A Delphi Panel to Identify Optimal Clinical Outcome Measures (COAs) in Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

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Background

- CIDP is a rare autoimmune neuropathy, involving both cellular and humeral components of the immune system,[1] affecting 2.81 per 100,000 people globally.[2]
- CIDP is clinically heterogenous, with clinical subtypes divided into two main categories – typical CIDP, characterized by symmetrical symptom distribution, and atypical variants, characterized by varied regional and modular (motor or sensory) symptoms.[2-4]
- Due to the heterogeneity of CIDP and variability of symptoms observed, no single outcome measure can capture all relevant domains and diverse outcome measures are needed to assess treatment response and disease progression.[5-6]
- There are no validated biomarkers for monitoring therapeutic response.[6]
- The lack of a universally agreed definition of a meaningful response in clinical practice adds further complexity, with differing views between patients and healthcare professionals.[6,7]

Objective

This study seeks to reach consensus on optimal clinical assessments that accurately and appropriately reflect the impact of CIDP on patients via a multi-stakeholder Delphi panel.

Methods

- This ongoing study started in December 2024 using a double-blinded modified Delphi method **(Figure 1)**: an established method of eliciting consensus from experts.[8,9]
- Preliminary results from first-round survey from 18 HCPs and 13 PAGs (total N=31) are presented here; full results are expected by July 2025.
- The remaining phases of this research will include a second-round survey, and a virtual consensus meeting.
- A nine-point Likert scale (from 1 [strongly disagree] to 9 [strongly agree]) was used during the first round. Consensus was defined as ≥80% of panellists providing a response of 7–9 (indicative of strongly agree) or 1–3 (strongly disagree)
- A steering committee compromising of two independent neurologist experts and a patient advocacy group representative ensured insights were reflective of real-world practice, were clinically valid, and were comprehensible to a patient audience.

Figure 1. Modified Delphi panel

Inclusion criteria

- ✓ All clinical experts were required to have ≥2 years experience within their role, treating at least 10 patients with CIDP in the last 12 months. Clinical experts were also required to be familiar with current treatment guidelines, and outcome measures used in CIDP.
- ✓ Patient advocates included: individuals living with CIDP, those caring for an individual living with CIDP, those who are patient representatives for CIDP, or an individual supporting the family and caregivers of patients with CIDP.
- ✓ All patient representatives were required to have an understanding outcome measures used to track disease progression for CIDP.

Recruitment of 31 panelists (18 HCPs and 13 patients advocates)

Delphi panel round 1: Online Questionnaire (n=31) – *completed*

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Analysis of **Delphi panel** Round 1 results

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Delphi panel round 2: Online Questionnaire (n=31) - *ongoing*

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Analysis of **Delphi panel** Round 2 results

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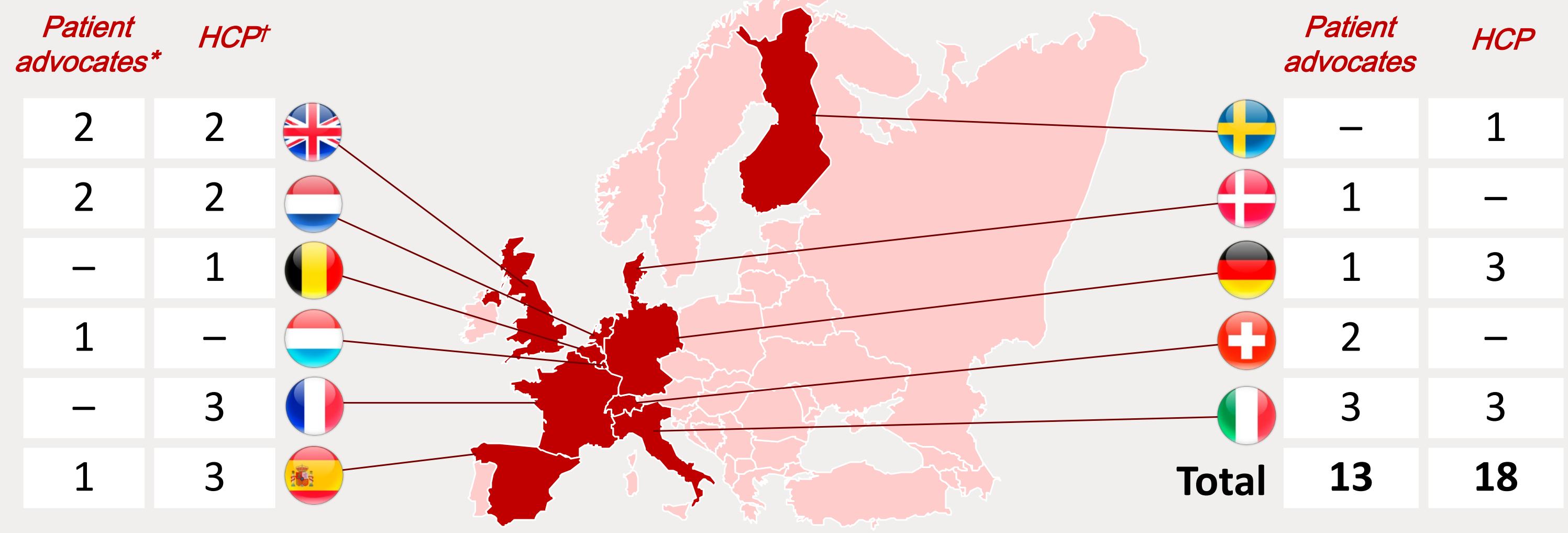
Delphi panel round 3: Consensus Meeting (n=12) – *to commence following round 2*

