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RESEARCH PROTOCOL

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IgM anti-MAG± peripheral neuropathy (IMAGiNe) study protocol: An international, observational, prospective registry of patients with IgM M-protein peripheral neuropathies

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Abstract

Background: International consensus on IgM ± anti-MAG ± PNP (IgM PNP) is lacking. Despite increasing interest in clinical trials, validated disease-specific measures are needed to adequately capture limitations and changes over time. The IMAGiNe (IgM ± anti-myelin associated glycoprotein [MAG] peripheral neuropathy) study surges as an international collaboration to create a standardized registry of patients with IgM ± anti-MAG PNP. The consortium, which currently consists of 11 institutions from 7 countries, presents here the IMAGiNe study design and protocol.

Aims: Functional outcome measures will be constructed at the level of impairment, as well as activity and participation. We aim to describe the natural history of the cohort, the role of anti-MAG antibodies, the presence of clinical subtypes, and potential biomarkers.

Methods: The IMAGiNe study is a prospective, observational cohort study with a 3-year follow-up. At each assessment, researchers collect clinical data and subjects complete a list of preselected outcome measures. Among these, the "Pre-Rasch-built Overall Disability Scale (Pre-RODS)" questionnaire will be submitted to Rasch analysis to assess classic and modern clinimetric requirements.

Results: The final measures will include the IgM-PNP-specific RODS and Ataxia Rating Scale (IgM-PNP-ARS). Descriptions of the disease course, clinical heterogeneity, treatment regimes, variations in laboratory values, and antibody titers will help reach consensus on diagnosis and follow-up strategies.

Conclusion: The constructed interval scales will be cross-culturally valid and suitable for use in future clinical trials and daily practice. The ultimate goals are to improve

† IMAGiNe Consortium: Group Authorship are listed by Appendix 1.

functional individualized assessment, reach international consensus, and lay the foundations for successful designs in future studies.

KEYWORDS
anti-MAG antibodies, clinimetry, IgM neuropathies, monoclonal gammopathy of undetermined significance, paraproteinemic neuropathies

1 | INTRODUCTION

IgM monoclonal gammopathy-associated peripheral neuropathy (IgM PNP) is a rare and clinically heterogeneous disease that may cause functional disabilities and severe limitations in daily activities and quality of life.[1–3] To date, a direct causal relationship between gammopathies of any class and neuropathies has only been commonly recognized for the IgM subtype. Approximately 30%–60% of neuropathies associated with gammopathies are IgM related.[4–6]

Anti-MAG (Myelin Associated Glycoprotein) antibody titers have been documented in approximately 50%–60% of patients with IgM PNP, and such coexistence has the strongest recognized evidence for causal pathomechanism in typical clinical cases.[7–9] There is a multiplicity of studies demonstrating colocalization of antigen and antibody binding and histopathological and animal model evidence of functional effects of anti-MAG antibodies.[10–12] However, there is no certain correlation between the severity of neuropathy and serum antibody levels. Some authors have reported no correlation,[11,13] yet other studies reported that antibody presence appeared to be associated with a lower risk of severe disease progression, and a therapeutic reduction in titers resulted in clinical stabilization or improvement.[1,14] In the few well-designed randomized controlled trials, there is no evidence to support the use of anti-MAG antibody titers as a reliable predictor of the clinical course of anti-MAG antibody-associated disease, and they are not universally used in practice to monitor disease severity or treatment response.[8,15]

The prognosis and extent to which patients experience limitations are as variable as the clinical presentation.[16–18] Various reports indicate increasing rates of disability during follow-up, ranging from 20% to 50%.[19–21] However, considering the relatively small numbers studied, the nature of this association should be examined with a follow-up of a larger cohort to properly discriminate between causality and coincidence and determine whether this is attributed to aging or variation in subtypes.[22]

In the past, assessing changes and clinical outcomes in IgM PNP has proven to be very difficult.[4,23] Unfortunately, most published clinical trials lack adequate evidence to support treatments for anti-MAG-associated neuropathy. Potential factors contributing to negative trial results include: small cohorts with low numbers of treated patients; a trial duration too short to capture relevant changes for an indolent disease course; the lack of uniformity in applied outcome measures that were usually ordinal-based, inadequate, insensitive, and deficient; study designs too flawed to extract confident conclusions or comparisons between individual treatments; inadequate dose and duration of drug regimens; and inconsistent definitions of treatment response.[24–28]

