Connecting impairment, disability, and handicap in immune mediated polyneuropathies

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Methods: Four impairment measures (fatigue severity scale, MRC sum score, “INCAT” sensory sum score, grip strength with the Vigorimeter), five disability scales (nine hole peg test, 10 metres walking test, an overall disability sum score (ODSS), Hughes functional grading scale, Rankin scale), and a handicap scale (Rotterdam nine items handicap scale (RIHS9)) were assessed in 113 clinically stable patients (83 with Guillain–Barré syndrome, 22 with chronic inflammatory demyelinating polyneuropathy, eight with a gammopathy related polyneuropathy). Regression analyses with backward and forward stepwise strategies were undertaken to determine the correlation between the various levels of outcome (impairment on disability, impairment on handicap, disability leading to handicap, and impairment plus disability on handicap).

Results: Impairment measures explained a substantial part of disability (R² = 0.64) and about half of the variance in handicap (R² = 0.52). Disability measures showed a stronger association with handicap (R² = 0.76). Combining impairment and disability scales accounted for 77% of the variance in handicap (RIHS9) scores.

Conclusions: In contrast to some suggestions, support for the ICIDH model is found in the current study because significant associations were shown between its various levels in patients with immune mediated polyneuropathies. Further studies are required to examine other possible contributors to deficits in daily life and social functioning in these conditions.

Background: In the World Health Organisation (WHO) International Classification of Impairments, Disabilities, and Handicaps (ICIDH), it is suggested that various levels of outcome are associated with one another. However, the ICIDH has been criticised on the grounds that it only represents a general, non-specific relation between its entities.

Objective: To examine the significance of the ICIDH in immune mediated polyneuropathies.

METHODS

Patients
We recruited 113 clinically stable patients (83 with Guillain–Barré syndrome, 22 with chronic inflammatory demyelinating polyneuropathy, eight with a gammopathy related polyneuropathy) from the Rotterdam immune mediated polyneuropathy databank and the Dutch Guillain–Barré syndrome study group (stable group). Patients with these three conditions were recruited as it is argued that they represent parts of a continuum with respect to their pattern of neuromuscular dysfunction. The selected patients still had residual symptoms or signs of their illness, representing a broad range of combined impairment and disability measures. We believed that these evaluations would increase our knowledge of how these conditions influence life in the long term. Also, the strength of the relations between items representing the various levels of outcome would help physicians to use them as a proxy for measuring other levels of clinical deficit. For example, grip strength (an impairment measure) could be an indicator of arm disability, because it shows a moderate to good association with an arm disability scale.

Abbreviations: f score, Hughes functional grading scale; FSS, fatigue severity scale; ICIDH, WHO international classification of impairments, disabilities, and handicaps; INCAT, inflammatory neuropathy cause and treatment; ISS, INCAT sensory sum score; MRC, Medical Research Council; ODSS, overall disability sum score; RIHS9, Rotterdam nine items handicap scale
disability. Nine patients with chronic inflammatory demyelinating polyneuropathy required interval treatment with intravenous immunoglobulin over periods ranging from weeks to months. With this treatment their clinical condition has been stable for more than six months. Six patients with gammapathy related polyneuropathy (three with IgG type, two with IgM type, and one with IgG+IgM type) had an associated demyelinating polyneuropathy with minor concurrent axonal damage in three. An axonal polyneuropathy was diagnosed in the remaining two patients with gammapathy related polyneuropathy (one IgA type and one IgG type). All patients with Guillain–Barré syndrome and chronic inflammatory demyelinating polyneuropathy met the international criteria for their illness. The diagnosis of gammapathy related polyneuropathy was established after excluding all possible causes for the gammapathy and polyneuropathy.