Results

Demographic characteristics

- A total sample of 31 panellists were recruited through a third party-fieldwork agency and a patient association group using pre-defined screening criteria.
- The panel comprised of 18 clinical experts in neurology and 13 patient advocates from a range of European countries (**Figure 2**).

Figure 2. Panel composition



Patient advocates*	HCP†	
2	2	🇬🇧
2	2	🇳🇱
–	1	🇧🇪
1	–	🇱🇺
–	3	🇫🇷
1	3	🇪🇸

	Patient advocates	HCP
🇸🇪	–	1
🇩🇰	1	–
🇩🇪	1	3
🇨🇭	2	–
🇮🇹	3	3
Total	13	18

*10 patients with CIDP, 2 caregivers and 1 patient representative
†11 neuromuscular specialists, 3 neuropathy specialists, 2 general neurologists, 1 neuromuscular and neuropathy specialist and 1 neuroimmunologist

Relative of importance of outcome domains

- **Consensus was reached for the following eight domains as the most important outcome domains to consider when assessing therapeutic benefit (Figure 3).**

Figure 3. Domains where consensus was reached on importance for assessment (% agree)

🟥 Mobility, gait and balance (100%)	🟥 Upper and lower limb function (97%)	🟥 Manual dexterity and strength (97%)	Functional independence (94%)
Health-related quality of life (87%)	Pain (84%)	Activity and social participation (81%)	Cognitive functioning (81%)

