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1. Introduction

Twenty researchers in the field of neuromuscular disorders from eight different countries (USA, Canada, Spain, Italy, France, Belgium, The Netherlands, UK), and a patient representative of the GBS/CIDP Foundation International (Glennys Sanders) participated in the 196th ENMC international workshop in Naarden, The Netherlands from February 8th to 10th 2013 to discuss the results of the peripheral neuropathy outcome measurement standardisation (PeriNomS) study and to strive for consensus on a specific core set of outcome measures to be used in future clinical trials and follow-up studies in patients with Guillain–Barre syndrome (GBS), chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), monoclonal gammopathy of undetermined significance related polyneuropathy (MGUSP), and multifocal motor neuropathy (MMN).

In 2004, the first workshop on outcome measures in peripheral neuropathies was held on the auspice of the European Neuromuscular Centre (ENMC). At this 131st workshop, inadequate agreement was reached regarding which outcome measures should be used at the impairment and activity and participation levels in future trials involving patients with inflammatory neuropathies, like GBS, CIDP, MGUSP (IgM paraproteinemia with positive anti-myelin associated glycoprotein antibodies), and MMN [1]. Recommendations were provided to perform a comparison study between outcome measures that formed the basis of the current workshop. Based on these recommendations, the PeriNomS study was conducted between 2007 and 2012.

2. Background

2.1. PeriNomS study: background and recruitment findings

The PeriNomS study (2 years of preparation, 5 years of data collection; kick-off 2007, PNS, Utah, USA; dbase closed 31st December 2012) is an international collaborative effort of 26 neuromuscular centres with special interest in inflammatory neuropathies. Through comparative responsiveness studies, the most responsive measures were selected at the various levels of interest of assessing outcome. The study consisted of two parts: the cross-sectional part and the longitudinal part (Fig. 1). The cross-sectional part mainly focused on examining validity and reliability in 122 recruited patients (GBS: 30, CIDP: 30, MGUSP: 20, MMN: 22, inflammatory small fibre neuropathy (SFN): 20) with a clinical stable condition with residual symptoms and signs. These patients were examined twice (interval 2–4 weeks) by two well trained and independent observers to obtain inter-/intra-observer reliability scores. Patient-reported outcomes were assessed twice by patients in the same way, without having access to the previous scores. The longitudinal studies were performed worldwide (at the collaborating centres) and the data were centrally collected (Erasmus MC and Maastricht UMC, The Netherlands), and were used to determine comparative responsiveness scores between equally valid and reliable pre-selected outcome measures in inflammatory neuropathies. A total of 163 newly diagnosed patients (GBS: 55, CIDP: 30, MGUSP: 20, MMN: 22, inflammatory small fibre neuropathy (SFN): 20) with a clinical stable condition with residual symptoms and signs.
were enrolled and examined during a one-year period (GBS and CIDP: examined at T0, T1, T3, T6, and T12 months; MGUSP and MMN: examined at T0, T3, and T12 months). Basic characteristics of these patients were presented including treatment regimens if reported. The workshop mainly focused on the cross-sectional validity and reliability and longitudinal responsiveness results by comparing the (modified) Medical Research Council (MRC) sum score versus neuropathy impairment scale (NIS) motor subset, the modified inflammatory neuropathy cause and treatment (INCAT) sensory sum score versus NIS sensory subset, the Jamar dynamometer versus the Martin Vigorimeter, the INCAT disability 10-point scale, the overall disability sum score (ODSS), the overall neuropathy limitations scale (ONLS) versus the newly devised inflammatory Rasch-built overall disability scale (R-ODS) [2,3].

