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Predicting Outcome in Guillain-Barré Syndrome: International Validation of the Modified Erasmus GBS Outcome Score

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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) is a clinical model that predicts the risk of walking inability in GBS patients, and was developed with data from Dutch patients. The study objective was to validate the mEGOS in the International GBS Outcome Study (IGOS) cohort and to improve its performance and region-specificity.

Methods. We used prospective data from the first 1500 patients included in IGOS, aged ≥ 6 years and unable to walk independently. We evaluated if 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 two measures for model performance: (1) discrimination: area under the receiver operating characteristic curve (AUC), and (2) calibration: observed versus 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=56), and 671 for validation of mEGOS at week 1 (Europe/North America n=563, Asia n=65, other=43). AUC-values were >0.7 in all regional subgroups. In the Europe/North America subgroup observed outcomes were worse than predicted, while 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. The mEGOS is a validated tool to predict the inability to walk unaided at 4 and 26 weeks in GBS patients, 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 GBS patients.

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Introduction

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 diarrhoea [4, 5]. With this model a patient >60 years with a severe tetraparesis and preceding diarrhoea will have the worst predicted outcome (Table 1). The mEGOS was developed with data from Dutch GBS patients, and until now has been validated in a Dutch cohort and two Asian cohorts [6, 7]. In our previous study, based on the first 1000 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 GBS patients most frequently showed the demyelinating subtype of GBS, with involvement of both sensory and motor nerves. In Asia the Miller Fisher syndrome (MFS) was more frequent, and the overall outcome was better[8]. Therefore, 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 if we could improve the mEGOS predictions by applying region-specific adjustments.

Materials and Methods

Modified Erasmus GBS Outcome Score (mEGOS)

Details of the development of the mEGOS model have been published previously [4], see Table 1 for a summary. The model was developed using multivariable logistic regression analysis and was based on data from 394 severely affected GBS patients who were unable to walk independently and were enrolled in two randomised controlled trials (RCTs) and one pilot study [9-11]. Patients in the development cohort were mainly enrolled in Dutch centres, but some were enrolled in Belgian or German centres. The model was validated in an independent prospective cohort of 191 GBS patients who were enrolled in two Dutch studies, one open label pilot study and one observational study [12, 13]. The observational study also included GBS patients 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 1500 patients included in IGOS, an ongoing prospective multicentre 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, UK, USA.

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 the Miller Fisher syndrome (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 CIDP). We also excluded children under six years, because the 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 re-estimating the coefficients for age, diarrhoea 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 three 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 UK) and Asia. This subdivision was based on previously identified differences in clinical presentation, disease course and subtypes of GBS 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 the 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 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 GBS patients.

Results

From the IGOS-1500 cohort we excluded 85 patients (6%) because of an alternative diagnosis, 32 (2%) because of a protocol violation, and seven (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 GBS patients 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 of America (n=132). In total, 6% of the data points (2624/41280) were missing for the mEGOS predictors (age, preceding diarrhoea, 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 the Miller Fisher syndrome (MFS) were excluded from the mEGOS development cohort, but were included in the IGOS validation cohorts (Table 2 and eTable 1).

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 the mEGOS at week 1), but 95% confidence intervals (CI) 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 the MRC sum score, and a smaller, non-significant effect for diarrhoea upon external validation (diarrhoea 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, diarrhoea was a significant predictor in both the full IGOS cohort and the Eu/NA subgroup (diarrhoea 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 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 post-recalibration) 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 two 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% to 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. These results do need to be interpreted with caution as confidence intervals for the AUC-values were relatively wide. The Malaysian study also provided AUC-values which 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 GBS patients 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 favourable 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 Europe/North America 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 two 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 diarrhoea 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 diarrhoea 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 re-estimation of the odds ratio's for age, preceding diarrhoea and the 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 electrophysiological subtypes, preceding infections, anti-ganglioside antibodies, cerebrospinal fluid protein and serum ΔIgG 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 ΔIgG levels 2 weeks after standard IVIg treatment were independently associated with a worse outcome at 6 months. In this study, the effect of serum ΔIgG on outcome was corrected for the age of the patient, preceding diarrhoea 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 six 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].

How can the mEGOS model be used in clinical practice? The 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 on online tool[25]. Currently, 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. Unfortunately, aside from the standard course of IVIg or plasma exchange, at present no additional treatment is available for patients with a poor expected outcome[26-29]. Several trials with new treatments for GBS are currently 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, i.e. 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 cut-off values for the predicted outcome.

In conclusion, 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.