🟥 Physical domains
▨ Non-physical domains

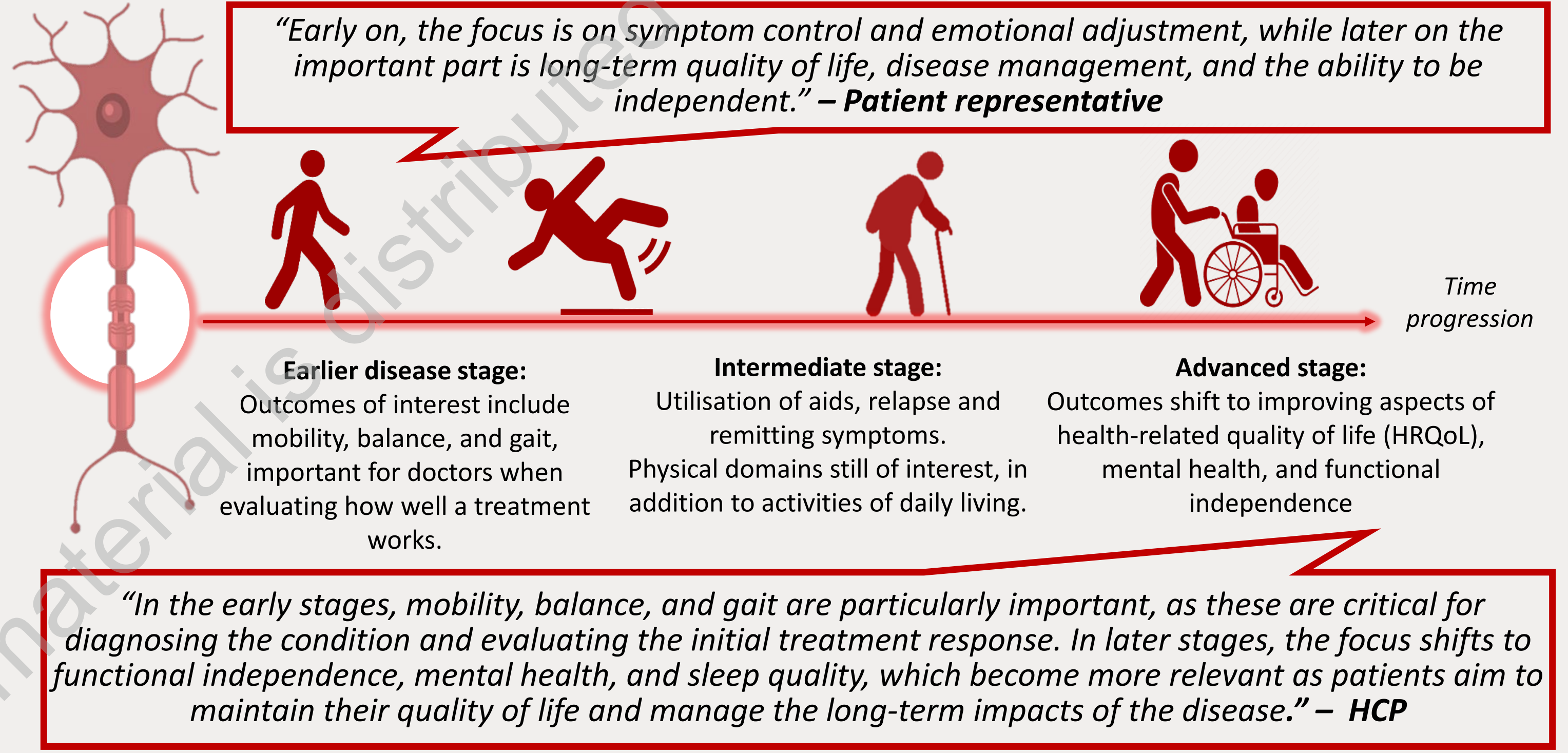
- Over half of the panel (63%; 12 HCPs and 7 PAGs) agreed that improvements in physical domains are more meaningful, as they lead to improvements in other domains (such as the non-physical domains above).
- Overall, 43% of the panel felt all domains had a cyclical relationship with equal importance, however, these insights were largely derived from patient advocates (noted by 10 patient advocates and one HCP).

Applicability of COAs during routine assessments over time

Over half of the panel (77%; 15 HCPs and 9 patients) agreed that domains for assessment should be

- **adapted over time**
- dependent on the **disease stage**
- reflective of the **evolution of symptoms**

Despite this, over half of the patient advocates (54%) highlighted that the type of **assessments have not varied** from after diagnosis to present day.



> *"Early on, the focus is on symptom control and emotional adjustment, while later on the important part is long-term quality of life, disease management, and the ability to be independent." –* ***Patient representative***

Earlier disease stage: Outcomes of interest include mobility, balance, and gait, important for doctors when evaluating how well a treatment works.

Intermediate stage: Utilisation of aids, relapse and remitting symptoms. Physical domains still of interest, in addition to activities of daily living.

Advanced stage: Outcomes shift to improving aspects of health-related quality of life (HRQoL), mental health, and functional independence

> *"In the early stages, mobility, balance, and gait are particularly important, as these are critical for diagnosing the condition and evaluating the initial treatment response. In later stages, the focus shifts to functional independence, mental health, and sleep quality, which become more relevant as patients aim to maintain their quality of life and manage the long-term impacts of the disease." –* ***HCP***

Results *cont.*

Relevance of physical impairment and disability related COAs

- **Among the HCP cohort only (n=18), consensus was reached for INCAT, I-RODS and the MRC sum score as measures that can adequately assess therapeutic benefit in patients with CIDP. However, HCPs acknowledged their limitations (Figure 4).**