Assessment tools/scales

Rationale for scale selection

Scales were selected by a panel of 13 expert neurologists, all members of the Inflammatory Neuropathy Cause and Treatment Group (INCAT)—a collaborating force of European neurologists with a special interest in neuroimmunological illnesses. Selection was based on their experience, taking into account the clinical spectrum of sensory-motor immune mediated polyneuropathies. Because the motor and sensory systems are primarily affected in these conditions, the MRC sum score and a new sensory sum score were selected to examine the deficits. As distal weakness could predominate, grip strength was used to measure “focal impairment” of the hand. A fatigue scale was also selected, as fatigue has been found to be a major complaint in patients with immune mediated polyneuropathies. Various scales were selected to measure different aspects of disability. An overall disability scale (measuring arm and leg function) was chosen as the final disability target for the regression studies, based on its comprehensive nature compared with the other disability measures. Finally, a handicap measure that has been subjected to psychometric evaluation in immune mediated polyneuropathies was chosen to complete the set of scales.

Description of the scales

The MRC sum score is a summation of the Medical Research Council grades (range 0–5) for the following muscle pairs: upper arm abductors, elbow flexors, wrist extensors, hip flexors, knee extensors, and foot dorsal flexors. The MRC sum score ranges from 0 (“total paralysis”) to 60 (“normal strength”). The subdivisions MRC-arms (range 0–30) and MRC-legs (range 0–30) were also incorporated separately in the univariate regression analyses.

The INCAT sensory sum score (ISS) has recently been evaluated in patients with immune mediated polyneuropathies. In brief, this scale comprises pin prick and vibration sense plus a two point discrimination test in the arms and legs, and ranges from 0 (“normal sensation”) to 20 (“most severe sensory deficit”). The sensory modes representing the ISS were also analysed separately in the univariate regression analyses to determine their impact on disability and handicap (pin prick, arm + leg: range 0 (no deficit) to 8 (maximum deficit); vibration, arm + leg: range 0 (no deficit) to 8 (maximum deficit); two point discrimination: range 0 (no deficit) to 4 (maximum deficit)).

The Vigorimeter (Martin, Tuttlingen, Germany) is a hand held dynamometer used to measure grip strength. A medium sized bulb was used in the patients selected. The pressure in the bulb is registered on a manometer and expressed in kilopascals (kPa; range 0–160). The Dutch version of the fatigue severity scale (FSS) was used to assess fatigue. The FSS is a brief and simple self assessed questionnaire containing nine items with answers ranging from 1 (“strongly disagree”) to 7 (“strongly agree”) for each inquiry. The mean score of the nine inquiries ranges from 1 (“no signs of fatigue”) to 7 (“most disabling fatigue”).

The overall disability sum score (ODSS) is derived from a recent arm and leg disability scale, with a total score ranging from 0 (“no sign of disability”) to 12 (“most severe disability”). The ODSS comprises a good functional description of the arms and legs in checklist form suitable for interviewing patients. Daily arm activities such as dressing the upper part of the body, doing up and undoing buttons and zips, washing and brushing the hair, using a knife and fork, and turning a key in a lock are investigated. Problems with walking are also evaluated taking into account the use of a walking aid. The ODSS, its arm disability scale, and its leg disability scale were examined separately in the univariate regression analyses to determine their association with the handicap level.

The modified Hughes functional grading scale (FSS) was used to assess functional ability, particularly mobility, and ranges from 0 (no symptoms or signs) to 5 (requiring artificial ventilation for at least part of the day).

The Rankin scale has primarily been used in patients with stroke. The grades of this scale range from 0 (no deficit) to 8 (maximum deficit): two point discrimination: range 0 (no deficit) to 8 (maximum deficit); vibration, arm + leg: range 0 (no deficit) to 8 (maximum deficit). The recently constructed Rotterdam nine items handicap scale (RIHS9) has been evaluated in immune mediated polyneuropathies. The RIHS9 comprises nine inquiries (mobility indoors, mobility outdoors, kitchen tasks, domestic tasks indoors, domestic tasks outdoors, leisure activities indoors, leisure activities outdoors, ability to drive a car/go by bus/ride a bicycle, and ability to work/study), with a total score ranging from 9 (“unable to fulfil any applicable task or activity”) to 36 (“able to fulfil all applicable tasks and activities”).

Test procedures

General aspects

All participants gave their informed consent before the study. All procedures were done in a quiet and comfortably warm room at our outpatient clinic. The assessments were undertaken in random order. All participants received instructions on how to fill in the FSS form.