Table 1. mEGOS scoring system [4]

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

mEGOS = modified Erasmus GBS Outcome Score; MRC = Medical Research Council.
[a] Diarrhoea in the 4 weeks preceding onset of weakness.

Table 2. Clinical characteristics of mEGOS development and validation cohorts

Characteristics	Validation cohort: Patients unable to walk unaided at entry (n = 809)	Validation cohort: Patients unable to walk unaided at week 1 (n = 671)	Development cohort[4] (n = 394)
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, USA	Argentina, Australia, Belgium, Canada, China, Denmark, France, Germany, Greece, Italy, Japan, Malaysia, The Netherlands, South Africa, Spain, Taiwan, UK, USA	The Netherlands, Belgium, Germany
Age	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
Sex (male)	459 (57%)	388 (58%)	215 (55%)
Preceding diarrhoea[a]	194/797 (24%)	162/660 (25%)	89/392 (23%)
Time onset[b] to admission, days	2 (1-4)	2 (1-4)	*NA*
Time onset[b] to entry, days	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%)
00-30	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%)
00-30	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%)
Time onset[b] to start IVIg/PE, days	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%)

This table provides an overview of the characteristics of the (non-imputed) development and validation cohorts. Numbers are provided as median (IQR) or n (%), unless stated otherwise. mEGOS = modified Erasmus GBS Outcome Score; CNI = cranial nerve involvement; GBS-DS = GBS disability score; NA = not available/applicable.

[a] Symptoms of a gastro-intestinal 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 and hyponatraemia etc.
[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's brainstem encephalitis etc.
[e] Treated with IVIg and/or plasma exchange. This variable was based on the first two treatment episodes reported in the IGOS study.
f Proportion of patients unable to walk independently

Table 3. Discriminative ability

	mEGOS entry		mEGOS w1	
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)

Values between brackets represent 95% CIs.
mEGOS = modified Erasmus GBS Outcome Score; AUC = area under the receiver operating characteristic curve; Eu/NA = Europe/North America

Figure 1. Study population

IGOS = International GBS Outcome Study; mEGOS = modified Erasmus GBS Outcome Score; GBS-DS = GBS disability score; Eu/NA = Europe/North America

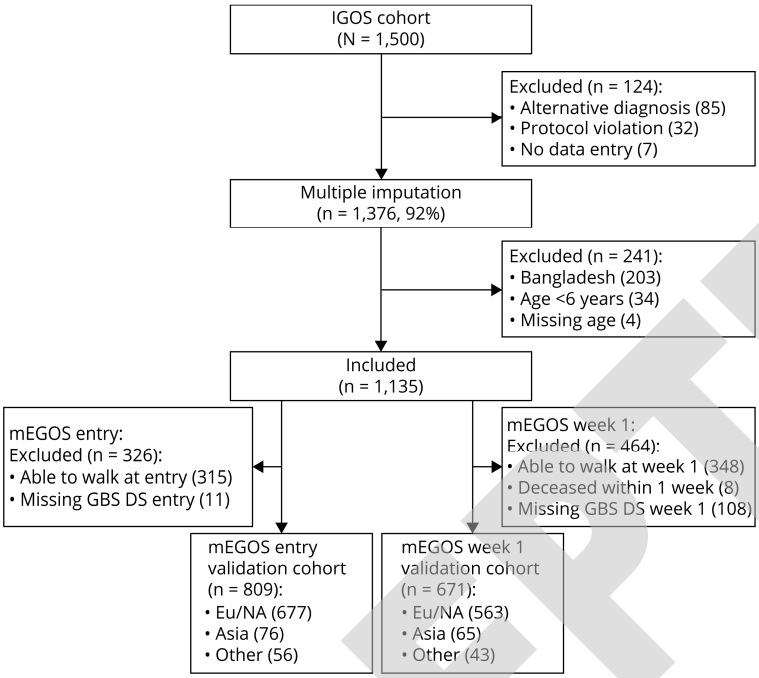


Figure 2. Mean observed probabilities of poor outcome versus mean predicted risks based on the original mEGOS model

Panel A: mean observed and predicted risks based on the mEGOS at entry. Panel B: mean observed and predicted risks based on the mEGOS at 1 week. mEGOS = modified Erasmus GBS Outcome Score; Eu/NA = Europe/North America. mEGOS entry validation cohort: full IGOS cohort n=809, Europe/North America n=677, Asia n=76; mEGOS w1 validation cohort: full IGOS cohort n=671, Europe/North America n=563, Asia n=65.