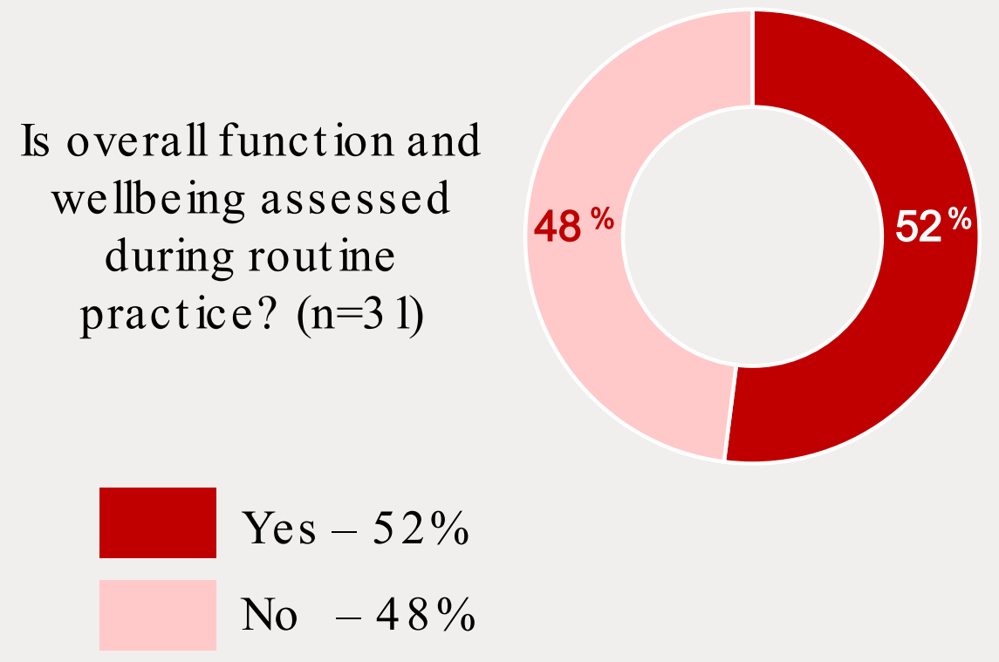
Figure 4. Criticisms of physical disability and impairment related scales from the HCP cohort

INCAT	I-RODS	MRC sum score
Limited disease sensitivity and ceiling effects Scoring system lacks granularity Dependent on subjective interpretation of the clinician Limited to muscular aspects of CIDP	Subjectivity concerns due to the patient-reported nature of this PRO Lacks ecological validity; response options are too restrictive and may have multiple reasons for not being feasible Limited sensitivity for minor improvements Lacks specificity to CIDP	Limited to muscular aspects of CIDP Does no consider all muscles and/or muscle groups that may be impacted by CIDP Limited sensitivity for minor improvements Scoring system is non-linear Inter-rater variability

- Only 38% of the PAG cohort reported familiarity with the above scales.

Relevance and applicability of HRQoL measures

Assessment of overall function and wellbeing in clinical practice was divisive



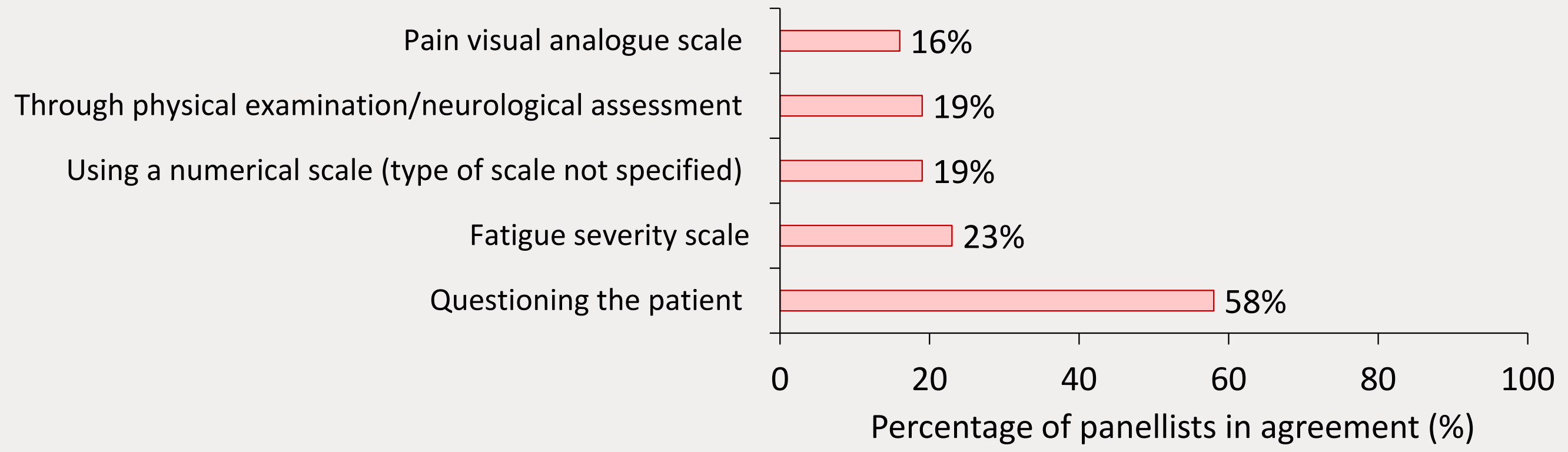
HRQoL was highlighted as an assessment conducted informally through patient questioning/recollection by 41% of the panel, rather than though the use of validated COAs.

