# The impact of neuromuscular diseases on functioning and quality of life

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**Isaäc Bos**

**Colofon**

This study was conducted within the Department Neurology and the SHARE and BCN research institutes of the Graduate School of Medical Sciences, University Medical Center Groningen, University of Groningen.

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# The impact of neuromuscular diseases on functioning and quality of life

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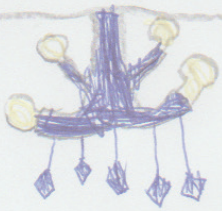
## Contents

# 1

# THE IMPACT OF NEUROMUSCULAR DISEASES ON FUNCTIONING AND QUALITY OF LIFE



General introduction, aims and outline

Neuromuscular diseases (NMDs) include many diseases which impair muscle function, either directly through pathologies of the muscles, or indirectly through pathologies of the nerves or neuromuscular junctions. NMDs are progressive diseases which can cause muscle weakness or spasticity and an increasing demand for supportive devices and medical and non-medical support.

The aim of this thesis is to provide insight into the impact of having an NMD on functioning and quality of life. Therefore, the main focus of this thesis was to identify the most relevant disease-specific and health-related disabilities, to develop a psychometrically sound measurement instrument based on these disabilities, and to evaluate the impact of these disabilities on perceived quality of life. A second objective was to develop an easy to apply instrument to measure disease severity in NMDs. The third objective was to examine the prevalence and severity of stigmatization in persons diagnosed with an NMD and its impact on quality of life.

This chapter introduces the central concepts of this thesis and specifies its aims and outline.

## Neuromuscular diseases

Neuromuscular diseases (NMD) can be acquired or hereditary. Their causes are dysfunction of the anterior horn cell or sensory ganglion cell (neuronopathy), peripheral nerve (neuropathy), neuromuscular junction (myasthenia) or muscle (myopathy).[1] These diseases vary according to their characteristics, such as pattern of inheritance, origin of genetic mutation, incidence, symptoms, age at onset, rate of progression and prognosis. Today, the manifestations of neuromuscular diseases span several medical specialities including neurology, rehabilitation, rheumatology, immunology, cardiology, pulmonology and gastroenterology. An integrated and multidisciplinary approach to the management of these patients has become a standard of care.[2]

NMDs is a very broad term which encompasses many diseases which vary greatly in their onset and diagnosis, such as a common neuropathy (due to diabetes) or rare diseases such as Amyotrophic Lateral Sclerosis and congenital Arthrogryposis multiplex. Therefore, epidemiology in NMDs is an active field of inquiry. Epidemiologic interest is growing in NMDs in the world's

more advanced healthcare regions.[3] NMDs occur worldwide and the determination of prevalence and incidence depends on a consensus of diagnostic criteria.[4] In the Netherlands the ISNO foundation CRAMP database provides a good indication of Dutch adult individuals with NMDs diagnosed in university hospitals.[5] Its estimated prevalence rate is as least similar to that of Parkinson's disease, from around 100 to 300 incidents per 100.000 based on the published peer reviewed literature for the available incidence and prevalence rates within a group of about 30 neuromuscular disorders. If we assume this group is the tip of the iceberg, the true incidence rates are likely to be much higher.[4]

The large number of NMDs can be classified[6] into four major subgroups based on their most common characteristics: motor-neuron disorders, muscle disorders, junction disorders and peripheral nerve disorders. For the characteristics and some examples of these NMD subgroups, see Box 1.

## Consequences of neuromuscular diseases

Most NMDs involve loss of sensation and the progressive loss of physical functioning from progressive muscle weakness in the upper and lower extremities. These are the most common symptoms alongside weakness in the muscles responsible for breathing or swallowing and speech functions.[17, 18] Around 59% of patients perceive difficulties in physically demanding mobility activities in the common muscle diseases,[19, 20] for example difficulty in walking long distances, up to a total inability to perform essential activities of daily living such as walking, going to the toilet and preparing meals. This declining physical functioning impacts on mental and social functioning.[17, 21]

It is known that the balance of emotional and psychological functioning is usually impaired in people with a neuromuscular disease.[17, 22] The impact of NMDs on mental functioning, however, depends on the symptoms related to a specific NMD and their severity. In general, mental function

**Box 1** NMD subgroups

NMDs can be classified into four major subgroups based on their most common characteristics:

*Motor-neuron disorders* are disorders where the motor-neurons in brain and or spinal cord deteriorate or die. They can be inherited as well as acquired. A well-known disease is Amyotrophic Lateral Sclerosis (ALS),[7] and less well-known are Progressive Spinal Muscular Atrophy[8] and Primary Lateral Sclerosis.[9]

*Muscle disorders* are disorders which affect the muscles based on abnormalities in the genes and/or enzymes. The most common inherited muscle disorder in childhood is Duchenne muscular dystrophy, in which the cytoskeletal protein dystrophin enzyme is lacking due to a gene mutation.[10] Another inherited muscle disorder with an onset at different life stages is Myotonic Dystrophy,[11, 12] a progressive systemic condition due to abnormally high trinucleotide expansion.

*Junction disorders* are disorders with impaired neuromuscular transmission leading to fluctuating muscle weakness. Most junction disorders are acquired and caused by autoimmune dysregulation. Myasthenia Gravis[13] is the most common junction disorder.

*Peripheral nerve disorders* are diseases which concern peripheral neuropathies. They can be inherited and acquired and present variously.[14] A common peripheral nerve disorder is Polyneuropathy.[15] Hereditary Motor and Sensor Neuropathy is a neuromuscular disease which also includes motor and sensor abnormalities.[16]

is negatively associated with pain[23], fatigue[24, 25] and depression.[26] The impact of an NMD on social functioning depends on the severity of the disease.[27] For example, severely fatigued patients have poorer 'social functioning' than those without fatigue,[24] and decline in physical functioning due to NMDs impacts negatively on occupational functioning.[28] Some NMDs include cognitive impairments which can deteriorate interpersonal and social relationships and contribute to a reduced HRQoL.[29-31]

## International Classification of Functioning, Disability and Health

The International Classification of Functioning, Disability and Health[32] (ICF) describes all aspects of human functioning and can therefore help describe the consequences of NMDs. The ICF is a framework for organizing and documenting information on functioning and disability[32]. The ICF is based on the biopsychosocial model, which integrates a person's features (medical model) and the

overall context in which the person lives (social model). The functioning of an individual in a specific domain reflects an interaction between the health condition and the contextual: environmental and personal factors.

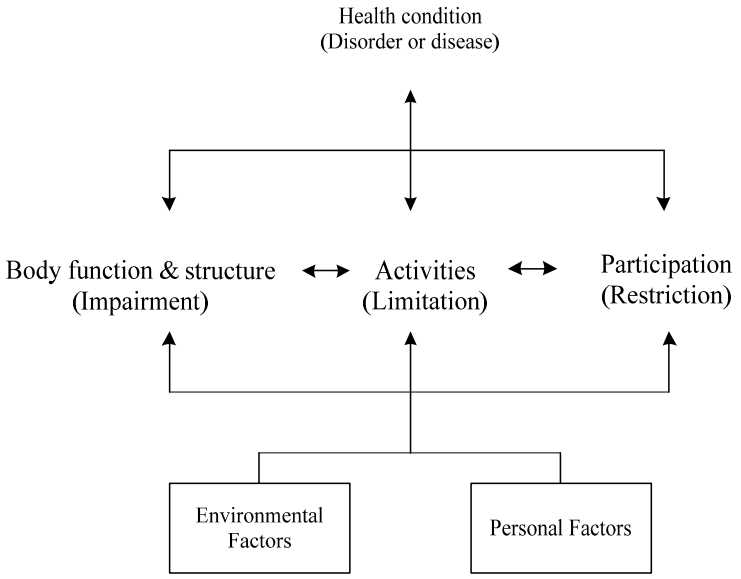



**Figure 1** ICF framework representing the interactions between the components.[32]

In other words a person's functioning in a specific domain is a dynamic interaction or complex relationship between the health condition and contextual factors. NMDs (health conditions) are the reason for a variety of NMD-related disabilities affecting functioning. The ICF is a framework for describing and organizing information on functioning and disability and describes four components into which human functioning is classified: body functions, activities, participation and environment, functioning and disability, and the ICF components are defined in Box 2.

The ICF provides a standard language and a conceptual basis for the definition and measurement of disability, and it also provides classifications and codes, hence providing a common framework for the development of health outcome measures.[32-34] It recognises the role of environmental factors in the development of disability, as well as the role of health conditions.[35]

**Box 2** ICF-definitions of functioning and disability and specifications for the ICF- components.[32]

Definitions:

*Functioning*: functioning is an umbrella term for body functions, body structures, activities and participation. It denotes the positive aspects of the interaction between an individual (with a health condition) and that individual's contextual factors (environmental and personal factors).

*Disability*: disability is an umbrella term for impairments, activity limitations and participation restrictions. It denotes the negative aspects of the interaction between an individual (with a health condition) and that individual's contextual factors (environmental and personal factors).

Functioning and disability in each ICF component

*Body functions*: body functions are the physiological functions of body systems (including psychological functions).

*Body structures*: body structures are the anatomical parts of the body such as organs, limbs and their components.

*Impairments*: Impairments are problems in body function and structure such as significant deviation or loss.

*Activity*: activity is the execution of a task or action by an individual.

*Activity limitations*: activity limitations are difficulties an individual may have in executing activities.

*Participation*: Participation is the involvement in a life situation.

*Participation restrictions*: participation restrictions are the problems an individual may experience in life situations.

*Environmental factors*: environmental factors are the physical, social and attitudinal environment in which people live and conduct their lives. These are either barriers to or facilitators of the person's functioning.

## Stigmatization

Health-related stigmatization is typically characterized by the social disqualification of individuals and populations with particular health problems.[36] To understand stigma or disgrace in chronic and acute diseases better, Scambler and Hopkins introduced a recognisable and generally accepted distinction between 'enacted' and 'felt' stigma.[37, 38] Enacted stigma refers to actual discrimination and is often associated with conditions which have particular moral attributes attached to them

(such as HIV/AIDS). Felt stigma refers to feelings of shame rather than an experience of actual discrimination.

Although it seems reasonable to assume that NMD patients are at risk of stigmatization, little is known about the prevalence and severity of health-related stigma in NMDs. Stigmatization of NMDs could be caused by the enduring disabilities they entail, which can impair almost any aspect of our physical, emotional, social or cognitive functioning.[39, 40] For instance, differences in illness manifestation appear to contribute to differences in quality of life across populations: greater anxiety and lower perceptions of control have been documented for epileptic populations relative to healthy populations and other groups living with chronic illnesses.[41] Certain characteristics of neurological disorders (e.g. seizures and tremors) could also be visible to others, resulting in stigmatizing social experiences.[42] Finally, stigma associated with neurological conditions and illness manifestation can contribute to poorer quality of life outcomes.

## Quality of Life

Healthcare developments in the 1980s resulted in an emerging consensus on the importance of the patient's perspective in monitoring medical care outcomes.[43, 44] The main concerns at that time were the rising costs of healthcare and improvement in the quality of care by managing medical care outcomes.[45] As a result, the development of measurement instruments for the evaluation of health-related quality of life (HRQoL) has become increasingly important in evaluating healthcare outcomes. In the mid-1980s, the World Health Organization (WHO) initiated the conceptualization and development of measurement instruments to evaluate people's subjective QoL. The WHO defines QoL as individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.[46, 47] This focus resulted in projects assessing QoL around the world. QoL is a broad-ranging, complex concept affected by a person's physical health, psychological state, level of independence, social relationships, personal beliefs and relationship to salient features in the

environment.[48] Unfortunately, there is no absolute consensus in the scientific literature on the essential domains of QoL.[49-52]

The consequences of NMDs have an enormous impact on QoL.[17, 53, 54] Generic QoL measures for QoL in NMDs are available,[44, 55] as well as some NMD-specific QoL measures.[20, 56-58]

## Patient-reported outcome measurements

Patient-reported outcome measurements (PROMs) are measurement instruments based on a report that comes directly from the patient (i.e., a study subject) about the status of a patient's health condition without amendment or interpretation of the patient's response by a clinician or anyone else.[59] A PROM can be recorded by the patient directly, or by an interviewer, provided the interviewer records the patient's response exactly.[59]

PROMs can be divided into generic and disease-specific measures. Generic measurement instruments consist of generic questions and permit the comparison of results between different populations and different programmes, a very important objective for policy analysis and decision making.[60] Disease-specific measurement instruments consist of disease-specific questions and can be more responsive to the attributes of patients with the disease of interest.[61]

## Psychometric properties

The psychometric properties of measurement instruments reflect their strength in outcome measurement, and need to be sound for obtaining evidence. These properties include reliability, validity and sensitivity to change.[62, 63]

Reliability concerns the overall consistency of a measure. A measure is said to have a high reliability if it produces similar results under consistent conditions. Reliability can be evaluated by examining the internal reliability consistency, which refers to high correlations among test items, and by examining repeatability: test-retest reliability is established by administrating the test to two groups of subjects at different time points and correlating the scores obtained.[64]

Validity refers to the relationship between the concept measured and the instrument used to assess it.[65] Validity concerns content, construct and criterion validity. Content validity is the extent to which a measure is representative of the conceptual domain which it is intended to cover. This is established by putting the measure into the context of present knowledge and is not measured statistically.[65] Construct validity relates to the theoretical foundations of a test and is evaluated by demonstrating that certain explanatory constructs account for test performance. The most important factor in construct validity is thus the explicitness of the theory behind the test in question. Good construct validity requires a strong, well-articulated theoretical rationale underpinning the measure, and there must be evidence of a consistent pattern of findings across a range of studies.[64] Criterion-related validity determines whether a measure discriminates between individuals who are known to differ on a marker external to the measurement instrument itself. Criterion validity is often represented in terms of the sensitivity and specificity of the measurement instrument in question.[64] Furthermore, the relative validity estimate for each measure in a given test indicates in proportional terms the empirical validity of the scale in question, relative to the most valid scale in that test.[44, 66, 67] Briefly, a measure is more efficient, relative to another, if it yields the right information with greater accuracy (less error).[67]

Sensitivity to change applies to an instrument's ability to detect clinically important change in outcomes over time and is also referred to as longitudinal validity.[68]

An important point to bear in mind is that overall acceptability of the measurement instrument to respondents and administrators will reduce factors which can disturb data collection. The respondent's burden – defined as the time, energy and other demands placed on those to whom the instrument is administered – and the administrative burden – defined as the demands placed on those who administer the instrument – can have a negative impact on the acceptability of a measurement instrument.[69, 70]

## Aims of this thesis

The aim of this thesis is to provide insight into the consequences of having an NMD for functioning and QoL. Therefore, the main focus of this thesis was to identify the most relevant disease-specific and health-related disabilities, to develop a psychometrically sound measurement instrument based on these disabilities and to evaluate the impact of these disabilities on perceived quality of life. A second objective was to adapt and combine two known extremity functioning scales, so that they can serve as an easy to apply indicator for disease severity in NMDs. The third objective was to examine the prevalence and severity of stigmatization in persons diagnosed with an NMD and its impact on their quality of life. This resulted in the following research questions:

1 What is the content validity of the initial ICF Core Set for NMDs?

2 How should the prevalence and severity of NMD-related disabilities, using the ICF Core Set for NMDs, be assessed?

3 What is the impact of a broad range of NMD-related disabilities on QoL?

4 How should disability severity be assessed when focusing on extremity functioning in patients with an NMD?

5 What is the impact of stigma on the QoL of patients with an NMD?

## Outline

**Chapter 2** reports on the results of the study on the content validity of the initial ICF Core Set for NMD. **Chapter 3** reports on the development of the Neuromuscular Diseases Impact Profile designed for the evaluation of NMD-related disabilities and the examination of their psychometric properties. In **Chapter 4** the psychometric evaluation of the NMDIP is continued by examining the test-retest reliability and the Relative Validity of the NMDIP. **Chapter 5** describes the impact of NMD-related disabilities on QoL using the NMDIP. **Chapter 6** describes the translation and adaptation of two valid extremity function scales, and reports on the examination of the psychometric properties of this easy to apply self-report measurement instrument, the Extremity Function Index, designed for the evaluation of disability severity. **Chapter 7** reports the translation of a well-known measurement instrument for the assessment of stigma and describes the impact of stigma on QoL. The main results of this thesis are summarized and discussed in **Chapter 8**, followed by a consideration of some methodological issues, their implications for practice and possibilities for further research.

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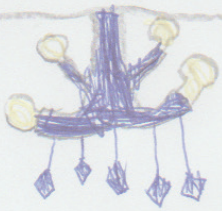
# 2

## Validation of the ICF Core Set for Neuromuscular Diseases



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## Abstract

**Background**: Understanding of the consequences of a neuromuscular disease (NMD) can improve when a valid sample of disease-specific categories based on the International Classification of Functioning, Disabilities, and Health (ICF) is available.

**Objective**: To examine the content validity of the initial ICF Core Set for neuromuscular diseases (NMDs). The initial ICF Core Set was developed for three chronic neurological diseases.

**Design**: A qualitative method.

**Methods**: To examine the content validity of the initial ICF Core Set for NMD, concepts in established disease-specific health-related Quality of Life Questionnaires (HRQOL) were compared with ICF categories. Next, the selected ICF categories were linked to the ICF categories in the initial ICF Core Set.

**Results**: All concepts in the HRQOL questionnaires, except one body function concept, were covered by the initial ICF Core Set. However, the NMD Core Set reflects a broader scope concerning health problems than the concepts in the HRQOL questionnaires do, especially concerning the "Participation" and "Environmental Factors" components.

**Conclusion**: The NMD Core Set, as well as a measurement based on this Core Set, can contribute to a better understanding of the consequences of NMDs and can also serve as a basis for clinical practice, research, social security systems, and educational programs.

**Clinical rehabilitation impact:** The newly developed NMD Core Set can be a basis for enhancing the development of rehabilitation interventions and improving overall health care for patients with a NMD.

**Keywords**: Neuromuscular Diseases, International Classification of Functioning, Disabilities and Health, ICF Core Set.

## Introduction



A neuromuscular disease (NMD) is a chronic and progressive neurological disorder that affects the muscle and/or the peripheral nervous system. Neuromuscular diagnoses may be classified into four major NMD groups: (i) motor neuron disorders (MND), (ii) muscle disorders (MD), (iii) nerve-muscle junction disorders (NMJD), and (iv) peripheral nerve disorders (PND).[1] Patients with a MND suffer from progressive muscle weakness and muscle atrophy; eventually most patients will die as a result of problems with swallowing and breathing.[2-4] Patients with a MD suffer from chronic and progressive muscle weakness leading to an insidious decline in mobility[5]; the clinical course in these diseases varies greatly in different patients and different diseases. Patients with a NMJD may suffer from droopy eyelids, double vision, swallowing and speech problems, and a limb-girdle weakness. Symptoms fluctuate and stabilize or even improve over the course of time.[6] Finally, patients with a PND may suffer from impaired sensory feeling, muscle twitching, cramping, numbness, tingling, and a host of other symptoms. Symptoms are, in most cases, slowly progressive.[7]

Symptoms of NMDs can lead to vulnerability, with a considerable impact on general health status and everyday life, and with possible limitations in terms of tasks or participation in social life with regard to housing, work, and income. The impact of these symptoms may increase with the progressive course of most of the NMDs.[8, 9]

Due to better diagnostics, a increasing number of NMD patients is identified and receiving medical treatment. Therefore, life expectancy for patients with a NMD has increased.[10]

In order to reduce the patient's vulnerability and to improve his or her independent daily functioning, it is important for healthcare professionals and researchers to deepen the knowledge of a patient's actual functioning and disability. Health-status measuring instruments can be helpful tools.

Over the last two decades many health-measuring instruments have been developed for the use in both, clinical practice as well as in research. There are generic HRQOL instruments, for example,

the 36-item Short Form Health Survey Questionnaire (SF-36).[11] In addition, there are generic and domain specific measuring instruments to assess activities of daily living, for example, GARS (Groningen Activity Restriction Scale)[12] or to assess participation in life situations, for example, the IPAQ (Impact on Participation and Autonomy Questionnaire).[13] An example of a disease specific HRQOL instrument with a broad scope concerning the consequences of a NMD is the Individual Neuromuscular Quality of Life Questionnaire (INQOL).[14]

Due to the prolific development and the increasing use of health-measuring instruments, there are now "competing" instruments in many areas, and there is no consensus about which components are important and how to measure these components.[15] Furthermore, comparisons of health status across chronic diseases are problematic; the differences in aspects contributing to the content of physical, emotional, or social functioning constructs is a good example of this. Consequently, it is opportune to develop an internationally accepted frame of reference in order to measure functioning, disability and health in patients with a MND.

Since HRQOL can be defined as an individual's perceptions of health and health-related domains of well-being, the ICF categories can serve as the basis for the operationalization of HRQOL.[16] These ICF categories systematically describe all aspects of functioning and health. Health domains are classified in the "Body Functions and Structures" component and in the "Activity and Participation" component. Since an individual's functioning and disability occurs in a context, the ICF also includes a list of "Environmental Factors".[17]

However, the ICF in its original form with about 1500 categories is hardly practicable and lacks feasibility.[18] Therefore, Stucki and colleagues[19, 20] have suggested defining short lists – so-called Core Sets – of ICF categories which are relevant for specific conditions (e.g., stroke)[21] or multiple sclerosis.[22, 23] An example of a measuring instrument based on a selection of ICF categories, and reflecting the broad scope of consequences of Multiple Sclerosis is the Multiple Sclerosis Impact Profile (MSIP).[24]

For the development of an assessment tool reflecting the broad range of the most important consequences of NMDs, the initial ICF Core Set for patients with a chronic neurological disorder [23] provides a good basis. Because this initial ICF Core Set was a consensus set for three neurological diseases and therefore not NMD-specific, we decided to further examine the content validity of the initial ICF Core Set with the goal to obtain an NMD Core Set.

The objective of this study is to develop an ICF Core Set for NMDs and to evaluate the content validity.

## Methods

### Design

To examine the content validity of the initial ICF Core Set, we used a qualitative method. We systematically linked the concepts in the questions belonging to the domains and scales of three established disease-specific HRQOL measuring instruments with the categories appraised as relevant for neurological diseases in the initial ICF Core Set.[23]

### Procedure

Linking the HRQOL concepts to the categories in the initial ICF Core Set was performed in three steps, namely: 1) meaningful concepts in the questions of the selected disease-specific questionnaires were identified by the two experts; 2) these concepts were linked to the categories of the full version of the ICF employing the ICF linking-rules[25, 26]; and 3) the matched ICF categories were compared with the categories in the initial ICF Core Set. Newly identified ICF categories were included in the final NMD Core Set when this category was found in at least two of the three measuring instruments.

The linking procedure was performed by two healthcare professionals: one professional with expertise in ICF (HAS: member of the Dutch WHO-FIC collaborating center) and one professional

with expertise in NMDs (IB: Nurse Practitioner NMDs). These experts worked independently within the steps of the linking procedure.

Categories were included in the sample when both investigators unequivocally considered the selected category to be appropriate for analysis. Differences were resolved through discussion with reference to a third and fourth reviewer (JBMK, KW) if necessary.[26]

**The initial ICF Core Set**

The initial ICF Core Set was developed to indicate relevant categories of functioning and health for patients with a chronic neurological disorder such as multiple sclerosis, Parkinson's Disease, and neuromuscular disease. Therefore, a written Delphi study was performed using three disease-specific panels composed of patients and proxies, and medical and non-medical healthcare professionals (n=98). The panels were asked to make a selection from among the 1500 categories found in the ICF reflecting relevant disease-specific health problems. As a result, sixty-eight ICF categories were considered to be the most relevant and they belonged to the ICF components: "Body Functions and Structures" (20 categories), "Activities" (21 categories), "Participation" (17 categories), and "Environmental Factors" (10 categories). No significant differences were found between the appraisal of categories by patients/proxies and healthcare professionals. Agreement across the disease panels appeared to be very strong.[23]

**Disease-specific HRQOL measuring instruments**

We searched for HRQOL measuring instruments that at least covered the dimensions of "physical functioning," "psychological functioning," and "social functioning," and represented at least one of the four groups in the classification of NMD according to Rowland and McLeod.[1]

We searched the Medline, Embase, Psychinfo, and Pubmed databases from 2000 until 2010 using the following keywords: (i) neuromuscular disease, (ii) quality of life, (iii) disability, and (iv) outcome assessment. No measurement was found for the peripheral nerve disorder group.

We found the following instruments used for analysis:

**Individual Quality of Life Questionnaire (INQOL)**

The INQOL is a measurement developed to assess HRQOL among patients with muscle disorders[14] and consists of 42 questions within ten domains. Four of the domains focus on the impact of key muscle disease symptoms (weakness, locking, pain, and fatigue), five of the domains concern the impact on particular areas of life (e.g., independency, relationships, body image), and one domain concerns the effects of treatment. The test-retest reliability demonstrated good stability[14] in eight subscales. In an Italian study, the Cronbach's alpha was estimated twice in the test-retest sample. In both cases its values were high, varying from 0.88 to 0.95.[27]

**Amyotrophic Lateral Sclerosis Assessment Questionnaire (ALSAQ-40)**

The ALSAQ-40 is a measurement developed to assess HRQOL among patients with amyotrophic lateral sclerosis, a disease within the motor neuron disorder group.[28] The ALSAQ-40 consists of 40 questions within five domains, namely: (i) Eating and Drinking, (ii) Communication, (iii) ADL/Independence, (iv) Physical Mobility, and (v) Emotional Well-being. The internal reliability coefficients of the five ALSAQ-40 dimensions at both administrations were all above the 0.91.[28] In an Italian study, the ALSAQ40 scales showed good internal consistency (Cronbach's alpha >0.86).[29]

**Myasthenia Gravis Quality of Life 60 (MGQOL-60)**

The MGQOL-60 is a measurement developed to assess HRQOL among patients with a junction disorder. The MGQOL-60 consists of 60 questions derived from interviews with experts and patient focus groups. Items were grouped into seven domains: (i) Mobility, with nine items, Cronbach's alpha = .89; (ii) Symptoms, with eight items, Cronbach's alpha = .74; (iii) Emotional Well-being, with eleven items, Cronbach's alpha = .88; (iv) General contentment, with seven items, Cronbach's alpha = .74; (v) Thinking and Fatigue, with four items, Cronbach's alpha = .91; (vi) Family/social

well-being, with nine items, Cronbach's alpha = .72; and (vii) Additional concerns, with twelve items, Cronbach's alpha = .60.[30]

## Results

### Linking procedure

We identified 142 concepts in the three HRQOL measurements: 42 concepts were derived from the INQOL, 40 concepts from the ALSAQ-40, and 60 concepts from the MGQOL-60.

Results of the linking procedure are provided in Tables 1-4, showing the content of the ICF components of "Body Function and Structures", "Activities", "Participation", and "Environmental Factors", respectively.

### Newly identified ICF categories not covered by the initial ICF Core Set

The initial ICF Core Set did not cover seven concepts. One newly identified ICF category was found in two measuring instruments (INQOL and MGQOL-60): Muscle endurance functions (b740).

From the MGQOL-60, three other concepts could not be linked to categories in the initial ICF Core Set: Functions of structures adjoining the eye (b215), Driving (a475), and Friends (e320). From the ASLSAQ-40, three concepts could be linked to the ICF categories: Voice functions (b310), Fluency and rhythm of speech functions (b330), and Climbing (a4551).

### Measurement concepts not covered by the ICF

Six concepts could not be linked to an ICF category. Three concepts from the INQOL: (i) "Independency" (in the question "Your independence"), (ii) "Appearance" (in the question "The way you look"), and (iii) "All kinds of activities" (in the question "Things you do"); and three concepts from the MGQOL-60: (i) "Bedridden" (in the question "I am forced to spend time in

bed"), (ii) "I am satisfied with my sex life", and (iii) "I am proud of how I am coping with my illness".



