Journal of the Peripheral Nervous System

WILEY

RESEARCH REPORT OPEN ACCESS

Feasibility and Reliability of a Monitoring App for Chronic Inflammatory Neuropathies

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Received: 23 October 2024 | **Revised:** 20 January 2025 | **Accepted:** 22 January 2025

Keywords: app | chronic inflammatory neuropathies | feasibility | reliability | tele-monitoring

ABSTRACT

Background and Aims: Multifocal motor neuropathy (MMN) and chronic inflammatory demyelinating polyneuropathy (CIDP) are immune-mediated neuropathies characterized by muscle weakness and/or sensory deficits. Identifying treatment response, relapse, and stability can be challenging in these chronic, sometimes unpredictable, conditions. This study explores the potential of a monitoring app designed to address these challenges.

Methods: Patients were monitored weekly or monthly, based on stability and patient preference, using grip strength, modified timed-up-and go (mTUG), and patient-reported outcome measures (PROMs). User experience was evaluated via a questionnaire addressing content and ease of use (scale 0–10). Adherence was measured as the percentage of completed mandatory assessments. We investigated reliability using intra-class correlation coefficients (ICCs) and standard errors of the mean (SEM) of repeated measurements. Longitudinal changes were analyzed using linear mixed-effects models.

Results: We included 38 patients, with a mean follow-up of 11 months (IQR 4.6–19.5). The mean user experience score was 8.35/10 (range 7–10). Adherence was 93% (95% CI: 91.9%–94.1%). Reported remote measurements for grip strength were 1358/1468 (93%), and 1343/1430 (94%) for mTUG. Grip strength and mTUG ICCs were both 0.96 (95% CI: 0.93–0.98 and 0.92–0.99, respectively). The average SEM was 8.46% (95% CI: 6.58–10.28) for grip strength and 8.18% (95% CI: 6.12–10.41) for mTUG. Only grip strength changed significantly, increasing by 3.1 pounds per 6 months (95% CI: 0.61–5.83; $p = 0.016$).

Interpretation: Our study demonstrates that tele-neuromonitoring is feasible and reliable, showing high adherence, positive user experience and high ICCs. We anticipate tele-neuromonitoring could complement routine follow-up, enabling clinicians to make better-informed treatment decisions.

1 | Introduction

Chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN) are immune-mediated neuropathies, most often characterized by prominent muscle weakness (CIDP/MMN) and/or sensory deficits (CIDP). Accurate and timely diagnosis of CIDP and MMN can be challenging [1, 2]. Although they are amenable to immune-modulating therapy, optimization of treatment may be arduous, due to the variable-disease course and treatment response [3, 4]. Moreover, there is no reliable disease activity biomarker that can identify patients who respond to treatment, may benefit from intensified treatment, or may be weaned off treatment [5, 6]. Consequently, treatment decisions are made based on clinical monitoring of symptoms and information patients recall during regularly scheduled outpatient clinic visits.

Guidelines for CIDP recommend collection of impairment outcomes, such as Medical Research Council (MRC) sum scores, hand-held dynamometry for grip strength, standardized walking tests, and patient-reported outcome measures (PROMs) (such as the Inflammatory Rasch-built Overall Disability Scale (I-RODS)) during clinic visits to increase the objectivity of clinical monitoring [7–9]. However, there are several limitations to this approach. Assessment of muscle strength using MRC-scores has low reproducibility, while rating and interpretation of PROMs such as the I-RODS, are complicated by relatively large subjective effects [10–12]. Hand-held dynamometry and standardized walking tests may be more reliable but are less valuable if collected infrequently. Important clinical changes may not be captured if the timing of the assessment does not align with changes in treatment or are not performed during clinical deterioration or improvement [13]. Enabling patients to track impairment and disability outcomes at home can provide continuous monitoring, without the burden of time-consuming hospital visits. This could facilitate identification of end-of-dose effects, aid in detecting early signs of relapses, or identify patients with stable disease. These observations can then be used to make more informed treatment decisions. Previous exploratory studies demonstrated the reliability of home-based measurements of grip strength and several PROMs [14, 15]. With the advance of e-health apps, the potential of remote-monitoring is promising [16–21].

Therefore, our team developed a novel tele-neuromonitoring app specifically designed for patients with immune-mediated neuropathies, and we conducted an implementation study with a prospective cohort to assess the feasibility and reliability of the app when used by patients with CIDP and MMN.

2 | Methods

2.1 | Patients

We performed a prospective cohort study of patients at the University Medical Center Utrecht (UMCU), a tertiary neuromuscular expert center in the Netherlands, between March 2021 and October 2022. Patients were included if they met the following criteria (1) diagnosed with CIDP or MMN based on the EAN/PNS or EFNS/PNS criteria [1, 2, 22], (2) receiving treatment with IVIg and/or steroids, (3) 18 years or older, and (4) had sufficient digital skills to report measurements in the app. Patients were excluded if they were not proficient in Dutch or English or did not own a smartphone or tablet (Android and IOS versions ≥ 7 respectively ≥ 12). All patients provided written informed consent.

2.2 | App Design

We co-designed a monitoring app (Polyneuropathie@home) with active input from patients, a panel of neuromuscular experts, and the Department of Digital Health of the UMCU. To capture the variability of the disease, four modules were developed: CIDP upper + lower limbs (1), CIDP focused on lower limbs (2), CIDP focused on upper limbs (3), and MMN (4). Eventually, within the timespan of this study, only the protocols CIDP upper + lower limbs and MMN were used. Different monitoring items are listed in Figure 1.

Monitoring frequency was scheduled either weekly or monthly, depending on disease stability and taking patients' own preferences into consideration. Most patients were initially enrolled in a weekly protocol, with those demonstrating a stable disease course being offered the option to switch to a monthly protocol. Moreover, patients had the option to report additional measurements between the required time points. As such, the timing of data collection in the app was not specifically synchronized with the patients' treatment schedules. All patients received a hand dynamometer (Saehan, hydraulic balloon) for home-based grip strength measurements. Single grip strength was recorded for each hand.