International consensus on proper assessment of patients with IgM PNP is lacking. Thus far, there has not been any systematically driven international cohort study focusing on the whole spectrum, including clinical, diagnostic, and potential laboratory predictors of outcome related to the clinical picture and various treatment regimens.[29,30] The IMAGiNe study is a collaborative initiative to establish new methods in diagnosis, disease classification, and treatment options. A close collaboration among neurologists, patient representatives, and hematologists/oncologists allows the IMAGiNe study to lay the foundation for future clinical trials by developing novel disease-specific patient-reported outcome measures at the level of impairment, activity and participation, and standardize multidimensional outcome assessment as emphasized during the European NeuroMuscular Center (ENMC) workshops.[23,31]

2 | THE IMAGiNe STUDY

2.1 | Objectives

The main objectives for the International IMAGiNe study discussed during the 230th ENMC International meeting[31] were:

1. Standardizing the documentation of clinical characteristics, including standardized neurological examinations, history of disease course, past and current treatments and response to therapy, data on nerve conduction findings, and laboratory testing, including antibody titers.
2. Describing the various clinical subtypes of IgM PNP[29,30] using a large cohort.
3. Constructing an IgM PNP-specific Rasch-built overall disability scale (IgM-PNP-RODS) and testing its clinimetric needs.[32,33]
4. Optional: collecting blood specimens allowing testing of titers, future antibody studies, DNA collection, and identification of other biomarkers in well-defined patients with IgM PNP, as well as performing bone marrow biopsies.

2.2 | Study design

The IMAGiNe study is an international, multicenter, prospective observational cohort study with a follow-up duration of 3 years for each participant. Examinations are performed at 0, 6, 12, 24, and 36 months. Treatment of the IgM PNP is at the discretion of

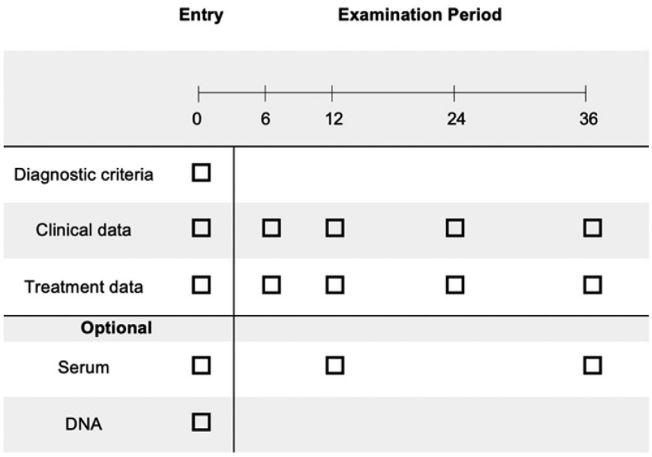

FIGURE 1 Overview of collection of data and biomaterial at the defined assessment times. When participants undergo treatment during the study period, additional follow-up visits are recommended to assess treatment effect.

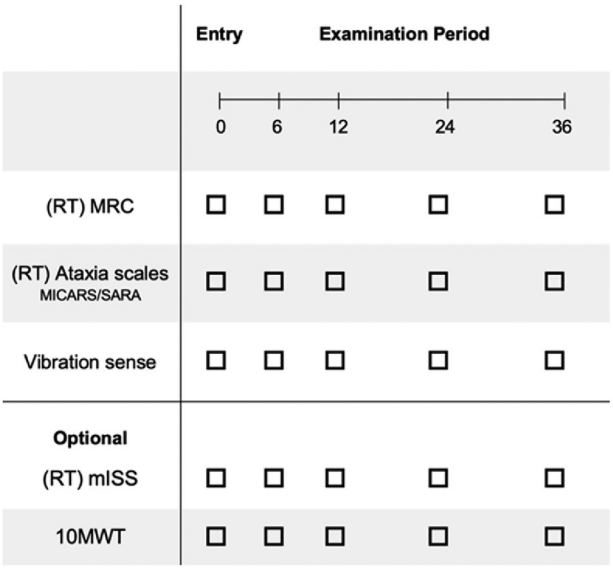

FIGURE 2 Study procedures: clinical data acquired during hospital visits. RT, Rasch transformed; MRC, Medical Research Council; mISS, modified INCAT sensory sum score, vibration sense will be measured using the Rydel-Seiffer tuning fork.