For the assessment of strength, the joint and limb position was standardised for each muscle group before the start of the study, as was the point at which counterforce was applied. Sensory modes were examined in triplicate under standard conditions with the patients lying in the supine position.

Grip strength with the Vigorimeter was assessed according to the recommendations of the American Society of Hand Therapists. Three grip strength measurements with maximum voluntary contractions for each hand were taken in alternating order. Between each trial there was a pause of 30 seconds. The results of three trials for each hand were averaged and considered to represent the grip strength score for that hand.

All patients received training in assessing the nine hole peg test before the start of the study; to exclude any training effect. The patients were asked—under the prescribed standard conditions in alternating order for both hands—to pick up nine pegs from a tray at table height and place them as quickly as possible into nine holes in a neighbouring horizontal board. After this procedure, the pegs then had to be removed as fast as possible. Patients were also requested to walk 10 metres in a straight line at their preferred speed, using whatever aid was needed.

Three measures were completed for each of these tests and the corresponding time was recorded at each assessment (in seconds). For each test separately, the mean time of completion was calculated by averaging the three measures obtained.
Validity and reliability
The minimum entry requirement for regression model analyses was that a scale had been shown to be valid and reliable. These criteria had already been fulfilled for the MRC sum score, ISS, grip strength with the Vigorimeter, FSS, F score, ODSS, and RHIS9. The remaining scales (Rankin scale, nine hole peg test, and 10 metres walking test) were declared valid by the panel of experts.

For the assessment of the validity and reliability of the scales, two neurologists and six experienced residents in neurology formed 28 different couples. Preceding the study, all investigators received instructions in assessing the outcome measures. Twenty seven (“variable”) couples investigated a total of 68 patients (two to three patients for each couple). The remaining 43 stable patients were investigated by the “experienced” couple (1M + 3S). The latter couple was formed to examine the effect of training (and thus a possible increase in reliability) when using the scales often. The patients were examined on two different occasions at our outpatient clinic. During the first visit the two members of an appointed pair arrived at their scores independently and consecutively (usually within two hours) (interserver variability). Within two to four weeks, the patient returned for a second visit and only one investigator of the earlier assigned pair examined the patient again (intrarerver variability) without having access to the previous results. The assessment sequence at entry and the examination at the second visit were equally distributed among the members of an assigned couple. Eventually, each member of a couple examined approximately the same number of patients. With the exception of the f score, all scales were assessed at each visit in all patients. For the validity and regression model studies, only the scale values obtained at entry were used. The study took place between December 1998 and January 2000 and was performed on behalf of the INCAT group.

Statistics
Validity and reliability of scales not thoroughly evaluated in immune mediated polyneuropathies

The correlation between the Rankin scale, the nine hole peg test, and the 10 metres walking test was analysed using the Spearman rank correlation test. Inter-rater and intrarater reliability was quantified by estimation of the intraclass correlation coefficient using a one way random effects analysis of variance model for the two investigator (“experienced” and “variable”) groups.

Regression model studies
Univariate and multivariate linear regression analyses were done to determine the association between impairment, disability, and handicap outcome measures. The ODSS was used as the disability dependent variable in the studies analysing the association with impairment measures (explanatory variables). The ODSS was chosen because of its comprehensiveness in monitoring disability compared with the f score and Rankin scale. The latter two scales assess disability with a strong emphasis on mobility and do not provide information on the arms. The RHIS9 was the dependent variable for the analyses of impairment and disability measures leading to handicap. If necessary, a transformation of the various scales was done to obtain a normal distribution.

Table 1: Basic characteristics of stable patients with immune mediated polyneuropathies