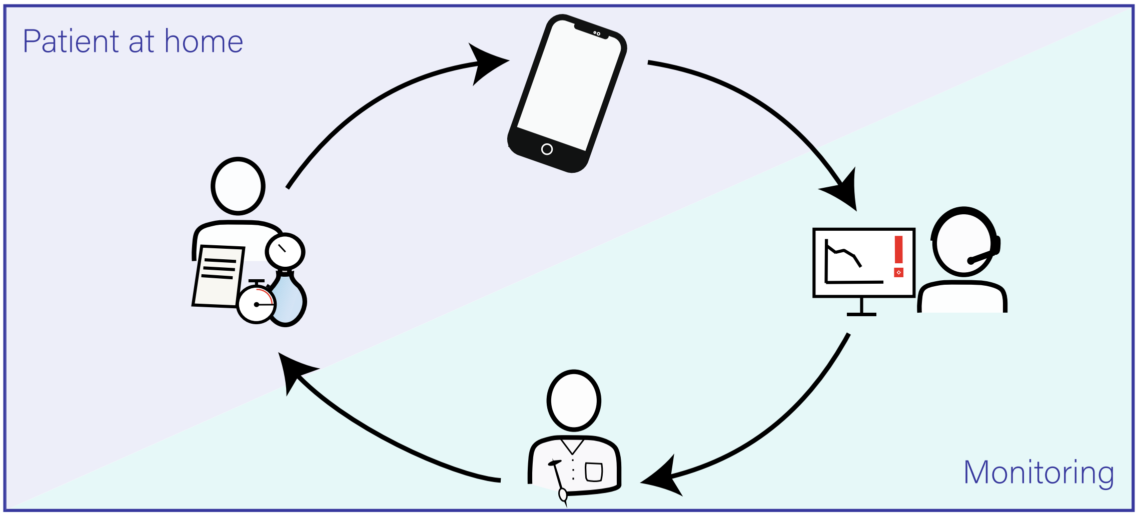
Patients were trained in person and received instructions during an outpatient clinic visit. Additionally, relevant information about executing the home measurements was available on the hospital website. The app allowed patients to monitor their own measurements, and a digital dashboard was created for physicians to display longitudinal trends. Importantly, we had several security requirements for the use of our CIDP/MMN monitoring app, and a two-factor authentication was built into the app to fulfill privacy requirements.

2.3 | User Experience

In the implementation test phase, we evaluated the first version of the monitoring app in a pilot group of 12 patients. After 6 weeks, targeted feedback was sought using a focus group (consisting of patients and physicians) to discuss points for improvement. Participants were also issued a 28-item questionnaire to evaluate the user experience. We aggregated this feedback to refine the app. Subsequently, a novel app version (update) was launched for all end-users (November 2021). In this current version, the item “fine motor skills” (Can you rate your fine motor skills on a scale from 0 to 5?) has been replaced by the item “hand motor skills,” which comprises a subset of five specific activities related to fine-hand motor skills (Figure 1). Moreover, the item “walking upstairs” (Can you rate your ability to walk up a flight of stairs on a scale from 0 to 5?) was removed. In addition, the item “walking, running, and standing” was added, which consists of a subset of three questions, asking the patient to rate these activities each on a scale from 0 to 5, with a potential maximum total score of 15 points.

2.4 | Monitoring and Adherence

Once the patients had been registered for participation, they received a manual and were guided by phone through the installation process of the app. All information in the app was monitored by the Medical Direction Center. The Direction Center is a department in our hospital specialized in screening incoming measurements from monitoring apps, based on predefined measurement thresholds. If a change in outcome exceeded a



Reported items	CIDP/MMN	Maximum score	Alert thresholds
PROMs			
Hand motor skills	CIDP/MMN	25 points	≤5 points or Δ ≥ 5 points decrease
Walking running and standing	CIDP/MMN	15 points	≤3 points or Δ ≥ 3 points decrease
General well-being	CIDP/MMN	3 points	≥1 point
Medical aids	CIDP/MMN	1 point	≥1 point
Walking distance	CIDP	1 point	≥1 point
Trip or fall	CIDP	1 point	≥1 point
Numbness	CIDP	1 point	≥1 point
Quantitative assessments			
Grip strength (Saehan dynamometer)	CIDP/MMN		Decrease ≥ 11 pounds
Modified Timed-up and go test (mTUG)	CIDP/MMN		≥ 21 Seconds

FIGURE 1 | Infographic with most important aspects of tele-neuromonitoring and the reported outcome measures. Hand motor skills subquestions: To what extent are you able to perform the following activities (0 not possible, 5 no restrictions): Opening jars and packaging (1), opening a door with a key (2), using buttons, belt, zippers (3), using a phone or sending text messages (4), lifting a heavy object and putting it on the ground (5). General well-being: Comprises physical well-being, mental well-being and energy level, each scored as 1 point. Alerts for an item arise if the scores are lower or equal to their threshold value or the difference with the previous measurement (Δ) exceeds the threshold value. For grip strength, an alert appears if either left- or right-hand grip strength decreases by 10 pounds, and for the mTUG, there is an alert if time exceeds 20 s. MDC, Medical Direction Center; mTUG, modified timed-up-and go; PROM, patient-reported outcome measure.

predefined threshold (Figure 1), staff were alerted, and patients or healthcare providers were contacted. The course of action was highly dependent on the specifics of each individual case. If an alert was escalated to notify the treating physician, the appropriate response was determined based on the physician's clinical judgment and their assessment of the situation. If deemed necessary, the patient was seen at the outpatient clinic. Baseline was determined based on the first measurement and updated manually if it appeared not to be appropriate. Threshold values for alerts were based on expert opinion and could be switched off in agreement with a patient and their physician. On reporting days, patients received a first notification in the app at 09.00 a.m. and a reminder at 08.00 p.m. if the values had not yet been reported. If two subsequent measurements were missing, patients were contacted via a personal message after 3 days. If data were still missing on Day 4, patients were contacted by phone.

2.5 | Statistical Analysis

Descriptive statistics were used to describe the patient characteristics at baseline. We performed Student's *t*-tests or Wilcoxon signed rank tests to compare differences in baseline characteristics. To evaluate the feasibility, we evaluated adherence together with the results of the user experience questionnaire. Adherence was calculated as the number of reported outcomes divided by the number of scheduled measurements for each individual. The difference in adherence between monitoring protocols was calculated using the *t*-test or Wilcoxon signed rank test.

To evaluate the reliability of grip strength measurements and the mTUG, we estimated the intra-class correlation coefficient (ICC) and the standard error of the mean (SEM) over time, using the first eight repeated measurements following study inclusion. Data were $_{10}$log transformed to account for heteroscedasticity, and a linear mixed model (LME), with only a random intercept per patient, was fitted. The ICC was obtained by calculating the ratio of the between-patient variability and the total variability, which is the sum of the within- and between-patient variability. The SEM was derived from within-patient variability and expressed as a percentage of the observed score by multiplying the square root (within-patient variability) × 100 × ln (10) [23]. Confidence intervals around these estimates were obtained by means of bootstrapping ($n = 1000$). The minimal detectable change (MDC) at an individual level was calculated as $MDC = SEM * \sqrt{2} * 1.96$ [24]. For illustrative purposes, we calculated the monitoring bands for one patient based on the MDC. MDC can be interpreted as the 95% CI around the expected difference between two observations for one patient.

To estimate longitudinal changes in grip strength, mTUG, hand motor skills and walking, running and standing, LMEs were fitted. The fixed part of the model contained an intercept and a linear effect for time per 6 months. The random effect contained a random intercept and random slope for time per patient. We used a likelihood ratio test to determine whether the change over time was statistically significantly different from zero. To test the variability in progression rates between patients, we used a likelihood ratio test to compare a model with only a random intercept versus a model with a random intercept and random slope for time per patient. All statistical analyses were performed using R (version 1.3.1093).