the local investigator; therefore, the study will not affect treatment decisions made. However, if participants enrolled in the study are receiving treatment, additional visits are recommended to assess treatment effect. An overview of the data collection is presented in Figure 1.

2.3 | Study population

Subjects over 18 years of age, fulfilling the international criteria for IgM monoclonal gammopathy, with or without (±) anti-MAG antibodies and peripheral neuropathy will be eligible.[34–37] Participants will be both newly diagnosed and follow-up participants, with and without treatment. Exclusion is primarily based on concomitant diseases or medication possibly interfering with assessments. Participants with an active malignancy with poor prognosis or undergoing treatment aside from IgM PNP will be excluded.

In the sample size calculation for the IgM-PNP RODS development, at least 250 participants are needed in order to create stable outcome measures. A sample size of approximately 250, with at least 150 participants undergoing active treatment, is necessary to obtain a 99% confidence with a stable item calibration within ±0.5 logits, hence providing a robust and stable model when performing Rasch analysis.[38,39] However, to achieve proper cross-cultural validity, the aim is to include at least 500 subjects in total with a good geographical distribution.

2.4 | Study parameters

The following study parameters will be measured:

- Weakness, using the (Rasch Transformed [RT]-) Medical Research Council (MRC) sum score.[40]
- Vibration sense, using the Rydel-Seiffer tuning fork at pre-specified anatomic locations.
- Ataxia, using a face/content validity preselected list of items originating from the Modified International Cooperative Ataxia Rating Scale (MICARS) and Scale for the Assessment and Rating of Ataxia (SARA).[41,42]
- Activity and participation, using the preliminary RODS and after its construction, the IgM-PNP-RODS.[43]
- Quality of life, using the EuroQol EQ-5D Health Questionnaire (EQ-5D).[44]
- Pain, using the Pain-Intensity Numerical Rating Scale (PI-NRS).[45,46]
- Health changes, using the Patients' Global Impression of Change (PGIC).[45,46]
- Optional: sensation using the (RT)-Modified INCAT Sensory Sum Score (mISS) and walking ability with the 10-m walking test (10-MWT).[47,48]

2.5 | Study procedures

Data will be collected during hospital visits and by questionnaires completed at home. If participants are treated, it is optional to add extra visits at the discretion of the treating physician. At study entry and at each assessment during the 3-year follow-up, data including medical history, demographics, and current clinical situation defined by subjects' complaints, neurological deficits, and various outcome measures will be collected (Figure 2). Additionally, diagnostic data regarding results from diagnostic work-up, including electrophysiological and other examinations, as well as prior and current treatments and treatment response, will be collected.

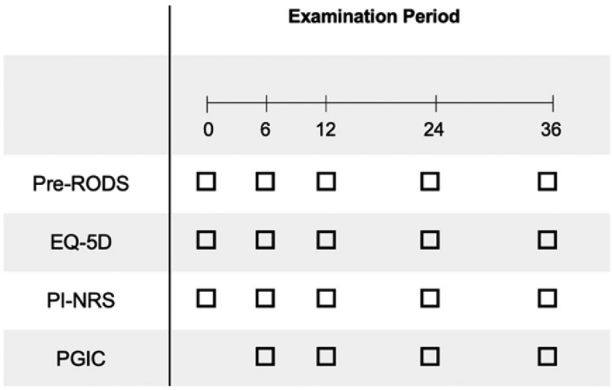

FIGURE 3 Study Procedures: Patient-reported questionnaires. Pre-RODS, pre-defined (Raw) Rasch-built Overall Disability Scale; EQ-5D, EuroQol EQ-5D Health Questionnaire; PI-NRS, Pain Intensity Numeric Rating Scale; PGIC, Patients' Global Impression of Change.