2.2. Historical background of clinical assessments in inflammatory neuropathies

Richard Hughes, UK reviewed the historical background of the development of outcome measures focussing on strength, sensation and disability, relying in part on the historical essay provided by Dyck and colleagues [4]. In 1917 Robert Lovett, a Boston orthopaedist introduced a system for scoring weakness by manual muscle testing, ranging from 1 being normal to 6 paralysis [4]. In 1942 the order of scoring was reversed by the Medical Research Council to provide a scale for scoring strength ranging from 0 for paralysis to 5 for normal [4]. The MRC grading system was developed derived adding the scores of 6 pairs of muscles to try to represent the overall strength of a patient. This composite measure has served through the years as an outcome measure in numerous trials involving patients with inflammatory neuropathies [5]. In parallel, the Mayo Clinic developed what came to be called the neuropathy impairment score with more grades of severity for milder weakness than the MRC grading system: muscle weakness is scored as follows: 0 = normal; 1 = 25%; 2 = 50%; 3 = 75% weak; 3.25 = movement against gravity just possible; 3.5 = movement with gravity eliminated just possible; 3.75 = flicker; and 4 = paralysed [4]. Alternative methods of scoring sensory impairment have been developed, the INCAT sensory sum score (ISS) in Europe and the neuropathy impairment sensory score (NISsen) at the Mayo clinic [4,6]. Disability measures have been developed for inflammatory neuropathies such as 7-point disability scale for GBS and the 10-point inflammatory neuropathy cause and treatment (INCAT) disability for chronic inflammatory neuropathies. The latter has been further modified into the overall disability sum score (ODSS) and finally the overall neuropathy limitations score (ONLS) [3].

2.3. Trial design and outcome models in GBS and other inflammatory neuropathies

Pieter van Doorn, The Netherlands, discussed the issues in trial design and outcome models. For rare disorders like inflammatory neuropathies, it may be important to use advanced prognostic modelling, which enables researchers to reduce the required sample size, thereby considerably shortening the length of trials in these conditions. In order to obtain comparability between trials, the use of previously used outcome measures was proposed. However, this statement was debated, since persistent use of improper outcome measures may continue to jeopardise the results in the same way as seen in the past. Proper attention should be given to the choice of the best outcome measure, particularly choosing outcome measures that have been tested in terms of their clinimetric properties in the disease of interest and fulfilling modern requirements [7]. Also, time of assessment during the course of the illness of interest is important, since the course of inflammatory neuropathies may vary and with this possible improvement in patients [8]. Possible reasons for trials in the inflammatory field being negative were addressed highlighting the possibility of insensitive outcome measures contributing to this. Finally, the need for international collaboration in these rare disorders was emphasised.

2.4. Requirements for outcome measures: traditional aspects

Ingemar Merkies, The Netherlands, presented on behalf of David R. Cornblath (USA) the traditional basic requirements for outcome measures. Several types of data
were discussed. Outcome measures at the nominal and ordinal level are descriptive and the collected data are qualitative without having a numerical value. Despite this general knowledge, we have been allocating numbers to descriptive response categories of each item and have been doing parametric analyses on calculated sum scores, assuming linearity [9]. Measurements at the interval or ratio level increase the level of precision in the assessment of interest since the recruited data have a numerical value. The distance between the categories is known, and therefore meaningful calculations can be performed.

The international classification of functioning, disability and health (ICF) is an international framework classifying the consequences of a health condition [10]. The ICF was discussed addressing its domains: body functions and structures (limitation in one of these is addressed as impairment, e.g., paresis) and activities and participation (capturing daily activities and social functioning, e.g., dressing up, fulfill a job). Limitations at any of these levels may contribute to the concept of quality of life that embraces patients’ reaction to the discrepancy between actual and expected achievements arising as a consequence of their illness [7].

Outcome measures should be simple, valid, reliable and responsive [7]. The advantages and disadvantages of traditional ‘classic test theory’ ordinal based composite outcome measures were summarized [9]. In brief, outcome measures in inflammatory neuropathies are generally ordinal multi-items composite measures that recruit items arbitrarily. Sum scores are generally used, assuming that all items have equal weight, hence assuming a fixed unit and thus treating the data as if these were at the linear level. Additionally the differences obtained in a sum score throughout the range of the constructed sum score have been equally treated. All these assumptions are highly unlikely and hamper the interpretation of the results in/between clinical trials [9].