An exploratory analysis was conducted to examine the occurrence of different alert types, and corroboration with clinical data, specifically for grip strength alerts. In general, grip strength alerts were only escalated to notify the physician in certain conditions: For example, a first single grip strength alert was not escalated unless it was accompanied by other alerts for which this was necessary, or the patient provided relevant information in the message option. As a result, not all grip strength alerts were linked to outpatient clinic data. To further explore the clinical impact, the frequency with which grip strength alerts were followed by an escalation in treatment was assessed.

3 | Results

3.1 | Baseline Characteristics

Forty patients were invited to participate during routine outpatient clinic visits; two patients declined, resulting in a total enrolled population of 38 patients (20 with CIDP and 18 with MMN); the patient characteristics are summarized in Table 1. One patient with MMN discontinued home monitoring after 5 weeks due to stressful personal circumstances, not related to the disease or home monitoring project, and one patient with CIDP paused home monitoring after 79 weeks due to a severe relapse, resulting in tetraplegia and prolonged hospitalization. Overall, the mean follow-up time per patient was 11 months (IQR 4.6–19.5 months). We found no significant differences in baseline characteristics between patients with CIDP and MMN, except for lower mean age in the MMN group. In all but two patients, multiple weekly measurements were carried out before they continued with the monthly program. Two patients with MMN started with the monthly program straight away.

3.2 | User Experience

Twelve patients participated during the implementation test phase. CIDP and MMN patients spent on average 7.5 min completing data entry in the app. On a scale of 0–10, participants gave the app a total score of 8.35 out of 10 for both ease of use and content (minimum score 7/10 and maximum score 10/10).

TABLE 1 | Baseline table.

	Total (n = 38)	CIDP (n = 20)	MMN (n = 18)	p-value
Sex, male (%)	26 (68)	13 (65)	13 (72)	0.90
Age, years	57 (10)	60 (10)	53 (9)	0.03
Disease duration (months)	48 (26–80)	48 (25–72)	46 (27–93)	0.81
I-RODS (n = 19) Missing	40.6 (5.5) 19	40.6 (5.5) 1	N/A	N/A
Hand grip strength at baseline, pound-force	37.0 (24.1–53.3)	32.5 (24.9–47.62)	40.5 (17.1–59.8)	0.60
Treatment at baseline				
IVIg/ScIg	38 (100%)	20 (100%)	18 (100%)	N/A
Steroids	2–4[a] (5.2%–10.5%)	2–4[a]	0	
Other[b]	1	1	0	
App schedule				N/A
Monthly	10 (26.3%)	5 (25%)	5 (27.8%)	
Weekly	28 (73.7%)	15 (75%)	13 (72.2%)	
Follow-up (weeks)	31 (20–85)	70 (24–85)	22 (16–79)	0.15

Note: Data are expressed as mean (SD), n (%), or median (interquartile range).
Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; I-RODS, Inflammatory-Rasch-built Overall Disability Scale; IVIg, Intravenous immunoglobulin; MMN, multifocal motor neuropathy; ScIg, subcutaneous immunoglobulin.
[a]In the case of two patients, it is not clear whether they did or did not receive steroids, as they were participating in a double-blind trial with IVIg + steroids versus IVIg + placebo.
[b]Plasmapheresis, rituximab, and cyclophosphamide.

These patients responded to the following statements using answering options "agree," "disagree," or "both," categorized below based on the percentage who "agreed" with a statement.

- The app is easy to find, downloading and installation are easy, the app works intuitively and is self-explanatory, the layout is clear, additional information is clear, and the notifications in the app are useful. It is clear to me when to take up contact regarding care-related/health-related issues. Contact with the medical direction center via the app was pleasant and useful. I would recommend the app to other people (100%).
- The text and explanations in the app are all clear and comprehensive, and the measurements in the app are easy to perform at home. I am able to provide an explanation in the app when necessary. I can indicate when I would like to be called. I find the app a useful addition to the current healthcare standard (92%).
- It is easy to track and evaluate my own disease course in the app. The app provides useful insight into my disease. The e-mail reminders are useful (83%).
- The frequency of completing the questions and measurements in the app is just right (75%). The questions and measurements I have to report in the app apply to me (64%).

3.3 | Adherence

Nine patients had personalized adjustments to their monitoring protocol. This mainly included the removal of the item "use of medical aids," as this was not applicable to them. One MMN patient requested he would no longer be required to report the mTUG, as leg function was not affected, and one MMN patient only reported grip strength. Overall adherence was 93% (95% CI: 91.9%–94.1%). Adherence per protocol is visualized in Figure S1. For grip strength, 1358/1468 (93%) planned remote measurements were reported, and 1343/1430 (94%) for mTUG. There were no adherence differences between the weekly and the monthly protocols (Table S1) with the exception of the mTUG, which was found to have slightly higher adherence in the weekly group compared with the monthly group (95% vs. 90%). Patients with CIDP had a more favorable adherence profile than patients with MMN, but all individual assessments had 89% or greater adherence, also for MMN patients (Table S1). For the item "use of medical aids," seven patients in the MMN protocol scored adherence $< 85\%$. In contrast, in the CIDP group, all adherence scores for this item were $\geq 85\%$, indicating CIDP patients embraced the use of medical aids more than MMN patients did—likely as a result of distinct functional disability levels.

3.4 | Reliability

We found an average ICC for the first 8 repeated measurements of 0.96 for both grip strength and the mTUG (95% CI: respectively 0.93–0.98 and 0.92–0.99). The ICC of grip strength increased after the first measurements from 0.88 to 0.98. The average SEM was 8.46% (95% CI: 6.58–10.28) for grip strength and 8.18% (95% CI: 6.12–10.41) for the mTUG (Figure 2).

3.5 | Longitudinal Monitoring

The majority of patients showed a relatively stable hand grip strength and mTUG time (Figure 3). A change of 3.1 (95% CI: 0.61–5.83) pounds per 6 months was observed for grip strength, but we found no significant changes for the outcomes mTUG, "hand motor skills" and "walking, running, and standing." The half-yearly changes in each outcome are presented in Table 2. For each outcome, adding a random slope for each patient significantly improved model fit (all $p < 0.001$), reflecting the wide variability between patients in their longitudinal trajectories. Patients with shorter follow-up duration had higher between-subject variability. Originally, for the group of 38 patients, the between-subject variability for grip strength was 6.7 with a slope of 3.1 ($p = 0.016$). By excluding patients with < 25 weeks of follow-up, between-subject variability was 5.8 and the slope was not significant ($p = 0.13$).