**Table 1** The number of categories belonging to the component of "Body Function and Structures" associated with INQOL, MGQOL-60 and ALSAQ-40 items

| ICF category | | INQOL | MGQOL-60 | ALSAQ-40 |
|---|---|---|---|---|
| | *Mental functions* | | | |
| b1300 | Energy level | -[#] | 4 | - |
| b134 | Sleep functions | - | 1 | - |
| b140 | Attention functions | - | - | - |
| b144 | Memory functions | - | - | - |
| b152 | Emotional functions | 3[##] | 19 | 12 |
| b160 | Thought functions | - | 1 | - |
| | *Sensory functions and pain* | | | |
| b210 | Seeing functions | - | - | - |
| b280 | Sensation of pain | 4 | - | 1 |
| | *Voice and speech functions* | | | |
| b320 | Articulation functions | - | 1 | 2 |
| | *Functions of cardiovascular and respiratory systems* | | | |
| b455 | Exercise tolerance functions | 4 | 1 | 1 |
| | *Ingestion functions* | | | |
| b5105 | Swallowing | - | - | 1 |
| b525 | Defecation functions | - | - | - |
| | *Genitourinary and reproductive functions* | | | |
| b620 | Urination functions | - | - | - |
| b640 | Sexual functions | - | - | - |
| | *Muscle and movement functions* | | | |
| b730 | Muscle power functions | 4 | 2 | - |
| b735 | Muscle tone functions | 4 | - | - |
| b740 | **Muscle endurance functions*** | 3 | 3 | - |
| b760 | Control of voluntary movement functions | - | - | - |
| b765 | Involuntary movements functions | - | - | - |
| b770 | Gait pattern functions | - | - | - |
| b780 | Sensations related to muscle and movement functions | - | 1 | - |

***** Newly added ICF category; [#]a dash indicates the ICF category is not addressed by the HRQOL measurement concept; [##] a digit indicates the frequency at which an ICF category was addressed by an HRQOL measurement concept

**Table 2** The number of categories belonging to the component of "Activities" associated with INQOL, MGQOL-60, and ALSAQ-40 items

| ICF category | | INQOL | MGQOL-60 | ALSAQ-40 |
|---|---|---|---|---|
| | *Communication* | | | |
| a330 | Speaking | -[#] | - | 1 |
| a350 | Conversation | - | - | - |
| a360 | Using communication devices and techniques | - | - | - |
| | *Mobility* | | | |
| a410 | Changing basic body position | - | - | 3 |
| a415 | Maintaining a body position | - | - | - |
| a420 | Transferring oneself | - | - | - |
| a440 | Fine hand use | - | - | 2 |
| a445 | Hand and arm use | - | - | 2 |
| a450 | Walking and moving | - | 1 | 5 |
| a465 | Moving around using equipment | - | - | - |
| a470 | Using transportation | - | - | - |
| | *Self-care* | | | |
| a510 | Washing oneself | - | - | 1 |
| a520 | Caring for body parts | - | 1 | 1 |
| a530 | Toileting | - | - | - |
| a540 | Dressing | - | - | 1 |
| a550 | Eating | - | 1 | 2 |
| a560 | Drinking | - | - | 1 |
| a570 | Looking after one's health | - | 1 | - |
| | *Domestic life* | | | |
| a630 | Preparing meals | - | - | - |
| a640 | Doing housework | - | - | 1 |
| | *Community, social and civic life* | | | |
| a920 | Recreation and leisure | 1[##] | - | - |

[#]a dash indicates the ICF category is not addressed by the HRQOL measurement concept;

[##] a digit indicates the frequency in which an ICF category was addressed by an HRQOL measurement concept

**Table 3** The number of categories belonging to the component of "Participation" associated with INQOL, MGQOL-60, and ALSAQ-40 items

| ICF category | | INQOL | MGQOL-60 | ALSAQ-40 |
|---|---|---|---|---|
| | *Communication* | | | |
| p350 | Conversation | -[#] | - | 1 |
| p360 | Using communication devices and techniques | - | - | - |
| | *Mobility* | | | |
| p465 | Moving around in different locations | - | - | - |
| p470 | Using transportation | - | - | - |
| | *Self-care* | | | |
| p510 | Washing oneself | - | - | - |
| p520 | Caring for body parts | - | - | - |
| p530 | Toileting | - | - | - |
| p540 | Dressing | - | - | - |
| p570 | Looking after one's health | - | - | - |
| | *Domestic life* | | | |
| p610 | Acquiring a place to live | - | - | - |
| p630 | Preparing meals | - | - | - |
| | *Interpersonal interactions and relationships* | | | |
| p750 | Informal social relationships | 5[##] | - | - |
| p760 | Family relationships | 3 | 1 | - |
| p770 | Intimate relationships | - | - | - |
| | *Major life areas* | | | |
| p850 | Remunerative employment | 1 | 1 | - |
| | *Community, social and civic life* | | | |
| p910 | Community life | - | 1 | - |
| p920 | Recreation and leisure | - | 1 | - |

[#]a dash indicates the ICF category is not addressed by the HRQOL measurement concept;

[##] a digit indicates the frequency in which an ICF category was addressed by an HRQOL measurement concept

**Table 4** The number of categories belonging to the component of "Environmental Factors" associated with INQOL, MGQOL-60, and ALSAQ-40 items

| ICF category | | INQOL | MGQOL-60 | ALSAQ-40 |
|---|---|---|---|---|
| | *Products and technology* | | | |
| e115 | Products and technology for personal use in daily living | -[#] | - | - |
| e120 | Products and technology for personal indoor and outdoor mobility and transportation | - | - | - |
| e125 | Products and technology for communication | - | - | - |
| e155 | Design, construction and building products and technology of buildings for private use | - | 1 | - |
| | *Support and relationships* | | | |
| e310 | Immediate family | - | 6 | - |
| e340 | Personal care providers and personal assistants | - | - | - |
| | *Services, systems and policies* | | | |
| e5400 | Transportation services | - | - | - |
| e5700 | Social security services | - | - | - |
| e5702 | Social security policies | - | - | - |
| e580 | Health services, systems and policies | 7[##] | 6 | - |

[#]a dash indicates the ICF category is not addressed by the HRQOL measurement concept;

[##] a digit indicates the frequency in which an ICF category was addressed by an HRQOL measurement concept

**Categories in the initial ICF Core Set not covered by the measurement concepts**

In total 58 categories of the initial ICF Core Set were not covered by the concepts in the INQOL: fifteen categories for the "Body Function and Structures" component, twenty categories for the "Activities" component, fourteen categories for the "Participation" component, and nine categories for the "Environmental Factors" component.

In total 51 categories of the initial ICF Core Set were not covered by the concepts in the ASLSAQ-40: fifteen categories of the "Body Functions and Structures" component, ten categories of the "Activities" component, sixteen categories of the "Participation" component, and ten categories for the "Environmental Factors" component.

In total 49 categories of the initial ICF Core Set were not covered by the concepts in the MGQOL-60: twelve categories of the "Body Functions and Structures" component, seventeen categories of the "Activities" component, thirteen categories of the "Participation" component, and seven categories of the "Environmental Factors" component.

**Final NMD Core Set**

As a result the ICF category, "Muscle endurance function" (b740) was added to the "Body Functions and Structures" component of the initial ICF Core Set. The final NMD Core Set now consists of 69 "very relevant" categories, belonging to the ICF components: "Body Functions and Structures" (21 categories), "Activities" (21 categories), "Participation" (17 categories), and "Environmental Factors" (10 categories).

## Discussion

The objective of this study was to examine the content validity of the initial ICF Core Set for the NMDs.

Based on our findings, we can conclude that the initial ICF Core Set covered all the relevant health problems of NMDs except for one "Body Function" category. The final NMD Core Set consists of 69 ICF categories that belonged to all ICF components.

In comparison with concepts in the disease-specific HRQOL measurement instruments, the NMD Core Set has a broader scope, especially for the "Participation" and "Environmental Factors" components. The under representation of "Environmental Factors" in the three HRQOL measurements was also found in comparable studies using an HRQOL measurement for stroke[31], and multiple sclerosis measurement.[23]

As a result of this study, we were able to add an important category to complete the NMD Core Set: "Muscle endurance functions" (b740). Furthermore, in clinical practice this is an important and recognizable issue. Fatigue and muscle weakness have a major impact on the functioning of NMD patients.

Some concepts belonging to "Personal Factors" – such as "Independency", "Appearance", "Coping", and "Satisfaction" – could not be linked to ICF categories, because "Personal Factors" have not been classified in the ICF up until now.

We decided to use HRQOL measuring instruments for the validation of the initial ICF Core Set because of the expected broad scope of these questionnaires. However, it turned out that these instruments were few in number. Furthermore, we found that each of these measuring instruments mainly focused on one specific ICF component. For example, the ASLSAQ-40 has a strong focus on the "Activity" component, while the INQOL gears its focus towards the "Body Functions" component, and the MGQOL-60 mainly focuses on the "Body Functions" component. These findings further justify our intention to develop a new ICF-based functional health-status measurement with a broad and balanced scope that includes all ICF components.

We think the methods and procedures applied contributed in a positive way to the results of our study. There are reasons for assuming this. First, because we validated the initial ICF Core Set that was meticulously developed in a Delphi study, in which the ICF categories were selected by a varied and extensive Delphi panel. Second, we applied a proven method to evaluate the content validity of this initial ICF Core Set by linking concepts from established disease specific measuring instruments, representing three of the four NMD-classification groups, to the items in the initial ICF Core Set. Finally, a reliable linking procedure was carried out by experts in NMDs and ICF so that all relevant expertise was present.

As a consequence of the meager number of disease-specific measuring instruments with a broad scope available, one potential limitation of this study is that we could not find an established measurement for the NMD peripheral nerve disorders group. Therefore, we were not able to validate the initial ICF Core Set for this group of NMDs. However, considering our findings for the other three groups, we think that no essential items are missing in our final NMD Core Set.

In the ICF, the "Activity" and "Participation" components are listed together. In this context the NMD Core Set does not consist of 69 but of 59 ICF categories, because ten categories are listed in both components. For example, for the "Recreation and Leisure" category d920, we made a distinction between a920, "Can you participate in recreation and leisure"? (Capacity) and p920, "Do you take part in recreation and leisure"? (Performance).

We decided to apply the distinction between both components (Table 2 and Table 3) with respect to the participants in the Delphi study and the initial ICF Core Set (23). Furthermore, Jette and colleagues[32] identified distinct concepts within physical functioning that conformed to the components "Activity" and "Participation" as proposed in the ICF. Another important reason for our decision was that the distinction between these components is common in HRQOL measuring instruments and is reflected in the domains of physical and social functioning. This distinction is also relevant for the development of the next step, an ICF-based questionnaire.

Our choice for the biomedical classification of Rowland (1) could provide a potential limitation because of its medical focus. Therefore, this classification may not accurately portray the consequences of the disease, namely, functioning and disabilities. However, based on our findings, we can now conclude that the NMD Core Set is a consensus set for functioning and disabilities for all NMDs.

The ICF proved to be a useful classification for the linking of the concepts in the HRQOL questionnaires.[26] The ICF categories concerning mobility and muscles are goals of nursing interventions both in specialized rehabilitation nursing as well as in general health care.[17] The newly developed NMD Core Set can be a basis for enhancing the development of rehabilitation interventions and improving overall health care for patients with an NMD.

Based on our findings, we can conclude that the NMD Core Set is a valid selection of categories reflecting a broad scope of functioning and disabilities related to NMD, one that is broader than the established disease-specific HRQOL measuring instruments, especially in terms of the components of "Participation" and "Environmental Factors". Therefore, the NMD Core Set provides a solid basis for the development of a health-status measuring instrument reflecting the most relevant aspects of functioning and health for patients with NMDs.

**Conclusion**, the NMD Core Set as well as a measurement based on this Core Set can contribute to a better understanding of the NMDs and can also serve as a basis for clinical practice, research, social security systems, and educational programs.

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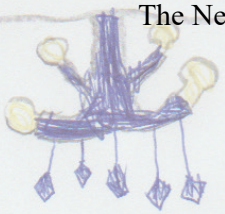
# 3

Development and testing psychometric properties of an ICF-based health measure: The Neuromuscular Disease Impact Profile



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## Abstract

**Objectives:** To develop a measure that is based on the International Classification of Functioning, Disability and Health (ICF), and reflects the prevalence and severity of disabilities related to neuromuscular disorders, and to evaluate the psychometric properties of this measure.

**Methods:** A preliminary questionnaire was developed, based on the categories of the ICF Core Set for Neuromuscular Diseases. Next a cross sectional postal survey was carried out among 702 patients (70% response rate) diagnosed with a neuromuscular disease. Finally, psychometric properties were examined.

**Results:** The preliminary Neuromuscular Disease Impact Profile (NMDIP) consisted of 45 items. Factor analysis showed that the NMDIP comprised domains representing 3 ICF-components: 5 factors in the Body Functions component, and 2 factors in the Activities component, and 1 factor in the Participation component. Scales showed moderate to good internal consistency ($\alpha$=0.63-0.92) and mean inter-item correlation coefficients (0.38-0.77). Convergent and discriminant validity analysis indicated that the NMDIP measures the impact of neuromuscular disease on physical, mental, and social functioning. The NMDIP discriminates between groups who differ in extent of limitations.

**Conclusion:** The NMDIP is an ICF-based measure that reflects the neuromuscular disease-related disabilities. It consists of 36 items divided over 8 scales with satisfactory psychometric properties and 4 single items.

**Keywords**

Neuromuscular disease; Health measure; International Classification of Functioning Disability and Health; Psychometric properties.

## Introduction

Neuromuscular diseases (NMD) may be acquired or hereditary. Causes are dysfunction of the anterior horn cell or sensory ganglion cell (neuronopathy), peripheral nerve (neuropathy), neuromuscular junction (myasthenia), or muscle (myopathy).[1] Common symptoms of neuromuscular diseases include muscle weakness, impairment in muscle endurance, involuntary muscle activity (stiffness, myotonia, cramp, and fasciculation), sensory loss, autonomic dysfunction and impairment in control of voluntary movements. Sensations of pain and fatigue are common consequences of these muscle and nerve disturbances.[2, 3] These symptoms have a profound impact on daily activities and participation in life situations.[4, 5]



In clinical practice and research there is a need for reliable and validated assessment tools as well as outcome measures that cover the broad range of health problems in neuromuscular patients.[6]

Over the last two decades many health measurement instruments have been developed for use both in clinical practice and in research. As a result, there are generic health-related quality of life (HRQoL) instruments with a broad scope, for example, the Medical Outcome study Short Form Questionnaire (SF-36).[7] An example of a disease-specific HRQoL instrument with a broad scope is the Amyotrophic Lateral Sclerosis Assessment Questionnaire (ALSAQ-40).[8] In addition, there are generic and domain-specific measures to assess limitations in daily living, for example the Groningen Activity Restriction Scale (GARS)[9], or to assess participation in life situations, for example, the Impact on Participation and Autonomy Questionnaire (IPAQ).[10]

The International Classification of Functioning, Disability, and Health (ICF) is a classification developed by the World Health Organization (WHO) and aims at providing a unified and standardized language for describing and classifying health domains and health-related states, and hence providing a common framework for the development of health outcome measures.[11, 12]

The ICF comprises 4 key components. The first component, *Body Functions and Structures*, refers to functions of body systems, and to anatomic parts. The second component, A*ctivities*, refers to “task or action execution by the individual”. The third component, *Participation*, refers to

"involvement in life situations". The *Environmental Factors* that interact with these 3 components, are described in the fourth component of the ICF.[11]

In the model of functioning that underlies the ICF classification system, the components body functions and structures, activities and participation are summarized under the concepts "functioning" and "disability". These are associated both with health status and with personal and environmental factors. Functioning is an umbrella term encompassing all body functions, activities and participation. Similarly, disability is an umbrella term for impairments in body functions, limitations in activities and restrictions in participation.[11] ICF Core Sets have been the first approach to providing ICF-based instruments for clinical practice and research.[13] An example of such ICF-based measures is the Multiple Sclerosis Impact Profile (MSIP).[14] This measurement instrument has shown to be a feasible assessment tool in practice and psychometrically sound measures in research. To the best of our knowledge there is no broad ICF-based health measure covering all 600 NMDs. Therefore the aim of this study was to develop an ICF-based measure, the Neuromuscular Disease Impact Profile (NMDIP), with the intention of reflecting the prevalence and severity of a broad range of disabilities related to neuromuscular diseases, using the ICF features such as ICF terminology and ICF qualifiers and to evaluate the psychometric properties of this new measurement instrument.

## Methods

### Sample and procedures

A cross-sectional postal survey was conducted among patients diagnosed with a neuromuscular disease and registered at the department of Neurology of the University Medical Center Groningen, the Netherlands. Criteria for inclusion were: diagnosed with a neuromuscular disease, aged 18 years or older, and able to read and write in Dutch.



In total 1003 eligible patients were selected from the hospital patient record system with the aim of representing the four major NMD groups defined by Rowland: motor neuron disorders, muscle disorders, junction disorders and, peripheral nerve disorders.[15] To prevent any inappropriate sending of the questionnaire, we crosschecked for deceased patients using the national population register.

Patients received information about the study and were invited to participate. Respondents completed the preliminary NMDIP, generic and domain-specific questionnaires, along with some demographic and disease-specific questions. Reminders were sent out after two weeks.

Ethical approval was obtained from the local ethics committee. Reference: METc 2009.310.

### Preliminary NMDIP

The preliminary NMDIP was developed as a disease-specific and ICF-based measure to assess disability among patients with an NMD. We used the 69 ICF categories of the NMD-Core Set.[3] These categories are divided over the 4 ICF components. Selected categories were operationalized in order to estimate the patient's objectified opinion (impairment in body functions, limitations in activities or restrictions in participation) of the incidence and severity of a disability, and to estimate the support from relevant environmental factors. Furthermore, ICF terminology for "disabilities" was applied, ICF item labels were used when formulating the subject of the question (e.g., "urination" functions instead of "bladder" functions), and ICF codes (e.g., b280 or p920) were documented for each question.(14) Illustrative examples were annexed (using fourth-level ICF-items) to some questions to ensure an adequate response. To record the presence and severity of a

problem in functioning, we applied response scales with scoring options specified for each ICF component, based on "qualifiers" proposed by the ICF.[14]

The preliminary questionnaire was reviewed by patients, clinicians, nurse specialists, experts on the ICF and methodologists (n=24) for clarity, comprehensiveness, redundancy and patient burden. A modified questionnaire was pre-tested in a random sample of 3 clinicians and 50 patients who were not involved in the first appraisal of the questionnaire. Unclear or ambiguous items and instructions were identified and some modifications of the questionnaire were made.

Finally, the preliminary NMDIP reflects an objectified view of the prevalence and severity of NMD-related disabilities and consists of 45 items representing the 4 ICF components.

**Measurement instruments**

For evaluating the psychometric properties of the NMDIP, 2 generic and 2 domain-specific measures were used.

The SF-36 is a broad and generic HRQOL measure that consists of 36 items divided over 8 domains.[7] For each domain, item scores were transformed to a scale that ranges from 0 (worst health) to 100 (best health). In a previous study among Dutch multiple sclerosis patients the SF-36 domains showed satisfactory levels of internal consistency: Cronbach's alpha ranged between 0.74 and 0.96.[14]

The World Health Organization Quality Of Life (abbreviation version) (WHOQOL-BREF) is a broad and generic measure of global QoL[16], and consists of 26 items divided over 4 domains. For each domain, item scores were transformed to a scale that ranges from 0 (worst health) to 20 (best health). In a previous study among Dutch multiple sclerosis patients the WHOQOL-BREF showed good levels of internal consistency: Cronbach's alpha ranged between 0.80 and 0.81.[14]

The GARS is a domain-specific instrument to measure limitation, and consists of 18 items divided over 2 domains.[9] A 4-category response format is used, ranging from 1 (no problem in performing without help) to 4 (impossible to perform). Scores are summed for each subscale. The

GARS showed strong levels of internal consistency: Cronbach's alpha ranged between 0.95 and 0.97 in a study in a Dutch sample of multiple sclerosis patients.[14]

The IPAQ is a domain-specific questionnaire focusing on person-perceived participation and autonomy.[10, 17] The instrument assesses 2 aspects of participation: perceived participation and the perceived problem. In this study we applied the perceived participation part that consists of 24 items divided over 5 domains. Items are scored on a 5-point rating scale with discrete responses, ranging from 1 (very good) to 5 (very poor). Scores are summed for each domain. In a previous study among Dutch multiple sclerosis patients, the IPAQ showed good levels of internal consistency: Cronbach's alpha ranged between 0.86 and 0.94.[14]



**Item reduction**

Exploratory factor analysis with oblique rotation (Geomin)[18, 19] was used to examine whether the domains measured by the NMDIP represent the 4 ICF components. To improve the content validity the prevalence of each item was examined before entering items in the factor analysis. Items with a low prevalence (≤ 20%) were excluded from further analysis.[20, 21] Factor analyses were performed using Mplus 6 software.[18] Given the categorical nature of the variables, methods based on polychoric correlations and the robust-weighted least squares estimators[22] were used. Goodness-of-fit of the underlying factorial structure was measured by the root mean squared error of approximation (RMSEA, adequate if below 0.06) and the standardized root mean square residual (SRMR, adequate if below 0.08), the Comparative Fit Index and the Tucker-Lewis Index. For the latter 2 indices, it is recommended that values should be greater than 0.95.[19, 23] Items with factor loadings ≥0.40 were selected for scale construction.

Items that could not meet the criteria of scalability were taken into consideration for use as a single indicator.

**Missing items**

The maximum number of missing items allowed to be replaced by the mean scale score was determined by a sufficient Cronbach's alpha in relation to the number of scale items.[21, 24]

**Psychometric evaluation**

The distribution of scale scores was evaluated by calculating the median, mean and standard deviation and observed score range. Proportion of patients with worst and best possible scores (floor and ceiling effect) were calculated. Proportions ≤20% were considered acceptable.[20]

Internal consistency was examined with Cronbach's alpha[25] and the mean inter-item correlation coefficient (MICC) for each scale.[26, 27] Alpha was considered sufficient if ≥ 0.70.[28, 29], and MICC if ≥ 0.30.[26]

To test whether NMDIP scales measure physical, psychological, social, and environmental domains of functioning, as they purport to measure, convergent and discriminant validity were assessed by examining the extent to which correlation values between NMDIP scales and concurrent measures were consistent with hypotheses.[30, 31] Regarding convergent validity, we hypothesized that the NMDIP scales would have a strong correlation (≥0.70)[32] with scales that cover the same domain in concurrent measures. For example, NMDIP scales for physical functions should correlate highly with the SF-36 "Physical Functioning scale". To support discriminant validity, we hypothesized that the NMDIP scales would correlate weakly (<0.40) with scales measuring different domains in NMDIP or concurrent measures. For example, NMDIP scales for physical function would correlate weakly with mental or emotional scales of the SF-36.

Regarding known-groups validity[30, 31], we hypothesized that the NMDIP scales should be able to discriminate between subgroups of respondents known to differ on relevant clinical characteristics. The level of limitations due to a neuromuscular disease was used to create such relevant subgroups of respondents. Therefore, the generic question "Extent of limitations" was used. Respondents were asked to answer the question "To what extent are you limited due to a neuromuscular disease?" on

an 11-point scale with a score range from 0 (not limited at all) to 10 (severely limited). Next, respondents were divided into 2 groups: those with a "lower extent of limitations" (score 1-4), and those with a "higher extent of limitations" (score 5-10).



### Statistics

Patient characteristics were analysed using descriptive statistics. Spearman's correlation coefficient (rho) was used to examine convergent and discriminant validity. Known-groups validity was assessed using the independent Mann-Whitney *U* test.

To estimate the magnitude of the difference in scores between subgroups of respondents, the nonparametric effect size (coefficient *r*) for unrelated samples was calculated for statistically significant group differences (alpha=0.05).[33] Coefficient *r* is calculated by dividing the z statistic (obtained from the Mann-Whitney *U* test) by the root of the sample size (*n*). To interpret the nonparametric effect sizes using coefficient *r*. Cohen suggested the following thresholds for interpretation: an $r$ of $< 0.10$ indicates a trivial effect, an $r$ of $\geq 0.10$ to $< 0.24$ a small effect, an $r$ of $\geq 0.24$ to $< 0.37$ a moderate effect, and an $r \geq 0.37$ a large effect. An $r \geq 0.10$ reflects a clinically relevant difference between groups.[33, 34] IBM SPSS statistics version 20 was used.

## Results

### Patient characteristics

In total 702 participants (70% response rate) completed the questionnaires. Demographics and disease-specific characteristics are described in Table 1. Average age was 59 years (SD 16, range 19-92 years), while slightly more than half of the patients were younger than 65 years. Mean number of "Years since diagnosis" was 12 years (SD 11, range 0-65 years).

Approximately 30% of the patients were retired due to a neuromuscular disease. The motor neuron disorder subgroup was a relatively small sample compared with the other neuromuscular disease subgroups according to the classification of Rowland.[15]

**Table 1** Sample characteristics (n = 702)

| *Variable* | *Total sample* |
|---|---|
| *Gender* (%) | |
| Female | 350 (50) |
| Male | 352 (50) |
| Age, years mean (SD)[range] | 59(16)[19-92] |
| Years since diagnosis MEAN (SD) [range] | 12 (11) [0-65] |
| *Relationship status (%)* | |
| Relationship (married/partnership) | 498 (71) |
| Single (unmarried/widowed/divorced) | 186 (27) |
| *Educational level (%)* | |
| Primary school/vocational training | 235 (33) |
| Secondary school/vocational training | 270 (38) |
| Higher education/vocational training | 161 (23) |
| University | 28 (4) |
| *Employment status (more answers possible) (%)* | |
| Enrolled in a training or study course | 36 (5) |
| Employment (part-time or full-time) | 173 (25) |
| Voluntary work (part-time or full-time) | 42 (6) |
| (Partially) retired due to NMD | 213 (30) |
| Housewife/househusband | 171 (24) |
| Retired due to age | 244 (35) |
| *NMD category (%)* | |
| Motor neuron disorder | 43 (6) |
| Muscle disorder | 154 (22) |
| Junction disorder | 234 (33) |
| Peripheral nerve disorder | 271 (39) |

NMD: neuromuscular diseases; SD=standard deviation.

Non-respondents did not differ from respondents in terms of gender, but were significantly younger (mean 53, SD 19 years) than respondents (mean 59, SD 16 years).

**Content validity**

Nine of the original 45 items showed a low prevalence (≤ 20%) and were not entered in the factor analysis. These items were from the component "Activities" ("a350 Conversation", "a360 Using communication devices and techniques", and "a465 Moving around using equipment"), the component "Participation" (p510-p540 items concerning "Personal care", "p360 Communication devices and techniques, "p630 Eating and drinking", "p610 Acquiring a place to live", and "p850 Remunerative employment"), and from the component "Environmental Factors" ("e340 Personal care providers and personal assistants").

**Item reduction**

The EFA models showed a (very) good fit for the 5-factor model for the Body Functions component, the 2-factor model for the Activities component, and the 1-factor model for the Participation component. Comparative Fit Index and Tucker-Lewis Index values were above 0.95, SRMR values were below 0.08 as recommended. The RMSEA values were below 0.06 for the Body Functions component and Participation component, while the value for the Activities component was slightly higher (0.069) but still acceptable. For the Environmental Factors component no satisfying fit was found. Factor analysis reduced the remaining 36 items of the initial NMDIP to 32 items:

- Five factors within the Body Functions component included 15 items (Table 2). Interpretation of item content, using the ICF first- and second level category labels led to the following scale labels: “Muscle Functions” (MuF), “Movement Functions” (MoF), “Swallowing and Speech Functions” (SSF), “Excretion and Reproductive Functions” (ERF), and “Mental Functions and Pain” (MFP).
- Two factors within the Activities component included 14 items (Table 3)These factors were given the labels, “Activities of Moving around”(AMA) and “Self-care and Domestic Activities” (SDA).
- One factor within the Participation component included 3 items (Table 4). This factor was labelled “Participation in Life Situations” (PLS).

Finally the Body Functions component items “Seeing functions” and the Environmental Factor component items “Immediate family”, “Social security services”, and “Health services” with a sufficient prevalence and clinical relevance were added to the questionnaire as single items.

**Table 2** Factor Analysis with Body Functions component categories (n=702)

| | Factor 1 | Factor 2 | Factor 3 | Factor 4 | Factor 5 |
|---|---|---|---|---|---|
| *Muscle Functions (MuF)* | | | | | |
| Impairment in… | | | | | |
| b730 Muscle power functions | **0.612** | 0.473 | 0.032 | 0.015 | -0.054 |
| b740 Muscle endurance functions | **0.677** | 0.329 | -0.003 | -0.020 | 0.195 |
| *Movement Functions (MoF)* | | | | | |
| Impairment in… | | | | | |
| b760 Control of voluntary movements functions | 0.009 | **0.777** | -0.100 | 0.023 | -0.038 |
| b765 Involuntary movements functions | -0.315 | **0.849** | 0.106 | -0.022 | 0.044 |
| b780 Sensation related to muscles and movement | 0.045 | **0.590** | -0.041 | 0.053 | 0.198 |
| *Swallowing and speech functions(SSF)* | | | | | |
| Impairment in… | | | | | |
| b320 Speech functions | 0.024 | 0.144 | **0.842** | 0.008 | -0.013 |
| b5105 Swallowing functions | 0.246 | -0.035 | **0.687** | 0.053 | 0.054 |
| *Excretion and reproductive Functions(ERF)* | | | | | |
| Impairment in… | | | | | |
| b525 Defecation functions | 0.022 | -0.030 | -0.002 | **0.656** | 0.168 |
| b620 Urination functions | -0.052 | 0.028 | 0.036 | **0.785** | -0.032 |
| b640 Sexual functions | 0.046 | 0.281 | 0.026 | **0.426** | 0.043 |
| *Mental Functions and Pain(MFP)* | | | | | |
| Impairment in… | | | | | |
| b134 Sleep functions | -0.028 | -0.008 | -0.055 | 0.091 | **0.680** |
| b1300 Fatigue | 0.460 | 0.019 | 0.062 | 0.011 | **0.593** |
| b152 Emotional functions | -0.020 | -0.014 | 0.100 | -0.148 | **0.725** |
| b160 Thought functions | -0.230 | 0.040 | 0.259 | 0.023 | **0.539** |
| b280 Sensation of pain | 0.078 | 0.267 | -0.238 | 0.040 | **0.527** |

Bold figures are sufficient factor loadings selected for scale construction.