3. Modern requirements for outcome measures

3.1. Requirements for outcome measures: modern aspects through Rasch analyses

Catharina Faber, The Netherlands, explained the ‘modern’ clinimetric approach through the concept of the Rasch model [11,12]. This model is based on a logical assumption: a patient with a high ability (a term used for any particular trait of interest; e.g., mobility, or performing daily and social activities etcetera; in essence, a less ill patient) will have a higher probability of affirming a particular task compared to a patient with a lower ability (more ill patient) [11]. The Rasch method enables researchers to transform ordinal obtained data into an interval metric, hereby increasing the level of precision. Both the ability of a patient and the difficulty of a task, having a logarithmic relation, are placed on the same ruler (with logits as the fixed unit) [11]. Items and patients are ordered according to the Guttman scaling procedure. An example of ordering items in terms of their difficulty and patients in terms of their ability on the same metric was provided in lay terms. The RUMM (Rasch unidimension measurement model) was presented explaining through various real data examples some of its model requirements (like fit statistics, disordered thresholds, local dependency, item bias, and proper targeting). Emphasis was put on the need to review data that are not fulfilling model expectations and if possible to modify (“clean-up”) these to improve model fitting.

3.2. ACTIVLIM, a measure of activity limitations in children and adults with various neuromuscular disorders

Peter Van den Bergh, Belgium, discussed the development of the first Rasch-built measures addressing activity limitations (ACTIVLIM) in both adults and children with various neuromuscular disorders in order to follow patients’ evolution over time. This measurement fulfilled basic and Rasch model requirements [13]. In addition, their experience through the years using this outcome measure and efforts to introduce its use nationally in the 6 accredited neuromuscular reference centres by means of a dedicated Belgian neuromuscular Disease Registry website application were addressed. Also, the availability of obtaining an online score for the ACTIVLIM was shown. It was agreed upon, that the item weights obtained with this scale differed from those obtained from the GBS, CIDP, and MGUSP specific R-ODS [2]. The differences were explained by the differences in cohorts of patients examined (ACTIVLIM examining patients with all forms of neuromuscular illnesses, R-ODS being disease specific). Finally, the construction of the ABILHAND measure through Rasch analyses, a tool to assess upper limb activity limitations was also discussed [14].

3.3. The concept of MCID and defining a responder

Ingemar Merkies, The Netherlands, explained the concept of MCID and defining a responder. Traditional clinical trials tend to demonstrate the efficacy of a particular intervention by looking at p-values for groups’ comparison or by comparing proportions of patients reaching an arbitrary pre-defined meaningful cut-off for an endpoint of interest. However, all these comparisons assume a fixed standard error (SE) across the metric being used. The concept of MCID was also addressed, highlighting its complexity due to the various available techniques [15]. The MCID represents a change that is considered meaningful and worthwhile by the patient such that they would consider repeating the intervention [16]. The MCID anchor-based methods and distribution-based methods were discussed [15,17]. Currently, there is no consensus regarding which MCID technique should be used.
Responsiveness techniques like the effect size can be misleading when doing groups comparison of the calculated responsiveness scores found between outcome measures in the same population at study [18]. However, using modern techniques like the Rasch method, comparison at the ‘individual level of being a responder’ can be made by using the model’s provided individual standard errors for each patient at the various assessment time points. Outcome measures evaluated through Rasch demonstrate a ‘U’-shape SE across the outcome measure range being used (see Fig. 2 for an example) [18,19].

For the comparison purposes of the PeriNomS study, a responder was defined as a patient in whom the clinical condition improved enough to fall outside the MCID threshold boundaries of $1.96 \times SE$ for the scale at study (see Fig. 2C) [18,19].

By using this method, responders could be determined at the individual level in addition to groups’ comparison (Fig. 3). For the Jamar versus Vigorimeter comparison, a combined (1 anchored-based and 1 distribution-based MCID technique) approach was used as previously suggested [17].

4. Impairment measures

4.1. MRC grading system: original versus Rasch-built modification

Ingemar Merkies, The Netherlands, presented data on the ordinal-based 6-point MRC grading system, showing that the MRC did not meet Rasch model’s expectations, despite being used over 7 decades and in various neuromuscular clinical trials. In 1065 patients, with 7 different neuromuscular illnesses, almost 80% of all muscles were not properly scored by physicians, most showing disordered thresholds. The ability to properly discriminate between the different response options was hardly influenced by factors like experience of the physician and type of illness. Using the Rasch model, the 6-point MRC score was modified to a proposed four-points grading system [20]. Its use is, however, suggested only as part of Rasch-transformed composite scores in future clinical studies, since the four response categories are still ordinal based.