2.6 | Data collection and statistics

A web-based data entry system was developed to facilitate international data collection. The IMAGiNe database is pseudonymized: all registered participants are assigned a unique study number. The website provides time-stamped electronic audit trails to identify what, when, and by whom changes were made in the records. After every visit, participants will fill out questionnaires online through a direct, secured link they receive from the database by e-mail (Figure 3). Validity and reliability studies will be performed as previously reported.[43,49]

2.7 | IgM-PNP-RODS development

One of the core activities of the study is to create a disease-specific IgM-associated Neuropathy-RODS, based upon prior research on modern scientific scales construction in other peripheral neuropathies.[43] The IgM-PNP-RODS will be developed following these steps:

Step 1: Accepted standardized scale development procedures will be applied to create a disease-specific activity and participation scale.[50,51] We have critically reviewed potential items listed under the heading "activity and participation" according to the international classification of the consequences of an illness by the World Health Organization (ICF-WHO) and after systematic literature review with reference tracing.[52] We selected items to form a large item pool, the so-called "preliminary Rasch-built overall disability scale" (preliminary RODS), which contains 146 items and has been used previously.[43] The same pool of items will be used in the current study. These items have been described in a concise, simple and unambiguous way, and an instruction guideline for completion is available for researchers. This pre-metric scale has been translated into numerous languages according to international requirements.[53]

Step 2: Eligible participants will be requested to complete the preliminary RODS. Participants will be requested to answer all questions by themselves and to answer "[0] impossible to perform" when unable to complete an item or "[1] able to perform, but with difficulty" when special devices or other forms of assistance were needed. If the task is completed without any perceived difficulty, the participant will rate the item as "[2] easily performed, without difficulty". A scoring manual will be provided to improve the scoring.

Step 3: Experts in the field of immune-mediated neuropathies will judge Items of the preliminary RODS. Based on the clinical characteristics of IgM PNP items with insufficient face and content validity will be removed.[51]

Step 4: Items with >10% missing values and participants with >10% unanswered items will be omitted as a quality control procedure. The remaining responses of the preliminary RODS will be examined in terms of modern scientific values using Rasch analysis on RUMM2030 software.[43,54] The finally constructed IgM-PNP-RODS should be unidimensional, free from item bias, and without disordered thresholds or local dependency.[33]

2.8 | Longitudinal studies

Longitudinal data will be used to describe the natural history of the disease, variation in clinical and electrophysiological subtypes, associated dynamics of antibody titers, and other hematological parameters, to identify biomarkers for monitoring and predicting disease activity and treatment response. Since these parameters are gathered from the routine medical care practice, the statistical plan for their analysis will be described in the future depending on the available data at the end of the study. Naive participants not being treated (natural course responsiveness studies) and those initiating treatment (whether naive or known participants with a deterioration; treatment-related responsiveness studies) will be part of the follow-up study to determine the clinical dynamics (changes over time) with the selected and newly constructed outcome measures. Responsiveness will be obtained through anchor and distribution-based setting.[55,56] All data will be compared to baseline values. In addition, the study will also be looking at the patients' voice, capturing responsiveness (using PGIC) including other approach forms.

3 | DISCUSSION

In this study, the IgM ± anti-MAG PNP registry will provide a unique cohort of prospectively collected and highly standardized clinical data from a large group of well-defined participants. This will allow us to describe the core typical features of this neuropathy and identify other phenotypes that are associated with anti-MAG antibodies. Comprehensive demographic and historic data will be collected, as well as data on antibody status. We will explore the specificity of the antibodies for detecting both a typical phenotype and possible disease-related phenotypes, as well as the false positive identifications. Likewise, other hematological, neurophysiological, and therapeutic records will be analyzed to conjunctly identify markers for disease course and outcome.

Data will be collected at the level of impairment, activity and participation, and quality of life. Symptoms such as weakness, loss of sensation, impaired balance, ataxia, tremor, and pain will be recorded using carefully selected outcome measures with newly devised metrics if needed. The core set of patient-reported outcome measures selected for the IMAGiNe study contains the EQ-5D, PI-NRS, and PGIC. Furthermore, using the scores of the Pre-RODS questionnaires, the IgM-PNP-RODS will be constructed to accurately measure limitations at the level of activity and social participation.