**Table 3** Factor Analysis with Activities component categories (n=702)

| | Factor 1 | Factor 2 |
|---|---|---|
| *Activities of Moving around (AMA)* | | |
| Limitations in… | | |
| a410 Changing body position | **0.860** | 0.005 |
| a415 Maintaining body position | **0.639** | 0.270 |
| a420 Transferring oneself | **0.711** | 0.251 |
| a450 Walking | **0.952** | -0.035 |
| a470 Using transportation | **0.589** | 0.330 |
| a920 Recreation and leisure | **0.411** | 0.354 |
| *Self-care and Domestic Activities (SDA)* | | |
| Limitations in… | | |
| a440 Fine hand use | -0.003 | **0.758** |
| a445 Hand and arm use | -0.102 | **0.894** |
| a510 Washing oneself | 0.272 | **0.709** |
| a520 Caring for body parts | -0.007 | **0.904** |
| a530 Toileting | 0.335 | **0.585** |
| a540 Dressing | 0.200 | **0.754** |
| a630 Preparing meals | 0.057 | **0.863** |
| a640 Doing housework | 0.398 | **0.458** |

Bold figures are sufficient factor loadings selected for scale construction.

**Table 4** Factor analysis with Participation components (n = 702)

| | Factor 1 |
|---|---|
| *Participation in Life Situations(PLS)* | |
| Restriction in… | |
| p460/p470 Mobility | **0.690** |
| p740-p760 Relationships | **0.719** |
| p910/p920 Recreation and leisure | **0.903** |

Bold figures are sufficient factor loadings selected for scale construction.



Scale features are shown in Table 5. Internal consistency for seven NMDIP scales for the total sample was good and moderate for one scale. Cronbach's alpha ranged from 0.63 to 0.92 and mean inter-item correlation coefficient ranged from 0.38 to 0.77. Four scales showed a high floor effect.

The NMDIP scales within the NMD groups showed acceptable to good internal consistency. (Table 6). For some scales the Cronbach's alpha was weak but this was compensated by a sufficient mean inter-item correlation coefficient, except for the "Swallowing and Speech Functions" scale in the peripheral nerve disorder group and the "Excretion and Reproductive Functions" scale in the muscle disorder group.

The final version of the NMDIP consists of 36 items divided over 8 scales and 4 single items. (See Appendix I).

**Table 5** Scale features of the Neuromuscular Disease Impact Profile (NMDIP) scales (n = 702)

| | Cases (n) | Items (k) | Possible score range | Observed score range | Floor effect (%) | Ceiling effect (%) | Median | Mean | SD | Alpha | MICC |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *NMDIP scales* | | | | | | | | | | | |
| Muscle Functions | 658 | 2 | 0-8 | 0-8 | 8 | 3 | 4 | 3.4 | 1.9 | 0.87 | 0.77 |
| Movement Functions | 594 | 3 | 0-12 | 0-12 | 18 | 0 | 2 | 2.4 | 2.1 | 0.72 | 0.47 |
| Swallowing and Speech Functions | 669 | 2 | 0-8 | 0-6 | 59 | 1 | 0 | 0.7 | 1.1 | 0.69 | 0.53 |
| Excretion and Reproductive Functions | 509 | 3 | 0-12 | 0-12 | 27 | 0 | 1 | 1.8 | 3.1 | 0.63 | 0.38 |
| Mental Functions and Pain | 597 | 5 | 0-20 | 0-16 | 7 | 0 | 4 | 1.8 | 1.8 | 0.80 | 0.59 |
| Activities of Moving around | 702 | 6 | 0-18 | 0-18 | 18 | 2 | 4 | 5.1 | 4.8 | 0.90 | 0.62 |
| Self-care and Domestic Activities | 701 | 8 | 0-24 | 0-24 | 28 | 1 | 2 | 4.7 | 6.0 | 0.92 | 0.59 |
| Participation in Life Situations | 695 | 3 | 0-12 | 0-12 | 49 | 0 | 1 | 1.7 | 2.4 | 0.72 | 0.47 |
| *NMDIP single item* | | | | | | | | | | | |
| Seeing functions | 666 | 1 | 0-4 | 0-4 | | | 0 | 0.68 | 0.88 | | |
| Immediate family | 697 | 1 | 0-2 | 0-2 | | | 0 | 0.51 | 0.73 | | |
| Social security services | 268 | 1 | 0-2 | 0-2 | | | 1 | 0.74 | 0.77 | | |
| Health services | 693 | 1 | 0-2 | 0-2 | | | 0 | 0.66 | 0.75 | | |

MICC=mean inter-item correlation coefficient. SD=standard deviation.

**Table 6** Internal consistency (Cronbach's alpha) and the mean inter-item correlation coefficient (MICC) of the Neuromuscular Disease Impact Profile (NMDIP) scales per neuromuscular diseases group

| | Motor neuron disorders (*n*=43) | | Muscle disorders (*n*=154) | | Junction disorders (*n*=234) | | Peripheral nerve disorders (*n*=271) | |
|---|---|---|---|---|---|---|---|---|
| | Alpha | MICC | Alpha | MICC | Alpha | MICC | Alpha | MICC |
| Muscle Functions | 0.86 | 0.77 | 0.79 | 0.67 | 0.87 | 0.78 | 0.86 | 0.76 |
| Movement Functions | 0.72 | 0.48 | 0.72 | 0.48 | 0.67 | 0.42 | 0.67 | 0.41 |
| Swallowing and Speech Functions | 0.82 | 0.72 | 0.74 | 0.59 | 0.63 | 0.47 | 0.42 | 0.27 |
| Excretion and Reproductive Functions | 0.71 | 0.47 | 0.54 | 0.30 | 0.63 | 0.36 | 0.68 | 0.45 |
| Mental Functions and Pain | 0.69 | 0.34 | 0.77 | 0.40 | 0.73 | 0.36 | 0.72 | 0.33 |
| Activities of Moving around | 0.90 | 0.62 | 0.90 | 0.60 | 0.85 | 0.50 | 0.90 | 0.59 |
| Self-care and Domestic Activities | 0.95 | 0.69 | 0.93 | 0.63 | 0.83 | 0.43 | 0.88 | 0.47 |
| Participation in Life Situations | 0.80 | 0.57 | 0.74 | 0.49 | 0.67 | 0.40 | 0.67 | 0.41 |

**Psychometric testing**

Table 7 provides evidence of convergent and discriminant validity for the NMDIP scales, reflecting the impact of a neuromuscular disease on physical, psychological, and social aspects of functioning. The predictions were consistent with the direction, magnitude, and patterns of correlations.

Convergent validity was supported by a strong correlation between the NMDIP "Muscle Functions" scale and the SF-36 "Physical Functioning" scale, and a strong correlation between the NMDIP "Activities of Moving Around" and "Self-care and Domestic Activities" scales, and the GARS "Activities of Daily Living" and "Instrumental Activities of Daily Living" scales. The NMDIP "Participation in Life Situations" scale was moderately correlated with the IPAQ participation scales.

Discriminant validity was supported by weak correlation values found, for example, between the NMDIP "Mental Functions and Pain" scale and the SF-36 "Physical Functioning" scale, and the GARS "Activities of Daily Living" and "Instrumental Activities of Daily Living" scales. Similarly, the NMDIP "Muscle Functions" scale correlated weakly with the SF-36 "Mental Health and "Role Emotional" scales, and the NMDIP "Participation in Life Situations" scale correlated weakly with the SF-36 "Mental Health" scale.

**Table 7** Results of convergent and divergent validity analyses of the Neuromuscular Disease Impact Profile (NMDIP) scales (n = 702)

| | Body Functions | | | | | Activities | | Participation | |
|---|---|---|---|---|---|---|---|---|---|
| *NMDIP* | MUF | MOF | SSF | ERF | MFP | AMA | SDA | PLS | Alpha |
| *NMDIP* | | | | | | | | | |
| Muscle Functions (MuF) | 1 | | | | | | | | 0.87 |
| Movement Functions (MoF) | 0.57 | 1 | | | | | | | 0.72 |
| Swallowing and Speech Functions (SSF) | 0.26 | 0.23 | 1 | | | | | | 0.69 |
| Excretion and Reproductive Functions (ERF) | 0.35 | 0.43 | 0.31 | 1 | | | | | 0.63 |
| Mental Functions and Pain (MFP) | *0.49* | *0.59* | *0.34* | *0.48* | 1 | | | | 0.80 |
| Activities of Moving around (AMA) | **0.72** | 0.58 | 0.23 | 0.41 | 0.48 | 1 | | | 0.90 |
| Self-care and Domestic Activities (SDA) | **0.63** | 0.52 | 0.31 | 0.45 | 0.51 | **0.79** | 1 | | 0.92 |
| Participation in Life Situations (PLS) | 0.54 | 0.46 | 0.26 | 0.38 | 0.53 | 0.68 | 0.61 | 1 | 0.72 |
| *SF-36* | | | | | | | | | |
| Physical functioning | **-0.71** | -0.52 | -0.23 | -0.40 | -0.47 | **-0.85** | **-0.77** | -0.61 | 0.94 |
| Role physical | -0.43 | -0.42 | -0.26 | -0.37 | -0.52 | -0.43 | -0.45 | -0.40 | 0.88 |
| Bodily pain | -0.38 | -0.51 | -0.17 | -0.32 | -0.65 | -0.42 | -0.40 | -0.38 | 0.91 |
| General health | -0.49 | -0.49 | -0.32 | -0.44 | -0.60 | -0.49 | -0.48 | -0.46 | 0.78 |
| Mental health | *-0.21* | -0.33 | -0.18 | -0.18 | **-0.53** | *-0.21* | *-0.25* | *-0.32* | 0.83 |
| Role emotional | *-0.18* | -0.30 | -0.20 | -0.21 | -0.39 | *-0.23* | *-0.26* | -0.25 | 0.87 |
| Social functioning | *-0.44* | -0.46 | -0.29 | -0.40 | -0.63 | -0.46 | -0.46 | **-0.51** | 0.77 |
| Vitality | -0.41 | -0.42 | -0.34 | -0.33 | -0.68 | -0.35 | -0.39 | -0.39 | 0.81 |
| *WHOQOL-BREF* | | | | | | | | | |
| Physical health and autonomy | -0.29 | -0.30 | -0.22 | -0.29 | -0.49 | -0.29 | -0.29 | -0.33 | 0.84 |
| Psychological health | *-0.25* | *-0.33* | *-0.25* | *-0.23* | *-0.43* | *-0.29* | *-0.30* | -0.35 | 0.80 |
| Social relation | *-0.23* | *-0.22* | *-0.14* | *-0.40* | *-0.37* | *-0.26* | *-0.25* | **-0.33** | 0.60 |
| Environment | *-0.34* | *-0.39* | *-0.24* | *-0.27* | *-0.51* | *-0.41* | *-0.39* | -0.46 | 0.82 |
| *GARS* | | | | | | | | | |
| Activities of daily living | 0.64 | 0.54 | *0.26* | 0.45 | 0.44 | **0.81** | **0.81** | *0.62* | 0.95 |
| Instrumental activities of daily living | 0.67 | 0.49 | *0.30* | 0.44 | 0.49 | **0.78** | **0.84** | *0.62* | 0.93 |
| *IPAQ* | | | | | | | | | |
| Autonomy indoors | 0.54 | 0.52 | 0.25 | 0.43 | 0.50 | 0.66 | 0.65 | **0.56** | 0.94 |
| Family role | 0.53 | 0.52 | 0.30 | 0.41 | 0.59 | 0.61 | 0.61 | **0.53** | 0.92 |
| Autonomy outdoors | 0.57 | 0.50 | 0.34 | 0.48 | 0.63 | 0.68 | 0.66 | **0.66** | 0.84 |
| Social relations | 0.34 | 0.35 | 0.32 | 0.41 | 0.53 | 0.41 | 0.45 | **0.48** | 0.85 |

NMDIP: *n* = 484–658; SF-36: *n* = 654–657; WHOQOL-BREF: *n* = 628–649; GARS: *n* = 655–658; IPAQ: *n* = 654–657.
Bold correlations = expected convergent correlations. Italic correlations = expected discriminant correlations.
MuF: Muscle functions; MoF: Movement functions; SSF: Swallowing and Speech functions; ERF: Excretion and Reproductive functions; MFP: Mental functions and Pain; AMA: "Activities of Moving around"; SDA: "Self-care and Domestic Activities"; PLS: Participation in life situations; GARS: Groningen Activity Restriction Scale; IPAQ: Impact on Participation and Autonomy Questionnaire..

Evidence of known-groups validity was obtained for all NMDIP scales by statistically significant group differences and clinically relevant effect sizes (Table 8). Patients classified as having a higher extent of limitation had statistically significant higher scores on all NMDIP scales compared with those classified as having a lower extent of limitation. Effect sizes were moderate for 2 scales, and large for 6 scales.

**Table 8** Results of known-groups validity analyses of the Neuromuscular Disease Impact Profile scales (n=702)

| | Low (1-4) versus high (5-10) Extent of limitations | | | | |
|---|---|---|---|---|---|
| | N | Low Mean Rank | High Mean Rank | p-value (Z-statistic) | Effect Size |
| Muscle Functions (MuF) | 640 | 197.84 | 390.25 | 0.000 (-12.973) | 0.51 |
| Movement Functions (MoF) | 577 | 201.52 | 342.52 | 0.000 (-9.994) | 0.42 |
| Swallowing and Speech Functions (SSF) | 651 | 273.86 | 359.14 | 0.000 (-6.445) | 0.25 |
| Excretion and Reproductive Functions (ERF) | 495 | 198.34 | 279.74 | 0.000 (-6.374) | 0.29 |
| Mental Functions and Pain (MFP) | 581 | 201.45 | 346.38 | 0.000 (-10.170) | 0.42 |
| Activities of Moving around (AMA) | 683 | 210.67 | 422.72 | 0.000 (-13.704) | 0.52 |
| Self-care and Domestic Activities (SDA) | 682 | 227.58 | 411.25 | 0.000 (-11.956) | 0.46 |
| Participation in Life Situations (PLS) | 677 | 239.81 | 400.46 | 0.000 (-11.110) | 0.43 |

## Discussion

The objective of this study was to develop a psychometrically sound ICF-based measure for estimating the prevalence and severity of a broad range of disabilities related to neuromuscular diseases using ICF features such as ICF terminology and ICF qualifiers.



The results provide evidence to support the validity and reliability of the final version of the Neuromuscular Disease Impact Profile (NMDIP) as an instrument to measure the prevalence and severity of a broad spectrum of consequences of a neuromuscular disease including disabilities in Body Functions, Activities and Participation, and lack of support from Environmental Factors. The NMDIP can be used as a clinical and research instrument for the assessment of the impact of a neuromuscular disease.

The original 45 items in the preliminary NMDIP could be reduced to 36 items: 32 items covering 8 domains representing 3 ICF-components, and 4 clinically relevant items (1 Body Functions item and 3 Environmental Factors items), which were applied as single items in the questionnaire (See final version in Appendix).

Although the NMDIP used the same items as the initial MSIP[14], results of the factor analysis showed some differences compared to the final MSIP scales. For example, the MSIP "Muscle and Movement functions" 4-item scale is represented in the NMDIP in 2 separate and recognizable scales "Muscle functions" with 2 items and "Movement functions", also with 2 items. Furthermore, the 3-item "Mental functions" MSIP scale appeared in the NMDIP as a 5-item version: new scale items were Fatigue and Pain. This can be explained by the fact that pain and fatigue are the direct result of (using) weakened muscles, which is a common symptom in neuromuscular diseases. Unlike neuromuscular diseases fatigue in multiple sclerosis is most likely related to the process of inflammation, while pain originates from spasticity and/or neuropathy. Furthermore, scale construction also identified a construct that was not present in the MSIP: "Swallowing and Speech Functions". This can be explained by the fact that some myopathies and the myasthenia's tend to

affect bulbar musculature. Finally, analysis showed no consistent factor for the Environmental Factors items.

Reliability of the NMDIP scales of the total sample was sufficient for 2 scales and good for 6 scales. The scales per NMD group showed overall sufficient alpha's and good MICC's. Except for two scales the "Swallowing and Speech Functions" scale in the peripheral nerve disorder group and the "Excretion and Reproductive Functions" scale in the muscle disorder group. Some caution is advised in the interpretation of the results. Convergent and discriminant validity analysis indicated that the NMDIP measures the impact on physical, mental, and social functioning for people with a neuromuscular disease.

The correlation between the NMDIP "Participation in Life Situations" scale and the SF-36 "Physical Functioning" scale was unexpectedly higher. It is likely that the activity-related participation items in the NMDIP scale are responsible for this moderate correlation.

Known-groups validity was supported for the 8 NMDIP scales. Scales discriminated sufficiently between groups of patients with a neuromuscular disease that differed in extent of limitations.

An important strength of this study is the large and broad group of participating patients with a neuromuscular disease, and the sound conceptual basis in developing the NMDIP.[3, 35]

A possible limitation in this study is the small sample size of the motor neuron disorder group, compared to the sample size of the 3 other NMD groups. However, in our opinion the disabilities in this group are sufficiently represented in the NMDIP because the basis of the NMDIP, the NMD ICF-Core set, covers all items of the disease-specific Amyotrophic Lateral Sclerosis Assessment Questionnaire-40.[8] Another limitation could be the high floor effect of some scales that might affect the reliability of these scales.[36] However, these floor effects match with the course of the slowly progressive nature in most NMDs. This means that some disabilities appear years after onset, such as speech and swallowing functions or upper extremity activities.

Further research should focus on psychometric evaluation concerning stability and sensitivity to change of the NMDIP scales, and validation across other populations of neuromuscular disease

patients in other cultures. It would also be interesting to examine the differences in prevalence and severity of disabilities between the 4 major NMD groups as defined by Rowland.[15] Finally, it would be interesting to investigate the impact of the broad range of NMDIP related disabilities on HRQOL of neuromuscular disease patients.



We considered the possibility to undertake the group invariance testing, however the sub groups are relative small and will affect the test of Differential Item Functioning. We therefore suggest further examination of the factor structure in a new sufficient sample.

Clinical practice, especially in multidisciplinary rehabilitation teams, the NMDIP may contribute to better understanding the patients' health problems when used as an assessment tool. Although positive results were found in the feasibility studies with the preliminary NMDIP and the MSIP, it is advisable to combine this application with research; for example, in order to investigate the effects on the health care plan when using the NMDIP.

**Acknowledgements**

We wish to thank the patients with a neuromuscular disease who participated in this study and were so kind as to share personal information about the consequences of their disease, and for taking the time to fill out the questionnaires. We also wish to thank the students who sent out the questionnaires and entered the data from the questionnaires: Kyra van der Beek, Hanna Bosman, Annelies, Carolien and Marieke Verschure, and Ronald Brans. We finally thank Josué Almansa Ortiz (PhD) for his statistical support.

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**Appendix I** Neuromuscular Disease Impact Profile (NMDIP). (Final 36-item version)

Neuromuscular Disease Impact Profile (NMDIP).

| NMDIP | | Body functioning questions |
|---|---|---|
| Scale | | Response options<br>0 = no, not at all<br>1 = yes, I have a slight impairment<br>2 = yes, I have a moderate impairment<br>3 = yes, I have a severe impairment<br>4 = yes, I have a complete impairment |
| MuF | b1 | Do you face loss of your **muscle power functions**? (b730) |
| MuF | b2 | Do you face loss of **muscle endurance functions**? (b740) |
| MoF | b3 | Do you face loss of **control of voluntary movements**? (b760) |
| MoF | b4 | Do you face **involuntary movements**? (e.g., tremors or tics) (b765) |
| MoF | b5 | Do you face **muscle stiffness or muscle spasm**? (b7800 / b7801) |
| SSF | b6 | Do you face impairment in your **speech functions**? (b320) |
| SSF | b7 | Do you face impairment in your **swallowing functions**? (b5105) |
| ERF | b8 | Do you face impairment in your **defecation functions**? (e.g., changes in frequency, constipation, incontinence) (b525) |
| ERF | b9 | Do you face impairment in your **urination functions**? (e.g., frequency of urination, incontinence, difficulties with urination) (b620) |
| ERF | b10 | Do you face limitations in **sexual functions**? (b640) |
| MFP | b11 | Do you face impairment in your **sleep functions**? (e.g., onset of sleep, the maintenance of sleep or the quality of sleep) (b134) |
| MFP | b12 | Do you experience **fatigue**? (b1300/b455) |
| MFP | b13 | Do you face **changes** in your **emotional functions**? (e.g., fear, depression, happiness) (b152) |
| MFP | b14 | Do you face **changes** in your **thought functions**? (e.g., the ability to think logically, the ability to memorize, the ability to concentrate) (b160) |
| MFP | b15 | Do you experience **sensation pain**? (b280) |
| single | b16 | Do you face impairment in your **seeing functions**? (With eyeglasses on or item lenses in) (b210) |

| NMDIP | | Activities questions |
|---|---|---|
| Scale | | Response options<br>0 = No<br>1 = Yes, but assistance devices and/or adaptations *are not* necessary<br>2 = Yes, and assistance devices and/or adaptations *are* necessary<br>3 = Yes, and assistance devices and/or adaptations *and* another person's help are necessary |
| AMA | a1 | Do you face limitations in **changing** your **body position**? (e.g., moving from lying down to standing up or from standing to sitting) (a410) |
| AMA | a2 | Do you face limitations in **maintaining** your **body position**? (e.g., maintaining kneeling, standing, and sitting postures) (a415) |
| AMA | a3 | Do you face limitations in **transferring** yourself? (e.g., moving from a chair into bed; from a wheelchair into a car) (a420) |
| AMA | a4 | Do you face limitations in **walking**? (a450) |
| AMA | a5 | Do you face limitations in **using transportation**? (a470) |
| AMA | a6 | Do you face limitations in activities you would like to undertake for **recreation and leisure**? (a920) |
| SDA | a7 | Do you face limitations in your **fine hand use**? (e.g., picking up small objects; |

| | | |
|---|---|---|
| | | manipulating a keyboard) (a440) |
| SDA | a8 | Do you face limitations in your **arm(s) and hand(s) use**? (e.g., pulling or pushing objects; turning or twisting knobs or handles; reaching for kitchen cupboard) (a445) |
| SDA | a9 | Do you face limitations in **washing yourself**? (a510) |
| SDA | a10 | Do you face limitations in **caring for body parts**? (e.g., brushing teeth, clipping your nails, combing your hair, shaving) (a520) |
| SDA | a11 | Do you face limitations in **toileting**? (a530) |
| SDA | a12 | Do you face limitations in **dressing** yourself? (a540) |
| SDA | a13 | Do you face limitations in **preparing meals**? (a630) |
| SDA | a14 | Do you face limitations in **doing housework**? (a640) |
| **NMDIP** | | **Participation questions** |
| Scale | | Response options<br>0 = no<br>1 = Yes, as a consequence I have **some** trouble with ….<br>2 = Yes, as a consequence I have trouble with...<br>3 = Yes, as a consequence I have **a lot of** trouble with …<br>4 = Yes, as a consequence …. is (nearly) impossible |
| PLS | p1 | Are there **obstacles** in your **environment** that complicate your participation in **community, recreation, and leisure**? (e.g., accessibility of clubs or associations) (p910/p920) |
| PLS | p2 | Are there **obstacles** in your **environment** that complicate the **maintenance** of your **relationships with your closest family, friends, or relatives**? (e.g., the travel distance, the attitude of others) (p740-p760) |
| PLS | p3 | Are there **obstacles** in your **environment** that complicate your **mobility inside** or **outside** your home? (e.g., thresholds; curbs; absence of elevators) (p460 / 470) |
| **NMDIP** | | **Environmental factors questions** |
| Scale | | Response options<br>0 = Yes, very supportive;<br>1 = Yes, somewhat supportive;<br>2 = No, not supportive |
| Single Item | e1 | Is your relationship with your **immediate family** supportive for you? (e.g., partner, children, parents, brothers, sisters) (e310) |
| Single Item | e2 | Are the **social security services** supportive for you? (e.g., income support) (e570) |
| Single Item | e3 | Are the **health services** supportive for you? (e.g., medical and nursing care) (e580) |

MuF = Muscle Functions; MoF=Movement Functions; SSF = Swallowing and Speech Functions; ERF = Excretion and Reproductive Functions; MFP = Mental Functions and Pain; AMA = Activities of Moving Around; SDA = Self-care and Domestic Activities; PLS = Participation in Life Situations.

# 4

## Stability and Relative Validity of the Neuromuscular Disease Impact Profile (NMDIP)

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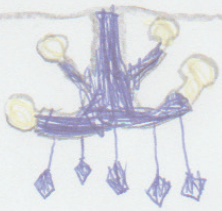

BMC Neurology 2017; 17(1), 87

## Abstract

**Background:** The aim of this study was to examine the stability and relative validity (RV) of the Neuromuscular Disease Impact Profile (NMDIP) using criterion-related groups. In a previous study the NMDIP-scales showed good internal consistency, convergent and discriminant validity. Known-groups analysis showed that the NMDIP discriminates between categories of extent of limitations.

**Methods:** A cross-sectional postal survey study was performed on patients diagnosed with a NMD and registered at the Department of Neurology, University Medical Center Groningen, the Netherlands.

Participants were asked to complete the preliminary NMDIP, the Medical Outcome study Short Form Questionnaire (SF-36), the World Health Organization Quality Of Life-abbreviation version (WHOQOL-bref), and two generic domain specific measures: the Groningen Activity Restriction Scale (GARS) and the Impact on Participation and Autonomy Questionnaire (IPAQ). The variables 'Extent of Limitations' and 'Quality of Life' were used to create criterion-related groups. Stability over time was tested using the Wilcoxon Signed Rank Test for paired samples and the intraclass correlation coefficients for repeated measures. RV was examined by comparing the ability of NMDIP with generic multidimensional health impact measures, and domain specific measures in discriminating between criterion-related subgroups using the Kruskal-Wallis H-test.

**Results:** Response rate was 70% (n=702). The NMDIP-scales showed sufficient stability over time, and satisfactory or strong RV. In general, the NMDIP scales performed as well as or better than the concurrent measurement instruments.

**Conclusions**: The NMDIP proved to be a valid and reliable disease-targeted measure with a broad scope on physical, psychological and social functioning.

**Keywords**

Neuromuscular Disease Impact Profile; Relative validity; Test-retest reliability; Stability; Criterion validity.

## Background

Neuromuscular Diseases (NMDs) may be caused by an abnormality of the anterior horn cells, sensory ganglion cells (neuronopathy), the peripheral nerves (neuropathy), neuromuscular junctions (myasthenia), or muscle (myopathy). Common symptoms and signs of NMD include muscle weakness, impairment in muscle endurance, involuntary muscle activity (stiffness, myotonia, cramps, and fasciculations), sensory loss, autonomic dysfunction and impairment in control of voluntary movements. Sensations of pain and fatigue are common consequences of muscle and nerve pathology.[1,2] Easy to apply NMD-specific reliable and validated self-report assessment tools are essential for obtaining insight into the prevalence and severity of the broad range of patient perceived health-related problems in NMDs. This is important for research and for clinical practise as well, in order to narrow the gap between the clinician's and patient's view on the actual health situation and to help to tailor care plans to the patient's need and preferences.[3] We therefore developed the disability-severity Neuromuscular Disease Impact Profile (NMDIP) based on the ICF-Core set for NMDs, a set of categories selected from the International Classification of Functioning, Disability and Health (ICF).[2,4]

The NMDIP consists of 36 items that cover all ICF-components and are divided into eight scales and four single items. The NMDIP-scales showed moderate to good Cronbach's alpha and mean inter-item correlation coefficients. Convergent and discriminant validity analysis indicated that the NMDIP measures the impact of neuromuscular disease on physical, psychological and social functioning. The NMDIP discriminates between groups of patients who differ in 'Extent of limitations'. The four single items represent the Environmental Factors component (three items) and one Body Functions item (Seeing function).[4]

The objective of this study was to further examine the psychometric properties of the NMDIP and to build on previous studies on this measurement instrument.[2,4] We examined its stability over time by assessing the test-retest reliability of the NMDIP-scales. We furthermore compared the ability of the NMDIP scales to discriminate between criterion related subgroups with

this ability of four established concurrent measurement instruments, by assessing the Relative Validity (RV).[5,6] The RV coefficient indicates how much more or less valid each outcome measure is related to the best outcome measure.