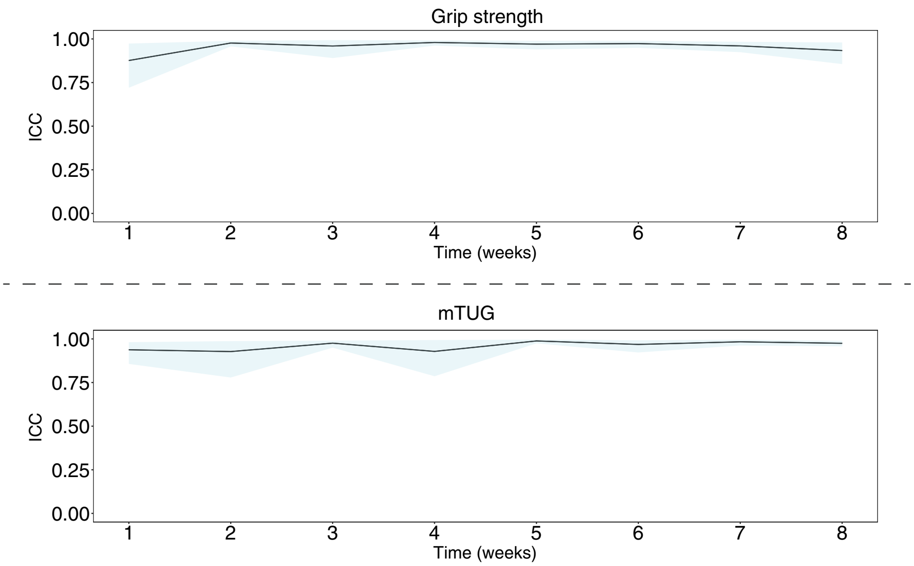


FIGURE 2 | Intra-class correlation for the first eight repeated measurements. ICC, intra-class correlation; mTUG, modified timed-up-and go.

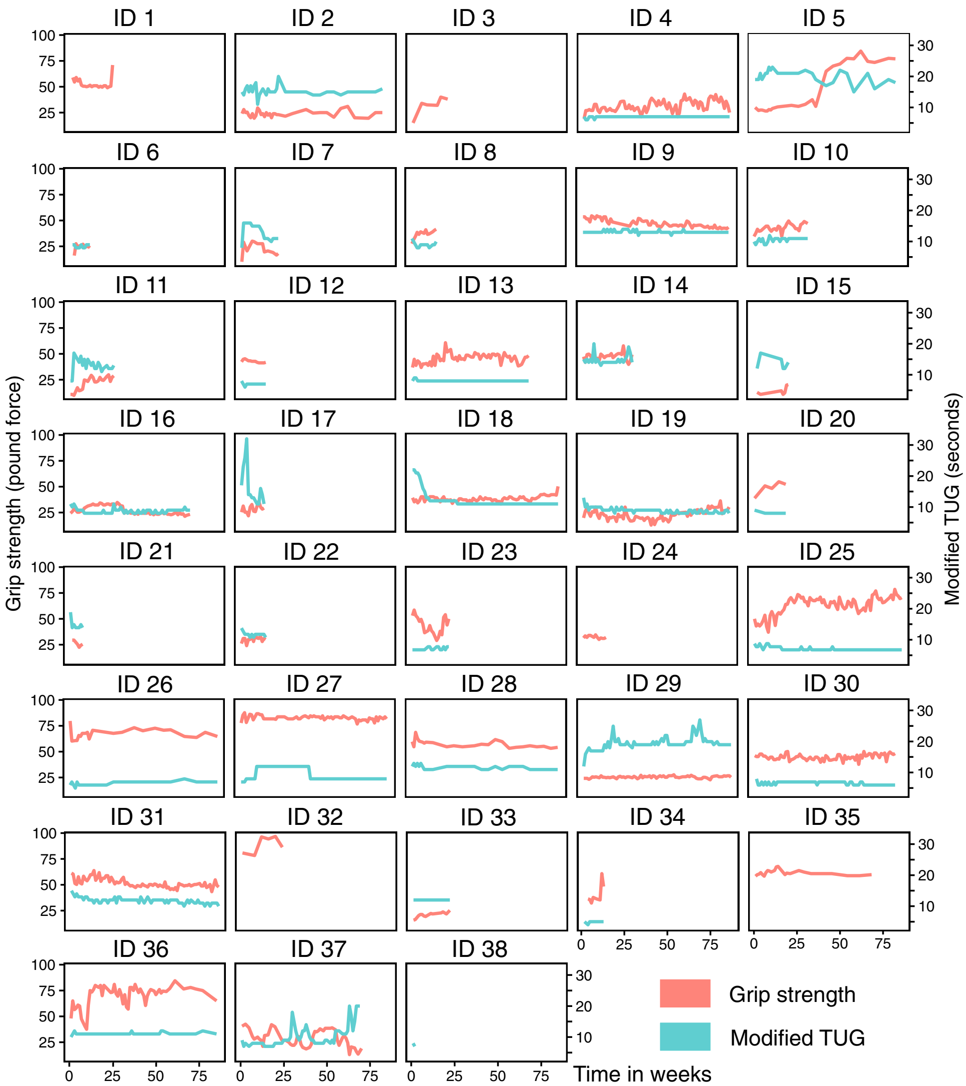


FIGURE 3 | Course over time of grip strength (in pound-force) and mTUG test (in seconds) for all patients. 20 patients remained on stable immunoglobulin treatment (dosing and frequency) during the study. In Patients 1 and 27, the IVIg dosing frequency decreased, and in patient 10 maintenance dosing increased. Nine patients had one additional IVIg loading dose during the tele-monitoring period, after which for ID 5, 9, 23, and 25, the maintenance dose or interval was changed. Six patients had multiple additional loading doses and/or other immune-modulating treatments. IVIg, intravenous immunoglobulins; mTUG, modified timed-up-and go.

TABLE 2 | Output of the linear mixed models for the outcomes grip strength, hand motor skills, mTUG, and walking, running, and standing.

Outcome	Intercept	Slope (pounds per 6 months)	95% CI	*p*-value	Between-subject variability	95 percentiles change per 6 months
Grip strength (pounds)	40.9	3.1	0.61, 5.83	0.016	6.7	−12.5, 19.0
Hand motor skills (0–25 points)	17.3	−0.8	−1.78, 0.19	0.111	2.4	−6.5, 4.9
mTUG (s)	12.8	−1	−2.25, 0.23	0.111	3.2	−8.5, 6.5
Walking, running, and standing (0–15 points)	7.4	−0.2	−0.65, 0.39	0.448	0.8	−2.2, 2.0

Note: Between-subject variability is the standard deviation of the random slope and indicates the change due to individual heterogeneity. 95 percentiles change per 6 months indicates the range within which the outcome can vary in 6 months for an individual. This is calculated by taking the lower and upper bound of the fixed slope 95% CI and respectively subtract or add (1.96*between-subject variability.).
Abbreviations: CI, Confidence interval; mTUG, modified timed-up-and go.