<table>
<thead>
<tr>
<th>Demographic variables and tests</th>
<th>Number of patients</th>
<th>Guillain–Barre syndrome (n)</th>
<th>CIDP (n)</th>
<th>MGUSP (n)</th>
<th>Age at entry (years)</th>
<th>Duration of symptoms to onset of study (years)</th>
<th>Sex distribution (n (%))</th>
<th>MRC sum score at entry (kPa)</th>
<th>INCAT sensory sum score at entry (kPa)</th>
<th>Grip strength values with the Vigorimeter at entry (kPa)</th>
<th>Fatigue severity scale score at entry</th>
<th>f Score at entry</th>
<th>Overall disability sum score at entry (kPa)</th>
<th>ISS</th>
<th>RotAm six item handicap scale at entry (kPa)</th>
<th>Nine hole peg test at entry (s)*</th>
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</thead>
<tbody>
<tr>
<td>Total</td>
<td>113</td>
<td>83</td>
<td>22</td>
<td>8</td>
<td>54.3 (15.1)</td>
<td>6.9 (3.1), 0.5 to 28</td>
<td>Male 59 (52)</td>
<td>53.3 (7.7), 16 to 60</td>
<td>4.4 (4.1), 0 to 15</td>
<td>66.9 (33.6), 0 to 156</td>
<td>2.1 (0.9), 1 to 4</td>
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<td>31 (20), 15 to 135</td>
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</tr>
</tbody>
</table>

Values are mean (SD) and range unless stated otherwise.
*Five patients could not fulfil the nine hole peg test.
†Seven patients were unable to walk.

Table 2: Validity of the selected scales in 113 patients with immune mediated polyneuropathies

<table>
<thead>
<tr>
<th>Rankin</th>
<th>9HPT-RH</th>
<th>9HPT-LH</th>
<th>10MWT</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Experienced” examiners (couple No 1); n=45 (Spearman’s rank correlation coefficient)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rankin</td>
<td>–</td>
<td>0.52**</td>
<td>–</td>
</tr>
<tr>
<td>9HPT-RH</td>
<td>0.52**</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>9HPT-LH</td>
<td>0.56**</td>
<td>0.50*</td>
<td>0.49*</td>
</tr>
<tr>
<td>10MWT</td>
<td>0.51*</td>
<td>0.50*</td>
<td>0.49*</td>
</tr>
</tbody>
</table>

| “Variable” examiners (couples Nos 2–28); n=68 (Spearman’s rank correlation coefficient) |         |         |        |
| Rankin                      | –       | 0.44*   | –      |
| 9HPT-RH                     | 0.44*   | –       | –      |
| 9HPT-LH                     | 0.42*   | –       | –      |
| 10MWT                       | 0.65**  | 0.66**  | 0.61** |

The validity and reliability have already been established for the MRC sum score, “INCAT” sensory sum score, grip strength by Vigorimeter, fatigue severity scale, Hughes’ functional grading scale (f score), and the Rotterdam nine item handicap scale. The validity and reliability values of the remaining scales are presented in this table.

*p < 0.001; **p < 0.0001.

10HPT-LH, nine hole peg test, left hand; 9HPT-RH, nine hole peg test, right hand; 10MWT, 10 metres walking test; RHIS9, Rotterdam nine item handicap scale.
pattern. The other scales showed a Gaussian distribution pattern. Univariate regression studies were performed first, aiming for the best fit between the dependent and independent variable through a systematic evaluation of graphs showing the linear regressions, including a restricted cubic spline function on the independent variable. Subsequently, multivariate linear regressions were carried out for the various linkages (disability on impairment, handicap on impairment, handicap on disability, and handicap on impairment plus disability), using stepwise backward eliminating, forward adding strategies. The strength of the association between the dependent variable and the explanatory variables was presented as $R^2$: the fraction of the variance explained by the independent variables from the regression model.

In the multivariate regression models, only the right hand grip strength and nine hole peg values are presented, because the regressions for the right hand and the left hand values were similar.

All analyses were done using Stata 6.0 for Windows 98 (Stata Statistical Software, release 6.0; Stata Corporation, Texas, USA). A probability (p) value of < 0.05 was considered statistically significant.

## RESULTS

### General aspects

The group of patients (54 female and 59 male) had a mean duration of symptoms up to the time of the study of 6.9 years. Seven were bed bound and 14 required assistance or a device to walk short distances. The remaining 92 patients could walk without support. The values for all the scales in these patients are listed in table 1.

### Validity and reliability

Validity and reliability have already been demonstrated for the MRC sum score, ISS, Vigorimeter, FSS, I score, ODSS, and RH59. The correlation studies between the remaining scales are presented in table 2. In general, moderate to good correlations were obtained for each scale, thus demonstrating their validity. Significant reliability values were also found for these scales (table 3). Hence the basic requirements were fulfilled for these outcome measures, enabling their participation in the regression studies.