4.2. MRC sum score versus NIS motor subset

Els Vanhoutte, The Netherlands, presented the equivalent validity and reliability findings in the cross-sectional comparison of the NIS motor subset versus the MRC sum score. Comparison between the scales was performed after Rasch transformation (RT-) and modifying the data as much as possible to meet model requirements, as important steps preceding comparison of the findings. The significant meaningful improvement (SigChange) was equivalent between the RT-MRC sumscore and the RT-NIS motor subset. SigChange for motor scales was mainly seen in patients with GBS (50%) and to a lesser extent in CIDP (20%). For both scales, SigChange was hardly seen in MMN. There was no
SigChange found in MGUSP, but most of these patients received no active therapy.

4.3. Modified INCAT sensory scale versus NIS sensory subset

Els Vanhoutte, The Netherlands, presented the comparison data between the modified ISS versus the NIS sensory subset. The ISS was modified (mISS) by incorporating in a standardized manner the examination of light touch sense, joint position sense, and the 2-point discrimination cut-offs that were based on recruited normative values [21]. Differences in their construction were addressed (mISS having a proximal gradient in its assessment versus sensory examination being only distally located in the NIS). The NIS sensory subset and the mISS had equivalent validity and reliability findings with a slightly better targeting of the mISS (better fitting to the patients’ location on the metric by the mISS items’ thresholds).

Thereafter, Kenneth Gorson, US, showed that the proportion of patients reaching the significant change cut-off ($\pm 1.96 \times SE; \text{SigChange}$) were higher for the mISS compared to the NIS sensory subset. Furthermore, SigChange was mainly seen in patients with GBS (40%) (in CIDP only 10%). The SigChange was even less in patients with MGUSP (<10%).

4.4. Jamar versus Vigorimeter

Els Vanhoutte, The Netherlands, showed that there were no differences in validity and reliability aspects between the Martin Vigorimeter and the Jamar. However, in all illnesses, most patients preferred the Vigorimeter. Since both instruments are at the ratio level, a combined MCID anchor-based (SF-36, question number 2) and a MCID distribution-based approach (unified rule of $\frac{1}{2} \times SD$) were adopted for comparison purposes [17]. In essence, a patient was labelled as being a responder, if both MCID cut-offs were exceeded. Significant meaningful grip strength changes were equivalent between the two instruments. The longitudinal findings validated the suggested “many faces” of MCID, since the magnitude of the results varied depending on the MCID technique used [15]. Meaningful changes were mainly seen in patients with GBS (up to 81% with the Vigorimeter and 84% with the Jamar at 1 year follow-up), followed by the patients with CIDP (~40% for both instruments). SigChange was relatively low in MMN (Vigorimeter: 23.5%, Jamar 12.5% at 1 year follow-up) and hardly seen in MGUSP (6.7% versus 13.3%, respectively). The preference of patients for the Martin Vigorimeter was validated in the longitudinal group of patients throughout all illnesses.

4.5. Is there a place for skin biopsy as an outcome in inflammatory neuropathies?

Giuseppe Lauria, Italy, discussed the state of the art in skin biopsies, focusing on facts and pitfalls. Skin biopsy
for determining intraepidermal nerve fibre (IENF) density may be used in follow-up studies, as has been shown in some experimental studies. For clinical use, age and gender-adjusted normative data for the IENF density at the distal leg are available [22]. IENF density at the distal leg was reduced in GBS, CIDP and anti-MAG inflammatory neuropathies [23]. Furthermore, the IENF density at the distal leg correlated with early pain in GBS [23]. Several questions remain to be answered such as right-to-left variability, intra- and inter-individual variability over time and normal values for IENF density at proximal sites.

Dermal nerves may also reveal important information [24], particularly in inflammatory neuropathies like GBS, CIDP, and MGUSP. However, the value of morphological changes, length measurement, myelin disruption, Ig, cell and complement depositions in the skin need further validation. In addition, the recruitment of normative values for dermal nerve assessment and determining potential differences in counting between laboratories were discussed. A place for skin biopsy findings as secondary outcome or exploratory outcome was proposed.