3.6 | Alerts and MDC

On average, 11 alerts per 6 months occurred per patient, ranging from 0 to 50 alerts per 6 months. In the case of two patients, there were no alerts (follow-up duration 22 and 24 weeks). Alerts per outcome and following action are reported in Table 3. The most common reason for an alert was generally feeling unwell, followed by changes in sensation and mobility. Alerts were only classified as "clinical action" if the medical direction center was directly involved in changing therapy based on an alert; this occurred three times.

For grip strength, 49 alerts were generated in 19 different patients in total. The number of grip strength alerts per patient ranged from 1 to 14, with all but one patient generating 1–4 alerts. Sixteen alerts were closely followed by changes in treatment (Table 4). A more detailed description of grip strength alerts can be found in the Supporting Information.

In Figure 4, grip strength course, and hand motor skills, and their alerts are visualized for one patient. The grip strength alert threshold was set at a decrease in left or right hand of 11 pounds, or a grip strength below 11 pounds. For hand motor skills, this was a 5-point decrease or a score of <5 out of 25.

4 | Discussion

Our study shows that the utilization of a monitoring app in CIDP and MMN patients is feasible and reliable. Although adherence was slightly better in CIDP patients compared to MMN patients, it was greater than 90% in both groups for nearly all assessments.

TABLE 3 | Alerts and action for each outcome including optional outcomes: adverse effects, blood pressure, and wish to contact caregiver.

Alert	*N*	Clinical action	Contacted via message	Contacted via phone	No action	Other
All alerts	823 (100%)	3 (0.4%)	162 (19.7%)	100 (12.2%)	477 (58.0%)	81 (9.8%)
General well-being	172 (20.9%)	1	59	25	76	11
Numbness	124 (15.1%)	1	24	14	71	14
Walking upstairs + walking, running, and standing	125 (15.2%)	0	13	0	88	24
Use of medical aids	72 (8.7%)	1	7	3	55	6
Fine motor skills (old item) + hand motor skills (new item)	62 (7.3%)	0	13	1	41	7
Grip strength	49 (6.0%)	0	4	15	27	3
Walking distance	44 (5.3%)	0	9	2	29	4
mTUG	44 (5.3%)	0	9	0	31	4
Trip or fall	24 (2.9%)	0	0	9	13	2
Adverse effects of treatment	31 (3.8%)	0	2	16	13	0
Blood pressure	8 (1%)	0	0	2	5	1
Wish for contact	68 (8.3%)	0	22	13	28	5

Note: Outcome "walking upstairs" and "fine motor skills" were replaced by respectively "walking, running, and standing" and "hand motor skills" on November 2021.
Abbreviation: mTUG, modified timed-up-and go.

TABLE 4 | Grip strength alerts in relation to treatment changes.

Number of grip strength alerts (*X*)	Number of patients with *X* grip strength alerts	Grip strength alerts are closely followed by treatment escalation
1	11	3
2	1	1
3	2	0
4	4	7
≥ 5	1	5
Total	19	16

Note: Nineteen patients generated 49 grip strength alerts during the study, of which 16 were closely followed with changes in treatment.

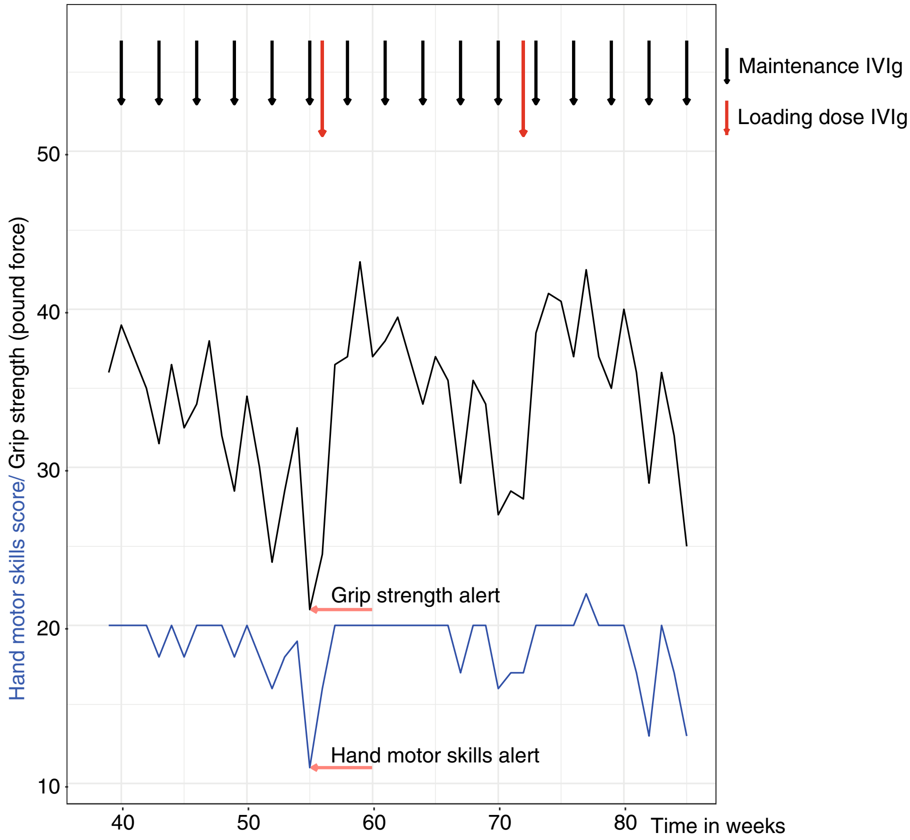


FIGURE 4 | Home monitoring observations for one individual. Measurements over time for a patient receiving 55 g IVIg every 3 weeks combined with additional loading doses every 4 months (3 days 50 g/day), showing an end-of-dose effect visible in grip strength (black) and hand motor skills score (blue) fluctuations. Horizontal red arrows indicate alerts in grip strength and hand motor skills. IVIg, intravenous immunoglobulins.

We found that home-based measurements of grip strength and mTUG test were reliable (both ICC 0.96), indicating that they are appropriate for use by patients at home without direct observation by a clinician. In addition, we found a lower correlation in grip strength for the first repeated measurements, indicating a learning effect for the first measurement.

We evaluated standardized home-based assessments to capture disease activity in CIDP and MMN. Our results are in line with previous studies that demonstrate the practicality and benefits of frequent collection of grip strength in CIDP and MMN patients at home [14, 15, 25]. However, our study goes a step further by integrating these assessments with a mobile app, which facilitates and coordinates the data collection process and gives a real-time overview of disease course for patients and physicians. Additionally, we did not only capture grip strength, but a set of patient-tailored PROMs. Consequently, utilization of an app in CIDP and MMN may significantly expand the capabilities of monitoring in clinical practice, making it easier for healthcare providers to track disease course and adjust treatment plans as needed.