Participant recruitment began in September 2016 in the Netherlands and is ongoing. At the time of manuscript submission, a total of 236 participants from centers in The Netherlands, Spain, Serbia, Denmark, Italy, France, and the United States of America had been included. Other centers in Belgium, the United States of America, Brazil, Italy, and the United Kingdom are currently working on their review board approval and will start including subjects in 2023. The IMAGiNe study aims to lay the foundation for success in future clinical trials and unravel the issues surrounding the IgM ± anti-MAG PNP disorder.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to report.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, TH, upon reasonable request.

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REFERENCES

1. Steck AJ. Anti-MAG neuropathy: from biology to clinical management. *J Neuroimmunol*. 2021;361:577725.
2. Bardel B, Molinier-Frenkel V, Le Bras F, et al. Revisiting the spectrum of IgM-related neuropathies in a large cohort of IgM monoclonal gammopathy. *J Neurol*. 2022;269(9):4955-4960.
3. Campagnolo M, Ruiz M, Falzone YM, et al. Limitations in daily activities and general perception of quality of life: long term follow-up in patients with anti-myelin-glycoprotein antibody polyneuropathy. *J Peripher Nerv Syst*. 2019;24(3):276-282.
4. Kyle RA, Dyck PJ. Neuropathy associated with the monoclonal Gammopathies. In: Dyck PJ, Thomas PK, eds. *Peripheral Neuropathy*. 4th ed. Elsevier Saunders; 2005:2255-2276.
5. Yeung KB, Thomas PK, King RH, et al. The clinical spectrum of peripheral neuropathies associated with benign monoclonal IgM, IgG and IgA paraproteinaemia. Comparative clinical, immunological and nerve biopsy findings. *J Neurol*. 1991;238(7):383-391.
6. Rison RA, Beydoun SR. Paraproteinemic neuropathy: a practical review. *BMC Neurol*. 2016;16:13.
7. Steck AJ, Stalder AK, Renaud S. Anti-myelin-associated glycoprotein neuropathy. *Curr Opin Neurol*. 2006;19(5):458-463.
8. Nobile-Orazio E. Update on neuropathies associated with monoclonal gammopathy of undetermined significance (2008-2010). *J Peripher Nerv Syst*. 2010;15(4):302-306.
9. Katz JS, Saperstein DS, Gronseth G, Amato AA, Barohn RJ. Distal acquired demyelinating symmetric neuropathy. *Neurology*. 2000;54(3):615-620.
10. Ritz MF, Erne B, Ferracin F, Vital A, Vital C, Steck AJ. Anti-MAG IgM penetration into myelinated fibers correlates with the extent of myelin widening. *Muscle Nerve*. 1999;22(8):1030-1037.
11. Nobile-Orazio E, Manfredini E, Carpo M, et al. Frequency and clinical correlates of anti-neural IgM antibodies in neuropathy associated with IgM monoclonal gammopathy. *Ann Neurol*. 1994;36(3):416-424.
12. Vital C, Vital A, Deminiere C, Julien J, Lagueny A, Steck AJ. Myelin modifications in 8 cases of peripheral neuropathy with Waldenström's macroglobulinemia and anti-MAG activity. *Ultrastruct Pathol*. 1997;21(6):509-516.
13. Latov N. Antibody testing in neuropathy associated with anti-myelin-associated glycoprotein antibodies: where we are after 40 years. *Curr Opin Neurol*. 2021;34:625-630.
14. Renaud S, Fuhr P, Gregor M, et al. High-dose rituximab and anti-MAG-associated polyneuropathy. *Neurology*. 2006;66(5):742-744.
15. Joint Task Force of the EFNS and PNS. European Federation of Neurological Societies/peripheral nerve society guideline* on management of paraproteinemic demyelinating neuropathies. Report of a joint task force of the European Federation of Neurological Societies and the peripheral nerve Socie. *J Peripher Nerv Syst*. 2010;15:185-195.
16. Stork AC, Notermans NC, Vrancken AF, Cornblath DR, van der Pol WL. Rapid worsening of IgM anti-MAG demyelinating polyneuropathy during rituximab treatment. *J Peripher Nerv Syst*. 2013;18(2):189-191.
17. Dalakas MC. Advances in the diagnosis, immunopathogenesis and therapies of IgM-anti-MAG antibody-mediated neuropathies. *Ther Adv Neurol Disord*. 2018;11:1756285617746640.
18. Falzone YM, Campagnolo M, Bianco M, et al. Functioning and quality of life in patients with neuropathy associated with anti-MAG antibodies. *J Neurol*. 2018;265(12):2927-2933.
19. Smith IS. The natural history of chronic demyelinating neuropathy associated with benign IgM paraproteinaemia. A clinical and neurophysiological study. *Brain*. 1994;117(Pt 5):949-957.
20. Notermans NC, Wokke JH, Lokhorst HM, Franssen H, van der Graaf Y, Jennekens FG. Polyneuropathy associated with monoclonal gammopathy of undetermined significance. A prospective study of the prognostic value of clinical and laboratory abnormalities. *Brain*. 1994;117(Pt 6):1385-1393.
21. Nobile-Orazio E, Meucci N, Baldini L, Di Troia A, Scarlato G. Long-term prognosis of neuropathy associated with anti-MAG IgM M-proteins and its relationship to immune therapies. *Brain*. 2000;123(Pt 4):710-717.
22. Galassi G, Tondelli M, Ariatti A, Benuzzi F, Nichelli P, Valzania F. Long-term disability and prognostic factors in polyneuropathy associated with anti-myelin-associated glycoprotein (MAG) antibodies. *Int J Neurosci*. 2017;127(5):439-447.
23. Vanhoutte EK, Faber CG, Merkies IS. 196th ENMC international workshop: outcome measures in inflammatory peripheral neuropathies 8-10 February 2013, Naarden, The Netherlands. *Neuromuscul Disord*. 2013;23(11):924-933.