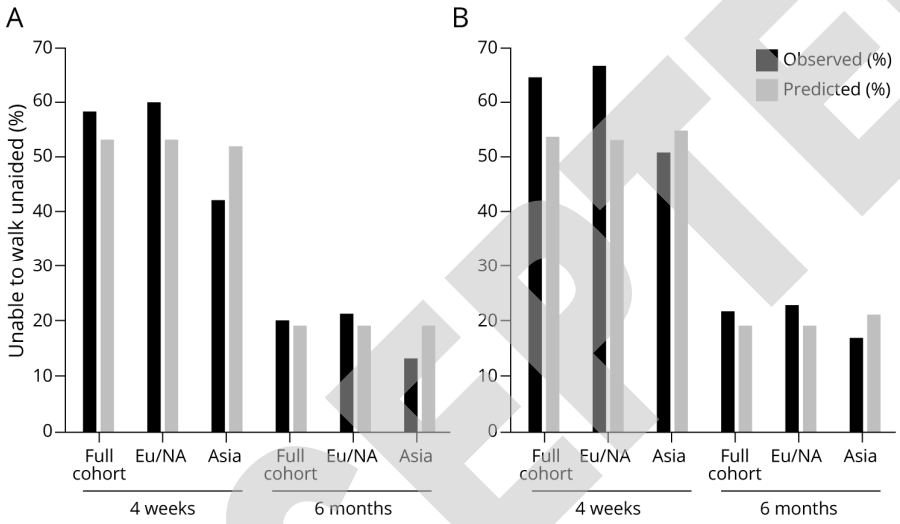


Figure 3. Predicted proportion of patients unable to walk independently based on original and recalibrated mEGOS

This figure provides the predicted probabilities of not being able to walk independently at 4 weeks and 6 months based on the mEGOS score at entry (panel A) and the mEGOS score at week 1 (panel B). Probability graphs are based on the original mEGOS model (red) and the recalibrated model for the Europe/North America subgroup (green). Dashed and grey areas around the curves represent the 95% CIs. 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 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 GBS patients the probability of poor outcome can be determined using the probability graphs based on the recalibrated model (green lines). For predictions in GBS patients from countries outside Europe and North America the probability graphs based on the original mEGOS model can be used (red lines). mEGOS = modified Erasmus GBS Outcome Score; 4w = 4 weeks; 6m = 6 months.