### 4.6. Is there a place for EMG as an outcome in inflammatory neuropathies?

Vera Bril, Canada, discussed nerve conduction studies (NCS) in inflammatory neuropathies mainly focusing on the results of the ICE trial [25]. In addition, the value of having a central core lab for quality control and guidance purposes of NCS in multi-centre trials was discussed. NCS are necessary for diagnosis, and are considered objective measures that reflect clinical change and provide supportive evidence for positive therapeutic results. The use of NCS as an endpoint is also proposed by the FDA. NCS as a secondary outcome measure was proposed.

### 4.7. Pathophysiology of CIDP

Ivo van Schaik, The Netherlands, questioned whether we should re-focus on unravelling pathophysiological mechanisms underpinning inflammatory neuropathies. A historical overview of pathophysiological studies including possible biomarkers in inflammatory neuropathies was discussed. Understanding all these may contribute to determine future trial strategies and/or directions for treatment regimens.

Biomarkers could be useful to define subgroups with different pathogenic mechanisms and with different responses to treatment. Different possible antibodies and genetic factors were discussed, particularly highlighting the approach shown recently in a group of patients with anti-contactin antibodies [26]. The need for CIDP (and other inflammatory neuropathies) registry and biobanking was stated.

### 5. Activity and participation

#### 5.1. Disability measures in inflammatory neuropathy trials

Michael Lunn, UK, discussed the definition of disability as presented by the WHO in 1980 and 2001 and then gave an overview of the disability measures used in inflammatory neuropathy trials up to 2013 [10]. The term disability was replaced by the positive concept of ‘activities’ in the 2001 WHO definitions and is described as ‘the nature and extent of executing a task or action by an individual’. The clinimetric aspects of the disability measures used in trials so far were discussed and the advantages and disadvantages of classical test theory and Rasch built scales were highlighted. In turn, the GBS Disability scores, the modified Rankin score, the functional Independence measure, the Rivermead Mobility Index, the Guy’s originated disability scores (GNDS, INCAT, ODSS and ONLS), the AMC linear disability scale [27], the ALDS item bank [28], the ACTIVLIM [13] and the R-ODS [2] scales were illustrated in detail. Lunn concluded that activity and participation should be the primary outcome level in trials in inflammatory neuropathies mainly because of its meaning to patients and care-givers, and the general ease and applicability of scales in this domain.

#### 5.2. The R-ODS family: their construct and (dis)advantages

Els Vanhoutte, The Netherlands, presented the development of a patient-based, linearly-weighted Rasch-built overall disability scale (R-ODS) and the evaluation of its clinimetric properties. The 24-item R-ODS for GBS, CIDP and MGUSP fulfilled all Rasch model expectations [2]. However, the R-ODS as it is currently used showed item bias in 6 of the 24 (25%) items when examining cultural differences. Cross-cultural validation is mandatory for international use of any scale. Therefore, re-modelling of the R-ODS should be undertaken. The most widely used activity scale in GBS and CIDP is the INCAT 10-points disability measure [29]. Its construct is quite similar to the ODSS and ONLS. For comparison purposes, the collected longitudinal data of the ONLS was transformed through Rasch and demonstrated improper targeting with large gaps between items, local dependency, and misfit statistics for all items. Comparison between the RT-ONLS and the R-ODS showed a significant higher proportion of meaningful improvement (SigChange; cut-off \(>1.96 \times SE\)) in the R-ODS when compared to INCAT-OSS-ONLS. With respect to the R-ODS, a higher proportion of SigChange was seen in patients with GBS (up to 100% at 1 year of follow-up; INCAT-ONLS: 80%) compared to CIDP (≈45% at 1 year follow-up; INCAT-ONLS 28%). The SigChange was poor in patients with MGUSP (at 3 months 20%; most probably determined by the few patients that received therapy; at 1 year 6%).
5.3. The R-ODS family – for MMN

Ingemar Merkies, The Netherlands, demonstrated the composition of the R-ODS specifically for MMN including its validation, reliability and responsiveness findings using Rasch. A relatively low SigChange was seen in the R-ODS for MMN (only 20% being a responder at 1 year; cut-off 1.96 × SE). This was most probably explained by most patients not being naive treated patients. Based on these findings the following suggestions were made for evaluating patients with MMN:

– Perhaps examining ‘being a responder’ should be performed using a much lower cut-off, e.g. at 1 × SE or the definition of being a responder should be revisited, not only including the subgroup of significant improvement, but also non-significant improvement, and stability (i.e. responders are those patients that do not deteriorate).
– MMN (and MGUSP) should be examined for a longer period over time due to their indolent course to capture relevant changes.