This proof-of-concept study was designed to show the feasibility and reliability of home-based monitoring. Our study was not primarily designed to directly guide management decisions. Consequently, there were relatively few registered treatment changes that were directly based on alerts generated by the app. For example, an alert was only classified as "clinical action" if the medical direction center was directly involved in a change in treatment, which probably underestimates the number of clinical decisions made based on alerts. More often, the medical direction center contacted patients and documented this in the patient file or sent an order to the physician, who later decided to change management or not, hence these changes were not coupled directly to an alert.

By demonstrating feasibility and reliability of home-based collection of outcomes using the app, we have set the stage for application of this model in patients starting treatment, and patients who are withdrawing from treatment. Before doing so, we have identified several modifications that are needed. At this time the app did not have the flexibility to adjust alert thresholds based upon individual patient characteristics (e.g., threshold for grip strength is a decrease of 11 pounds, in all patients). We also collected a high number of alerts—many more than is practical to manage during busy routine clinical care. Moreover, it is worth noting that almost all subjective alerts were reported more often than grip strength and mTUG, especially the less disease specific "general well-being" is reported most frequent (Figure 5). As we accrue data from individual patients, we expect to learn more about how changes in the data can be collected and reported in a more targeted way. As a case in point, by calculating grip strength MDC boundaries for one of our patients, we were able to generate monitoring bands that could be individualized for each patient and automated for monitoring (Figure 6). Methods like this may be utilized in future studies to personalize threshold values to individual patients.

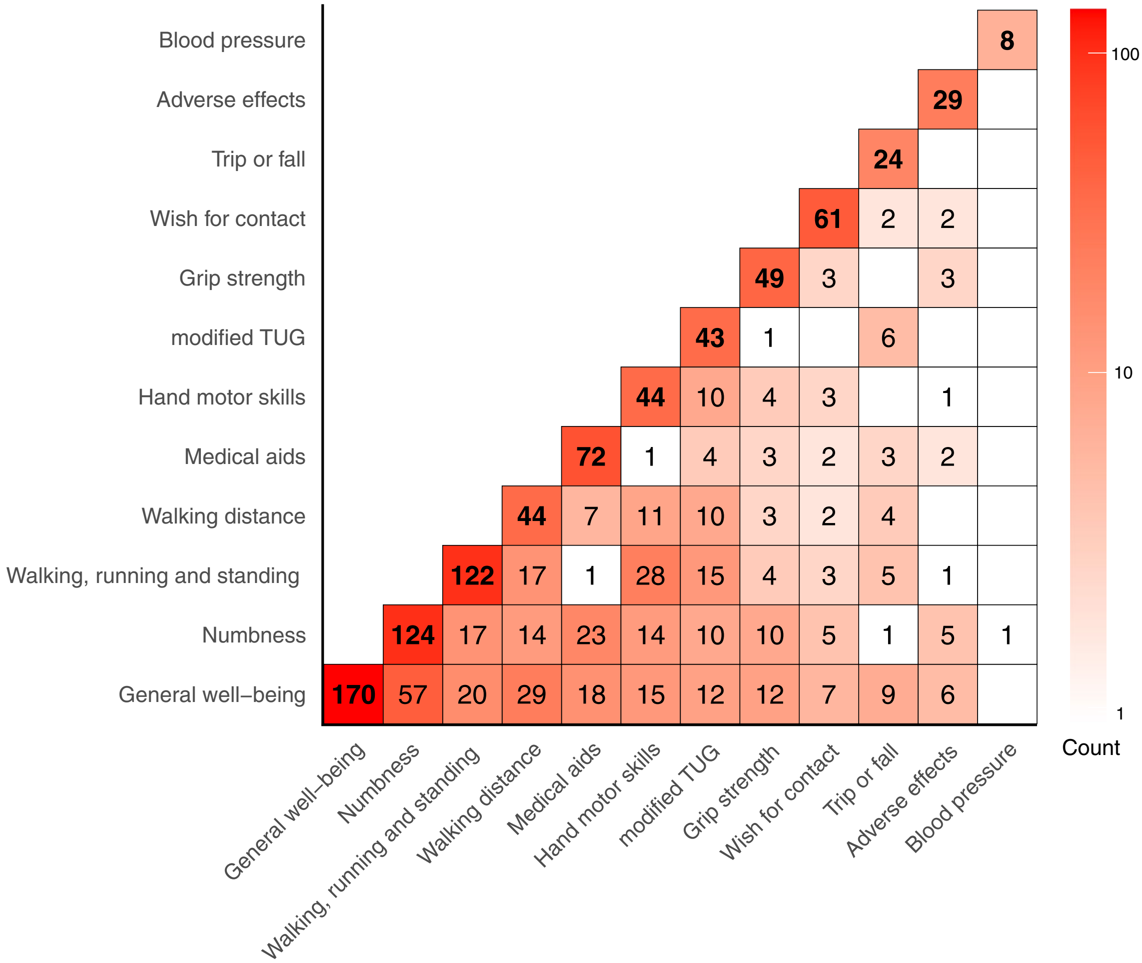


FIGURE 5 | Simultaneous occurrence of alerts. Absolute count and co-occurrence of alerts for all patients per app-item during the total monitoring period. Fourteen alert duplicates (i.e., patient reported an app-item more than once on the same day) were excluded. "Fine motor skills" and "walking upstairs" have not been included in this figure as they were replaced in the new app version.

Our study has several limitations. The included patients were also relatively stable under active treatment, and smaller sample size of our study may lead to potential spectrum bias. However, other clinical characteristics were variable such as disease duration and treatment characteristics, representing the diverse patient population at our outpatient clinic. Additionally, remote monitoring may not be feasible for all patients, including those with lack of digital technology skills or lower motivation to evaluate their disease activity more regularly. The outcomes collected included patient-reported outcomes designed to capture the participants' subjective experience (general well-being, numbness, mobility perception and fine hand motor skills). These have not been validated in CIDP and MMN, and as such, the significance of changes in the scores is not known. While these parameters may give valuable insights, they are non-specific and many times did not reflect clinically meaningful changes. We selected these patient-reported outcome measures because patients reported these as most relevant for their disease. A large number of alerts were generated by the PROM general well-being. Since our hospital has the capability to manage alerts through the medical direction center, we were able to respond to these notifications, which may have influenced patient participation engagement and adherence. However, the clinical relevance of these subjective alerts is debatable. Over time, we expect to gain a better understanding of which changes can be considered less relevant and potentially dismissed, and which ones are crucial. In the context of setting up the system without an extensive triage team, it may be worthwhile to prioritize collecting objective measurements, such as grip strength.

In this exploratory setting, we have not performed a cost analysis. However, we foresee that monitoring apps will play an increasingly crucial role in reducing the need for in-person follow-up visits and enabling medication adjustments without requiring additional physical appointments. This trend is especially significant in regions with vast geographical distances, where travel can be time-consuming and costly. We realize that, in contrast to the Netherlands, home administration of IVIg is not widespread globally, and some patients still need to travel for their treatment even when monitored with a monitoring app. However, in addition to other benefits of remote monitoring—such as more frequent insights into disease course, and potential reduction of unnecessary appointments with specialists—we anticipate that the need for frequent travel for treatment will decrease as well due to the growing adoption of subcutaneous immunoglobulin (ScIg) and the emergence of new therapies. We believe that remote monitoring can lower healthcare costs by reducing the need for in-person visits. However, further cost analyses will be needed to confirm and quantify these savings.