## Methods

### Sample and procedure

A cross sectional study, using a postal survey, was administered to patients diagnosed with a NMD who were registered at the Department of Neurology of the University Medical Center Groningen, University of Groningen, the Netherlands. Inclusion criteria for this study were: diagnosis with a NMD and representing one of Rowland's NMD classification groups: motor-neuron disorders, muscle disorders, junction disorders and peripheral nerve disorders[7]; being aged 18 or older; being able to read and write in Dutch; and being able to give informed consent. No exclusion criteria were formulated.

A total of 1003 eligible patients were selected from the hospital patient records system. To avoid inappropriately sending the questionnaires, we crosschecked for deceased patients using the national population register. Patients received information about the study and were invited to participate.

Respondents completed demographic and disease specific questions, the NMDIP, two criterion variables to measure the 'Extent of Limitations' and 'Quality of Life'. Also, concurrent measures were completed: two generic multidimensional health impact measures (the Medical Outcome study Short Form Questionnaire (SF-36)[8] and the World Health Organization Quality Of Life-abbreviation version (WHOQOL-bref)[9], and two generic domain specific measures the Groningen Activity Restriction Scale (GARS)[10] and the Impact on Participation and Autonomy Questionnaire (IPAQ).[11] To assess stability over time, the NMDIP was administered on two occasions to patients who agreed to fill in the questionnaire twice. We, arbitrary, selected a time frame from eight to ten

weeks to be sure that patients could not remember their answers on the first questionnaire, and the likelihood of changes in the health situation was minimal.

**Measurement instruments**



The NMDIP includes 36 items and consists of eight scales and four additional items. The 36 items were divided over the four ICF components. For the Body Functions component items and for the Participation component items scoring options ranged from 0 (no disability) to 4 (complete disability); for the Activities component items scoring options ranged from 0 (no disability) to 3 (complete disability); and for the Environmental Factors component items scoring options ranged from 0 (no support) to 2 (full support).[4] Item scores were summed into a scale with higher scores indicating more disability. To evaluate the RV, we used the 'Physical Functioning' construct as represented by the 'Activities of Moving around' and 'Self-care and Domestic Activities' scales, the 'Psychological Functioning' construct as represented by the 'Mental Functions and Pain' scale, and the 'Social Functioning' construct as represented by the 'Participation in Life Situations' scale. These scales were selected because items in these scales are closely associated with the scales in the concurrent measures.

The SF-36 was selected as a well-known reliable and valid generic multidimensional health-impact measure used for NMD.[12,13] The SF-36[8] comprises 36 items with eight functional dimensions. Three scales were used to examine the RV: 'Physical Functioning', 'Mental Health' and 'Social Functioning'. Item scores were coded, summed and transformed to a score of 0 (worst health) to 100 (best health) for each scale. The overall Cronbach's alpha for these scales was 0.79 in a study of Amyotrophic Lateral Sclerosis patients.[14] In our previous study the Cronbach's alpha for the selected scales ranged from 0.77 and 0.94.[4]

The WHOQOL-bref[9] was selected as a generic measurement instrument for a broad evaluation of quality of life. It consists of 28 items in four constructs and two separate questions. Three scales were used to examine the RV: 'Physical Health and Autonomy', 'Psychological

Health', and 'Social Relations'. Item scores from each scale were coded, summed and transformed to a score of 0 (worst health) to 20 (best health). The Cronbach's alpha ranged from 0.63 to 0.81 in a study of Multiple Sclerosis patients.[15] In our previous study the Cronbach's alpha for the selected scales ranged from 0.60 to 0.84.[4]

The GARS[10] is a domain specific generic measurement instrument for assessing disability in 'Activities of daily living' (ADL) and 'Instrumental activities of daily living' (IADL). It consists of eleven ADL items and seven IADL items. A four-category response format was used, and ranged from 1 (no problem in performing without help) to 4 (impossible to perform). The scores were summed for each subscale. The Cronbach's alpha ranged from 0.95 to 0.97 in a study of Multiple Sclerosis patients.[15] In our previous study the Cronbach's alpha ranged from 0.93 to 0.95.[4]

The IPAQ[11,16] is a domain specific generic measurement instrument for assessing participation. It consists of fifteen items focusing on person-perceived participation and autonomy. The instrument assesses two aspects of participation: perceived participation and the perceived problems with participation. In this study the perceived participation aspect was used since this construct is closely associated with the 'Participation in Life Situations' construct in the NMDIP questionnaire. The sub-domains were 'Autonomy Indoors', 'Family Role', 'Autonomy Outdoors', and 'Social Relations'. The response options ranged from 1 (very good) to 5 (very poor). Scores were summed for each domain. The Cronbach's alpha ranged from 0.86 and 0.94 in a study of Multiple Sclerosis patients.[15] In our previous study the Cronbach's alpha ranged from 0.84 to 0.94.[4]

**Criterion variables**

Two questions were selected as criterion variables: 'Extent of limitations' and 'Quality of life'.

To evaluate the 'Extent of Limitations' respondents were asked to answer the question: 'To what extent are you limited due to your NMD?' Responses were on a ten-point scale ranging from 1 (not limited at all) to 10 (completely limited). Respondents were classified into one of four groups: Group A with a 'very low extent of limitation' (score 1-2), Group B with a 'moderate extent of

limitation' (score 3-5), Group C with a 'high extent of limitation' (score 6-8) and, Group D with a 'very high extent of limitation' (score 9-10).

The second criterion variable for evaluation of quality of life was one of the two single items adapted from the WHOQOL-bref. Respondents were asked: 'How would you rate your quality of life?'. Response options were: 1=very poor, 2=poor, 3=neither poor nor good, 4=good and 5=very good. Respondents were classified into three groups: Group A– 'very poor or poor quality of life', Group B– 'neither poor nor good', and Group C– 'good or very good quality of life'.



**Analysis**

Descriptive statistics were used to characterize the total sample and the test-retest sample. Differences between both samples were examined using the difference in proportions test, the two-sample t-test, and if data are not normally distributed a non-parametric test for independent samples were used.

Test-retest reliability or stability over time was examined using the Wilcoxon Signed Test and the one-way random intraclass correlation coefficients (ICCs).[17]

Relative Validity was examined in several steps. First, the Chi-square was computed for each scale by calculating the Kruskal-Wallis H-test. Second, the RV of each scale was computed by dividing each H-statistic by the H-statistic for the scale with the highest H-statistic, and multiplied by one hundred. The resulting RV-estimate indicates the extent to which a scale or construct is able to discriminate between two groups compared to the measure with the highest H-statistic.[18,19] Finally, the clinical relevance of the differences between respondent subgroups, and the nonparametric effect size (coefficient *r*) for unrelated samples, was calculated for statistically significant group differences ($\alpha$=0.05) with post hoc tests (Bonferroni correction).[20] Effect sizes where estimated through coefficient *r,* which was calculated by dividing the *z*-statistic (obtained from the Mann-Whitney U test) by the root of the sample size (n). To interpret this nonparametric effect sizes (coefficient *r)*, Cohen suggested the following thresholds: an *r* of < 0.10 indicates a

trivial effect, an $r$ of ≥ 0.10 to < 0.24 a small effect, a $r$ of ≥ 0.24 to < 0.37 a moderate effect, and an $r$ ≥ 0.37 a large effect. A $r$ ≥ 0.10 reflects a clinically relevant difference between groups.[20,21]

IBM SPSS statistics version 22 was used.

## Results

A total of 702 participants (70% response rate) completed the questionnaires. Of the 202 patients who agreed to complete the NMDIP twice 185 participants (92% response rate) actually returned the questionnaire.

The non-respondents from the 1003 eligible patients did not differ from respondents in terms of gender, but non-responders were significantly younger than respondents (p-value<0.001 not in table).

The total sample (n=702) and the test-retest sample (n=185) differed in Age, Years since diagnosis. Participants in the total sample were older and were diagnosed more recently with a NMD compared to the test-retest sample. Also a significant larger proportion of respondents in the total sample was 'Retired due to age' compared to test-retest sample (p-value=0.007) (Table 1). Finally the NMD category distribution differed significantly between the samples with less patients with Motor-neuron disorders and Muscle disorders and more patients with Peripheral nerve disorders in the total sample compared to the test-retest sample.

### Test-retest reliability

Wilcoxon Signed Rank Test (Table 2) showed no significant score differences between time points for most of the NMDIP scales, indicating stability over time, except for the 'Mental Functions and Pain' scale. However this difference was not clinically relevant (ES 0.18, not shown in table). The ICC of all scales showed sufficient agreement and ranged from 0.79 to 0.97, indicating good stability over time.

**Table 1** Patient characteristics of total sample and test-retest sample

| Variable | Total sample N=702 | Test-retest sample N=185 | p-value |
|---|---|---|---|
| Gender (%) | | | |
| Female | 350 (50) | 105 (57) | 0.095^ |
| Male | 352 (50) | 80 (43) | 0.095^ |
| Age | | | 0.024## |
| Median (IQR) | 61 (21) | 57 (18) | |
| Range | 19-92 | 19-92 | |
| Year since diagnosis | | | 0.003## |
| Median (IQR) | 7 (11) | 10 (14) | |
| Range | 0-65 | 1-64 | |
| Extent of limitations | | | 0.329## |
| Median (IQR) | 5 (4) | 6 (4) | |
| Range | 1-10 | 1-10 | |
| Quality of life (WHOQOL-bref) | | | 0.129## |
| Median (IQR) | 4 (1) | 4 (1) | |
| Range | 1-5 | 1-5 | |
| Relationship status (%) | | | |
| Relationship (married/partnership) | 515 (73) | 135 (76) | 0.910^ |
| Single (unmarried/widowed/divorced) | 186 (27) | 45 (24) | 0.549^ |
| Educational level (%) | | | |
| Primary school/vocational training | 235 (33) | 57 (31) | 0.492^ |
| Secondary school/vocational training | 270 (38) | 81 (44) | 0.188^ |
| Higher education /vocational training | 161 (23) | 37 (20) | 0.394^ |
| University | 28 (4) | 8 (4) | 0.837^ |
| Employment status (more answers possible) (%) | | | |
| Following a training or study | 36 (5) | 12 (7) | 0.468^ |
| Employment (part-time or full time) | 173 (25) | 43 (23) | 0.693^ |
| Voluntary work (part-time or full time) | 42 (6) | 15 (8) | 0.294^ |
| (Partially) retired due to NMD | 213 (30) | 67 (36) | 0.126^ |
| Housewife/househusband | 171 (24) | 55 (30) | 0.136^ |
| Retired due to age | 244 (35) | 45 (24) | 0.007^ |
| NMD category (%) | | | |
| Motor neuron disorder (MND) | 43 (6) | 20 (11) | 0.027^ |
| Muscle disorder (MD) | 154 (22) | 69 (37) | <0.001^ |
| Junction disorder (JD) | 234 (33) | 66 (36) | 0.549^ |
| Peripheral nerve disorder (PND) | 271 (39) | 30 (16) | <0.001^ |

^Difference in proportions test, ## Mann-Whitney U test. Interquartile range (IQR)=Q3-Q1.

**Table 2** Test-retest reliability for the NMDIP scales (n=185).

| | Comparison of scores at measurement 0 and 1 | | | | | | Intraclass correlation (one way random) |
|---|---|---|---|---|---|---|---|
| | Cases (N) | Median (IQR) 0 | Cases (N) | Median (IQR) 1 | Z-statistic | p-value* | |
| Muscle Functions | 177 | 4 (2) | 179 | 4 (2) | -2.08 | 0.037 | 0.85 |
| Movement Functions | 161 | 2 (3) | 153 | 2 (2) | -.006 | 0.995 | 0.88 |
| Excretion and Reproductive Functions | 135 | 2 (3) | 144 | 1 (3) | -1.00 | 0.318 | 0.85 |
| Swallowing and Speech Function | 172 | 0 (2) | 180 | 0 (2) | -0.23 | 0.818 | 0.91 |
| Mental Functions and Pain | 164 | 4 (4) | 162 | 4 (3) | -3.39 | 0.001 | 0.90 |
| Activities of Moving around | 185 | 4 (6) | 185 | 4 (6) | -1.23 | 0.219 | 0.96 |
| Self-care and Domestic Activities | 185 | 3 (9) | 185 | 3 (7) | -0.41 | 0.683 | 0.97 |
| Participation in Life Situations | 180 | 1 (2) | 182 | 0 (2) | -1.70 | 0.090 | 0.79 |

* Wilcoxon Signed Rank Test, 2-tailed. Interquartile range (IQR)=Q3-Q1.

**Criterion-related relative validity**

Median scores of patients with a low 'Extent of limitation' (Table 3) or very poor or poor 'Quality of life' level (Table 4) were significantly different in the hypothesized direction when compared to the next higher group mean.

**Extent of limitations**

About 16% (n=110) of the respondents reported 'low extent of limitations' (Group A) due to NMD, while 36% (n=250) reported a 'moderate extent of limitation' (Group B), and 39% (n=270) reported a 'high extent of limitation' (Group C). About 8% (n=58) of the respondents reported a 'very high extent of limitations' (Group D).

Comparisons of the RV coefficients, as summarized in Table 3, revealed that the NMDIP 'Activities of Moving around' scale and SF-36 'Physical Functioning' scale were the most valid in discriminating between groups with an increasing extent of limitation.

We then examined the performance of the NMDIP-scales in indicating the differences between extreme groups (A-D) and subgroups (A-B, B-C, C-D) regarding the physical-, psychological- and social functioning constructs, as they relate to similar constructs in the concurrent measurement instruments. Regarding physical functioning, we found that both NMDIP activity scales turned out to be the most sensitive (followed by the 'Muscle Functions' scale) for measuring differences

between extreme groups and subgroups. However, the performance of the concurrent SF-36 'Physical functioning' scale and both GARS scales were almost identical. Regarding the psychological functioning construct we found that the NMDIP 'Mental Functions and Pain' scale was the best performing scale compared to the SF-36 'Mental Health' scale and the WHOQOL-bref 'Psychological Health' scale, showing the highest extreme group and subgroup differences. Regarding the social functioning construct the NMDIP 'Participation in Life Situations' scale performed better than the SF-36 'Social Functioning' and the WHOQOL-bref 'Social Relations' scales, and roughly as well as the same as the comparable constructs in the domain-specific IPAQ.



In summary, the NMDIP scales performed sufficient to good in discriminating between (sub) groups with an increasing extent of limitations compared to similar constructs in concurrent measures regarding physical functioning, psychological functioning and social functioning constructs.

**Table 3** Relative validity of the NMDIP, domain specific and generic measurement instruments compared, using subgroups of extent of limitations (n=702 )

| | Group A (n=110) low extent of limitation | | Group B (n=250) moderate extent of limitation | | Group C (n=270) high extent of limitations | | Group D (n=58) very high extent of limitations | | Kruskal-Wallis H | | Group A-B* | Group B-C* | Group C-D* | Group A-D* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | Median (IQR) | n | Median (IQR) | n | Median (IQR) | n | Median (IQR) | Chi Square | RV[#] | ES | ES | ES | ES |
| **NMDIP** | | | | | | | | | | | | | | |
| Muscle Functions | 97 | 2 (2) | 231 | 3 (2) | 263 | 4 (2) | 56 | 6 (3) | 221.3 | 88 | 0.44 | 0.30 | 0.44 | 0.78 |
| Movement Functions | 92 | 0 (1) | 210 | 2 (2) | 232 | 3 (2) | 49 | 5 (4) | 149.3 | 59 | 0.34 | 0.30 | 0.29 | 0.72 |
| Excretion and Reproductive Functions | 82 | 0 (1) | 182 | 1 (2) | 194 | 2 (3) | 43 | 3 (3) | 47.1 | 19 | 0.16 | 0.18 | - | 0.51 |
| Swallowing and Speech Function | 107 | 0 (0) | 238 | 0 (1) | 258 | 0 (1) | 55 | 1 (2) | 48.6 | 19 | 0.17 | 0.11 | 0.18 | 0.50 |
| Mental Functions and Pain | 95 | 2 (2) | 205 | 4 (3) | 237 | 5 (4) | 50 | 6.5 (5) | 128.0 | 51 | 0.30 | 0.29 | 0.21 | 0.64 |
| Activities of Moving around | 110 | 0 (2) | 250 | 3 (4) | 272 | 6 (7) | 58 | 13 (9) | 251.0 | 99 | 0.42 | 0.39 | 0.39 | 0.79 |
| Self-care and Domestic Activities | 109 | 0 (1) | 250 | 2 (3) | 272 | 4 (8) | 58 | 16.5 (14) | 219.7 | 87 | 0.36 | 0.35 | 0.37 | 0.81 |
| Participation in Life Situations | 108 | 0 (0) | 249 | 0 (1) | 271 | 2 (4) | 55 | 4 (4) | 168.5 | 67 | 0.24 | 0.33 | 0.30 | 0.76 |
| **SF-36** | | | | | | | | | | | | | | |
| Physical Functioning | 109 | 27 (6) | 250 | 21 (8) | 272 | 16 (7) | 58 | 11 (3) | 252.9 | 100 | 0.41 | 0.38 | 0.43 | 0.78 |
| Mental Health | 110 | 25 (3) | 250 | 25 (5) | 271 | 24 (6) | 58 | 21.5 (7) | 35.2 | 14 | - | 0.12 | 0.14 | 0.40 |
| Social Functioning | 110 | 10 (1) | 250 | 8 (2) | 271 | 7 (3) | 58 | 5.5 (4) | 129.8 | 51 | 0.31 | 0.26 | 0.22 | 0.62 |
| **WHOQOL-bref** | | | | | | | | | | | | | | |
| Physical Health and Autonomy | 108 | 3 (1) | 244 | 3 (0) | 271 | 3 (0) | 57 | 3 (1) | 68.0 | 27 | 0.21 | 0.19 | - | 0.47 |
| Psychological Health | 106 | 4 (0) | 246 | 3.5 (0.5) | 271 | 3.5 (1) | 57 | 3 (0) | 68.0 | 27 | 0.19 | 0.14 | 0.25 | 0.55 |
| Social Relations | 104 | 4 (1) | 238 | 4 (0) | 261 | 4 (1) | 55 | 4 (1) | 30.8 | 12 | - | 0.14 | - | 0.35 |
| **GARS** | | | | | | | | | | | | | | |
| Activities of Daily Living | 110 | 11 (1) | 250 | 13 (6) | 272 | 17 (10) | 58 | 27 (17) | 213.5 | 84 | 0.31 | 0.35 | 0.39 | 0.79 |
| Instrumental Activities of Daily Living | 109 | 7 (2) | 250 | 10 (7) | 270 | 15 (9) | 58 | 24 (5) | 215.0 | 85 | 0.33 | 0.35 | 0.39 | 0.78 |
| **IPAQ** | | | | | | | | | | | | | | |
| Autonomy Indoors | 110 | 7 (3) | 250 | 13 (6) | 272 | 14 (6) | 57 | 19 (11) | 174.3 | 69 | 0.37 | 0.27 | 0.32 | 0.75 |
| Family Role | 110 | 8.5 (7) | 248 | 15 (7) | 271 | 18 (7) | 58 | 22 (9) | 177.3 | 70 | 0.40 | 0.28 | 0.22 | 0.71 |
| Autonomy Outdoors | 110 | 5.5 (4) | 249 | 9 (3) | 272 | 11 (5) | 56 | 14 (4) | 238.5 | 94 | 0.39 | 0.40 | 0.31 | 0.76 |
| Social Relations | 110 | 9 (6) | 250 | 12 (4) | 272 | 13 (5) | 56 | 13 (4) | 87.0 | 34 | 0.24 | 0.23 | - | 0.52 |

NMDIP, GARS, and IPAQ: higher scores = more unable to perform activity; SF-36 and WHOQOL-bref scales: higher scores=better quality of life and more able to perform activity. Interquartile range (IQR)=Q3-Q1. -=not statistically significant. Bonferroni correction *=0.0125 (p-value 0.05/4). RV=relative validity, [#]=score indicating the relative validity with score 100 related to the highest H-statistic. ES=effect size

**Table 4** Relative validity of the NMDIP, domain specific and generic measurement instruments compared, using subgroups of Quality of Life (n=702)

| | Group A (n=53) Very poor or poor QoL | | Group B (n=175) Neither poor nor good QoL | | Group C (n=474) Good or very good QoL | | Kruskal-Wallis H Chi Square | RV[#] | Group A-B* ES | Group B-C* ES | Group A-C* ES |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | Median (IQR) | n | Median (IQR) | n | Median (IQR) | | | | | |
| **NMDIP** | | | | | | | | | | | |
| Muscle Functions | 52 | 5 (2) | 167 | 4 (2) | 439 | 3 (2) | 81.4 | 50 | 0.34 | 0.23 | 0.35 |
| Movement Functions | 46 | 4 (3) | 148 | 3 (2) | 400 | 2 (3) | 83.8 | 51 | 0.30 | 0.27 | 0.35 |
| Excretion and Reproductive Functions | 36 | 3 (5) | 129 | 2 (2) | 344 | 1 (2) | 40.6 | 25 | 0.21 | 0.22 | 0.25 |
| Swallowing and Speech Function | 49 | 2 (3) | 162 | 0 (1) | 458 | 0 (1) | 43.6 | 27 | 0.26 | 0.14 | 0.27 |
| Mental Functions and Pain | 45 | 8 (4) | 147 | 6 (4) | 405 | 3 (4) | 147.7 | 90 | 0.28 | 0.42 | 0.40 |
| Activities of Moving around | 53 | 10 (8) | 175 | 4 (6) | 474 | 3 (5) | 75.2 | 46 | 0.36 | 0.19 | 0.35 |
| Self-care and Domestic Activities | 53 | 10 (13) | 175 | 3 (8) | 473 | 2 (4) | 79.9 | 49 | 0.32 | 0.22 | 0.33 |
| Participation in Life Situations | 52 | 4.5 (5) | 175 | 2 (4) | 468 | 0 (2) | 103.7 | 63 | 0.32 | 0.26 | 0.39 |
| **SF-36** | | | | | | | | | | | |
| Physical Functioning | 53 | 12 (4) | 175 | 17 (8) | 473 | 21 (10) | 85.7 | 52 | 0.38 | 0.23 | 0.34 |
| Mental Health | 53 | 20 (6) | 175 | 22 (6) | 473 | 25 (4) | 132.5 | 81 | 0.27 | 0.35 | 0.38 |
| Social Functioning | 53 | 5 (3) | 175 | 7 (2) | 473 | 9 (2) | 138.3 | 84 | 0.31 | 0.36 | 0.38 |
| **WHOQOL-bref** | | | | | | | | | | | |
| Physical Health and Autonomy | 53 | 3 (5) | 173 | 3 (0) | 466 | 3 (0) | 117.7 | 72 | 0.21 | 0.41 | 0.34 |
| Psychological Health | 53 | 3 (0) | 173 | 3 (1) | 466 | 4 (0) | 163.8 | 100 | 0.31 | 0.40 | 0.41 |
| Social Relations | 50 | 3 (1) | 170 | 4 (1) | 450 | 4 (0) | 61.3 | 37 | - | 0.25 | 0.25 |
| **GARS** | | | | | | | | | | | |
| Activities of Daily Living | 53 | 26 (16) | 175 | 17 (10) | 474 | 13 (7) | 80.6 | 49 | 0.37 | 0.20 | 0.35 |
| Instrumental Activities of Daily Living | 52 | 22 (12) | 175 | 15 (9) | 472 | 11 (9) | 82.8 | 51 | 0.34 | 0.23 | 0.33 |
| **IPAQ** | | | | | | | | | | | |
| Autonomy Indoors | 53 | 19 (9) | 175 | 14 (5) | 473 | 12 (7) | 109.6 | 67 | 0.32 | 0.29 | 0.36 |
| Family Role | 53 | 24 (8) | 175 | 20 (8) | 471 | 15 (8) | 127.6 | 78 | 0.28 | 0.34 | 0.37 |
| Autonomy Outdoors | 53 | 15 (4) | 174 | 11 (5) | 471 | 8 (5) | 157.6 | 96 | 0.42 | 0.35 | 0.43 |
| Social Relations | 53 | 15 (6) | 175 | 13 (3) | 472 | 11 (5) | 134.1 | 82 | 0.26 | 0.35 | 0.37 |

NMDIP, GARS, IPAQ scales: higher scores = lower quality of life, SF-36, and WHOQOL-bref scales: higher scores=higher quality of life. Interquartile range (IQR)=Q3-Q1. -=not statistically significant. Bonferroni correction *=0.02 (p-value 0.05/3). RV= relative validity. [#]=score indicating the relative validity with score 100 related to the highest H-statistic. ES= effect size

**Quality of life**

Eight percent (n=53) of the respondents reported poor or very poor quality of life (Group A), while 25% (n=175) experienced their quality of life as neither poor nor good (Group B) and 67 % (n=474) reported a good or very good quality of life' (Group C).

Comparisons of the RV-coefficients, as summarized in Table 4, revealed that the SF-36 'Psychological Health' scale and IPAQ 'Autonomy outdoors' scales were the most valid in discriminating between groups with differences in quality of life. The 'Mental Functions and Pain' NMDIP scale was the third most valid scale.

When examining the performance of the NMDIP-scales in indicating the differences between extreme and subgroups for quality of life, we found about the same extreme group differences for the physical functioning scales for all concurrent constructs with moderate Effect Sizes (ESs). The same goes for the subgroup differences, although the NMDIP 'Mental Functions and Pain' scale, and the WHOQOL-bref 'Psychological Health' scale performed slightly better than the SF-36 'Mental Health' scale. Finally, when examining the social functioning scales we found that the comparable NMDIP 'Participation in Life Situations' scale performed about as well as the SF-36 'Social Functioning' scale and the IPAQ scales with a moderate to large ESs for extreme group differences. The NMDIP 'Participation in Life Situations' scale also performed better compared to the social functioning construct of the WHOQOL-bref, the 'Social Relations' scale. The same goes for the subgroup differences.

In summary, the NMDIP scales performed well in discriminating between subgroups with differences in quality of life compared to similar constructs in concurrent measures concerning the physical functioning, psychological functioning and social functioning constructs.

## Discussion

In this study the NMDIP, that was developed to reflect the prevalence and severity of a broad range of NMD-related disabilities(4), showed stability and performed well in the criterion-related subgroups of NMD-patients who differed in the extent of limitation and quality of life.



The results of the test-retest reliability analysis were sufficient indicating stability in the eight NMDIP scales. Although the results showed a difference for 'Mental Functions and Pain' scale while the effect size was trivial, the intraclass correlation showed sufficient agreement for all NMDIP scales between the two measurement moments.

In general, the NMDIP scales performed well in discriminating between relevant subgroups with increasing extent of limitation. This was the case for constructs evaluating physical, psychological, and social functioning. The NMDIP scales showed satisfactory relative validity and moderate to strong ESs indicating the strength of the differences between subgroups. The NMDIP showed satisfactory performance in discriminating between relevant subgroups with decreasing Quality of Life. This was the case for constructs evaluating physical, psychological and social functioning.

Strength of this study is the inclusion of a large population of patients diagnosed with a NMD. Some potential study limitations should be mentioned. First, RV was examined as criterion-related validity value in this study. Because of the absence of a widely accepted criterion measure we chose to use self-report measures, which turned out to be a useful method. Secondly, the (relatively) small group sizes for 'very high extent of limitations' (Group D) and 'very poor or poor quality of life' (Group A) might have a negative impact on detecting group differences, though the difference between these subgroups and the adjacent groups showed sufficient ESs.

The results in this study permit us to recommend that researchers consider Relative Validity as a useful method to select a valid and 'with caution' a sensitive measure, especially

when data from longitudinal studies or intervention studies are lacking. At the same time, we want to stress that RV is not a substitute for the sensitivity-to-change test. The findings in this study cannot be generalized to longitudinal studies. We recommend further research to evaluate the sensitivity to change of the NMDIP scales.

Furthermore generic health measures have some disadvantages against disease-specific health measures in addressing topics of a particular relevance to patients with a specific disease. Therefore it is recommended that the individual items in a scale be examined to estimate the suitability of the scale for a particular patient population.[13]

## Conclusions

The results in this study confirmed the stability of the NMDIP over time, and showed good relative validity compared to generic QOL and domain-specific measures. In combination with the findings in our previous study[4], the NMDIP proved to be a valid and reliable disease-targeted measure with a broad scope on physical, psychological and social functioning. Further research should examine the responsiveness of the NMDIP scales.

## Abbreviations

**NMDIP**: Neuromuscular Disease Impact Profile; **RV**: relative validity; **WHOQOL-bref**: World Health Organization Quality Of Life-abbreviation version; **SF-36**: Medical Outcome study Short Form Questionnaire; **GARS**: Groningen Activity Restriction Scale; **IPAQ** : Impact on Participation and Autonomy Questionnaire ; **NMD**: Neuromuscular Diseases; **ADL**: Activities of daily living; **IADL**: Instrumental activities of daily living; **ICC**: Intraclass correlation coefficient.

