría J.P. Garrahan, Buenos Aires, Argentina	Major role in data acquisition; revising the manuscript for intellectual content
Girolama A. Marfia, MD	Tor Vergata University Hospital, Rome, Italy	Major role in data acquisition; revising the manuscript for intellectual content
Nortina Shahrizaila, FRCP, PhD	University of Malaya, Kuala Lumpur, Malaysia	Major role in data acquisition; revising the manuscript for intellectual content; IGOS Country Coordinator

Continued

Appendix 1 (continued)

Name	Location	Contribution
Giuliana Galassi, MD	University Hospital of Modena, Italy	Major role in data acquisition; revising the manuscript for intellectual content
Yann Péreón, MD, PhD	Reference Centre for NMD, CHU Nantes, France	Major role in data acquisition; revising the manuscript for intellectual content; IGOS Country Coordinator
Jan Bürmann, MD	Saarland University Medical School, Homburg-Saarland (previous); MVZ Pfalzkrlinikum, Kusel, Germany (current)	Major role in data acquisition; revising the manuscript for intellectual content
Krista Kuitwaard, MD, PhD	Albert Schweitzer Hospital, Dordrecht; Erasmus MC, University Medical Centre Rotterdam, the Netherlands	Major role in data acquisition; revising the manuscript for intellectual content
Ruud P. Kleyweg, MD, PhD	Albert Schweitzer Hospital, Dordrecht, the Netherlands	Major role in data acquisition; revising the manuscript for intellectual content
Cintia Marchesoni, MD	Hospital Británico, Buenos Aires, Argentina	Major role in data acquisition; revising the manuscript for intellectual content
María J. Sedano Tous, MD	Hospital Marques de Valdecilla, Santander, Spain	Major role in data acquisition; revising the manuscript for intellectual content
Luis Querol, MD, PhD	Hospital de la Santa Creu I Santa Pau, U.A.B. CIBERER and ERN-NMD, Barcelona, Spain	Major role in data acquisition; revising the manuscript for intellectual content; IGOS Country Coordinator
Isabel Illa, MD, PhD	Hospital de la Santa Creu I Santa Pau, U.A.B. CIBERER and ERN-NMD, Barcelona, Spain	Major role in data acquisition; revising the manuscript for intellectual content. IGOS Country Coordinator
Yuzhong Wang, MD	Affiliated Hospital of Jining Medical University, Shandong Province, China	Major role in data acquisition; revising the manuscript for intellectual content; IGOS Country Coordinator
Eduardo Nobile-Orazio, MD, PhD	IRCCS Humanitas Clinical and Research Institute, Milan University, Italy	Major role in data acquisition; revising the manuscript for intellectual content; IGOS Country Coordinator
Simon Rinaldi, MBChB, PhD	University of Oxford and Oxford University Hospitals NHS Foundation Trust, UK	Major role in data acquisition; revising the manuscript for intellectual content
Angelo Schenone, MD	University of Genova, Italy	Major role in data acquisition; revising the manuscript for intellectual content
Julio Pardo, MD, PhD	Hospital Clínico de Santiago, Santiago de Compostela (A Coruña), Spain	Major role in data acquisition; revising the manuscript for intellectual content

Appendix 1 (continued)