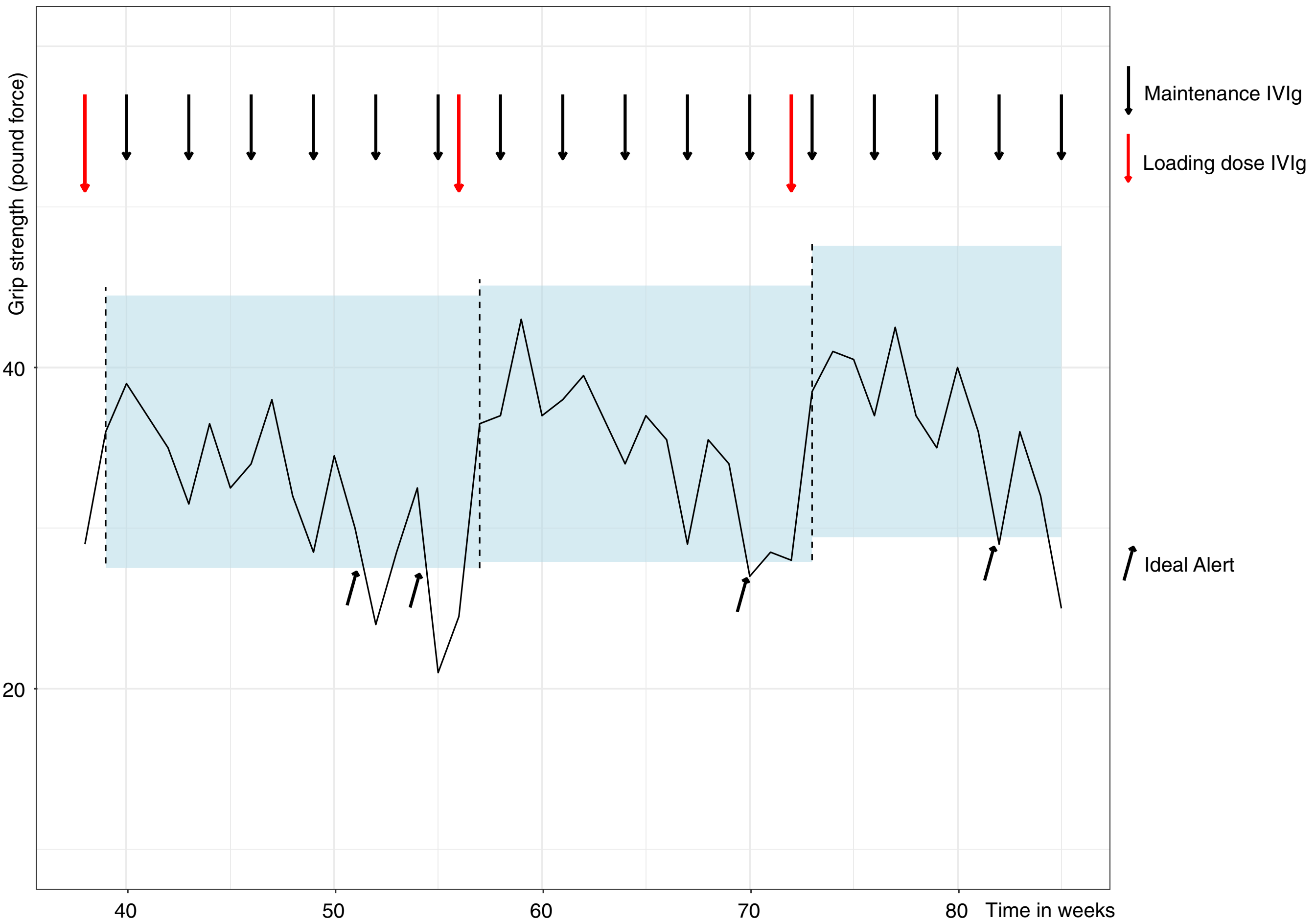


FIGURE 6 | Alerts and MDC. The same patient as in Figure 4, receiving 55 g IVIg every 3 weeks combined with additional loading doses every 4 months (3 days 50 g/day). The light blue band represents the MDC, updated with a new "baseline" grip strength value 1 week after each additional loading dose. Black diagonal arrows indicate when grip strength values drop below MDC boundaries, indicating a real decrease in grip strength. IVIg, intravenous immunoglobulins; MDC, minimal detectable change.

Our study shows that monitoring the clinical status of CIDP and MMN patients with an app is feasible and reliable. We furthermore introduce the functionality of the app and highlight the potential that home monitoring has to improve patient outcomes through early detection of relevant changes in disease activity. Moreover, home-based assessment with a monitoring app could in the future also be considered as a novel but reliable platform to collect data from patients during clinical trials. Monitoring outcomes for inflammatory neuropathy patients at home using smart devices is in its infancy. Larger cohorts of CIDP and MMN patients followed over time are needed to validate the monitoring app in a multicenter and culturally diverse setting. By doing so we expect that surveillance protocols can be developed and tailored to individual patient characteristics, and alerts can be automated and filtered to make them meaningful and practical for use in a busy outpatient clinic.

Acknowledgments

We would like to thank the staff of Digital Health, the eHealth department and the medical direction center for their contribution in developing, implementing and monitoring the polyneuropathie@home app. We also thank Brenda Vollers-King for assistance with language editing.

Disclosure

R.P.A. van Eijk receives support from the ALS Foundation Netherlands and the Dutch Research Council (NWO). J.A. Allen is a consultant for Argenx, Alexion, Annexon, Akcea, CSL Behring, Johnson & Johnson, Grifols, Sanofi, and Takeda. Y.A. Rajabally has received speaker/consultancy honoraria from LFB, Polyneuron, and Argenx, has received educational sponsorships from LFB and CSL Behring; and has obtained research grants from LFB and CSL Behring. L.H. van den Berg received an educational grant from Takeda, serves on the editorial boards of Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, and receives research support from the Netherlands ALS Foundation. W.L. van der Pol serves on the scientific advisory board for SAB SMA Europe; provides ad hoc consultancy for Argenx, Biogen, Biohaven, NMD Pharma, Novartis, Roche, and Scholar Rock (fee for service to employer); and receives research support from the Prinses Beatrix Spierfonds, Vriendenloterij, EU Horizon 2020, and Stichting Spieren voor Spieren. H.S. Goedee has received research grants from Prinses Beatrix Spierfonds, travel support from Shire/Takeda, and speaker fees from Takeda, paid to the institution.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

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

References

1. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of multifocal motor neuropathy, "Report of a Joint Task Force of the European Federation of Neurological Societies and the Peripheral Nerve Society–First Revision," *Journal of the Peripheral Nervous System* 15 (2010): 295–301.