**Ethics approval**

Ethical approval was obtained from the local ethics committee, the Medical Ethical Committee of the University Medical Center Groningen. Reference: METc 2009.310. Informed consent was obtained from all participants.



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# 5

## The prevalence and severity of disease-related disabilities and their impact on quality of life in neuromuscular diseases

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## Abstract

**Objective:** People with a Neuromuscular Disease (NMD) experience lower quality of life levels than people from the general population. We examined the prevalence and severity of a broad range of NMD-related disabilities and their impact on quality of life (QoL).

**Design:** Cross-sectional postal survey study.

**Setting:** Outpatient clinic of the Department of Neurology, University Medical Center Groningen, the Netherlands.

**Participants:** Adult out-patients diagnosed with an NMD

**Interventions:** Not Applicable

**Main Outcome Measures:** Patients completed the Neuromuscular Disease Impact Profile (NMDIP), a disease-related disability impact questionnaire, and two generic health-related QoL questionnaires: the Medical Outcome study Short Form Questionnaire (SF-36) and the World Health Organization Quality of Life-bref (WHOQoL-bref). The impact of disabilities on QoL was estimated using multiple regression analyses.

**Results:** 662 patients (68% response rate) completed the questionnaires. There were no differences in QoL between diagnosis-based subgroups. 'Impairments in Muscle Functions' had the highest prevalence and severity scores in the total sample and diagnosis-based subgroups. NMD-related disabilities showed strong and independent associations with all aspects of QoL. 'Impairments in Mental Functions and Pain' was the most important predictor of QoL followed by 'Restrictions in Participation in Life situations'. The assessed impact on QoL appeared to be dependent on the QoL measurement instrument applied.

**Conclusion:** Although 'impairment in Muscle Functions' is the most prevalent and severe disability, the 'impairments in Mental Functions and Pain' have the largest impact on QoL in NMD patients.

**Keywords**

Neuromuscular disease, Neuromuscular Disease Impact Profile, Disability, Quality of Life.

## List of abbreviations

| | |
|---|---|
| NMD | Neuromuscular Disease |
| QoL | Quality of Life |
| NMDIP | Neuromuscular Disease Impact Profile |
| ICF | International Classification of Functioning, Disability and Health |
| SF-36 | Medical Outcome Study 36-item Short Form Health Survey |
| WHOQol-bref | World Health Organization Quality of Life (abbreviated version) |
| VIF | Variance Inflation Factor |

## Introduction

Neuromuscular diseases (NMDs) can be caused by dysfunction of the anterior horn cell or sensory ganglion cell (neuronopathy), peripheral nerve (neuropathy), neuromuscular junction (myasthenia), or muscle (myopathy). Common impairments in functioning as a consequence of neuromuscular diseases include muscle weakness, impairment in muscle endurance, involuntary muscle activity (stiffness, myotonia, cramp and fasciculation), sensory loss, autonomic dysfunction and impairment in the control of voluntary movements. These impairments cause fatigue and pain in most people, which has a profound impact on their daily activities and participation in life situations.[1-5]

Quality of Life (QoL) has become increasingly important in evaluating healthcare outcomes in recent decades. Studies of QoL in NMDs generally report that people with an NMD experience lower QoL compared to the general population[4], which can be explained by NMD-related health problems such as poorer physical[4,6] and social functioning[7,8], pain[9-11], fatigue[12], cognitive impairments and impaired emotional functioning.[13]

Although these studies have generated clinically important information, they are limited by their typical focus on the impact of individual disabilities on QoL. Little is known of the relative impact of aggregated NMD-related disabilities on QoL. Insight into this could facilitate our understanding of the impact of disease-related disabilities in NMDs on QoL.

The aim of this study is therefore to examine the prevalence and severity of a large number of disease-related disabilities and their impact on QoL in a sample of patients diagnosed with a wide range of NMD.

## Methods

### Sample and procedure

A cross-sectional postal survey was conducted among patients diagnosed with an NMD and registered at the Department of Neurology of the University Medical Center Groningen, the Netherlands. The inclusion criteria in addition to an NMD diagnosis were: being aged 18 or older, and being able to read and write in Dutch.



A total of 980 eligible patients diagnosed with a neuromuscular disease were selected from the hospital patient record system. To avoid inappropriately sending questionnaires, we crosschecked for deceased patients using the national population register.

Patients received information about the study and were invited to participate. Respondents completed the Neuromuscular Disease Impact Profile (NMDIP), two generic health-related QoL questionnaires and some demographic and disease-specific questions. Reminders were sent after two weeks if there was no response.

### Measurement instruments

Disease-related disabilities were assessed using the NMDIP[5] This measurement instrument is based on the International Classification of Functioning, Disability and Health (ICF)[14] and consists of 36 items covering four ICF components. Its items are grouped into eight scales with four additional items. For the Body Functions and Participation component items, scoring options ranged from 0 (no disability) to 4 (complete disability); for the Activities component items, scoring options ranged from 0 (no disability) to 3 (complete disability); and for the Environmental Factors component items, scoring options ranged from 0 (no support) to 2 (full support). Scores are summed for each scale. To make the scores for each scale and the individual items comparable, the summed and individual scores were divided by the highest possible score and multiplied by 100 to obtain a result between 0 and 100. We

established in previous work that the NMDIP shows satisfactory levels of internal consistency: Cronbach's alphas ranged from 0.63 to 0.92, while mean inter-item correlations ranged from 0.38 to 0.77.[5] Test-retest reliability was good: Intraclass correlations ranged from 0.79 to 0.97.[15]

QoL was assessed using two generic health-related QoL measurement instruments, the Medical Outcome Study 36-item Short Form Health Survey (SF-36)[16] and the World Health Organization Quality of Life (abbreviated version) (WHOQoL-bref).[17] The SF-36 consists of eight scales and two separate questions covering physical, psychological and social aspects of health. Item scores were coded, summed and transformed to a scale ranging from 0 (worst QoL) to 100 (best QoL) for each dimension. The Cronbach's alpha for a recent NMD study ranged from 0.77 to 0.94.[5] The WHOQoL-bref consists of 26 items divided into four domains covering physical, psychological, social and environmental aspects and has two single-item questions. For each scale, item scores were coded, summed and transformed to a scale ranging from 0 (worst QoL) to 100 (best QoL). The Cronbach's alpha for a recent study of NMD patients ranged from 0.60 to 0.84.[5]

Contextual variables were assessed using three questions with a visual analogue scale: General health status was assessed using the EuroQol-visual analogue scale for the single question 'How good or bad is your health today?',[18] with the endpoints 'Best imaginable health state' scoring 100, and 'Worst imaginable health state' scoring 0. The extent of limitations was assessed using the single question 'To what extent are you limited due to your NMD?' Response options are on a ten-point scale ranging from 1 (not limited at all) to 10 (completely limited). And general QoL was assessed using the single question 'How do you rate your QoL?', with the endpoints 'Best imaginable QoL' scoring 10, and 'Worst imaginable QoL' scoring 0.

**Diagnosis-based subgroups**

To examine the differences in the prevalence and severity of disabilities between the relevant NMD subgroup we used the categorisation according to Rowland[19]: motor-neuron disorders, muscle disorders, junction disorders, and peripheral nerve disorders. Furthermore, the peripheral nerve disorders group was split into primary motor and primary sensor subgroups because of the differences in onset and expected differences in prevalence and disability severity.



**Data analyses**

Descriptive statistics were used to examine the patient characteristics. The prevalence of disabilities was calculated as the percentage of the patients who experience a disability (score >0). Severity scores were calculated as the mean score of the disability scores of all patients. To assess differences between diagnosis-based subgroups, Analysis of Variance and T-tests were performed for normally distributed continuous variables, a Chi-square test for categorical variables, and a Mann-Whitney U-test and Kruskal-Wallis test for not normally distributed variables.

The impact of the disease-related disabilities on QoL was assessed using a series of multiple regression analyses with each of the QoL variables as dependent variable. We first analysed the impact of patient characteristics (age, gender, years since diagnosis, employment status, and educational level) on QoL in Model 1 to control for patient characteristics. We then analysed the impact of the disease-related disabilities overall in Model 2. Before being entered into the regression analysis, the ordinal and categorical variables – gender, educational level and employment status – were dichotomized. The expected direction of standardized ß weights is negative, meaning that less disability equates to better QoL. Special attention was given to examining the multicollinearity between variables.[20]

Statistical analyses were performed using the SPSS 23.0 software package.

## Results

### Patient characteristics

Of the 980 eligible patients, 662 participants completed the questionnaires (68% response rate). The distribution of NMD diagnoses across the various NMD subgroups is described in supplementary table S1. Non-respondents did not differ from respondents in terms of gender, but were significantly younger than respondents (mean=53, SD=19, p=0.000).

**Table 1** Sample characteristics for the total sample (n=662) and subgroups

| | Total sample | Motor-neuron disorders | Muscle disorders | Junction disorders | Peripheral nerve disorders Primary motor | Peripheral nerve disorders Primary sensor | Subgroup differences |
|---|---|---|---|---|---|---|---|
| | (n=662) | (n=62) | (n=155) | (n=177) | (n=71) | (n=197) | p-value |
| *Gender* n (%) | | | | | | | 0.756 # |
| Female | 335 (51) | 31 (50) | 77 (50) | 115 (65) | 32 ( 45) | 80 (41) | |
| *Age (years)* | | | | | | | 0.000 ### |
| Mean (SD) | 59 (15.4) | 60.8 (12.7) | 51.6 (16.8) | 58.7 (15.7) | 55.7 (14.4) | 65.3 (12.3) | |
| Range | 19-92 | 29-86 | 19-92 | 22-89 | 26-82 | 32-91 | |
| *Relationship status n (%)* | | | | | | | 0.000 # |
| Married/partnership | 468 (71) | 51 (82) | 95 (61) | 128 (72) | 52 (73) | 142 (72) | |
| Unmarried/widowed/ Divorced | 193 (29) | 11 (18) | 60 (39) | 48 (27) | 19 (27) | 55 (28) | |
| *Educational level n (%)* | | | | | | | 0.000 # |
| Lower level | 480 (73) | 41 (66) | 114 (75) | 131 (74) | 51 (73) | 143 (73) | |
| Higher level | 177 (27) | 21 (34) | 37 (25) | 46 (26) | 19 (27) | 54 (27) | |
| *Employment status n (%)* | | | | | | | 0.000 # |
| Employment | 187 (28) | 18 (29) | 46 (30) | 60 (34) | 21 (30) | 42 (21) | |
| Unemployment | 475 (72) | 44 (71) | 109 (70) | 117 (66) | 50 (70) | 155 (79) | |
| Range | 0-65 | 1-64 | 1-62 | 0-65 | 0-55 | 0-61 | |
| *Health-state* | | | | | | | |
| EQ-VAS, median (IQR) | 67 (30) | 65 (23) | 65 (25) | 70 (25) | 70 (30) | 65 (30) | 0.058 ## |
| *Extent of limitations* | | | | | | | |
| median (IQR) | 5 (4) | 7 (3) | 6 (5) | 5 (3) | 6 (4) | 6 (5) | 0.000 ## |
| *Quality of Life* | | | | | | | |
| QoL-rate, median (IQR) | 7 (2) | 7 (2) | 7 (2) | 7 (2) | 7 (1) | 7 (2) | 0.129 ## |

#Chi-square test, ##Kruskal-Wallis test. ###Oneway Anova. IQR=Inter quartile range.

The mean age of respondents was 59 years and their mean disease duration was eleven years (Table 1). Most respondents were married or in a relationship, were of low education level and were retired. There was no significant difference in QoL between the NMD subgroups.

Respondents categorized in the NMD subgroups showed statistically significant differences in age, relationship status, education level, employment status, years since diagnosis and extent of limitations (Table 1).



### Prevalence and severity of disease-related disabilities

The most prevalent disability reported in the total sample (Table 2) was ‘impairments in Muscle Functions’, followed by ‘limitations in Activities of Moving Around’ and ‘impairments in Mental Functions and Pain’. The Peripheral nerve disorders subgroup, primary sensor group, had the highest prevalence for ‘impairments in Mental Functions and Pain’ and for ‘impairments in Excretion and Reproductive Functions’ compared to the other disorders. The most severe disability in the total sample was ‘impairments in Muscle Functions’ followed by ‘lack of support from Social security services’ and ‘Health services’, and ‘limitations in Activities of Moving Around’. Disability severity differed statistically significantly for most disabilities between NMD subgroups.

**Table 2** Prevalence and severity of disease-related disabilities in the total sample and in disease subgroups.

| | Total sample (n=662) | | Motor-neuron disorders (n=62) | | Muscle disorders (n=155) | | Junction disorders (n= 177) | | Peripheral nerve disorders Primary motor (n=71) | | Peripheral nerve disorders Primary sensor (n=197) | | Subgroup differences[#] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | % | mean (SD) | % | mean (SD) | % | mean (SD) | % | mean (SD) | % | mean (SD) | % | mean (SD) | p-value |
| Impairments in… | | | | | | | | | | | | | |
| Muscle Functions | 89 | 44.8 (23.0) | 98 | 58.7 (25.0) | 99 | 52.4 (21.8) | 93 | 35.3 (19.1) | 93 | 44.3 (22.2) | 91 | 42.3 (22.5) | 0.000 |
| Movement Functions | 70 | 22.0 (17.7) | 76 | 33.5 (20.5) | 69 | 21.5 (17.6) | 58 | 13.6 (13.3) | 86 | 23.4 (16.7) | 91 | 25.9 (17.5) | 0.000 |
| Excretion and Reproductive Functions | 47 | 15.9 (17.2) | 53 | 16.1 (18.1) | 43 | 15.8 (16.6) | 48 | 14.0 (14.2) | 51 | 12.3 (17.8) | 67 | 18.8 (19.2) | 0.119 |
| Swallowing and Speech Functions | 38 | 9.3 (14.5) | 37 | 13.8 (23.4) | 51 | 14.0 (16.8) | 50 | 11.5 (13.0) | 19 | 4.0 (10.0) | 26 | 4.4 (8.4) | 0.000 |
| Mental Functions and Pain | 79 | 22.6 (15.1) | 87 | 21.5 (14.4) | 80 | 24.3 (16.1) | 79 | 21.2 (14.4) | 89 | 18.3 (13.7) | 95 | 24.7 (15.4) | 0.033 |
| Seeing functions | 40 | 15.3 (20.8) | 21 | 5.7 (11.5) | 37 | 14.4 (20.8) | 68 | 26.1 (22.5) | 20 | 7.2 (17.4) | 34 | 11.8 (18.3) | 0.000 |
| Limitations in… | | | | | | | | | | | | | |
| Activities of Moving Around | 86 | 30.6 (27.4) | 98 | 48.8 (32.7) | 95 | 41.3 (29.3) | 73 | 16.4 (18.0) | 83 | 28.8 (24.5) | 88 | 29.9 (25.4) | 0.000 |
| Self-care and Domestic Activities | 76 | 21.8 (26.5) | 98 | 48.0 (36.2) | 86 | 31.0 (30.5) | 68 | 11.7 (15.5) | 75 | 17.3 (19.4) | 70 | 17.3 (22.1) | 0.000 |
| Restrictions in… | | | | | | | | | | | | | |
| Participation in Life Situations | 52 | 15.1 (20.7) | 63 | 25.3 (27.0) | 65 | 20.7 (22.8) | 39 | 9.3 (16.4) | 49 | 11.7 (17.8) | 53 | 13.9 (19.0) | 0.000 |
| Lack of support from… | | | | | | | | | | | | | |
| Immediate family | 35 | 23.8 (35.1) | 27 | 16.1 (28.3) | 37 | 24.8 (35.8) | 34 | 21.2 (32.2) | 32 | 21.1 (33.4) | 39 | 28.8 (39.1) | 0.204 |
| Social security services | 21 | 35.5 (38.2) | 20 | 28.6 (37.1) | 28 | 36.4 (36.8) | 18 | 33.6 (37.9) | 57 | 42.9 (42.3) | 52 | 35.3 (38.6) | 0.686 |
| Health services | 48 | 32.0 (36.7) | 55 | 33.9 (34.8) | 52 | 34.6 (36.9) | 42 | 28.2 (36.4) | 39 | 26.1 (35.7) | 52 | 34.9 (37.7) | 0.145 |

[^] Severity (mean disability) score: Score 0 = no disability; Score 100 = complete disability. 'Lack of support' score 0 = no support, score 100 = full support. [#] Independent Kruskal-Wallis H test.

**Impact of disease-related disabilities on QoL**

We obtained satisfactory results, and there was no multicollinearity: the variance inflation factor (VIF) for 'Activities of Moving Around' was 5.6 and the average VIF was 2.0. The mean tolerance was 0.59 and the range was from 0.20 to 0.85 and was never below the critical value of 0.2.

Disease-related disability variables contributed significantly and considerably to an important segment of the variance for all SF-36 and WHOQoL-bref domains. The significant standardized β weights were in the expected direction, meaning that patients who reported more disability experienced less QoL. The low significant positive direction of the β weight for the variable 'Seeing Functions' in relation to the SF-36 variable Bodily pain was somewhat unexpected.

The disabilities which were strong predictors for QoL evaluated using the SF-36 (Table 3) were:

- 'Impairments in Mental Functions and Pain' (impairments in sleep functions, fatigue, emotional functions, thought functions, and sensation of pain) was a significant predictor for six out of eight QoL variables
- 'Impairments in Muscle Functions' (impairments in muscle power functions and muscle endurance functions) and 'Limitations in Activities of Moving Around' (limitations in changing body position, maintaining body position, transferring oneself, walking, using transportation, and recreation and leisure) were important predictors in the 'Physical Functioning' QoL domain
- 'Restrictions in Participation in Life Situations' (restrictions in mobility, relationships and recreation and leisure) was an important predictor in the 'Role Physical' and 'Social Functioning' QoL domains

- ‘Limitations in Self-care and Domestic Activities’ (limitations in fine hand use, hand and arm use, washing oneself, caring for body parts, going to the toilet, dressing, preparing meals, and doing housework) and ‘Restrictions in Mental Functions and Pain’ were important predictors in the ‘Role Emotional’ QoL domain.

**Table 3** Impact of disease-related disabilities on the SF-36 QoL variables.

| SF-36 | Physical Functioning ß | Role Physical ß | Bodily Pain ß | Vitality ß | Social Functioning ß | Role Emotional ß | Mental Health ß | General Health ß |
|---|---|---|---|---|---|---|---|---|
| NMDIP | | | | | | | | |
| Impairments in ….. | | | | | | | | |
| Muscle Functions | **-0.20**$^{**}$ | -0.06 | 0.12 | -0.14 | -0.07 | 0.21 | -0.02 | -0.08 |
| Movement Functions | 0.09 | -0.01 | -0.06 | 0.14 | -0.06 | -0.02 | -0.10 | -0.10 |
| Excretion and Reproductive Functions | -0.00 | -0.11 | 0.04 | -0.04 | -0.11 | -0.06 | 0.11 | -0.14 |
| Swallowing and Speech Functions | 0.04 | -0.01 | -0.10 | -0.11 | 0.11 | 0.08 | -0.13 | -0.02 |
| Mental Functions and Pain | -0.08 | -0.16 | **-0.59**$^{***}$ | **-0.53**$^{***}$ | **-0.36**$^{***}$ | **-0.40**$^{**}$ | **-0.34**$^{**}$ | **-0.36**$^{**}$ |
| Seeing Functions | 0.09 | -0.00 | **0.11**$^{*}$ | 0.09 | -0.09 | -0.02 | -0.00 | -0.01 |
| Limitations in ….. | | | | | | | | |
| Activities of Moving Around | **-0.57**$^{***}$ | 0.20 | -0.08 | 0.02 | 0.24 | 0.29 | 0.15 | 0.19 |
| Self-care and Domestic Activities | -0.11 | 0.15 | -0.04 | 0.13 | -0.17 | **-0.42**$^{**}$ | -0.03 | -0.10 |
| Restrictions in ….. | | | | | | | | |
| Participation in Life Situations | -0.10 | **-0.46**$^{***}$ | -0.09 | -0.08 | **-0.32**$^{**}$ | -0.07 | -0.12 | -0.15 |
| Lack of support from….. | | | | | | | | |
| Immediate family | 0.04 | 0.04 | 0.02 | 0.04 | 0.01 | 0.01 | -0.13 | 0.03 |
| Social security services | -0.06 | 0.00 | -0.05 | -0.02 | 0.05 | -0.12 | -0.03 | 0.03 |
| Health services | 0.02 | 0.03 | -0.05 | -0.01 | -0.07 | 0.04 | -0.01 | 0.01 |
| $R^2$ | 0.73 | 0.31 | 0.52 | 0.51 | 0.49 | 0.27 | 0.29 | 0.43 |
| $\Delta R^{2\,\#}$ | 0.66 | 0.22 | 0.41 | 0.33 | 0.38 | 0.19 | 0.24 | 0.31 |
| F | 20.7$^{***}$ | 3.5$^{***}$ | 8.35$^{***}$ | 7.92$^{***}$ | 7.33$^{***}$ | 2.92$^{***}$ | 3.23$^{***}$ | 5.83$^{***}$ |
| F Change$^{\#}$ | 26.78$^{***}$ | 3.47$^{***}$ | 9.35$^{***}$ | 7.26$^{***}$ | 8.01$^{***}$ | 2.91$^{**}$ | 3.69$^{***}$ | 5.91$^{***}$ |

* =p<.05; **=p<.01; ***=p<.001. **In bold:** statistically significant ß values.
$^{\#}$ = compares Model 2 (disabilities) vs. Model 1 (patient characteristics)

The disabilities which were strong predictors for QoL evaluated using the WHOQoL-bref (Table 4) were:

- ‘Restrictions in Participation in Life Situations’ was a significant predictor for three out of four QoL variables
- ‘Impairments in Mental Functions and Pain’ was an important predictor in the ‘Physical Health’ and ‘Psychological Health’ QoL domains

**Table 4** Impact of disease-related disabilities on the WHOQOL-bref QoL variables.

| WHOQOL-bref | Physical Health ß | Psychological Health ß | Social Relationships ß | Environment ß |
|---|---|---|---|---|
| NMDIP | | | | |
| Impairments in ….. | | | | |
| Muscle Functions | -0.09 | -0.03 | 0.02 | -0.01 |
| Movement Functions | 0.06 | 0.10 | 0.20 | **0.21**$^{*}$ |
| Excretion and Reproductive Functions | -0.05 | -0.13 | **-0.41**$^{***}$ | -0.03 |
| Swallowing and Speech Functions | -0.06 | -0.05 | 0.14 | -0.06 |
| Mental Functions and Pain | **-0.54**$^{***}$ | **-0.28**$^{*}$ | -0.21 | -0.21 |
| Seeing Functions | 0.09 | -0.11 | -0.08 | -0.05 |
| Limitations in ….. | | | | |
| Activities of Moving Around | -0.04 | 0.19 | 0.00 | -0.13 |
| Self-care and Domestic Activities | 0.07 | -0.04 | -0.13 | -0.13 |
| Restrictions in ….. | | | | |
| Participation in Life Situations | **-0.21**$^{*}$ | **-0.25**$^{*}$ | -0.14 | **-0.27**$^{*}$ |
| Lack of support from ….. | | | | |
| Immediate family | 0.01 | 0.00 | **-0.20**$^{**}$ | **-0.24**$^{**}$ |
| Social security services | -0.12 | -0.07 | **-0.21**$^{*}$ | -0.07 |
| Health services | 0.09 | -0.05 | 0.09 | -0.07 |
| $R^2$ | 0.70 | 0.30 | 0.38 | 0.43 |
| $\Delta R^{2\,\#}$ | 0.46 | 0.23 | 0.34 | 0.36 |
| F | 17.94$^{***}$ | 3.33$^{***}$ | 4.76$^{***}$ | 5.86$^{***}$ |
| F Change$^{\#}$ | 16.60$^{***}$ | 3.58$^{***}$ | 5.99$^{***}$ | 6.86$^{***}$ |

* =p<.05; **=p<.01; ***=p<.001. **In bold:** statistically significant ß values.
$^{\#}$ = compares Model 2 (disabilities) vs. Model 1 (patient characteristics)

- ‘Impairments in Excretion and Reproductive Functions’ (impairments in defecation functions, urination functions, and sexual functions) was an important predictor in the ‘Social Relations’ QoL domain
- ‘Lack of support from Immediate Family’ and ‘Lack of support from Social Security Services’ showed significant contributions in the ‘Social Relationships’ QoL domain
- ‘Lack of support from Immediate Family’ showed a significant contribution in the ‘Environment’ QoL domain.

## Discussion

This study examined the prevalence, severity and impact of a broad range of disease-related disabilities on QoL in a large sample of NMD patients. The study’s most important finding is that disease-related disabilities have a strong and independent impact on all aspects of health-

related QoL. Although 'Impairments in Muscle Functions' was the most severe disability with the highest prevalence in all diagnosis-based subgroups, the 'Impairments in Mental Functions and Pain' was the most important predictor of health-related QoL, followed by 'Restrictions in Participation in Life Situations'.

Our finding that 'Impairments in Mental Functions and Pain' was an important predictor for QoL confirms previous studies.[4,21] The same applies to 'Restrictions in Participation in Life Situations'.[7,8]

Our finding that the most prevalent and severe disability 'Impairments in Muscle Functions' was not a strong predictor for QoL is also interesting. In contrast, the strongest predictor, 'Impairment in Mental Functions and Pain' that yielded relatively little impairment. Other studies also reported this phenomenon.[22,23] Graham et al.[4] reviewed the literature on how disabilities in Muscle Disorders affects QoL and noted this phenomenon. Awareness of this phenomenon can help support professionals aiming to improve patients' QoL.

We found no differences in QoL between diagnosis-based subgroups, which indicates the relatively minor contribution that medical diagnosis make to predicting QoL. We found that disease-related disabilities are important indicators of QoL. These findings underline the importance of attention to the broad spectrum of consequences of NMDs.

The positive impact of increased 'Impairments in Seeing Functions' on perceived QoL in the 'Bodily Pain' domain (SF-36), which means that worsening sight has a relatively small but positive impact on a patient's experienced pain, was an unexpected finding. Given the number of relationships under investigation, this could be a chance finding, but on the other hand, worsening sight could causes a decrease in activity and thereby a decrease in experienced activity-related muscle pain. A comparable unexpected finding is the relatively small positive impact of increased 'Impairments in Movement Functions' on quality of Environmental aspects (WHOQoL-bref). This can probably be explained by the beneficial

effects of adaptations in the environment and the use of assist devices such as mobility scooters.

We also found that the impact of disabilities on QoL was dependent on the QoL measurement instrument used. For example, when using the WHOQoL-bref, we found that limitations in activities did not affect one of the four domains of QoL. However, when using the SF-36, these limitations did affect QoL in the 'Physical Functioning' and 'Role Emotional' domains. Conversely, we found that environmental aspects had no impact on QoL when using the SF-36, while 'Lack of support from Immediate Family or Social Security Services' affected one or two of the four WHOQoL-bref domains. This finding indicates that QoL continues to be an evolving concept, which should be borne in mind when choosing a QoL measurement instrument and interpreting results.



We examined our expectation of differences in disability prevalence and severity between the peripheral nerve disorders subgroups. We found differences in 'impairments in Mental Functions and Pain' (difference of proportion test $p<0.01$, Mann Whitney U-test, $p=0.013$) and 'impairments in Excretion and Reproductive Functions' (difference of proportion test $p<0.01$, Mann Whitney U-test, $p=0.007$). The prevalence and severity of pain, and impairments in reproductive functions were higher in the primary sensor group, probably because the autonomous nervous system is more involved compared to the motor sensor group.

We did not expect a prevalence of more than 50% for 'impairments of Swallowing and Speech Functions' in our muscle group, but it should be realized that swallowing is a complex process not only comprising pharyngeal sphincters but also facial, lingual and chewing muscles. Self-evidently swallowing is an important factor for patients' prognosis and QOL.[24,25]

Our study might be limited concerning the representativeness for the population of NMD patients, because all patients in our study are adults and from the northeast part of the Netherlands.

Our study has some important strengths. First is the fact that we examined the impact on QoL of a broad range of disease-related disabilities, separately and in relation to each other, while most studies examined only one or some disabilities in one or some NMDs. As a result, this study offers a unique insight into the consequences of NMD. Second, this study examined the consequences of a large sample of NMDs representing all acknowledged diagnosis-based subgroups and not just one disease or a few diseases as is usually the case. Combined with our finding that it is the disease-related disabilities rather than the medical diagnosis which are relevant to predicting QoL, our findings are relevant to a broad population and could have important implications for the treatment of patients with chronic diseases such as NMD. Insight into the prevalence, severity and relative impact of a large number of disease-related disabilities could contribute to medical and non-medical support of NMD patients. Furthermore, if the focus of support is shifted from medical diagnoses to disabilities, the professionals who support patients with a chronic disease might exchange knowledge and experiences, or could integrate their activities. This 'joining forces' could contribute to the QoL of the chronically ill.