Among the HCP cohort only, both CAPPRI and SF-36 were considered valuable when assessing HRQoL in patients with CIDP, although, limitations of these measures were highlighted.

Relevance and applicability of symptomatic COAs for pain and fatigue

- When prompted to consider how pain and fatigue can be adequately assessed in routine practice, a variety of responses were received **(Figure 5).**

Figure 5. Group responses relating to optimal assessments of pain and fatigue in patients with CIDP



Barriers to optimal assessment of therapeutic benefit

- When asked to consider what the greatest challenges are when assessing therapeutic benefit, several factors were identified as key challenges that hinder assessment (**Figure 6).**

Figure 6. Overview of the challenges when assessing for therapeutic benefit in patients with CIDP

Clinical heterogeneity in CIDP precludes the use of a single metric that can capture all relevant outcomes (29%)	Objectivity issues and misalignment of COAs scores with patient experience (23%)
Lack of consistent and reoccurring therapeutic evaluations (standardisation) (16%)	Knowledge of a patients' condition/status at baseline (prior to treatment) (10%)

Conclusions and Key Takeaways

Significant outcome domains that must be considered when assessing treatment response in patients with CIDP include:

- Physical domains (mobility, gait and balance, manual dexterity and strength, and upper and lower limb function),
- Socio-functional domains (functional independence, activities of daily living and social participation),
- Symptomatic domains (pain),
- Cognitive domains (cognitive functioning),
- Overall HRQoL.

Using consistent COAs over time allows clinicians to identify improvement or deterioration, however, symptoms of CIDP can evolve over time and the relevance of domains may also therefore change over time. The domains prioritised for assessment should remain flexible to ensure outcomes are meaningful.

While several outcome measures exist for several different domains e.g., physical impairment, HRQoL, pain, and fatigue, existing COAs are considered to have limitations.

There remains an unmet need to identify COAs that are relevant to both clinicians and patients, considering individual experiences and the clinical heterogeneity of CIDP.

Further research is required to understand whether a composite outcome measure can be developed that includes all key relevant outcome domains to patients with CIDP.

Next steps

Based on insights collected within the first-round of this Delphi panel, a second-round survey is currently in development, with survey completion expected by June 2025, followed by a virtual meeting (with results expected in July 2025).

The second-round survey aims to probe further on first round insights, shifting the focus from outcome domains to specific scale items.

The second-round survey also aims to elicit consensus on what type of questions panellists would like to see included in a novel COA for CIDP, designed to capture a range of outcome domains considered important to both HCPs and patients, alongside their thoughts on the relevance and appropriateness of existing measures to help optimise CIDP management and patient care.

Disclosures

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CIDP: Chronic Inflammatory Demyelinating Polyneuropathy; COA: Clinical outcome assessment; HCP: Healthcare professional; HRQoL: Health-related Quality of Life; INCAT: Inflammatory Neuropathy Cause and Treat; I-RODS: Inflammatory Rasch-built Overall Disability Scale; MRC: Medical Research Council; PAG: Patient representatives

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