2. P. Y. K. Van den Bergh, P. A. van Doorn, R. D. M. Hadden, et al., "European Academy of Neurology/Peripheral Nerve Society Guideline on Diagnosis and Treatment of Chronic Inflammatory Demyelinating Polyradiculoneuropathy: Report of a Joint Task Force-Second Revision," *Journal of the Peripheral Nervous System* 26 (2021): 242–268.

3. L. Vlam, W. L. van der Pol, E. A. Cats, et al., "Multifocal Motor Neuropathy: Diagnosis, Pathogenesis and Treatment Strategies," *Nature Reviews Neurology* 8 (2012): 48–58.

4. W. L. van der Pol, E. A. Cats, and L. H. van den Berg, "Intravenous Immunoglobulin Treatment in Multifocal Motor Neuropathy," *Journal of Clinical Immunology* 30, no. Suppl 1 (2010): S79–S83.

5. A. L. Oaklander, M. P. Lunn, R. A. Hughes, I. N. van Schaik, C. Frost, and C. H. Chalk, "Treatments for Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP): An Overview of Systematic Reviews," *Cochrane Database of Systematic Reviews* 1 (2017): 1–33, https://doi.org/10.1002/14651858.CD010369.pub2.

6. L. Feyen, C. Schaub, J. Zimmermann, and L. Nitsch, "Parameters Associated With the Required Drug Dose of Intravenous Immunoglobulin in Stable Chronic Inflammatory Demyelinating Polyradiculoneuropathy," *Neurology International* 15 (2023): 405–414.

7. S. I. van Nes, E. K. Vanhoutte, P. A. van Doorn, et al., "Rasch-Built Overall Disability Scale (R-ODS) for Immune-Mediated Peripheral Neuropathies," *Neurology* 76 (2011): 337–345.

8. T. H. Draak, M. H. Pruppers, S. I. van Nes, et al., "Grip Strength Comparison in Immune-Mediated Neuropathies: Vigorimeter vs. Jamar," *Journal of the Peripheral Nervous System* 20 (2015): 269–276.

9. E. K. Vanhoutte, T. H. Draak, K. C. Gorson, et al., "Impairment Measures Versus Inflammatory RODS in GBS and CIDP: A Responsiveness Comparison," *Journal of the Peripheral Nervous System* 20 (2015): 289–295.

10. Y. A. Rajabally and F. Fatehi, "Outcome Measures for Chronic Inflammatory Demyelinating Polyneuropathy in Research: Relevance and Applicability to Clinical Practice," *Neurodegenerative Disease Management* 9 (2019): 259–266.

11. Y. A. Rajabally, R. Ouaja, F. Kasiborski, S. Pujol, and E. Nobile-Orazio, "Assessment Timing and Choice of Outcome Measure in Determining Treatment Response in Chronic Inflammatory Demyelinating Polyneuropathy: A Post Hoc Analysis of the PRISM Trial," *Muscle & Nerve* 66 (2022): 562–567.

12. E. K. Vanhoutte, C. G. Faber, S. I. van Nes, et al., "Modifying the Medical Research Council Grading System Through Rasch Analyses," *Brain* 135 (2012): 1639–1649.

13. E. K. Vanhoutte, N. Latov, C. Deng, et al., "Vigorimeter Grip Strength in CIDP: A Responsive Tool That Rapidly Measures the Effect of IVIG – The ICE Study," *European Journal of Neurology* 20 (2013): 748–755.

14. P. E. Doneddu, D. Mandia, F. Gentile, et al., "Home Monitoring of Maintenance Intravenous Immunoglobulin Therapy in Patients With Chronic Inflammatory Neuropathy," *Journal of the Peripheral Nervous System* 25 (2020): 238–246.

15. J. A. Allen, M. Pasnoor, M. M. Dimachkie, et al., "Quantifying Treatment-Related Fluctuations in CIDP: Results of the GRIPPER Study," *Neurology* 96 (2021): e1876–e1886.

16. H. M. R. van Goor, M. J. M. Breteler, K. van Loon, et al., "Remote Hospital Care for Recovering COVID-19 Patients Using Telemedicine: A Randomised Controlled Trial," *Journal of Clinical Medicine* 10, no. 24 (2021): 5940, https://doi.org/10.3390/jcm10245940.

17. D. Kauw, M. A. C. Koole, M. M. Winter, et al., "Advantages of Mobile Health in the Management of Adult Patients With Congenital Heart Disease," *International Journal of Medical Informatics* 132 (2019): 104011.

18. J. Helleman, R. Van Eenennaam, E. T. Kruitwagen, et al., "Telehealth as Part of Specialized ALS Care: Feasibility and User Experiences With "ALS Home-Monitoring and Coaching"," *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration* 21 (2020): 183–192.

19. F. A. C. Farias, C. M. Dagostini, Y. A. Bicca, V. F. Falavigna, and A. Falavigna, "Remote Patient Monitoring: A Systematic Review," *Telemedicine Journal and E-Health* 26 (2020): 576–583.

20. M. L. Dontje, E. Kruitwagen-van Reenen, E. van Wijk, E. Baars, J. M. A. Visser-Meily, and A. Beelen, "Evaluation of the Nation-Wide Implementation of ALS Home Monitoring & Coaching: An e-Health Innovation for Personalized Care for Patients With Motor Neuron Disease," *BMC Health Services Research* 22 (2022): 1389.

21. J. Hamel, P. D. Creigh, J. Dekdebrun, K. Eichinger, and C. A. Thornton, "Remote Assessment of Myotonic Dystrophy Type 1: A Feasibility Study," *Muscle & Nerve* 66 (2022): 336–339.

22. P. Y. Van den Bergh, R. D. Hadden, P. Bouche, et al., "European Federation of Neurological Societies/Peripheral Nerve Society Guideline on Management of Chronic Inflammatory Demyelinating Polyradiculoneuropathy: Report of a Joint Task Force of the European Federation of Neurological Societies and the Peripheral Nerve Society – First Revision," *European Journal of Neurology* 17 (2010): 356–363.

23. A. M. Euser, F. W. Dekker, and S. le Cessie, "A Practical Approach to Bland-Altman Plots and Variation Coefficients for Log Transformed Variables," *Journal of Clinical Epidemiology* 61 (2008): 978–982.

24. L. Furlan and A. Sterr, "The Applicability of Standard Error of Measurement and Minimal Detectable Change to Motor Learning Research-A Behavioral Study," *Frontiers in Human Neuroscience* 12 (2018): 95.

25. P. E. Doneddu and R. D. M. Hadden, "Daily Grip Strength Response to Intravenous Immunoglobulin in Chronic Immune Neuropathies," *Muscle & Nerve* 62 (2020): 103–110.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.