Conclusions: Although impairment of muscle function is the most prevalent and severe disability, impairment of mental function and pain have the greatest impact on QoL of NMD patients.

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**Ethical approval**

Ethical approval was obtained from the local ethics committee, the Medical Ethical Committee of the University Medical Center Groningen. Reference: METc 2009.310. Informed consent was obtained from all participants.

**Declaration of interest**

The authors report no declarations of interest.

**Supplementary Table S1**: Neuromuscular disorder subgroups and Diagnosis

| Motor-neuron disorders (n=62) | | Muscle disorders (n=155) | | Junction disorders (n= 177) | | Peripheral nerve disorders Primary motor (n=71) | | Peripheral nerve disorders Primary sensor (n=197) | |
|---|---|---|---|---|---|---|---|---|---|
| Diagnosis | n (%) | Diagnosis | n (%) | Diagnosis | n (%) | Diagnosis | n (%) | Diagnosis | n (%) |
| Amyotrophic lateral sclerosis | 23 (37) | Becker's muscular dystrophy | 14 (9) | Myasthenia Gravis | 171 (97) | Hereditary Motor and Sensory Neuropathy | 30 (42) | Distal symmetric polyneuropathy | 197 (100) |
| Progressive spinal muscular atrophy | 6 (10) | Duchenne muscular dystrophy | 4 (3) | Lambert-Eaton myasthenic syndrome | 6 (3) | Chronic inflammatory demyelinating polyneuropathy | 18 (25) | | |
| Primary lateral sclerosis | 3 (5) | Emery-Dreifuss muscular dystrophy | 1 (<1) | | | Guillain-Barré syndrome | 18 (25) | | |
| Spinal muscular atrophy | 20 (39) | Limb girdle muscular dystrophy | 20 (13) | | | Multi focal motor neuropathy | 3 (4) | | |
| Bulbospinal muscular atrophy | 1 (<1) | Desminopathy | 3 (2) | | | Hereditary neuropathy with liability to pressure palsies | 2 (3) | | |
| Focal motor neuron disease | 3 (5) | Facioscapulohumeral dystrophy | 27 (17) | | | | | | |
| Poliomyelitis | 1 (<1) | Oculopharyngeal muscular dystrophy | 7 (5) | | | | | | |
| Post-Polio Syndrome | 5 (8) | Myotonic dystrophy | 30 (19) | | | | | | |
| | | Inclusion body myositis | 6 (4) | | | | | | |
| | | Myositis | 8 (5) | | | | | | |
| | | Mitochondrial myopathy | 8 (5) | | | | | | |
| | | Proximal myotonic myopathy | 2 (1) | | | | | | |
| | | Myopathy, other | 17 (11) | | | | | | |
| | | Pompe disease | 3 (2) | | | | | | |
| | | Central Core Disease | 4 (3) | | | | | | |
| | | Hereditary spastic paraplegia | 1 (<1) | | | | | | |

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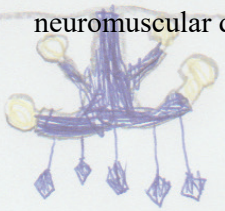
# 6

## The Extremity Function Index (EFI), a disability severity measure for neuromuscular diseases: psychometric evaluation



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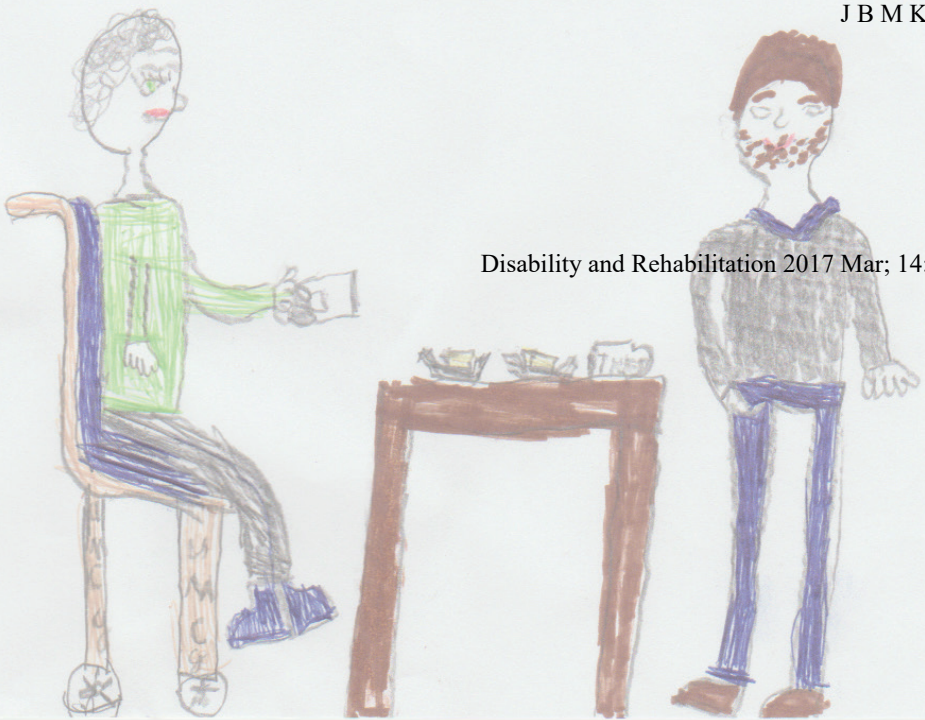

Disability and Rehabilitation 2017 Mar; 14:1-8

## Abstract

**Objective:** To adapt and to combine the self-report Upper Extremity Functional Index and Lower Extremity Function Scale, for the assessment of disability-severity in patients with a neuromuscular disease and to examine its psychometric properties in order to make it suitable for indicating disease-severity in neuromuscular diseases.

**Design**: A cross-sectional postal-survey study was performed among patients diagnosed with a neuromuscular disease.

**Methods**: Patients completed both adapted extremity function scales, questionnaires for psychometric evaluation, and disease-specific questions. Confirmatory factor analysis was performed, and reliability and validity were examined.

**Results**: Response rate was 70% (n=702). The Extremity Function Index model with a two-factor structure – for upper and lower extremities – showed an acceptable fit. The Extremity Function Index-scales showed good internal consistency (alphas: 0.97-0.98). The known-groups validity test confirmed that Extremity Function Index scales discriminate between categories of 'Extent of limitations' and 'Quality of Life'. Convergent and divergent validity tests confirmed that Extremity Function Index scales measure the physical impact of neuromuscular diseases. Relative Validity tests showed that the Extremity Function Index scales performed well in discriminating between subgroups of patients with increasing 'Extent of limitations' compared to concurrent measurement instruments.

**Conclusion**: The Extremity Function Index proved to be a sound and easy to apply self-report disability-severity measurement instrument in neuromuscular diseases.

**Key words**: disability; disability-severity; disease-severity; neuromuscular disease; psychometric evaluation; extremity function; questionnaire; activities; extent of limitations; upper extremity functioning; lower extremity functioning.

## Introduction

Neuromuscular diseases (NMDs) generally lead to progressive impairment in body functions and therefore have a profound impact on physical and psychosocial life, with loss of mobility as one of the main problems.[1, 2] Research into therapeutic approaches to neuromuscular disorders has progressed rapidly over the past decade and shows great promise for the future.[3] Therefore easy to apply and psychometrically sound assessment tools for evaluating disease-severity or impairments in body functions, are of growing importance.



Currently, the evaluation of disease-severity in NMDs is mainly achieved by assessing muscle power functioning using electromyography, measuring muscle strength using handheld dynamometry or by manual muscle tests. However, such tests can be experienced as harmful and time consuming, and do not reflect the subject's functional abilities.[4] In addition, there are observation-based measurements for NMD -as for example the Motor Function Measure scale[4], and the disease-specific Muscular Dystrophy Functional Rating Scale[5] but these measurements require patient exercise, a physiotherapy room and trained investigators. In order to overcome these disadvantages, self-report measuring instruments were developed, for example the disease specific Amyotrophic Lateral Sclerosis Functional Rating Scale[6, 7], measuring instruments administered by trained evaluators such as the Muscular Dystrophy Functional Rating Scale[5], and a measurement of activity limitations the ACTIVLIM[8], a combination questionnaire for children and adults. However, some of these instruments are disease specific, evaluator dependent or limited in feasibility. Also generic health related quality of life (QoL) measurements – the SF-36, for example – are used to measure the impact of disabilities on QoL.[2] Unfortunately, these generic measurements do not have specific items relevant for patients with a NMD, and therefore lacking sensitivity to change, while some of these items will be redundant when applied to NMDs.[1]

A well-known and commonly used disability-severity score, in clinical practice often used as indicator for disease-severity, is the Expanded Disability Scale (EDSS) developed for patients with Multiple Sclerosis[9]. This disability-severity score is based on limitations in mobility. The biggest advantages of the self-report version of the EDSS are that: 1) it is an easy instrument to administer in clinical practice and research, and 2) it expresses disability-severity in terms of a number, so that a change in disability-severity can easily be evaluated.[10] For these reasons we opted for limitations in mobility as a starting point for the development of a disability-severity measurement in NMDs that can serve as an indicator for disease-severity. This seems to be appropriate as it is known that muscle function related limitations in activities in NMDs are regarded as indicators of disease-severity.[11, 12]

In summary, a valid and reliable, easy to apply, self-report disability-severity measurement instrument for adults, reflecting the functioning of muscles in the upper and lower extremities involved in activities of daily living covering NMDs is not available yet. Therefore, the aim of this study was to adapt and to combine two validated self-report questionnaires, the Upper Extremity Functional Index[13] (UEFI) and the Lower Extremity Functional Scale[14](LEFS) as a disability severity measurement instrument in NMDs.

## Patients and Methods

### Sample

A cross-sectional postal-survey study was conducted among patients diagnosed with an NMD (n=1003). These patients were registered at the Department of Neurology of the University Medical Center Groningen, the Netherlands. The sample comprised patients from the four major NMD groups according to Rowland: motor neuron disorders, muscle disorders, junction disorders, and peripheral nerve disorders.[15] Patients were included if they could be assigned to one of these four NMD groups. Furthermore, patients also had to be aged 18 years or older, be able to read and write in Dutch, and able to provide informed consent.



### Procedure

Patients received information about the study and were invited to participate. Patient's informed consent was achieved by returning the completed questionnaire. Respondents completed both (adjusted) extremity function scales, questionnaires for psychometric evaluation, and answered demographic and disease specific questions. Reminders were sent after two weeks. After the questionnaires had been returned, they were checked for completeness. If a page had not been completed, a copy was returned with a request to complete the missing questions or, if this only concerned one or a few questions, patients were interviewed by telephone.

The Medical Ethical Committee of the University Medical Center of Groningen has assessed the study proposal and concluded that approval was not required (Reference METc 2009.310).

**Extremity Functioning Index**

The self-report Upper Extremity Functional Index (UEFI) and Lower Extremity Functional Scale (LEFS) were used as a basis for the disability-severity measure, the Extremity Functioning Index. Both scales were developed and validated for easy assessment of (limitations in) functioning. Each scale consists of twenty items assessing functional problems. Items were scored on a 5-point scale with discrete responses ranging from 0 (extremely difficult or unable to perform activity) to 4 (no difficulty). Items for both scales were summed for a total score ranging from 0 to 80 points, with higher scores representing higher levels of functioning. In previous studies both scales showed good internal consistency (Cronbach's alphas: 0.90[16] and 0.96[14] for the LEFS, and 0.95[13] for the UEFI), and stability (ICCs: 0.88[17] and 0.97[18] for the LEFS, and 0.85[19] for the UEFI).

For the purpose of this study the LEFS and the UEFI were translated into Dutch following the procedure proposed by Guillemin and colleagues.[20] First, the original Canadian English version was translated into Dutch by three researchers (IB, KvdB and HB) who have a working command of Dutch and English at academic level and who worked independently of each other. Secondly, the most satisfactory translation was chosen by consensus among the researchers. Thirdly, this Dutch translation was translated back into English by a native English speaker. Finally, the resulting English version was compared to the original English version, and all discrepancies were discussed by the three researchers. Any remaining discrepancies were discussed with the native English speaker.

The translated version of the LEFS and UEFI was reviewed by three medical specialists in NMDs (JBMK, GD and IB) and a methodologist (BM) on clarity, applicability and patient burden. As a result, six questions in the LEFS were adjusted for reasons of applicability in NMD-patients concerning disease specific limitations to walking distance (questions 11 and 12), sitting time (question 14), running (questions 16 and 17) and hopping (question 19).

These questions were adjusted to shorter distances (questions 11 and 12), shorter duration (question 14), walking (questions 16 and 17) and jumping (question 19). Because of these disease specific adjustments we have renamed the LEFS into the Lower Extremity Functional Index (LEFI). Next, the feasibility of the UEFI and LEFI was examined by pre-testing in a sample of twenty randomly selected NMD-patients. No barriers or unclear and ambiguous items were found. For the UEFI, the LEFI and the combination of both scales, the EFI, item scores were transformed for both subscales (score range from 0 to 80) and the total scale (score range from 0 to 160) into index scales with scores ranging from 0 (not difficult) to 100 (extremely difficult).



**Measurement instruments**

To examine the psychometric properties of the EFI the following measurement instruments were applied:

The Neuromuscular Disease Impact Profile (NMDIP), a broad and generic ICF-based disease impact measurement instrument that includes 36 items and consists of eight scales and four additional items.[21] The 36 items represent the four ICF components. For the Body Functions component items and for the Participation component items scoring options ranged from 0 (no disability) to 4 (complete disability); for the Activities component items scoring options ranged from 0 (no disability) to 3 (complete disability); and for the Environmental Factors component items scoring options ranged from 0 (no support) to 2 (full support). Item scores were summed into a scale, with higher scores indicating more disability. In a previous study among Dutch NMD patients, the NMDIP domains showed satisfactory levels of internal consistency: Cronbach's alpha ranged from 0.63 to 0.92 and Mean Inter-item Correlation Coefficient from 0.47 to 0.77.[21]

The Medical Outcome Study 36-item Short Form Health Survey (SF-36) is a broad and generic Health Related Quality Of Life (HRQoL) measurement and consists of 36 items divided over eight domains.[22] For each domain, item scores were coded, summed, and transformed on a scale from 0 (worst health) to 100 (best health). In a previous study among Dutch multiple sclerosis patients, the SF-36 domains showed satisfactory levels of internal consistency: Cronbach's alpha ranged from 0.81 to 0.94.[21]

The Groningen Activity Restriction Survey (GARS) is a domain-specific instrument for measuring Limitation in activities and consists of 18 items divided over two scales.[23] A four-category response format was used, ranging from 1 (no problem in performing without help) to 4 (impossible to perform). Scores were summed for each subscale. The GARS showed strong levels of internal consistency in a study among Dutch NMD patients: Cronbach's alphas were 0.93 and 0.95.[21]

**Single item variables**

The first variable 'Extent of Limitations' was evaluated with the Extent of Limitations Visual Analogue Scale (VAS)[24] Respondents were asked to answer the question: 'To what extent are you limited due to your NMD?' Scoring options ranged from 0 (no limitation at all) to 10 (most severely limited). The second variable 'Quality of Life' (QoL) was adapted from the WHOQOL-bref.[25] Respondents were asked to answer the question: 'How would you rate your quality of life?' Response options were: 1=very poor, 2=poor, 3=neither poor nor good, 4=good and 5=very good.

**Analysis**

Descriptive statistics were used for describing the patient characteristics.

To construct the EFI, we hypothesized a two-factor model in which extremity functioning is measured within domains for upper extremity functioning (using items from the UEFI)[13] and lower extremity functioning (using items from the LEFI).[14] Before testing the two-factor model the data were examined for the presence of univariate (standardized scores: $|z| \geq 3.30$) and multivariate outliers (Mahalanobis Distance: $p < 0.001$).[26, 27] Next, to test the two-factor model a confirmatory factor analysis (CFA) was conducted using M-Plus 7.1.[28] The CFA methods used in this software are suitable for not normally distributed ordinal items, and are based on polychoric correlations between standardized observed ordinal items.[29] Factor loadings of > 0.40 were considered sufficient.[30] Model fit was examined using multiple criteria: 1) as a measure of overall fit, the root means squared error of approximation (RMSEA): ≤ 0.05 indicate a close fit, whereas values up to 0.08 indicate an adequate fit; and 2) as descriptive measures: a Comparative Fit Index (CFI) ≥ 0.95 and a Tucker-Lewis Index (TLI) ≥ 0.95 indicate an adequate fit.[31] To merge the two domains into one disability-severity measurement, a strong correlation as expected (Spearman's correlation coefficient ≥ 0.70). For scale construction, the maximum number of missing items allowed to be replaced by the mean scale score was determined by a sufficient Cronbach's alpha in relation to the number of scale items.[32]

Next the EFI scale features were examined. The internal consistency was examined using Cronbach's alpha. Alpha was considered sufficient if ≥ .70.[33, 34] The distribution of scale scores was evaluated by calculating the median, mean, standard deviation, and the observed score range. Floor and ceiling effects were examined by calculating the proportions of patients with worst and best possible scores. Proportions ≤ 20% were considered acceptable.[35]

For examining psychometric properties the Kruskal-Wallis test and the Mann-Whitney U test were used for not normally distributed variables (Shapiro-Wilk test, $p < 0.05$).

Regarding known-groups validity[36, 37] we hypothesized that the EFI scales should discriminate between respondent subgroups known to differ on relevant clinical characteristics. The variables 'Extent of Limitations' and 'Quality of Life' were used to create such relevant respondent subgroups. Respondents were divided into two groups of 'Extend of Limitations': those with a lower 'Extent of Limitations' (score 0-4) and those with a higher 'Extent of Limitations' (score 5-10). Respondents were divided into two groups of 'Quality of Life': those with a poor Quality of Life' (response options 1-3) and those with good Quality of Life (response options 4-5).

Convergent and divergent validity was performed by examining the extent to which correlation values between EFI scales and concurrent measures were consistent with hypotheses. The Spearman rank order correlation coefficient (Rho, *p,* 2-tailed) was calculated between the EFI scales and concurrent scales. To support convergent validity, the EFI scales needed to have strong correlations ($\geq 0.70$), with scales covering the same domain in concurrent measurements (physical functioning scale and activity scales).[38] To support the divergent validity, the EFI scales should correlate weakly ($\leq 0.40$) with scales covering different domains (mental health scale) in concurrent measurements.[38]

Relative Validity (RV) indicates the extent to which a scale or construct is able to discriminate between groups compared to the concurrent measures.[22, 39] Respondents were divided into four groups of 'Extent of Limitations': Group A with a 'No to low extent of limitation' (score 0-4), Group B with a 'moderate extent of limitation' (score 5-6), Group C with a 'high extent of limitation' (score 7-8) and, Group D with a 'very high extent of limitation' (score 9-10). Next, RV of scales was examined in several steps. First, the Chi-square was computed for each scale by calculating the Kruskal-Wallis H-test. Second, the RV of each scale was computed by dividing each H-ratio by the H-ratio for the scale with the highest H-ratio, and multiplied by one hundred.

To estimate the magnitude of the clinical relevance of statistically significant group differences the nonparametric effect size (coefficient *r*) for unrelated samples was calculated.[38] The coefficient *r* was calculated by dividing the Z-statistic (obtained from the Mann-Whitney U test) by the root of the sample size (n). To interpret these nonparametric effect sizes, Cohen suggests the following thresholds for interpretation: $r < 0.10$ indicates a trivial effect; $r \geq 0.10$ to $< 0.24$ a small effect; $r \geq 0.24$ to $< 0.37$ a moderate effect; and $r \geq 0.37$ a large effect. An $r \geq 0.10$ reflects a clinically relevant difference between groups.[38, 40]



Statistical analyses were performed using SPSS 23.0 for Windows and CFA was performed using M-Plus 7.1.

## Results

### Patient characteristics

In sum, 702 patients (70% response rate) completed the questionnaires. The participants' demographic and disease specific characteristics are described in table 1. Mean age of participants was 59 years (SD=15,7), the mean number of years since diagnosis was 12 years, and about 30 percent of the respondents had retired due to an NMD. The motor neuron disorder group was relatively small compared to the other NMD subgroups (Rowland classification).

Non-respondents did not differ from respondents in terms of gender but were statistically significant younger (*p*-value: 0.000, 2-sided*)* than respondents.

### Extremity Function index (EFI) structure

CFA confirmed the expected two-factor model with good loadings (Table 2). Each observed aspect in terms of use of lower or upper extremities, loaded sufficiently on the expected factor. Model fit indicators were sufficient with RMSEA 0.086 (90% confidence interval:

0.084 - 0.089), CFI 0.96, and TLI 0.96, and confirmed a good fit of the two-factor model using the Upper Extremity Functional Index (UEFI) and the Lower Extremity Functional Index (LEFI). As expected, the correlation between the UEFI and LEFI was strong (0.87), such that both functioning domains can be merged into one disability-severity measure.

**Table 1** Sample characteristics (n = 702)

| *Variable* | *Total sample* |
|---|---|
| *Gender* (%) | |
| Female | 350 (50.1) |
| *Age* | |
| Median | 61 |
| IQR | 21 |
| Mean (SD) | 58.9 (15.7) |
| Range | 19-92 |
| *Year since diagnosis* | |
| Median | 7 |
| IQR | 11 |
| Mean (SD) | 11.6 (11.0) |
| Range | 0-65 |
| *Relationship status (%)* | |
| Married/partnership | 497 (70.8) |
| Unmarried/widowed/divorced | 186 (26.5) |
| Missing | 19 (2.7) |
| *Educational level (%)* | |
| Primary school/vocational training | 235 (33) |
| Secondary school/vocational training | 270 (38) |
| Higher education /vocational training | 161 (23) |
| University | 28 (4) |
| *Employment status (more answers possible) (%)* | |
| Enrolled in a training program or educational course | 36 (5.1) |
| Employment (part-time or full-time) | 173 (24.6) |
| Voluntary work (part-time or full-time) | 42 (6.0) |
| (Partially) retired due to NMD | 213 (30.3) |
| Housewife/househusband | 171 (24.4) |
| Retired due to age | 243 (34.6) |
| *NMD category (%)* | |
| Motor neuron disorder | 43 (6.1) |
| Muscle disorder | 154 (22.1) |
| Junction disorder | 234 (33.3) |
| Peripheral nerve disorder | 271 (38.5) |

IQR=Inter Quartile Range (Q3-Q1)

**Table 2** Factor loadings of the Extremity Function Index (EFI) model

| | *Upper Extremity Function Index* | *Factor* |
|---|---|---|
| 1 | Any of the activities involved in your usual work, housework, or schoolwork | 0.860 |
| 2 | Your usual hobbies, and recreational or sporting activities | 0.766 |
| 3 | Lifting a bag of groceries to waist level | 0.928 |
| 4 | Lifting a bag of groceries above your head | 0.900 |
| 5 | Grooming your hair | 0.829 |
| 6 | Pushing up on your hands (e.g., from bathtub or chair) | 0.855 |
| 7 | Preparing food (e.g., peeling, cutting) | 0.861 |
| 8 | Driving | 0.755 |
| 9 | Vacuuming, sweeping, or raking | 0.920 |
| 10 | Dressing | 0.915 |
| 11 | Buttoning your clothing | 0.839 |
| 12 | Using tools or appliances | 0.871 |
| 13 | Opening doors | 0.867 |
| 14 | Cleaning | 0.919 |
| 15 | Tying or lacing shoes | 0.883 |
| 16 | Sleeping | 0.494 |
| 17 | Laundering clothes (e.g., washing, ironing, folding) | 0.884 |
| 18 | Opening a jar | 0.810 |
| 19 | Throwing a ball | 0.846 |
| 20 | Carrying a small suitcase (with your affected limb) | 0.889 |

| | *Lower Extremity Function Index* | *Factor* |
|---|---|---|
| 1 | Any of the activities involved in your usual work, housework, or schoolwork | 0.897 |
| 2 | Your usual hobbies, and recreational or sporting activities | 0.809 |
| 3 | Getting into or out of the bathtub | 0.889 |
| 4 | Walking between rooms | 0.924 |
| 5 | Putting on your shoes or socks | 0.894 |
| 6 | Squatting | 0.886 |
| 7 | Lifting an object, like a bag of groceries from the floor | 0.914 |
| 8 | Performing light activities around your home | 0.928 |
| 9 | Performing intensive activities around your home | 0.927 |
| 10 | Getting into or out of a car | 0.873 |
| 11 | Walking 10 yards | 0.924 |
| 12 | Walking 200 yards | 0.897 |
| 13 | Going up or down 10 stairs (about 1 flight of stairs) | 0.897 |
| 14 | Standing for 1 hour | 0.859 |
| 15 | Sitting for 1 hour | 0.623 |
| 16 | Running on even ground | 0.886 |
| 17 | Running on uneven ground | 0.905 |
| 18 | Making sharp turns while running fast | 0.933 |
| 19 | Jumping | 0.943 |
| 20 | Rolling over in bed | 0.828 |

**Scale features**

Table 3 shows the scale features for the Extremity Function Index (EFI) total scale and EFI subscales for the total sample and for the four major NMD groups. Internal consistency for the EFI and both of the subscales was good. Cronbach's alphas ranged from 0.97 to 0.98. No negative floor and ceiling effects were found.

The final version of the EFI scale consists of two subscales each with twenty items, and also a total scale score can be calculated. (See appendix),

**Table 3** Scale features of the EFI total scale and subscales UEFI and LEFI (n=702)

| *Sample* and Scales | Cases (n) | Items (k) | Possible score range | Observed score range | Floor effect (%) | Ceiling effect (%) | Median | IQR | Mean | SD | Alpha |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *Total* | | | | | | | | | | | |
| EFI | 702 | 40 | 0-160 | 0-159 | 5.6 | 0.0 | 37 | 41 | 37.8 | 25.8 | 0.98 |
| UEFI | 701 | 20 | 0-80 | 0-79 | 9.1 | 0.0 | 31 | 42 | 33.9 | 25.7 | 0.97 |
| LEFI | 700 | 20 | 0-80 | 0-80 | 8.4 | 0.6 | 41 | 48 | 41.7 | 28.2 | 0.97 |
| *Motor neuron disorder* | | | | | | | | | | | |
| EFI | 43 | 40 | 0-160 | 0-158 | 2.3 | 0.0 | 54 | 49 | 55.1 | 28.2 | 0.98 |
| UEFI | 43 | 20 | 0-80 | 0-79 | 2.3 | 0.0 | 49 | 47 | 52.4 | 27.9 | 0.97 |
| LEFI | 43 | 20 | 0-80 | 0-80 | 4.7 | 4.7 | 61 | 50 | 57.4 | 32.1 | 0.98 |
| *Muscle disorder* | | | | | | | | | | | |
| EFI | 155 | 40 | 0-160 | 0-159 | 1.3 | 0.0 | 49 | 67 | 50.8 | 25.7 | 0.98 |
| UEFI | 154 | 20 | 0-80 | 0-79 | 3.2 | 0.0 | 44 | 40 | 46.1 | 26.4 | 0.97 |
| LEFI | 153 | 20 | 0-80 | 0-80 | 1.9 | 1.3 | 56 | 42 | 55.6 | 27.4 | 0.97 |
| *Junction disorder* | | | | | | | | | | | |
| EFI | 234 | 40 | 0-160 | 0-143 | 11.5 | 0.0 | 23 | 37 | 26.9 | 22.4 | 0.98 |
| UEFI | 234 | 20 | 0-80 | 0-72 | 14.1 | 0.0 | 25 | 36 | 26.8 | 22.3 | 0.96 |
| LEFI | 234 | 20 | 0-80 | 0-71 | 17.1 | 0.0 | 23 | 40 | 27.0 | 24.1 | 0.97 |
| *Peripheral nerve disorder* | | | | | | | | | | | |
| EFI | 270 | 40 | 0-160 | 0-152 | 3.7 | 0.0 | 36 | 37 | 37.1 | 23.3 | 0.98 |
| UEFI | 270 | 20 | 0-80 | 0-76 | 9.3 | 0.0 | 27 | 40 | 30.2 | 23.9 | 0.96 |
| LEFI | 270 | 20 | 0-80 | 0-76 | 5.2 | 0.0 | 44 | 38 | 44.0 | 25.2 | 0.97 |

EFI=Extremity Function Index; UEFI=Upper Extremity Functional Index; LEFI =Lower Extremity Functional Index; IQR=Inter Quartile Range (Q3-Q1); SD=Standard Deviation.

**Known-groups validity**

The known-groups validity of the EFI scales was confirmed by the expected group differences (Table 4). Patients classified as having greater 'Extent of Limitations' or higher 'Quality of Life' had significantly higher scores on the EFI scales compared with those classified as having lower 'Extent of Limitations' or lower reported 'Quality of Life'. Effect sizes were very large for 'Extent of Limitations' and moderate for 'Quality of Life' and confirmed clinical relevance.