### Univariate regression studies of impairment leading to disability

The univariate regression studies are presented in table 4. The MRC sum score and grip strength values were the strongest explanatory variables of disability, each accounting for 40–45% of the variance in ODSS scores. The MRC score for the legs had a higher impact than the score for the arms (table 4). The strongest explanatory sensory mode was the two point discrimination test (table 4). Fatigue had a non-significant impact on disability.

### Table 3

<table>
<thead>
<tr>
<th></th>
<th>“Experienced” couple of examiners (couple No 1; 45 patients)*</th>
<th>“Variable” couples of examiners (couples Nos 2–28; 68 patients)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Interobserver agreement</td>
<td>Intraobserver agreement</td>
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<tr>
<td>Rankin scale</td>
<td>0.77</td>
<td>0.89</td>
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<tr>
<td>Nine hole peg test</td>
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<td></td>
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<tr>
<td>Right hand</td>
<td>0.93</td>
<td>0.95</td>
</tr>
<tr>
<td>Left hand</td>
<td>0.93</td>
<td>0.89</td>
</tr>
<tr>
<td>10 metre walk test</td>
<td>0.99</td>
<td>0.85</td>
</tr>
</tbody>
</table>

*Intraclass correlation coefficient ($R$) ($p < 0.0001$ for all associations).

### Table 4

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Overall disability sum score</th>
<th>Rotterdam 9 item handicap scale</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$R^2$</td>
<td>p Value</td>
</tr>
<tr>
<td>Fatigue severity scale</td>
<td>0.03</td>
<td>0.4</td>
</tr>
<tr>
<td>MRC sum score</td>
<td>0.45</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MRC-arms</td>
<td>0.37</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MRC-legs</td>
<td>0.43</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>INCAT sensory sum score</td>
<td>0.21</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pin prick arm+leg</td>
<td>0.14</td>
<td>0.0003</td>
</tr>
<tr>
<td>Vibration arm+leg</td>
<td>0.10</td>
<td>0.002</td>
</tr>
<tr>
<td>2 point discrimination</td>
<td>0.19</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Grip strength</td>
<td>0.40</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Right hand</td>
<td>0.43</td>
<td>&lt;0.0001</td>
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<tr>
<td>Left hand</td>
<td>--</td>
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<tr>
<td>Functional grading scale</td>
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<tr>
<td>Overall disability sum score</td>
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<tr>
<td>Arm disability scale</td>
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<tr>
<td>Leg disability scale</td>
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<tr>
<td>Nine hole peg test</td>
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<tr>
<td>Right hand</td>
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<td>Left hand</td>
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</tbody>
</table>

INCAT, inflammatory neuropathy cause and treatment group; MRC, Medical Research Council.
Univariate regression studies of impairment leading to handicap

Approximately one third of the handicap was explained by the MRC sum score and grip strength, separately. A lower but still significant association was obtained between the ISS and RIHS9 values ($R^2 = 0.16$). Again, fatigue did not have a significant impact on handicap (table 4).

Univariate regression studies of disability leading to handicap

The overall disability sum score was the strongest explanatory variable of handicap, accounting for 65% of the variance in RIHS9 values. The functional grading scale and the Rankin scale were also both highly associated with handicap. The nine hole peg test had the weakest association with the RIHS9 of all disability measures (table 4).

Multivariate regression studies

In fig 1, the conceptual framework of the ICIDH is presented, showing the proportions of the variances that were obtained from multivariate regression studies between the various levels of outcome in patients with immune mediated polyneuropathies. As can be seen, approximately two thirds of the disability (assessed by the ODSS) was explained by impairment measures ($R^2 = 0.64$). Fatigue (FSS) was the only impairment measure that did not contribute significantly to this model.

All impairment measures remained significantly associated with handicap, accounting for a combined 52% of the variance in RIHS9 values (fig 1). Disability measures explained 76% of disturbances resulting from handicap. The Rankin scale and ODSS were the strongest contributors to this model. The nine hole peg test and the f score were eliminated.