Name	Location	Contribution
Frederique H. Vermeij, MD	Franciscus Gasthuis & Vlietland, Rotterdam, the Netherlands	Major role in data acquisition; revising the manuscript for intellectual content
Helmar C. Lehmann, MD, PhD	University Hospital of Cologne, Germany	Major role in data acquisition; revising the manuscript for intellectual content; IGOS Country Coordinator
Volkan Granit, MD	Montefiore Medical Center, New York, NY	Major role in data acquisition; revising the manuscript for intellectual content
Guido Cavaletti, MD	University Milano-Bicocca, Monza, Italy	Major role in data acquisition; revising the manuscript for intellectual content
Gerardo Gutiérrez-Gutiérrez, MD	Hospital Universitario Infanta Sofía, San Sebastián de los Reyes, Spain	Major role in data acquisition; revising the manuscript for intellectual content
Fabio A. Barroso, MD	Instituto de Investigaciones Neurológicas Raúl Carrea, FLENI, Buenos Aires, Argentina	Major role in data acquisition; revising the manuscript for intellectual content
Leo H. Visser, MD, PhD	St. Elisabeth-TweeSteden Hospital, Tilburg, the Netherlands	Major role in data acquisition; revising the manuscript for intellectual content
Hans D. Katzberg, MD	University Health Network, University of Toronto, Canada	Major role in data acquisition; revising the manuscript for intellectual content
Efthimios Dardiotis, MD	University Hospital of Larissa, Greece	Major role in data acquisition; revising the manuscript for intellectual content; IGOS Country Coordinator
Shahram Attarian, MD, PhD	Reference centre for NMD, CHU Timone ERN NMD, Marseille, France	Major role in data acquisition; revising the manuscript for intellectual content
Anneke J. van der Kooij, MD, PhD	Amsterdam University Medical Centre, University of Amsterdam, Neuroscience institute, Netherlands Neuromuscular Centre, Euro-NMD, the Netherlands	Major role in data acquisition; revising the manuscript for intellectual content
Filip Eftimov, MD, PhD	Amsterdam University Medical Centre, University of Amsterdam, Neuroscience institute, Netherlands Neuromuscular Centre, Euro-NMD, the Netherlands	Major role in data acquisition; revising the manuscript for intellectual content
Paul W. Wirtz, MD, PhD	Haga Hospital, The Hague, the Netherlands	Major role in data acquisition; revising the manuscript for intellectual content

Appendix 1 (continued)

Name	Location	Contribution
Johnny P.A. Samijn, MD	Maasstad hospital, Rotterdam, the Netherlands	Major role in data acquisition; revising the manuscript for intellectual content
H. Jacobus Gilhuis, MD, PhD	Reinier de Graaf Hospital, Delft, the Netherlands	Major role in data acquisition; revising the manuscript for intellectual content
Robert D.M. Hadden, MD, PhD	King's College Hospital, London, UK	Major role in data acquisition; revising the manuscript for intellectual content
James K.L. Holt, FRCP, PhD	The Walton Centre, Liverpool, UK	Major role in data acquisition; revising the manuscript for intellectual content
Kazim A. Sheikh, MD	University of Texas Health Science Centre at Houston	Major role in data acquisition; revising the manuscript for intellectual content
Summer Karafiath, MD	University of Utah School of Medicine, Salt Lake City	Major role in data acquisition; revising the manuscript for intellectual content
Michal Vytopil, MD	Lahey Hospital and Medical Center, Tufts University School of Medicine, Boston, MA	Major role in data acquisition; revising the manuscript for intellectual content
Giovanni Antonini, MD	University of Rome "Sapienza," Sant'Andrea Hospital, Rome, Italy	Major role in data acquisition; revising the manuscript for intellectual content
Thomas E. Feasby, MD	University of Calgary, Canada	Major role in data acquisition; revising the manuscript for intellectual content; IGOS Country Coordinator
Catharina G. Faber, MD, PhD	Maastricht University Medical Centre, the Netherlands	Major role in data acquisition; revising the manuscript for intellectual content
Cees J. Gijssbers, MD	Franciscus Gasthuis & Vlietland, Rotterdam, the Netherlands	Major role in data acquisition; revising the manuscript for intellectual content
Mark Busby, MD	Leeds Teaching Hospitals, UK	Major role in data acquisition; revising the manuscript for intellectual content
Rhys C. Roberts, MB BChir PhD	Addenbrooke's Hospital, Cambridge, UK	Major role in data acquisition; revising the manuscript for intellectual content
Nicholas J. Silvestri, MD	University at Buffalo Jacobs School of Medicine and Biomedical Sciences, NY	Major role in data acquisition; revising the manuscript for intellectual content
Raffaella Fazio, MD	Scientific Institute San Raffaele, Milano, Italy	Major role in data acquisition; revising the manuscript for intellectual content