The group discussed that in naive MMN patients significant improvement should be sought for. In addition, in those patients who are receiving management therapy, being a responder could be applied in the broader definition as presented above. A self-evaluation scale (SES) in MMN, based on the Canadian occupational performance measure (COPM) [30] demonstrated ~20% SigChange (1 year follow-up; cut-off 1.96 × SE). However, since the items vary per patient, no adaptations to Rasch model could be achieved using this outcome measure.

6. Quality of life

6.1. Patients perspective

Glennys Sanders, UK, urged for the recognition of the importance of patients’ experiences, expectations and emotions. Physicians should take factors like motivation, fatigue, pain and acceptance into account, since these factors can cause depression and affect concentration and confidence to focus on the challenges of their recovery. Furthermore these factors contribute significantly to disability and quality of life reduction. The importance of a positive and supportive/encouraging approach towards patients with inflammatory neuropathies was stressed. Attention for the impact of those receiving respiratory ventilation as well as for those being not able to smile were addressed. The group acknowledged that more attention for these aspects should be the focus of future studies in these conditions. Patients need an ability to express their anger, frustration and fears both for the present and future. Therefore, Sanders emphasised that all patients should be guided to relevant Support Groups to enable them to share knowledge, experiences and emotions.

7. Recommendations

After taking all the presented results into account, the group aimed to get consensus on a specific core set of outcome measures to be used in all future trials in patients with GBS, CIDP, MGUSP, and MMN separately. Table 1 provides an overview of the recommendations.

7.1. GBS

The primary outcome in GBS in future trials should be at the activity and participation level measured by the inflammatory R-ODS [2], since it has demonstrated significantly higher responsiveness compared to the INCAT–ONLS.

7.1.1. Minimal core set for future GBS studies

The minimum core set should include:

– At the impairment level: the Martin Vigorimeter, the Rasch-transformed-mISS, being ventilated (Y/N) and the duration of respiratory ventilation.
– At the activity and participation level: the R-ODS and the GBS disability scale. The latter was suggested for historical purposes.

7.1.2. Recommendations in GBS

It was recommended that future trials should also include the RT-FSS [31], the RT-MRC sum score, and the original MRC sum score, although no consensus was reached on this.

7.1.3. Future needs in GBS

Pain should be further evaluated in terms of its underlying pathophysiological mechanism as well as in terms of evaluating proper therapy. Also, measuring strength needs further exploration, since there was no consensus how, and if, strength should be measured; the possibility of including a muscle dynamometer and the RT-MRC sum score were discussed. The R-ODS could be further improved, by cross-cultural modification. At the quality of life level, a Rasch-transformed outcome measure based on the future findings of the PeriNomS study should be included.

7.2. CIDP

The primary outcome in CIDP in future trials should be at the activity and participation level measured by the R-ODS [2], since it has demonstrated significantly higher responsiveness compared to the INCAT–ONLS.

7.2.1. Minimum core set for future CIDP studies

The minimum core set should include:

– At the impairment level, the Martin Vigorimeter, the RT-mISS, and a ‘manual muscle testing’ procedure, not otherwise defined.
– At the activity and participation level: the R-ODS and the original INCAT disability score.
– At the quality of life level, the 5-points patient global impression of change (PGIC) [32] and SF-36 [33] should be used until the data of the PeriNomS study regarding quality of life measures are further analysed.

7.2.2. Recommendations in CIDP
It was recommended to use the RT-FSS and to include pain measurements such as the 11-point Pain-Intensity Numerical Rating Scale (PI-NRS) [32].

7.2.3. Future needs in CIDP
The RT-MRC sum score needs further development, and should possibly include additional muscles. The criteria for measuring pain should be examined. A walking test (2 or 6 min) could be considered. The R-ODS could be further improved, by cross-cultural modification. At the quality of life level, a Rasch-transformed outcome measure based on the future findings of the PeriNomS study should be included.