Combining the impairment and disability measures accounted for 77% of the variance in handicap scores. In this model, the Rankin scale, the ODSS, the 10 metre walking test, and fatigue (FSS) were the significant explanatory contributors. The values of sensation (ISS), dexterity (nine hole peg test), general strength (MRC sum score), grip strength (Vigorimeter), and functional grading scale (f score) were all excluded, as their contribution was not significant.

Adding patient variables (age, sex, and duration of illness) resulted in only a minor increase in the proportion of the variance explained (impairment to disability: $R^2$ from 0.64 to 0.67; handicap to handicap: $R^2$ from 0.80 to 0.83; disability to handicap: $R^2$ from 0.76 to 0.79; impairment + disability leading to handicap: $R^2$ from 0.77 to 0.80).

DISCUSSION

In this study, we found significant and meaningful associations between the levels of the ICIDH in patients with immune mediated polyneuropathies using validated and reliable outcome measures. These results are in contrast with some reports that have suggested only a marginal non-specific association between ICIDH levels of outcome. Our study provides further information on the extent to which an impairment measure contributes to the assessment of disability or handicap in comparison with other impairment variables. Physicians could use this information to choose a suitable scale acting as an outcome measure at a particular level and indirectly at another level, depending on the strength of its association with other variables. However, the minimum required strength of the association should be established by determining the significance of the correlations in the immune mediated polyneuropathies.

In the current study, only two thirds of the disability was explained by the impairment measures we used. The MRC sum score and grip strength (Vigorimeter) values were the strongest explanatory variables, which is consistent with earlier reports. Other explanatory variables should also be considered, as the associations were not absolute. In a study of patients with Guillain–Barré syndrome, psychological factors were consistently found to contribute to disability in addition to muscle weakness, sensory dysfunction, and fatigue.

To our knowledge, our study is the first to analyse the impact of impairments leading to handicap in the immune mediated polyneuropathies. However, only half (52%) of the variance in handicap was explained by impairment variables (table 4), suggesting a major contribution from other factors. The strongest association was obtained between the combined impairment and disability measures explaining handicap. Almost 80% of handicap variance was explained by these measures, thus supporting the assumed associations given in the ICIDH model. However, as the association was not absolute, other explanatory factors should be considered as potential contributors to handicap. Such factors might be pain, psychological influences such as anxiety, depression, coping mechanism, motivation, social support, and physical condition in terms of endurance.

The assessment and incorporation of these factors could be cardinal for further improvements in our understanding of the associations and consequences of immune mediated polyneuropathies at the various levels of outcome. We should, however, bear in mind that clinicians and other health workers (for example physical therapists) strive as much as possible to reduce the strength of the association between the various levels of outcome by prescribing medication, giving advice, recommending the use of certain aids, and creating a social support network. These “remedies” are generally in addition to any treatment that affects the impairment and disability directly. This is one of
the main reasons why the WHO recently published its second and more comprehensive edition of the ICIDH model for all diseases and disorders, integrating personal and external (social and environmental) factors as well."

Some methodological issues in our study need to be addressed. First, we must be aware that the rejection of an outcome measure (predictor) in a stepwise multiple regression model does not happen only when a variable has no relevance to the outcome, but also when other incorporated variables in the model already supply most, if not all, the information the rejected predictor contains. Second, the associations obtained in the current study were directly linked to the scales used and might vary if other outcome measures were employed. Our choice of outcome measures was determined by the views of experts in the field of neuromuscular disorders and by the established value of most of the scales selected.

Conclusions
We have shown that the framework of the WHO International Classification of Impairments, Disabilities, and Handicaps is applicable to the immune mediated polyneuropathies. Further information is provided on the consequences of these illnesses which may lead to deficits at various levels of outcome.

ACKNOWLEDGEMENT
This study was part of the Biomed project BMH4-CT96 0324.

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Competing interests: none declared

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Connecting impairment, disability, and handicap in immune mediated polyneuropathies

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*J Neurol Neurosurg Psychiatry* 2003 74: 99-104
doi: 10.1136/jnnp.74.1.99

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