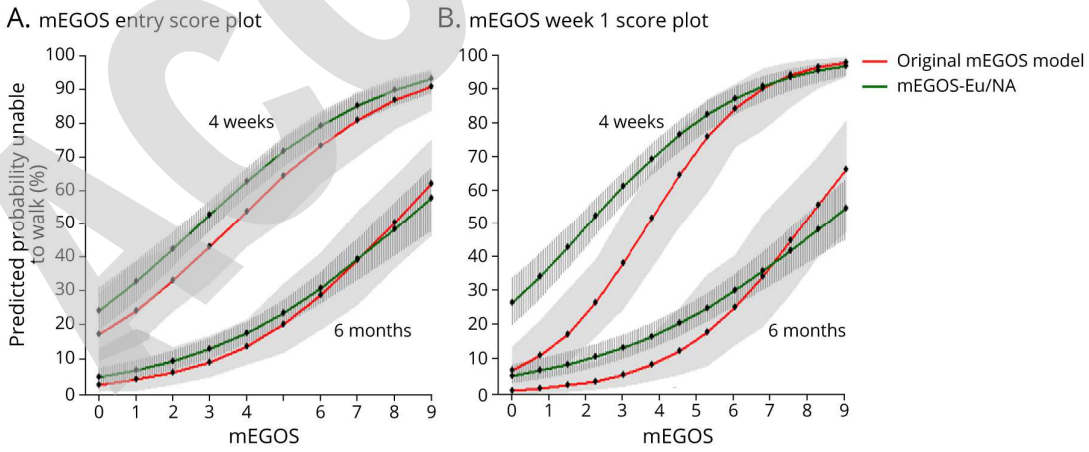
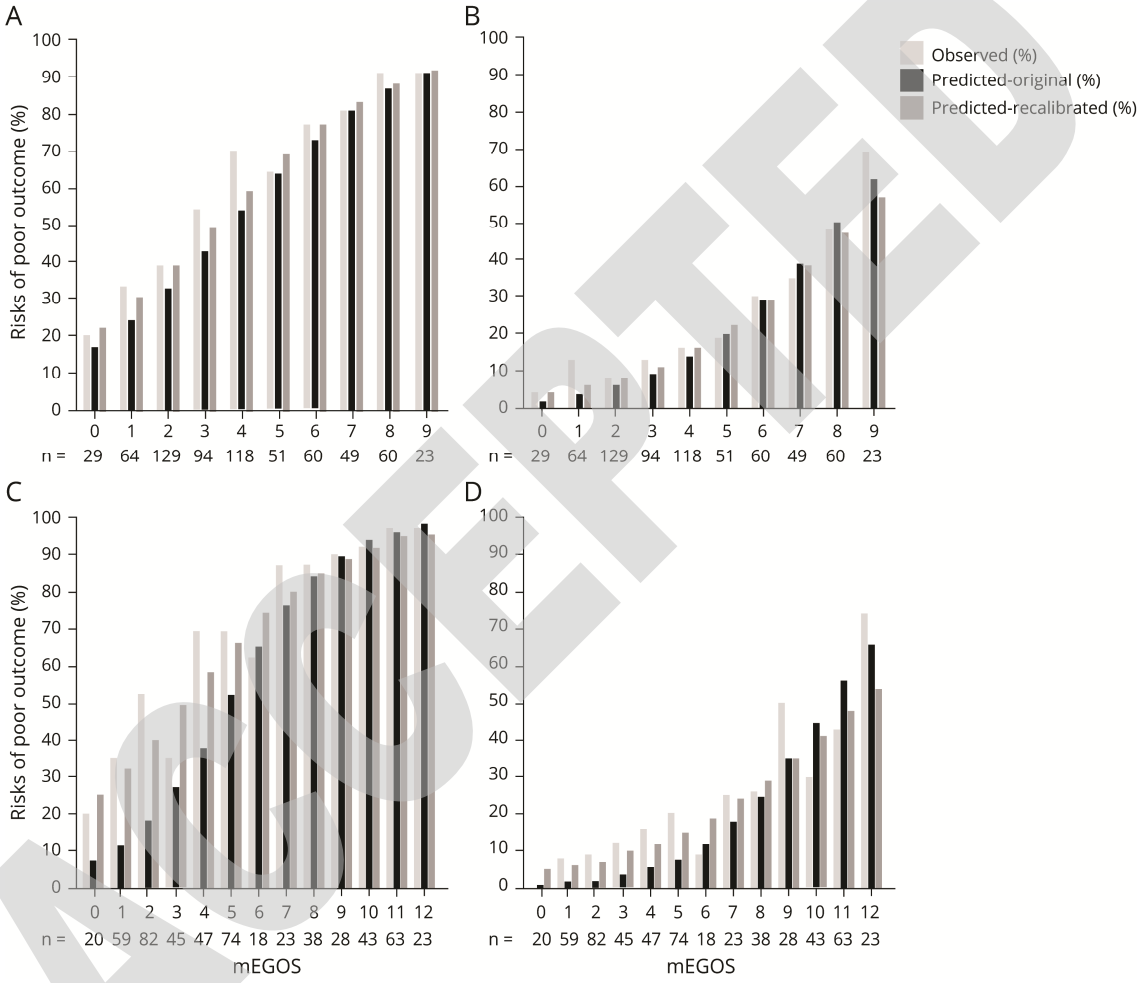


Figure 4. Observed versus predicted (pre- and post-recalibration) risks (%) of poor outcome per mEGOS score value for European and North American GBS patients

This figure compares the observed and predicted (pre- and post-recalibration) risks (%) of poor outcome per mEGOS score value for the Eu/NA subgroup. Panel A provides observed and predicted risks for the mEGOS at entry, predicting outcome at 4 weeks; panel B for the mEGOS at entry, predicting outcome at 6 months; panel C for the mEGOS at week 1, for predicting outcome at 4 weeks; and panel D for the mEGOS at week 1, predicting outcome at 6 months.