7.3. MMN

The primary outcome in MMN in future trials should be at the activity and participation level measured by the disease specific R-ODS [34].

7.3.1. Minimum core set for future MMN studies
– At the impairment level, the Vigorimeter should be used. In addition, patient-specific affected muscles should be incorporated and future studies are needed to re-determine these patient-specific MRC sum scores that may vary from patient to patient. The use of RT-MRC scores was proposed.
– At the activity and participation level, the RODS-MMN was suggested.
– At the quality of life level, a Rasch-transformed outcome measure based on the future findings of the PeriNomS study.

7.3.2. Future needs in MMN
The R-ODS could be expanded, possibly using the ALDS [27] or the ABILHAND [14]. At the quality of life level, a Rasch-transformed outcome measure based on the future findings of the PeriNomS study should be included.

7.4. MGUSP

7.4.1. Recommended outcome measures for future MGUSP studies
Changes were hardly captured in MGUSP patients. Since most patients have not received any therapy, the

Table 1 Overview of the minimum core set, recommendations, and future needs.

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<th>GBS</th>
<th>CIDP</th>
<th>MMN</th>
<th>MGUSP</th>
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<td>'Manual muscle testing’</td>
<td>RT-MRC scores</td>
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<td>GBS disability scale</td>
<td>Original INCAT disability score</td>
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<td>Quality of life level</td>
<td>5-PGIC</td>
<td>RT-QoL scale</td>
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<td>Activity and participation level</td>
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<td>R-ODS</td>
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<td>SF36 or Euro-QoL</td>
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<td>RT-MRCss</td>
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<td>Define core set</td>
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<td>Expanding the R-ODS</td>
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<tr>
<td>Quality of life level</td>
<td>RT-QoL scale</td>
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RT, Rasch transformed; mISS, modified INCAT sensory sumscore; R-ODS, Rasch-built overall disability scale; MRCss, Medical Research Council sum score; FSS, fatigue severity scale; 5-PGIC, 5-points patient global impression of change; 11-PI-NRS, 11-point pain-intensity numerical rating scale; QoL, quality of life.
obtained data could be considered as being historical. Therefore, a core set could not be defined. The group agreed upon extending the evaluation of patients with MGUSP over a longer period. In addition, more data on a larger sample size receiving therapy is needed before a minimum core set of outcome measures for future trials can be defined.

However, at this point, the RT-mISS was recommended at the impairment level, and the R-ODS was recommended at the activity and participation level (the latter as primary outcome suggested). Also the original INCAT 10-point disability should be included based on significant p-values seen in two previous trials [35] (1 not published yet). At the quality of life level, the PGIC and the SF-36 or Euro-QoL were arbitrarily recommended.

7.4.2. Future needs in MGUSP

Extending the evaluation of patients with MGUSP over a longer period is needed. More treated patients should also be examined. At the impairment level, pain evaluation, ataxia and a tremor score as well as the 9-hole PEG test could be further explored. At the quality of life level, a Rasch-transformed outcome measure based on the future findings of the PeriNomS study should be included.

8. Overall and closure

Consensus was reached for most illnesses at the various levels of assessing outcome, except regarding whether there is a need to perform manual muscle testing and how to handle the data. The Rasch-built activity and participation measures were proposed as the future primary outcome measures in all illnesses. Recommendations were made for additional evaluation of aspects like fatigue, pain, and mobility, and future needs were systematically highlighted. Additional evaluation in MGUSP over a longer period of time, particularly in patients receiving therapy was also agreed upon. The PeriNomS group will also be focusing on determining the impact of collected skin biopsy data as well as the construction of an inflammatory neuropathy specific Rasch-built quality of life metric.

Last but not least, the PeriNomS study is performing more than collecting and evaluating data in inflammatory neuropathies. The PeriNomS contributes to the wrinkles needed to create a paradigm shift in outcome assessment in future peripheral neuropathic studies and could serve as an example for other illnesses in neurology and medicine in general.

9. Participants (all members of the PeriNomS study group except*)

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References