**Table 4** Known groups validity of the Extremity Function Index (n=702)

| | Low (0-4) versus High (5-10) Extent of Limitations | | | | | Poor (1-3) versus Good (4-5) Quality of Life | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N Low/High | Low Mean Rank | High Mean Rank | p-value (Z-statistic)* | Effect Size | N Low/High | Poor Mean Rank | Good Mean Rank | p-value (Z-statistic)* | Effect Size |
| *Extremity Function Index* | 278/424 | 216.4 | 440.1 | 0.000 (-14.3) | 0.54 | 228/474 | 453.8 | 302.3 | 0.000 (-9.3) | 0.35 |
| Lower Extremity Function Index | 278/422 | 215.3 | 439.6 | 0.000 (-14.4) | 0.54 | 228/472 | 443.1 | 305.8 | 0.000 (-8.4) | 0.32 |
| Upper Extremity Function Index | 278/423 | 230.5 | 430.3 | 0.000 (-12.8) | 0.48 | 228/473 | 453.1 | 301.8 | 0.000 (-9.3) | 0.35 |

*Mann-Whitney U test, 2-sided.

**Convergent and divergent validity**

Table 5 summarizes our findings on the convergent and divergent test of EFI scales. The direction, strength and pattern of correlations are as hypothesized. We found the expected high correlations for most of the similar constructs (bold figures in the table) confirming convergent validity. Unexpected was the moderate correlation with the NMDIP 'Muscle Functions' variable. We found the expected low correlations (italic figures in the table) supporting divergent validity. Unexpected were the moderate correlations with the NMDIP 'Mental Functions and Pain' variable.

**Table 5** Results of convergent and divergent validity of EFI total and subscales (n=702).

| | EFI[#] | UEFI[#] | LEFI[#] |
|---|---|---|---|
| *NMDIP* | | | |
| Muscle Functions | **0.73** | **0.63** | **0.74** |
| Movement Functions | 0.59 | 0.50 | 0.59 |
| Swallowing and Speech Functions | 0.31 | 0.35 | 0.25 |
| Excretion and reproductive Functions | 0.46 | 0.44 | 0.42 |
| Mental Functions and Pain | *0.58* | *0.56* | *0.53* |
| Activities of Moving around | **0.82** | **0.69** | **0.86** |
| Self-care and Domestic Activities | **0.85** | **0.83** | **0.80** |
| Participation in Life Situations | 0.64 | 0.56 | 0.64 |
| *SF-36* | | | |
| Physical functioning | **-0.89** | **-0.76** | **-0.92** |
| Social Functioning | -0.53 | -0.52 | -0.49 |
| Role Physical | -0.51 | -0.49 | -0.47 |
| Bodily Pain | -0.48 | -0.44 | -0.48 |
| General Health | -0.58 | -0.55 | -0.53 |
| Mental health | *-0.29* | *-0.32* | *-0.25* |
| Role Emotional | *-0.32* | *-0.33* | *-0.28* |
| Vitality | -0.49 | -0.52 | -0.42 |
| *GARS* | | | |
| Instrumental activities of daily living | **0.89** | **0.83** | **0.86** |
| Activities of daily living | **0.86** | **0.77** | **0.87** |

[#]=Spearman rank order correlation coefficient, all correlations are significant at the 0.01 level (2-tailed); EFI=Extremity Function Index; UEFI=Upper Extremity Functional Index; LEFI =Lower Extremity Functional Index; NMDIP= Neuromuscular Disease Impact Profile; SF-36= Medical Outcome Study Short Form Questionnaire; GARS=Groningen Activity Restriction Scale.
Expected convergent validity scores (higher correlations >.70) in bold and expected divergent validity scores (lower correlations <.40) in italic. Relative Validity (RV)

About 40% (n=278) of the respondents reported 'low extent of limitations' (Group A) due to NMD, while 24% (n=169) reported a 'moderate extent of limitation' (Group B), and 28% (n=197) reported a 'high extent of limitation' (Group C). About 8% (n=58) of the respondents reported a 'very high extent of limitations' (Group D).

Comparisons of the RV coefficients, as summarized in table 6, revealed that the EFI 'Lower Extremity Function Index' subscale and the Extremity Function Index total scale were the most valid in discriminating between groups with an increasing 'Extent of Limitation'.

We then examined the performance of the EFI in indicating the differences between extreme groups (A-D) and subgroups (A-B, B-C, C-D) regarding the physical functioning construct, as it relates to the similar constructs in the concurrent measurement instruments.

**Table 6** Relative validity (RV) of the EFI, disease specific, domain specific and generic measurement instruments compared, using subgroups of Extent of Limitations (n=702)

| | Group A No to Low Extent of Limitations (score 0-4) | | Group B Moderate Extent of Limitations (score 5-6) | | Group C High Extent of Limitations (score 7-8) | | Group D Very high Extent of Limitations (score 9-10) | | Chi Square | RV | A-B | B-C | C-D | A-D |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | Median (IQR) | N | Median (IQR) | N | Median (IQR) | N | Median (IQR) | | | | | | |
| *Extremity Function Index (EFI)* | 278 | 16 (28) | 169 | 39 (28) | 197 | 51 (29) | 58 | 79 (30) | 258.0 | 96 | 0.43 | 0.23 | 0.42 | 0.59 |
| Lower Extremity Function Index (LEFI) | 278 | 18 (33) | 167 | 44 (31) | 197 | 59 (34) | 58 | 84 (26) | 268.8 | 100 | 0.41 | 0.26 | 0.45 | 0.61 |
| Upper Extremity Function Index (UEFI) | 278 | 14 (27) | 168 | 38 (31) | 197 | 44 (34) | 58 | 74 (43) | 201.5 | 75 | 0.39 | 0.17 | 0.36 | 0.54 |
| *NMDIP* | | | | | | | | | | | | | | |
| Muscle Functions | 249 | 25 (26) | 161 | 50 (25) | 192 | 50 (25) | 56 | 75 (37) | 244.6 | 91 | 0.40 | 0.26 | 0.43 | 0.63 |
| Movement Functions | 235 | 8 (17) | 140 | 17 (25) | 170 | 25 (16) | 49 | 42 (29) | 141.2 | 53 | 0.29 | 0.20 | 0.29 | 0.51 |
| Swallowing and Speech Functions | 270 | 0 (0) | 156 | 0 (13) | 188 | 0 (25) | 55 | 13 (25) | 57.3 | 21 | 0.22 | - | 0.18 | 0.37 |
| Excretion and reproductive Functions | 206 | 0 (17) | 120 | 8 (25) | 140 | 17 (31) | 43 | 25 (25) | 55.5 | 21 | 0.20 | - | - | 0.37 |
| Mental Functions and Pain | 237 | 10 (15) | 137 | 20 (20) | 173 | 30 (25) | 50 | 33 (25) | 135.7 | 50 | 0.29 | 0.23 | 0.19 | 0.47 |
| Activities of Moving around | 278 | 6 (17) | 169 | 17 (22) | 197 | 22 (28) | 58 | 56 (34) | 216.3 | 80 | 0.37 | 0.22 | 0.40 | 0.58 |
| Self-Care and Domestic Activities | 277 | 4 (4) | 169 | 17 (21) | 197 | 29 (45) | 58 | 75 (67) | 254.6 | 95 | 0.41 | 0.25 | 0.40 | 0.61 |
| Participation in Life Situations | 276 | 0 (8) | 168 | 8 (17) | 196 | 17 (33) | 55 | 33 (33) | 189.1 | 70 | 0.26 | 0.29 | 0.28 | 0.60 |
| *SF-36* | | | | | | | | | | | | | | |
| Physical Functioning | 277 | 25 (9) | 169 | 19 (8) | 197 | 16 (8) | 58 | 11 (3) | 254.7 | 95 | 0.39 | 0.26 | 0.44 | 0.61 |
| Social Functioning | 278 | 9 (2) | 169 | 8 (2) | 196 | 7 (1) | 58 | 6 (4) | 130.6 | 49 | 0.27 | 0.19 | 0.21 | 0.43 |
| Role Physical | 278 | 8 (3) | 168 | 5 (4) | 196 | 5 (2) | 57 | 4 (2) | 112.1 | 42 | 0.30 | - | - | 0.41 |
| Emotional Functioning | 278 | 6 (1) | 167 | 6 (2) | 196 | 6 (2) | 57 | 4 (3) | 33.0 | 12 | 0.18 | - | 0.16 | 0.28 |
| Mental Functioning | 278 | 25 (4) | 169 | 24 (5) | 196 | 24 (4) | 58 | 22 (7) | 32.4 | 12 | 0.13 | - | 0.16 | 0.27 |
| Vitality | 278 | 17 (6) | 169 | 15 (5) | 196 | 14 (5) | 58 | 11 (6) | 101.4 | 38 | 0.25 | 0.13 | 0.23 | 0.41 |
| General Health | 278 | 17 (6) | 169 | 14 (5) | 196 | 12 (5) | 58 | 10 (5) | 169.7 | 63 | 0.35 | 0.22 | 0.20 | 0.48 |
| Bodily Pain | 278 | 55 (16) | 169 | 44 (17) | 197 | 39 (20) | 58 | 33 (22) | 91.5 | 34 | 0.23 | 0.16 | 0.18 | 0.39 |
| *GARS* | | | | | | | | | | | | | | |
| Activities of Daily Living | 278 | 11 (4) | 169 | 15 (7) | 197 | 18 (10) | 58 | 27 (17) | 213.3 | 79 | 0.37 | 0.21 | 0.40 | 0.60 |
| Instrumental Activities of Daily Living | 277 | 8 (5) | 169 | 13 (8) | 195 | 16 (8) | 58 | 24 (9) | 225.8 | 83 | 0.40 | 0.17 | 0.40 | 0.60 |

NMDIP = Neuromuscular Disease Impact Profile; SF-36 = Medical Outcome study Short Form Questionnaire; GARS = Groningen Activity Restriction Scale. EFI, NMDIP and GARS scales: higher scores=worse health; SF-36 higher scores = better health; IQR=Inter Quartile Range (Q3-Q1). - = not statistically significant.

Regarding physical functioning, we found that the NMDIP 'Muscle Functions' performed slightly better compared to the 'Lower Extremity Function Index'. Subgroup differences (A-B, B-C and C-D) were statistically significant and clinically relevant for all EFI scales.

In summary, the EFI scales showed one small, and furthermore large effect sizes in discriminating between (sub) groups with an increasing 'Extent of Limitations' compared to similar physical functioning constructs in concurrent measures.

## Discussion

The Extremity Function Index (EFI) appears to be a valid and reliable instrument for evaluating disability-severity in adult patients with an NMD. The confirmed model for the EFI included a two-factor structure with two one-dimensional scales with twenty indicators in the upper extremity function domain and twenty indicators in the lower extremity function domain. The reliability of the EFI and both subscales was good. Known-groups validity was supported by statistically significant and clinically relevant differences between groups of patients with a NMD that differed in terms of 'Extent of Limitations' and 'Quality of Life'. Expectations regarding the direction and strengths of the convergent and divergent correlations were confirmed for most correlations. Unexpected was the moderate correlation with the 'Muscle Functions' variable. Apparently loss of muscle strength is more obvious in lower extremity function than in upper extremity function. Also unexpected were the moderate correlations with the NMDIP 'Mental Functions and Pain' variable. Probably the aspect of pain in this variable caused this stronger correlation with the EFI (sub)scales than expected. Finally, compared to concurrent domain specific and generic QOL measurement instruments the EFI performed well in discriminating between groups of NMD patients with an increasing 'Extent of Limitations' as indicated on the visual analogue scale.

A major strength of this study lies in the large and representative study population representing the four major NMD groups according to Rowland[15], which improves the

generalizability of the study results. As such the EFI may be considered applicable to the broad range of NMD patients that are encountered in clinical practice

A possible study limitation should be noted: the relatively small sample size of the motor neuron disorder group compared to the sample size of the other NMD groups. However, the complete study sample showed good representation of functional limitations in NMDs in terms of the use of upper and lower extremities in daily activities.

The EFI can have important implications for multidisciplinary care, research and for patients. Clinicians now have an easy to apply and patient-friendly disability-severity measurement instrument to evaluate the differences in disability-severity between relevant subgroups of NMD-patients. These differences can be seen as an indicator for the ability of this measurement instrument for detecting changes in disability over time. Researchers also can compare disability-severity between groups of NMD-patients. EFI could also have implications for patient self-management. For instance, EFI can offer patients a voice in making future decisions about assistive equipment and environmental adjustments.



Further research should focus on examining the relationship between objective and subjective disease-severity, psychometric evaluation concerning stability and sensitivity to change of the EFI, and validation across other populations of neuromuscular disease patients in other cultures.

In conclusion, this study showed that the Extremity Function Index (EFI) appears to be a reliable and valid disability-severity measurement instrument for NMDs. Moreover, the measure is an easy to apply and patient-friendly instrument for clinical practice, and can also support clinical trials and epidemiological studies.

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**Supplementary material**

## The 40-item Extremity Function Index

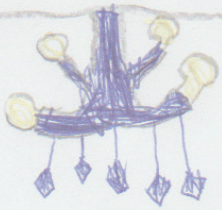
Response options
0 = not difficult
1 = slightly difficult
2 = moderately difficult
3 = quite difficult
4 = extremely difficult or impossible

| Upper Extremity Function Index (UEFI)<br>We are interested in whether the upper-limb problem for which you are seeking help is causing you any difficulty with the activities listed below. Please indicate how difficult each of the following activities is or would be for you today: | |
|---|---|
| 1 | Any of the activities involved in your usual work, housework, or schoolwork |
| 2 | Your usual hobbies, recreational or sporting activities |
| 3 | Lifting a bag of groceries to waist level |
| 4 | Lifting a bag of groceries above your head |
| 5 | Grooming your hair |
| 6 | Pushing up on your hands (e.g., from a bathtub or chair) |
| 7 | Preparing food (e.g., peeling, cutting) |
| 8 | Driving |
| 9 | Vacuuming, sweeping, or raking |
| 10 | Dressing |
| 11 | Buttoning your clothing |
| 12 | Using tools or appliances |
| 13 | Opening doors |
| 14 | Cleaning |
| 15 | Tying or lacing shoes |
| 16 | Sleeping |
| 17 | Laundering clothes (e.g., washing, ironing, folding) |
| 18 | Opening a jar |
| 19 | Throwing a ball |
| 20 | Carrying a small suitcase (with your affected limb) |

| Lower Extremity Function Index (LEFI)<br>We are interested in whether the lower-limb problem for which you are seeking help is causing you any difficulty with the activities listed below. Please indicate how difficult each of the following activities is or would be for you today: | |
|---|---|
| 1 | Any of the activities involved in your usual work, housework, or schoolwork |
| 2 | Your usual hobbies, recreational or sporting activities |
| 3 | Getting into or out of the bathtub |
| 4 | Walking between rooms |
| 5 | Putting on your shoes or socks |
| 6 | Squatting |
| 7 | Lifting an object (e.g., a bag of groceries) from the floor |
| 8 | Performing light activities around your home |
| 9 | Performing heavy activities around your home |
| 10 | Getting into or out of a car |
| 11 | Walking 10 yards |
| 12 | Walking 200 yards |
| 13 | Going up or down 10 steps (about 1 flight of stairs) |
| 14 | Standing for 10 minutes |
| 15 | Sitting for 1 hour |
| 16 | Walking on even ground |
| 17 | Walking on uneven ground |
| 18 | Making sharp turns while walking quickly |
| 19 | Jumping |
| 20 | Rolling over in bed |

# 7

# Experienced stigmatization reduced quality of life of patients with a neuromuscular disease: a cross-sectional study



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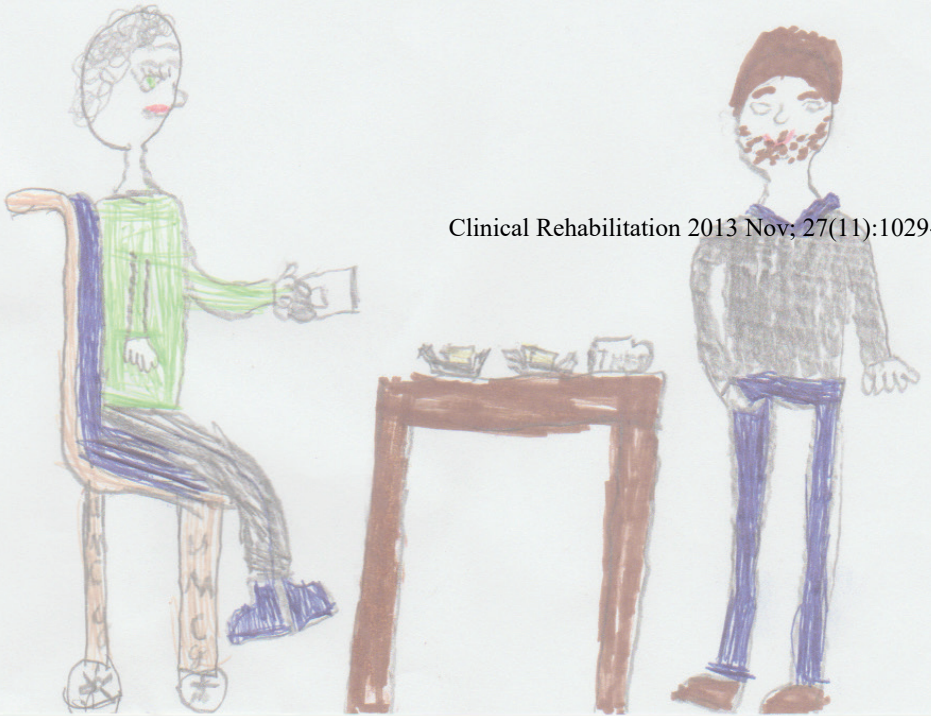

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## Abstract

**Background**: To examine the influence of stigma on the quality of life of patients with a neuromuscular disease.

**Design**: Cross-sectional postal survey.

**Setting**: Outpatient clinic of the Department of Neurology, University Hospital Groningen, the Netherlands.

**Subjects**: Patients diagnosed with a neuromuscular disease.

**Measures**: The Stigma Scale for Chronic Illness, the World Health Organization Quality of Life – abbreviated version questionnaires and some background and disease-related questions. The Stigma Scale for Chronic Illness was translated into Dutch according to international guidelines. The impact of stigma on quality of life was estimated using hierarchical multiple regression analysis after controlling for the extent of limitations and patient characteristics.

**Results**: In total 235 patients (75% response rate) were diagnosed with neuromuscular disease and represented all four categories of the approximately 600 neuromuscular diseases. Most patients (86%) reported self-stigma, while 64% reported to experience enacted stigma. Experienced quality of life was moderate to good. Stigma contributed to a unique and substantial extent to all domains of quality of life: explained variance for the impact of stigma on quality ranged from 0.13 (social relations) to 0.34 (physical functioning) for self-stigma and from 0.09 (social relations) to 0.11 (physical and psychological health, and quality of the environment).

**Conclusion**: Self stigma was a stronger predictor for poorer quality of life compared with enacted stigma. In other words: patients suffered more from shame and fear for discrimination (self-stigma) than from the really experienced discrimination and exclusion (enacted stigma).

## Keywords

Stigma, neuromuscular diseases, quality of life

## Introduction

Goffman (1963) was the first to define stigma as 'an undesired differentness'.[1] Since then, many scientists have studied stigma.[2–5] A recent and broad definition of stigma came from Scambler:4 'Stigma is typically a social process, experienced or anticipated, characterized by exclusion, rejection, blame or devaluation that results from experience, perception or reasonable anticipation of an adverse social judgement about a person or group'.

Health-related stigma is typically characterized by social disqualification of individuals and populations who are identified with particular health problems.[5] For better understanding stigma in (chronic) diseases, Scambler and Hopkins introduced a recognizable and generally accepted distinction between 'felt' and 'enacted' stigma.[6,7] In this dichotomy, enacted stigma refers to actually experiencing discrimination or exclusion, whereas felt stigma refers to shame of being deviant and the feeling that discrimination or exclusion will happen.[7–9] Van Brakel3 identified similarities in the perceived consequences of health-related stigma across diseases such as social avoidance, concealment of the condition, marital problems, shame and embarrassment, and reduced employment opportunities.

Experiences and negative feelings related to stigma are likely to increase psychological distress such as depression[7,10] and to decrease wellbeing and quality of life. Various studies reported a negative influence of stigma on the quality of life of patients with different kinds of chronic diseases, such as irritable bowel syndrome,[11] epilepsy,[12] mental illnesses[13,14] and hepatitis.[15]

Neuromuscular diseases comprises chronic neurological disorders that affect any part of the nerve and muscle with impact on sensation or movement.[16] There are approximately 600 neuromuscular diagnoses that can be classified in four major categories: motor neuron disorders, for example amyotrophic lateral sclerosis (ALS); muscle disorders, for example Duchenne muscular dystrophy; junction disorders, for example myasthenia gravis; and peripheral nerve disorders, for example Polyneuropathy.[17] Many of these neuromuscular

diseases have a genetic basis, are progressive and incurable.[16,18] Patients with a neuromuscular disease can have difficulties with speech or writing, can be wheelchair dependent or may need assistance with activities of daily living.[19]

Quality of life of neuromuscular disease patients has great potential to become negatively affected by the combination of a chronic and often progressive disease, and it seems plausible that stigma is a relevant variable in explaining quality of life of patients with a neuromuscular disease. We think that these patients can be at risk for stigmatization because of the eventually developed limitations, and dependency from assistance devices. However, the prevalence of stigma, and consequently the impact of stigma on quality of life among patients with a neuromuscular disease are, to our opinion, not investigated.

Therefore, the objective of this study was to examine the prevalence and seriousness of stigma in patients with a neuromuscular disease, and the effect of stigma on quality of life. We controlled for the extent of limitations when analysing the impact of stigma on quality of life, as it is known that the extent of limitations has a negative impact on quality of life.

## Methods

A cross-sectional postal survey was carried out among a sample of patients diagnosed with a neuromuscular disease (n = 315) attending the Department of Neurology of the University Hospital in Groningen, the Netherlands. The sample comprised patients from the four major neuromuscular disease categories, namely: motor neuron disorders, muscle disorders, junction disorders and peripheral nerve disorders. In total, 235 patients (75% response rate) completed the questionnaire.

Patients were included if they, according to the pre-specified clinical disease characteristics, without any doubt could be assigned to one of these four neuromuscular disease categories. After inclusion, patients received a mailed questionnaire. After the questionnaires were returned, they were checked for completeness. If a page had not been filled in, a copy was sent with a request to complete the questions or, if it concerned one or only a few questions, patients were interviewed by telephone.

Ethical approval was obtained from the local ethics committee.



## Measures

Patient characteristics, including age, gender, marital status, educational level and employment status were derived from patients' questionnaires. For application of the ordinal variables marital status, educational level and employment status in the regression analyses, they were dichotomized to (so-called) dummy variables.

Clinical variables, such as neuromuscular diagnosis of the patient's neuromuscular disease, were retrieved from medical records. For determining the disease severity, patients were asked to appraise their extent of limitations with the question "To what extent are you limited due to your neuromuscular disease?" on a visual analogue scale ranging from 0 (not limited at all) to 10 (severely limited).[20]

Subjective quality of life was assessed using the World Health Organization Quality of Life (WHOQOL) - BREF.[21] The WHOQOL-BREF consists of 26 items divided into four domains covering: physical health (for example ‘‘How well are you able to get around?’’), psychological health (for example ‘‘How much do you enjoy life?’’), social relations (for example ‘‘How satisfied are you with your personal relationships?’’) and environmental aspects (for example ‘‘How satisfied are you with your access to health services?’’) and two generic single-item questions (not considered in the scoring). For each scale, item scores were coded, summed and transformed to a scale ranging from 0 (worst health) to 20 (best health). In a previous Dutch study the WHOQOL-BREF showed satisfactory levels of internal consistency: Cronbach’s alpha ranged between 0.63 and 0.81.[20]

The Stigma Scale for Chronic Illness is a recently developed generic stigmatization measure in chronic neurological diseases.[22] The Stigma Scale for Chronic Illness consists of 24 items that can be examined as one overall stigma scale or as two subscales: one scale for enacted stigma and one for self or internalized stigma. The enacted-stigma scale measures the experienced discrimination or exclusion, and consists of 11 items (for example “Because of my illness, some people avoided me”). The self-stigma scale measures shame and the fear for discrimination or exclusion, and consists of 13 items (for example “Because of my illness, I felt embarrassed in social situations”). Response options range between 0 (never) and 4 (always). For each scale, item scores were summed and transformed to a scale ranging between 0 and 52 for the self-stigma scale, and between 0 and 40 for the enacted-stigma scale. Higher scores indicate more stigmatization. The American–English language version of the Stigma Scale for Chronic Illness showed satisfactory levels of internal consistency among patients with neurological disorders.[22] Cronbach’s alpha was 0.97 for the overall scale, while both subscales correlated considerably ($r = 0.81$). To avoid a biased estimate of reliability by the number of items, we used no overall stigma scale. For estimating the prevalence of health-

related stigma we assumed that a patient should report at least one symptom of enacted stigma or self-stigma, respectively.

For this study the Stigma Scale for Chronic Illness was translated into the Dutch language following the procedure proposed by Guillemin et al.[23] First, the original American–English version of the questionnaire was translated into Dutch by three researchers who had the command of the Dutch and English languages at academic level, working independently of each other. Second, the most satisfactory translation was chosen in consensus among the researchers. Third, this Dutch translation was translated back into the English language version by a native English speaker. Finally, the resulting American–English version was compared with the original American–English version and all discrepancies were discussed by the three researchers. Remaining discrepancies were discussed with a native English speaker.



## Statistical analysis

First, descriptive statistics were used to examine the patient characteristics, perceived stigma and quality of life scores. Continuous variables of self-stigma, enacted stigma and quality of life domains were not normally distributed (Shapiro-Wilk test, $p < 0.05$). Therefore, differences between the neuromuscular disease categories were analysed using the Kruskal–Wallis test with a post hoc Bonferroni correction to adjust for multiple comparisons with critical level of significance $p = 0.01$ ($p = 0.05/5$).

Reliability of all scales was examined with the internal consistency coefficient Cronbach's alpha and mean interitem correlation coefficient. According to the guidelines of Briggs and Cheek,[24] an mean interitem correlation coefficient of $\geq 0.25$ seems reasonable. For acceptable reliability of the scales we used the following criteria: Cronbach's alpha $\geq 0.70$ and $\leq 0.90$; and mean interitem correlation coefficient $\geq 0.25$.[24,25]

Second, a series of hierarchical regression analyses (the enter method) were employed to examine the impact of stigma on physical health, psychological health, social relations and environmental aspects, yielding standardized regression coefficients (beta). We used three models to explore the effect of stigma: Model 1 tested the crude effect of stigma on physical, psychological, social and environmental quality of life, respectively. Model 2 tested the effect of stigma on the quality of life variables when controlling for the extent of limitations by the neuromuscular disease, and finally in Model 3, patient characteristics (gender, age, marital status, educational level and employment status) were added. Ordinal variables were dichotomized (see Table 1) – for using them as so-called dummy variables – before entering them in the regression analysis: marital status – living without a partner (score 0) and living with a partner (score 1); employment status – employment without payment (score 0) and no employment with payment (score 1); educational level – lower level (score 0) and higher level (score 1).

In order to assume that our conclusions are true for a wider population of neuromuscular patients we tested the following assumptions. First, the risk for multicollinearity between the predictor variables (Type II error) was diagnosed by calculating the variance inflation factor and the tolerance statistic for all predictor variables in the regression model. Estimated beta-coefficients in the regression analysis are inflated when a predictor has a strong linear relationship with the other predictor(s) in case the variance inflation factors exceed four. Moreover, if the average variance inflation factor is substantially greater than one the regression may be biased by multicollinearity. Tolerance estimates below 0.1 (1/variance inflation factor) indicates a serious problem and tolerance estimates below 0.2 are worthy of concern or indicate a potential problem.[26,27] Furthermore (second assumption), the error terms or residuals should be uncorrelated or independent: the lack of autocorrelation was tested with the Durban–Watson test and finally (third assumption) the distribution of residuals should have a normal distribution was tested with the Kolmogorov–Smirnov test.[26,27]

Statistical analyses were performed using Statistical Product and Service Solutions 20 for Windows.

## Results

In sum 235 patients (75% response rate) completed the questionnaire.

Proportions of males and females in the study sample did not differ from the proportions among non-responders (n = 80). Although non-respondents were on average younger (mean age 50 years, SD 18.5) compared with participating patients (mean age 56 years, SD 15.5), this difference was not statistically significant (p = 0.97).