24. Lunn MP, Nobile-Orazio E. Immunotherapy for IgM anti-myelin-associated glycoprotein paraprotein-associated peripheral neuropathies. *Cochrane Database Syst Rev*. 2012;5(5):CD002827.
25. Lunn MP, Nobile-Orazio E. Immunotherapy for IgM anti-myelin-associated glycoprotein paraprotein-associated peripheral neuropathies. *Cochrane Database Syst Rev*. 2016;10(10):CD002827.
26. Dalakas MC, Quarles RH, Farrer RG, et al. A controlled study of intravenous immunoglobulin in demyelinating neuropathy with IgM gammopathy. *Ann Neurol*. 1996;40(5):792-795.
27. Mariette X, Brouet JC, Chevret S, et al. A randomised double blind trial versus placebo does not confirm the benefit of alpha-interferon in polyneuropathy associated with monoclonal IgM. *J Neurol Neurosurg Psychiatry*. 2000;69(2):279-280.
28. Pruppers MH, Merkies IS, Notermans NC. Recent advances in outcome measures in IgM-anti-MAG+ neuropathies. *Curr Opin Neurol*. 2015;28(5):486-493.
29. Stork AC, Jacobs BC, Tio-Gillen AP, et al. Prevalence, specificity and functionality of anti-ganglioside antibodies in neuropathy associated with IgM monoclonal gammopathy. *J Neuroimmunol*. 2014;268(1–2):89-94.
30. Stork AC, Notermans NC, van den Berg LH, et al. Fcγ receptor IIIA genotype is associated with rituximab response in antimyelin-associated glycoprotein neuropathy. *J Neurol Neurosurg Psychiatry*. 2014;85(8):918-920.
31. Pruppers MH, Merkies ISJ, Lunn MPT, Notermans NC. 230th ENMC International Workshop: Improving Future Assessment and Research in IgM Anti-MAG Peripheral Neuropathy: A Consensus Collaborative Effor, Naarden, The Netherlands 24–26 Februaryt. *Neuromuscul Disord*. 2017;27(11):1065-1072.
32. Rasch G. *Probabilistic Models for some Intelligence and Attainment Tests*. Danmarks Paedagogiske Institut; 1960.
33. Tennant A, Conaghan PG. The Rasch measurement model in rheumatology: what is it and why use it? When should it be applied, and what should one look for in a Rasch paper? *Arthritis Rheum*. 2007;57(8):1358-1362.
34. Latov N. Pathogenesis and therapy of neuropathies associated with monoclonal gammopathies. *Ann Neurol*. 1995;37(Suppl 1):S32-S42.
35. Notermans NC, Franssen H, Eurelings M, Van der Graaf Y, Wokke JH. Diagnostic criteria for demyelinating polyneuropathy associated with monoclonal gammopathy. *Muscle Nerve*. 2000;23(1):73-79.
36. Lehmann HC, Wunderlich G, Fink GR, Sommer C. Diagnosis of peripheral neuropathy. *Neurol Res Pract*. 2020;2(1):20.
37. Koike H, Katsuno M. Paraproteinemia and neuropathy. *Neurol Sci*. 2021;42(11):4489-4501.
38. Linacre JM. Sample size and item calibration stability. *Rasch Measur Transac*. 1994;7:328.