Appendix 1 (continued)

Name	Location	Contribution
Gert W. van Dijk, MD	Canisius Wilhelmina Hospital, Nijmegen, the Netherlands	Major role in data acquisition; revising the manuscript for intellectual content
Marcel P.J. Garszen, MD, PhD	Jeroen Bosch Hospital, 's-Hertogenbosch, the Netherlands	Major role in data acquisition; revising the manuscript for intellectual content
Chiara S.M. Straathof, MD, PhD	Leiden University Medical Centre, Leiden, the Netherlands	Major role in data acquisition; revising the manuscript for intellectual content
Kenneth C. Gorson, MD	St. Elizabeth's Medical Centre, Tufts University, School of Medicine, Boston, MA	Design and conceptualization of the study; interpretation of the data; drafting the manuscript; member of IGOS Steering Committee; IGOS Country Coordinator
Bart C. Jacobs, MD, PhD	Erasmus MC, University Medical Centre Rotterdam, the Netherlands	Design and conceptualization of the study; interpretation of the data; drafting the manuscript; member of IGOS Steering Committee (Chair); member of IGOS Coordinating Centre at Erasmus University MC Rotterdam; IGOS Country Coordinator

Appendix 2 Coinvestigators

Coinvestigators are listed at links.lww.com/WNL/B728

References

- Leonhard SE, Mandarakas MR, Gondim FAA, et al. Diagnosis and management of Guillain-Barré syndrome in ten steps. *Nat Rev Neurol*. 2019;15(11):671-683.
- van Koningsveld R, Steyerberg EW, Hughes RA, Swan AV, van Doorn PA, Jacobs BC. A clinical prognostic scoring system for Guillain-Barré syndrome. *Lancet Neurol*. 2007;6(7):589-594.
- Waalgaard C, Lingsma HF, Ruts L, et al. Prediction of respiratory insufficiency in Guillain-Barré syndrome. *Ann Neurol*. 2010;67(8):781-787.
- Waalgaard C, Lingsma HF, Ruts L, van Doorn PA, Steyerberg EW, Jacobs BC. Early recognition of poor prognosis in Guillain-Barré syndrome. *Neurology*. 2011;76(11):968-975.
- Kleyweg RP, van der Meche FG, Schmitz PI. Interobserver agreement in the assessment of muscle strength and functional abilities in Guillain-Barré syndrome. *Muscle Nerve*. 1991;14(11):1103-1109.
- Tan CY, Razali SNO, Goh KJ, Shahrizaila N. The utility of Guillain-Barré syndrome prognostic models in Malaysian patients. *J Peripher Nerv Syst*. 2019;24(2):168-173.
- Yamagishi Y, Suzuki H, Sonoo M, et al. Markers for Guillain-Barré syndrome with poor prognosis: a multi-center study. *J Peripher Nerv Syst*. 2017;22(4):433-439.
- Doets AY, Verboon C, van den Berg B, et al. Regional variation of Guillain-Barré syndrome. *Brain*. 2018;141(10):2866-2877.
- The Dutch Guillain Barré Study Group. Treatment of Guillain-Barré syndrome with high-dose immune globulins combined with methylprednisolone: a pilot study. *Ann Neurol*. 1994;35(6):749-752.
- van der Meche FG, Schmitz PI. A randomized trial comparing intravenous immune globulin and plasma exchange in Guillain-Barré syndrome: Dutch Guillain-Barré Study Group. *N Engl J Med*. 1992;326(17):1123-1129.
- van Koningsveld R, Schmitz PI, Meche FG, et al. Effect of methylprednisolone when added to standard treatment with intravenous immunoglobulin for Guillain-Barré syndrome: randomised trial. *Lancet*. 2004;363(9404):192-196.
- Garszen MP, van Koningsveld R, van Doorn PA, et al. Treatment of Guillain-Barré syndrome with mycophenolate mofetil: a pilot study. *J Neurol Neurosurg Psychiatry*. 2007;78(9):1012-1013.