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References

1. Leonhard SE, Mandarakas MR, Gondim FAA, et al. Diagnosis and management of Guillain-Barre syndrome in ten steps. Nat Rev Neurol 2019;15:671-683.
2. van Koningsveld R, Steyerberg EW, Hughes RA, Swan AV, van Doorn PA, Jacobs BC. A clinical prognostic scoring system for Guillain-Barre syndrome. Lancet Neurol 2007;6:589-594.
3. Walgaard C, Lingsma HF, Ruts L, et al. Prediction of respiratory insufficiency in Guillain-Barre syndrome. Ann Neurol 2010;67:781-787.
4. Walgaard C, Lingsma HF, Ruts L, van Doorn PA, Steyerberg EW, Jacobs BC. Early recognition of poor prognosis in Guillain-Barre syndrome. Neurology 2011;76:968-975.
5. Kleyweg RP, van der Meche FG, Schmitz PI. Interobserver agreement in the assessment of muscle strength and functional abilities in Guillain-Barre syndrome. Muscle Nerve 1991;14:1103-1109.
6. Tan CY, Razali SNO, Goh KJ, Shahrizaila N. The utility of Guillain-Barre syndrome prognostic models in Malaysian patients. J Peripher Nerv Syst 2019;24:168-173.
7. Yamagishi Y, Suzuki H, Sonoo M, et al. Markers for Guillain-Barre syndrome with poor prognosis: a multi-center study. J Peripher Nerv Syst 2017;22:433-439.
8. Doets AY, Verboon C, van den Berg B, et al. Regional variation of Guillain-Barre syndrome. Brain 2018;141:2866-2877.
9. The-Dutch-Guillain-Barre-Study-Group. Treatment of Guillain-Barre syndrome with high-dose immune globulins combined with methylprednisolone: a pilot study. . Ann Neurol 1994;35:749-752.
10. van der Meche FG, Schmitz PI. A randomized trial comparing intravenous immune globulin and plasma exchange in Guillain-Barre syndrome. Dutch Guillain-Barre Study Group. N Engl J Med 1992;326:1123-1129.
11. van Koningsveld R, Schmitz PI, Meche FG, et al. Effect of methylprednisolone when added to standard treatment with intravenous immunoglobulin for Guillain-Barre syndrome: randomised trial. Lancet 2004;363:192-196.
12. Garssen MP, van Koningsveld R, van Doorn PA, et al. Treatment of Guillain-Barre syndrome with mycophenolate mofetil: a pilot study. J Neurol Neurosurg Psychiatry 2007;78:1012-1013.
13. Ruts L, Drenthen J, Jacobs BC, van Doorn PA, Dutch GBSSG. Distinguishing acute-onset CIDP from fluctuating Guillain-Barre syndrome: a prospective study. Neurology 2010;74:1680-1686.
14. Jacobs BC, van den Berg B, Verboon C, et al. International Guillain-Barre Syndrome Outcome Study: protocol of a prospective observational cohort study on clinical and biological predictors of disease course and outcome in Guillain-Barre syndrome. J Peripher Nerv Syst 2017;22:68-76.
15. Asbury AK, Cornblath DR. Assessment of current diagnostic criteria for Guillain-Barre syndrome. Ann Neurol 1990;27 Suppl:S21-24.
16. Sejvar JJ, Kohl KS, Gidudu J, et al. Guillain-Barre syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine 2011;29:599-612.
17. Islam MB, Islam Z, Farzana KS, et al. Guillain-Barre syndrome in Bangladesh: validation of Brighton criteria. J Peripher Nerv Syst 2016;21:345-351.
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;172:971-980.
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;61:76-86.
21. Kuwabara S, Yuki N. Axonal Guillain-Barre syndrome: concepts and controversies. Lancet Neurol 2013;12:1180-1188.
22. Kuitwaard K, de Gelder J, Tio-Gillen AP, et al. Pharmacokinetics of intravenous immunoglobulin and outcome in Guillain-Barre syndrome. Ann Neurol 2009;66:597-603.
23. Yamagishi Y, Kuwahara M, Suzuki H, et al. Serum IgG anti-GD1a antibody and mEGOS predict outcome in Guillain-Barre syndrome. J Neurol Neurosurg Psychiatry 2020.
24. Martin-Aguilar L, Camps-Renom P, Lleixa C, et al. Serum neurofilament light chain predicts long-term prognosis in Guillain-Barre syndrome patients. J Neurol Neurosurg Psychiatry 2020.
25. IGOS GBS Prognosis Tool [online]. Available at: https://gbstools.erasmusmc.nl/prognosis-tool/0/0. Accessed July 28.
26. Verboon C, van den Berg B, Cornblath DR, et al. Original research: Second IVIg course in Guillain-Barre syndrome with poor prognosis: the non-randomised ISID study. J Neurol Neurosurg Psychiatry 2020;91:113-121.
27. Chevret S, Hughes RA, Annane D. Plasma exchange for Guillain-Barre syndrome. Cochrane Database Syst Rev 2017;2:CD001798.
28. Hughes RA, Swan AV, van Doorn PA. Intravenous immunoglobulin for Guillain-Barre 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-Barre syndrome. Cochrane Database Syst Rev 2020;1:CD008630.