39. Wright BD. Rack and stack: time 1 vs. time 2 or pre-test vs. *Post-Test Rasch Measur Transac*. 2003;17(1):905-906.
40. Vanhoutte EK, Faber CG, van Nes SI, et al. Modifying the Medical Research Council grading system through Rasch analyses. *Brain*. 2012;135(Pt 5):1639-1649.
41. Schmahmann JD, Gardner R, MacMore J, Vangel MG. Development of a brief ataxia rating scale (BARS) based on a modified form of the ICARS. *Mov Disord*. 2009;24(12):1820-1828.
42. Schmitz-Hübsch T, du Montcel ST, Baliko L, et al. Scale for the assessment and rating of ataxia: development of a new clinical scale. *Neurology*. 2006;66(11):1717-1720.
43. van Nes SI, Vanhoutte EK, van Doorn PA, et al. Rasch-built overall disability scale (R-ODS) for immune-mediated peripheral neuropathies. *Neurology*. 2011;76(4):337-345.
44. Rabin R, Charro F. EQ-SD: a measure of health status from the EuroQol group. *Ann Med*. 2001;33(5):337-343.
45. Farrar JT, Young JPJ, LaMoreaux L, Werth JL, Poole MR. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain*. 2001;94(2):149-158.
46. Haanpää M, Attal N, Backonja M, et al. NeuPSIG guidelines on neuropathic pain assessment. *Pain*. 2011;152(1):14-27.
47. Draak TH, Vanhoutte EK, van Nes SI, et al. Comparing the NIS vs. MRC and INCAT sensory scale through Rasch analyses. *J Peripher Nerv Syst*. 2015;20(3):277-288.
48. Watson MJ. Refining the ten-metre walking test for use with neurologically impaired people. *Physiotherapy*. 2002;88(7):386-397.
49. Fisher WJ. Reliability Statistics. *Rasch Measur Transac*. 1992;6:238.
50. Bombardier C, Tugwell P. A methodological framework to develop and select indices for clinical trials: statistical and judgmental approaches. *J Rheumatol*. 1982;9(5):753-757.
51. Streiner DL, Norman GR. *Health Measurement Scales: a Practical Guide to their Development and Use*. Oxford University Press; 1998.
52. World Health Organization International Classification of Functioning. *Disability and Health: ICF*. World Health Organization; 2001.
53. Streiner DL, Norman GR. *Health Measurement Scales: A Practical Guide to their Development and Use*. Oxford University Press; 2008.
54. Andrich D, Sheridan B, Luo G. *Rasch Models for Measurement: RUMM2030*. RUMM Laboratory Pty Ltd; 2009:1-10.
55. Draak TH, Vanhoutte EK, van Nes SI, et al. Changing outcome in inflammatory neuropathies: Rasch-comparative responsiveness. *Neurology*. 2014;83(23):2124-2132.
56. Hobart J, Cano S. Improving the evaluation of therapeutic interventions in multiple sclerosis: the role of new psychometric methods. *Health Technol Assess*. 2009;13(12):iii, ix-x, 1-177.

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APPENDIX 1

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