13. Ruts L, Drenthen J, Jacobs BC, van Doorn PA, Dutch Guillain Barré Study Group. Distinguishing acute-onset CIDP from fluctuating Guillain-Barré syndrome: a prospective study. *Neurology*. 2010;74(21):1680-1686.
14. Jacobs BC, van den Berg B, Verboon C, et al. International Guillain-Barré Syndrome Outcome Study: protocol of a prospective observational cohort study on clinical and biological predictors of disease course and outcome in Guillain-Barré syndrome. *J Peripher Nerv Syst*. 2017;22(2):68-76.
15. Asbury AK, Cornblath DR. Assessment of current diagnostic criteria for Guillain-Barré syndrome. *Ann Neurol*. 1990;27(Suppl):S21-S24.
16. Sejvar JJ, Kohl KS, Gidudu J, et al. Guillain-Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. *Vaccine*. 2011;29(3):599-612.
17. Islam MB, Islam Z, Farzana KS, et al. Guillain-Barré syndrome in Bangladesh: validation of Brighton criteria. *J Peripher Nerv Syst*. 2016;21(4):345-351.
18. Steyerberg EW. *Clinical Prediction Models*. Springer; 2009.
19. Vergouwe Y, Moons KG, Steyerberg EW. External validity of risk models: use of benchmark values to disentangle a case-mix effect from incorrect coefficients. *Am J Epidemiol*. 2010;172(8):971-980.
20. Janssen KJ, Moons KG, Kalkman CJ, Grobbee DE, Vergouwe Y. Updating methods improved the performance of a clinical prediction model in new patients. *J Clin Epidemiol*. 2008;61(2):76-86.
21. Kuwabara S, Yuki N. Axonal Guillain-Barré syndrome: concepts and controversies. *Lancet Neurol*. 2013;12(12):1180-1188.
22. Kuitwaard K, de Gelder J, Tio-Gillen AP, et al. Pharmacokinetics of intravenous immunoglobulin and outcome in Guillain-Barré syndrome. *Ann Neurol* 2009;66(suppl 1):597-603.
23. Yamagishi Y, Kuwahara M, Suzuki H, et al. Serum IgG anti-GD1a antibody and mEGOS predict outcome in Guillain-Barré syndrome. *J Neurol Neurosurg Psychiatry*. 2020;91(12):1339-1342.
24. Martin-Aguilar L, Camps-Renom P, Lleixa C, et al. Serum neurofilament light chain predicts long-term prognosis in Guillain-Barré syndrome patients. *J Neurol Neurosurg Psychiatry*. 2020.
25. *IGOS GBS Prognosis Tool [online]*. Available at: gbstools.erasmusmc.nl/prognosis-tool/0/0. Accessed July 28, 2021.
26. Verboon C, van den Berg B, Cornblath DR, et al. Original research: second IVIG course in Guillain-Barré syndrome with poor prognosis: the non-randomised ISID study. *J Neurol Neurosurg Psychiatry*. 2020;91(2):113-121.
27. Chevret S, Hughes RA, Annane D. Plasma exchange for Guillain-Barré syndrome. *Cochrane Database Syst Rev*. 2017;2(2):CD001798.
28. Hughes RA, Swan AV, van Doorn PA. Intravenous immunoglobulin for Guillain-Barré syndrome. *Cochrane Database Syst Rev*. 2014:CD002063.
29. Doets AY, Hughes RA, Brassington R, Hadden RD, Pritchard J. Pharmacological treatment other than corticosteroids, intravenous immunoglobulin and plasma exchange for Guillain-Barré syndrome. *Cochrane Database Syst Rev*. 2020;1(3):CD008630.