**Table 1** Patient characteristics (n=235)

| **Variable** | Sample |
|---|---|
| **Gender** | |
| Female (%) | 128 (55) |
| Male (%) | 107 (45) |
| **Age** | |
| Mean (SD) | 56 (15) |
| Range | 18–91 |
| **Marital status** (%) | |
| Married / partner(ship) | 173 (74) |
| Unmarried / widowed / divorced | 62 (26) |
| **Educational level** (highest level) (%) | |
| Primary or secondary school / vocational training | 178 (76) |
| Higher professional education / university | 57 (24) |
| **Employment status (%)** | |
| Employment for payment | 71 (30) |
| No employment for payment | 164 (70) |
| **Neuromuscular disease category** (%) | |
| Motor neuron disorder | 22 (9) |
| Muscle disorder | 91 (39) |
| Junction disorder | 84 (36) |
| Peripheral nerve disorder | 38 (16) |
| **Extent of limitations (0-10)*** | |
| Mean (SD) | 5.3 (2.5) |

* A higher score indicates a higher extent of limitations

All participating patients were diagnosed in one of the four neuromuscular disease categories (Table 1). Most patients had a muscle disorder or a junction disorder. Respondents

reported to be moderately limited owing to their neuromuscular disease. There were more women than men ($p = 0.09$). The average age was 56 years (SD 15.5) while 72% was younger than 65 years. About one-third of the respondents were retired owing to the disease, and about one-third was employed for payment. About three-quarters had a lower or secondary educational or vocational level.

Reliability of the quality of life and stigma scales was good. Cronbach's alpha for the WHOQOL-BREF scales ranged between 0.70 and 0.81, while the homogeneity of the scales was confirmed by the mean interitem correlation coefficients that ranged between 0.35 and 0.50. Cronbach's alpha for the self-stigma scale was 0.91 and for the enacted-stigma scale 0.89. Mean interitem correlation coefficients were 0.41 (self-stigma) and 0.45 (enacted stigma). Scale scores for both stigma scales were moderately correlated (Spearman's correlation coefficient: $Rho = 0.63$, $p < 0.01$), and explained variance ($R^2$) was 0.40 indicating that these scales measured related but distinct constructs.

Most respondents reported to experience self-stigma while two-thirds of the patients reported to experience enacted stigma. There were no differences between the neuromuscular disease categories when it comes to self-stigma (not in table); however patients with a peripheral nerve disorder experienced a lower level of enacted stigma than patients with muscle disorders (not in table: $p > 0.01$ Kruskal–Wallis post hoc analysis with Bonferroni correction).

Patients reported moderate to good levels of quality of life (Table 2), while there were no differences between neuromuscular disease categories (not in table).

**Table 2** Stigma and quality of life (n=235)

| Variable | Sample |
|---|---|
| **Stigma*** | |
| Self-stigma (0-52) | |
| Prevalence (> 0) (%) | 203 (86) |
| Mean (SD)** | 9.7 (8.0) |
| Enacted stigma (0-40) | |
| Prevalence (> 0) (%) | 155 (64) |
| Mean (SD)** | 4.5 (5.7) |
| **Quality of Life*** (0-20) mean (SD) | |
| Physical health | 13.6 (2.9) |
| Psychological health | 14.9 (2.4) |
| Social relations | 15.3 (2.6) |
| Environment | 15.6 (2.4) |

* a higher score indicates more stigma or better QOL, **Score among all respondents.



In analysing the impact of self-stigma and enacted stigma, indices of variance inflation factor were all close to 1.0 with an average variance inflation factor values that ranged from 1.08 to 1.09 and from 1.13 to 1.14 for the enacted-stigma and self-stigma models, respectively. As all variance inflation factor values were close to 1.0 and consequently, tolerance statistics (1/variance inflation factor value) were close to 1.0 as well and were not below the critical value of 0.2. Furthermore, in each of the four regression analysis the Durbin–Watson test was close to 2.0, and varied from 2.056 to 2.147 and from 1.996 to 2.055 for enacted and self-stigma, respectively. All residuals were tested against the normal distribution and each Kolmogorov–Smirnov test was non-significant indicating that the deviation from the normal distribution were owing to random variation (in other words: it is probably normal).

The results of the regression analysis to determine the effect of stigma on health-related quality of life are presented in Tables 3 and 4. Self-stigma, as well as enacted stigma, contributed to a unique segment of the variance for all quality of life domains. The standardized β weights were in the expected direction, meaning that patients who reported more stigmatization experienced less quality of life.

**Table 3** Impact of self-stigma on WHOQOL-BREF variables: hierarchical multiple regression analysis (n = 235).

| | Physical health β | Psychological health β | Social relations β | Environment β |
|---|---|---|---|---|
| **Model 1** | | | | |
| Self-stigma | –0.59*** | –0.55*** | –0.36*** | –0.50*** |
| *ssmc* | *** | *** | *** | *** |
| *R2* | *0.34* | *0.30* | *0.13* | *0.25* |
| **Model 2** | | | | |
| Self-stigma | –0.49*** | –0.56*** | –0.37*** | –0.44*** |
| Extent of limitations | –0.24*** | 0.04 | 0.03 | –0.16** |
| *ssmc* | *** | *ns* | *ns* | ** |
| *R2* | *0.40* | *0.30* | *0.13* | *0.27* |
| *ΔR2* | *0.05* | *0.001* | *0.001* | *0.02* |
| **Model 3** | | | | |
| Self-stigma | –0.56*** | –0.60*** | –0.46*** | –0.46*** |
| Extent of limitations | –0.22*** | 0.06 | –0.07 | –0.15* |
| Gender | –0.00 | 0.04 | 0.14* | –0.05 |
| Age | –0.25*** | –0.10 | –0.18* | –0.13* |
| Marital status | 0.04 | 0.06 | 0.18** | 0.08 |
| Educational level | 0.05 | 0.11 | 0.04 | 0.16** |
| Employment status | 0.04 | 0.04 | 0.02 | 0.02 |
| *ssmc* | *** | *ns* | ** | ** |
| *R2* | *0.46* | *0.33* | *0.21* | *0.32* |
| *ΔR2* | *0.07* | *0.03* | *0.08* | *0.05* |

*p < 0.05; **p < 0.01; ***p < 0.001.
ssmc: statistical significance of model change for the added variables.

Adjusting the impact of stigma for potential confounders (Models 2 and 3) did not affect the impact of stigma on the quality of psychological health. The impact of stigma on the quality of physical health was weakened when adjusted for the influence of extent of limitations and age, and (only for enacted stigma) gender. The impact of stigma on the quality of social relations was weakened by age, but strengthened by marital status (self-stigma) and gender (self-stigma).The impact of stigma on the quality of the environment was weakened by gender and strengthened by educational level.

**Table 4** Impact of enacted stigma on WHOQOL-BREF variables: hierarchical multiple regression analysis ($n$ = 235).

| | Physical health β | Psychological health β | Social relations β | Environment β |
|---|---|---|---|---|
| **Model 1** | | | | |
| Enacted-stigma | –0.34*** | –0.32*** | –0.30*** | –0.33*** |
| *ssmc* | *** | *** | *** | *** |
| *R2* | *0.11* | *0.11* | *0.09* | *0.11* |
| **Model 2** | | | | |
| Enacted-stigma | –0.252*** | –0.30*** | –0.29*** | –0.27*** |
| Extent of limitations | –0.35*** | –0.08 | –0.05 | –0.26*** |
| *ssmc* | *** | *ns* | *ns* | *** |
| *R2* | *0.23* | *0.11* | *0.10* | *0.18* |
| *ΔR2* | *0.12* | *0.01* | *0.002* | *0.07* |
| **Model 3** | | | | |
| Enacted-stigma | –0.31*** | –0.32*** | –0.33*** | –0.30*** |
| Extent of limitations | –0.34*** | –0.07 | –0.04 | –0.26*** |
| Gender | –0.13* | –0.08 | 0.07 | –0.13* |
| Age | –0.23*** | –0.08 | –0.16* | –0.12 |
| Marital Status | –0.02 | –0.01 | 0.12 | 0.03 |
| Educational level | 0.01 | 0.05 | 0.00 | 0.13* |
| Employment status | 0.06 | 0.06 | 0.03 | 0.04 |
| *ssmc* | ** | *ns* | *ns* | * |
| *R2* | *0.30* | *0.13* | *0.13* | *0.23* |
| *ΔR2* | *0.07* | *0.02* | *0.04* | *0.05* |

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.
ssmc: statistical significance of model change for the added variables.

## Discussion

In this study, the prevalence and impact of stigma on quality of life was examined among patients with a neuromuscular disease and represented the four categories of the approximately 600 neuromuscular diseases. The most important finding is that both self-stigma and enacted stigma have strong and independent associations with physical, psychological, social and environmental quality of life, both crude and after adjustment for the extent of limitation and patient characteristic variables. In other words, this study gives evidence that patients suffering from a neuromuscular disease who experienced stronger feelings of being stigmatized reported poorer quality of life. Furthermore, the patterns of

impact of self-stigma and enacted stigma on domains of quality of life, and the influence of confounding variables were similar (Tables 3 and 4).

We found evidence that self-stigma was a stronger predictor in all domains of quality of life compared with enacted stigma, meaning that neuromuscular disease patients suffered more from shame and their fear for discrimination, than from the really experienced discrimination and exclusion. As the saying goes 'people suffer most by the suffering that is feared'. We also found that the extent of limitations, which can be seen as a risk for stigma, had no impact on perceived quality of psychological health and quality social relations. This means that self-stigma, or the fear for discrimination and exclusion, was a stronger predictor of these quality of life variables than the actual risk for stigma, the extent of limitations, is. Thus, taking these findings into account, the conclusion could be that fear for stigma is a more important issue for health care professionals than (the risk for) actual discrimination is.

We also may conclude that the outcomes from the regression analyses were not biased by multicollinearity, correlated residuals or non-normally distributed errors and we assume that our conclusions are likely to be true for a wider population of patients with a neuromuscular disease.

As expected, the prevalence and severity of self-stigma was higher than of enacted stigma. Scambler and Hopkins6 also reported that about 90% of the epilepsy patients admitted to experience felt stigma that is closely related to self-stigma, while only a third of these patients could recall ever having encountered enacted stigma. Rao et al.,[22] who examined stigma among a sample of 511 patients with different chronic neurological disorders, found considerably higher stigma scores (total score range: 0–92, mean 42.2, SD 19.7) compared with results in our sample (mean 14.0, SD 12.4). An explanation could be found in the difference in the composition of the samples. The sample in the study of Rao et al.[22] mainly consisted of stroke (38%) and epilepsy (33%) patients. Maybe the consequences of these diseases are more pronounced and visible than in neuromuscular diseases. Another tempting

explanation could be found in cultural differences between the more individualistic oriented culture in the United States of America and the generally more social-oriented culture in the Netherlands.

Most of the respondents in our study perceived a good quality of life. Comparable results were found among people in the general population: the WHOQOL-group found relatively similar mean scores in 23 countries.[28] Probably the impact of a neuromuscular disease on the perceived quality of life is negligible. The same could be said for other chronic conditions because comparable findings for quality of life were also found among Multiple Sclerosis patients[29] and Sickle Cell disease patients,[30] while patients with HIV infection perceived a moderate quality of life.[31]



There are some possible limitations in our study. First, our sample is a convenience sample based on the patients attending the university hospital in the northeast part of the Netherlands. Therefore our sample might be limited concerning the representativeness for the population of neuromuscular disease patients. Second, there might be questions about the motivation of patients to participate in a study evaluating stigma and its impact on the findings, and therefore threaten the representativeness of the sample. However, this survey was part of a larger study in which a large number of questionnaires was administered, so we think the influence of this possible limitation is trivial. Third, despite our well-considered selection of confounding variables we might have overlooked relevant variables. We considered including stigma and quality of life-related variables like depression,[32] but had to decide against it considering the large number of questionnaires already administered. Finally, a possible, but acceptable, limitation in our study is our choice for a less well known quality of life measure, the WHOQOL-BREF. Therefore, the results concerning quality of life in neuromuscular disease are less comparable than when a well-known measure, such as the SF-36, was used. However, the relative validity of the WHOQOL-BREF seemed better compared with the SF-

36.[33] Furthermore, the WHOQOL-BREF is based on a more recent and broader definition of quality of life[34] than the SF-36 is,[35] including also environmental aspects.

In our opinion, this is the first time that the impact of stigma on health-related quality of life was investigated among patients with a neuromuscular disease. The recently developed Stigma Scale for Chronic Illness performed well within our sample. However, unlike Rao et al.,[22] we found a moderate correlation (Spearman's correlation coefficient: Rho = 0.63, $p < 0.01$) and explained variance ($R^2 = 0.40$) between the two subscales self-stigma and enacted stigma, indicating that these scales measured related but distinct constructs. Probably, the difference between self-stigma and enacted stigma is larger than in patients with stroke or epilepsy. Considering the relative low prevalence and severity of enacted stigma in our study, in combination with the more visible consequences of stroke and epilepsy, it seems reasonable to assume that this difference in findings is owing to the scores on the enacted stigma scale in our study.

Further psychometric evaluation of the Stigma Scale for Chronic Illness will strengthen the validation of this instrument, and comparisons across other neurological and non-neurological conditions will help to evaluate the generalizability of the Stigma Scale for Chronic Illness to other chronic conditions. However, cautiousness is desired in the merging of both subscales to one overall stigma scale. Furthermore, it would be valuable when the sensitivity for change of the Stigma Scale for Chronic Illness is examined, because the effectiveness from many stigma reduction interventions is often not known.[36]

Considering the findings in this study it is appropriate for scientist and healthcare professionals to pay attention to stigma and to apply (preventive) interventions targeted on decreasing the impact of stigma in patients with a neuromuscular disease to improve quality of life. Also, further psychometric evaluation of the Stigma Scale for Chronic Illness is necessary.

Clinical messages

- Patients suffering from a NMD who experienced stronger feelings of being stigmatized reported poorer quality of life.
- Fear for stigma is a more important issue than (the risk for) actual discrimination is.
- The extent of limitations owing to the NMD has no impact on perceived quality of psychological health and quality of social relations.


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# 8

General discussion

The objective of this thesis was to provide insight into the consequences of having an NMD. Therefore the main focus of this thesis was to identify the most relevant NMD-related disabilities, to develop a psychometrically sound measurement instrument based on these disabilities and to evaluate the impact of these disabilities on perceived quality of life. A second objective was to adapt and combine two known extremity functioning scales, so that they can serve as an easy to apply indicator for disease-severity in NMDs. The third objective was to examine the prevalence and severity of stigmatization in persons diagnosed with an NMD and its impact on QoL.

This chapter provides an overview of the main findings, including methodological considerations, and explains implications for practice and research.

## Main findings

Research question 1 (Chapter 2): **What is the content validity of the initial ICF Core Set for NMDs?**

This study examined the content validity of the initial ICF Core Set for NMDs. This initial ICF Core Set was developed for three neurological diseases. Concepts in three established disease-specific health-related QoL questionnaires were linked with ICF categories. Next, these selected ICF categories were linked to the ICF categories in the initial ICF Core Set.

The final ICF Core Set for NMDs is a valid selection of ‘very relevant’ categories, belonging to the four ICF components reflecting a broad range of functioning and disabilities related to NMDs. This ICF Core Set provides a solid basis for the development of a measurement instrument reflecting the most relevant aspects of functioning and health for patients with NMDs.

Research question 2 (Chapter 3 and 4): **How should the prevalence and severity of NMD-related disabilities, using the ICF Core Set for NMDs, be assessed?**

To answer this question we developed the Neuromuscular Disease Impact Profile (NMDIP), a self-report measurement instrument based on the ICF categories in the Core Set for NMD. The NMDIP reflects the disease-related disabilities in adult patients diagnosed with an NMD. We found that the NMDIP has a good fit for an eight-factor model within three ICF components with good reliability (internal reliability within disease-related subgroups and stability over time) and convergent, discriminant and known-groups validity. The NMDIP is sensitive to clinically important differences between the relevant subgroups and performed as well as or better than the concurrent measurement instruments. We may therefore conclude that the NMDIP is a psychometrically sound measurement instrument for the evaluation of a broad range of disease-related disabilities.



Research question 3 (Chapter 5): **What is the impact of a broad range of NMD-related disabilities on QoL?**

To answer this question, we first compared the diagnosis-related subgroups and found no differences in QoL between subgroups. We then performed multiple regression analysis and found that all NMD-related disabilities showed strong and independent associations with all aspects of QoL. 'Impairments in Mental Functions and Pain' was the most important predictor of QoL, followed by 'Restrictions in Participation in Life situations'. Although 'Impairments in Muscle Functions' showed the highest prevalence and severity scores, its impact on QoL was relatively limited.

Research question 4 (Chapter 6): **How should disability severity be assessed when focusing on extremity functioning in patients with an NMD?**

To answer this question we first translated, adapted and combined the self-report Upper Extremity Functional Index and Lower Extremity Function Scale, calling it the Extremity Function Index (EFI). The EFI represents all relevant upper and lower activity items reflecting NMD-related disability-severities in extremity function. We then examined the psychometric properties of the EFI and found good internal consistency, and convergent, divergent and known-groups validity. Relative Validity tests showed that the EFI scales performed well in discriminating between patients subgroups compared to concurrent measurement instruments. We may therefore conclude that the EFI is a sound and easy to apply self-report disability-severity measurement instrument in neuromuscular diseases.

Research question 5 (Chapter 7): **What is the impact of stigma on the QoL of patients with an NMD?**

To answer this question, we first translated the Stigma Scale for Chronic Illness and then examined the impact of stigma on QoL using a hierarchical multiple regression analysis after controlling for the extent of limitation and patient characteristics. Most patients (86%) reported self-stigma, while 64% reported experiencing enacted stigma. Stigma contributed to a unique and substantial extent to all QoL domains. Self-stigma was a stronger predictor for poorer QoL compared to enacted stigma, meaning that patients suffered more from shame and fear of discrimination (self-stigma) than from actually experienced discrimination and exclusion (enacted stigma).

## Reflection on the main findings

The following themes arise from the findings in this thesis. The overall theme was the consequences of having an NMD. This main theme can be specified into three subthemes: 1) measuring the consequences of an NMD, 2) the consequences of an NMD for functioning, and 3) the consequences of an NMD on QoL. These themes will be discussed below.

**Measuring the consequences of an NMD on functioning**

The main challenge in this study was to develop disease-specific measurement instruments to evaluate the consequences for functioning for all NMDs. We succeeded in developing two such instruments. The two instruments share ease of administration as self-report disability-severity measurement instruments, and differ in terms of goals, scope and use.



The NMDIP was primarily developed for organizing person-centred care and support for persons diagnosed with an NMD. Therefore, the International Classification for Functioning and Health (ICF) was chosen as the basis for developing the questionnaire. Furthermore, NMD patients and their representatives were given a lot of influence in the selection of relevant categories from the ICF. As a result, The NMDIP is a measurement instrument for assessing of a broad spectrum of specific consequences of NMDs on human functioning, representing categories from the ICF components ‘Body Functions’, ‘Activities and Participation’ and ‘Environmental Factors’. The EFI was primarily developed as a disability-severity measure capable of indicating disease severity. Therefore, two valid and reliable extremity function measurement instruments were translated into Dutch and adapted for people with an NMD to assess their daily activities, reflecting upper and lower extremity muscle function. As a result, the EFI is an instrument for the measurement of the specific consequences of NMDs for a broad spectrum of upper and lower extremity muscle function.

We also translated an instrument for the measurement of the prevalence and severity of stigma, the Stigma Scale for Chronic Illness. Stigma among NMD patients and the impact

of stigma on QoL are relevant but were not investigated. As a result, the two subscales of the translated Stigma Scale for Chronic Illness showed good internal consistency and performed well within our sample.

**The NMDIP reflects disease-specific characteristics of NMDs**

We were also able to demonstrate that the NMDIP reflects disease-specific characteristics by comparing results on disease-specific disabilities between NMDs and Multiple Sclerosis. We found differences between the two diseases, which underlines the strength of both measurement instruments, the NMDIP and the Multiple Sclerosis Impact Profile (MSIP).[1] The same ICF Core Set was used as the basis for the development of both measurement instruments, but we had to add the 'Endurance function' ICF category to improve the validity of the ICF Core Set for NMDs (Chapter 2). 'Endurance function' is strongly related to 'Muscle weakness' which is a characteristic aspect of NMDs. Two important differences between diseases became clear during the scale construction for the NMDIP (Chapter 3) and the MSIP.[1] First, the categories for 'Muscle Functions' and 'Movement Functions' were related within MS and formed a single scale, but the two categories were not related within the NMDs and formed separate scales. This could be because of the strong relationship between muscle endurance and muscle strength within NMDs, based on the etiological difference with MS: NMDs mainly cause muscle weakness, while MS is primarily a neurological disease. We also found a strong relationship between the disabilities Pain and Fatigue (Chapter 3) within NMDs, while this relationship was not found in MS. This can be explained by the fact that pain and fatigue are the direct result of having and using weakened muscles, which is a common symptom in NMDs. Unlike with NMDs, fatigue in MS is most likely connected to the process of inflammation, while pain originates from spasticity and/or neuropathy. Finally, scale construction (Chapter 3) also identified a construct which was not

present in the MSIP: 'Swallowing and Speech Functions'. This can be explained by the fact that some myopathies and myasthenias tend to affect bulbar musculature.

**The consequences of NMD on functioning**

We succeeded in obtaining unique insight into the prevalence and severity of a broad range of NMD-related disabilities covering a large sample of NMDs. These findings underlined the multidimensionality of the health-related problems related to having an NMD. We also found evidence of the differences in severity of disease-related disabilities among NMD subgroups. To the best of our knowledge, this is the first time that such an insight was obtained.

The most prevalent disability reported in the overall sample was 'impairments in muscle functions', followed by 'limitations in activities of moving around' and 'impairments in mental functions and pain' (Chapter 5). The most severe disability in the overall sample was also 'impairments in muscle functions' followed by 'lack of support from social security services' and 'lack of support from health services' and 'limitations in activities of moving around'. Disability severity differed statistically significantly for most disabilities among NMD-subgroups.



We were able to develop a valid and reliable instrument for the measurement of extremity functions and their limitations. We therefore had to translate and adapt two known extremity function measurement instruments to make them suitable for use in NMDs. It was particularly important that the measurement of the lower extremity functions was applicable to the evaluation in NMD patients of disease-specific limitations in terms of the ability to walk a certain distance, sit for a particular length of time, run and hop. These adjustments underline the disease-specific consequences of an NMD.

When comparing outcomes of the two measurement instruments, the NMDIP and the EFI (Chapters 3 and 6), we found that 'loss of muscle strength' is more obvious in lower extremity function than in the upper extremity function in the context of the impact of NMDs.

We also found that the pain aspect had a stronger relationship with extremity function than expected. These findings underline the importance of the combination of the two measurement instruments.

Concerning stigma, we found that most respondents reported experiencing self-stigma, while two-thirds of the patients reported experiencing enacted stigma. There were no differences between the NMD subgroup categories for self-stigma (shame and fear of discrimination). However, patients with a peripheral nerve disorder experienced a lower level of enacted stigma (actually experienced discrimination and exclusion) than patients with muscle disorders. The consequences of peripheral nerve disorders are probably less visible for others than the consequences of muscle disorders. This knowledge is important, as it is also known that stigmata associated with disability and assistive technology (AT) use are integrally related and have the potential to affect AT decision-making processes substantively.[2]

**The consequences of NMDs on QoL**

An important challenge in this thesis was to provide a detailed insight into the consequences of having an NMD on perceived QoL. Although it is known that having an NMD can seriously affect a person's QoL, little is known about the impact of the individual disease-specific disabilities. We succeeded in examining the relative impact of a broad range of NMD-related disabilities and their relative impact on QoL.

Most of the respondents in our study reported having a good quality of life. Comparable results were found in the general population (Chapter 7). Despite this finding, we also found that the disease-related disability variables contributed significantly and considerably to the variance for all QoL domains, meaning that patients who reported more disability experienced less QoL. Our most important finding was that although 'impairments in muscle functions' was the most prevalent and most severe disability in most NMDs,

'impairments in mental functions and pain' and 'restrictions in participation in life situations' showed the most significant impact on QoL (Chapter 5). Of interest in this context is our finding that there are no differences in perceived QoL among NMD subgroups, indicating the relatively small contribution made by the medical diagnosis in predicting QoL (Chapter 5).

Finally, we found that that most patients reported stigma, and that stigma contributed to a unique and substantial extent to all QoL domains. We also found that patients suffered more from shame and fear of discrimination (self-stigma) than from actually experienced discrimination and exclusion (enacted stigma). These findings were also found in epilepsy patients by Jacobi.[3,4]



## Methodological considerations

The main strengths of this study are the large and broad sample of NMD patients obtained, and the carefully selected and applied methods in the various studies. Nevertheless, some possible limitations should also be taken into account.

**Sample**

A major strength of this thesis is the large and varied sample of adult NMD patients used, representing all NMD subgroups – rather than just drawing from patients of only one disease or a few diseases as is usually the case – which improves the generalizability of the study results. The measurement instruments developed and validated in the various studies may be considered applicable to the broad range of NMD patients encountered in clinical practice. Another strength is the classification[5] we used, which offered a valid insight into the broad representation of NMDs in our sample.

A possible limitation is the relatively small sample size of the motor neuron disorder subgroup compared to the sample size of the other NMD subgroups. However, in our opinion the disabilities in this group are sufficiently represented in the NMDIP and EFI, because the

basis of the two instruments covers all the disabilities in this subgroup sufficiently. Another limitation could be the high floor effect of some NMDIP scales, which might affect the reliability of these scales.[6] However, these floor effects match the course of the slowly progressive nature of most NMDs. This means that some disabilities appear years after onset, such as impairments in speech and swallowing functions or limitations in upper extremity function.

**ICF and methods applied**

An important strength in the development of the NMDIP was the application of the ICF alongside strong methodologies. This permitted us to develop a valid and reliable measurement instrument which could provide a detailed insight into a broad spectrum of the impact of NMDs.

We first used the ICF to reach a valid selection of the most important and relevant ICF categories. We therefore validated the initial ICF Core Set, which was meticulously developed in a Delphi study,[6] in which relevant ICF categories were selected by a varied and extensive Delphi panel. It is important to mention the relative great influence of the NMD patients and their representatives in this selection. Second, we applied a proven method to evaluate the content validity of this initial ICF Core Set by linking concepts from established disease-specific measurement instruments, representing three of the four NMD subgroups according to Rowland,[5] to the items in the initial ICF Core Set. Finally, a reliable linking procedure was carried out by experts in NMDs and ICF so that all the relevant expertise was present.

We then used the ICF qualifiers to operationalize the selected ICF categories. These qualifiers were specified for each ICF component to record the presence and severity of a problem in functioning and were applied to each question. The preliminary questionnaire with the operationalized ICF categories was reviewed by experts and a modified questionnaire was

pre-tested with a random sample of clinicians and patients. The questionnaire was then evaluated psychometrically, and rigorous statistical tests were conducted.

## Implications for clinical practice

When used as an assessment tool, the NMDIP may contribute to understanding patients' health problems better, especially in multidisciplinary rehabilitation teams. Clinicians now have a valid and reliable assessment tool to assess a broad spectrum of disease-related disabilities (Chapter 2). The insight into the prevalence, severity and relative impact of a large number of disease-related disabilities could also contribute to medical and non-medical support of NMD patients. Furthermore, by shifting the focus of support from medical diagnoses to disabilities, the professionals who support patients with chronic diseases can exchange knowledge and experiences, or integrate their activities. This jointed up care could contribute to the QoL of the chronically ill.



The EFI could also have important implications for multidisciplinary care and for patients. Clinicians now have an easy to apply and patient-friendly instrument to evaluate changes in disability-severity over time (Chapter 6).

The NMDIP and the EFI could also have implications for patient self-management. For instance, the results of the combination of the two tools could give patients a say in future decisions concerning their healthcare.

**Implications for further research**

Future research could focus on the further psychometric evaluation of the measurement instruments we developed, adapted or translated for application in NMD patients. For example, we recommend further research to evaluate the sensitivity to change of the NMDIP scales. Examining and validating the subjective dimension of the NMDIP (Chapter 3) is also of interest because we learned from the psychometric evaluation of the MSIP[7] (for MS

patients) that the subjective dimension of functioning and health operationalized in disability perception is relevant to explaining QoL.

Further research using the EFI (Chapter 6) should focus on the applicability of this disability-severity measurement instrument. Psychometric evaluation of the EFI's stability and sensitivity to change, and validation across other NMD patient populations in other cultures could further strengthen the quality of the EFI. Finally, researchers could explore how the EFI can be used to compare disability severity between NMD patient groups.

We suggested that both the NMDIP and the EFI could also have clinical implications for patient self-management. Although positive results were found in the feasibility studies with the preliminary NMDIP and the MSIP, we recommend combining this application with research: for example, to investigate the effects on a healthcare plan when using the NMDIP.

Concerning the Stigma Scale for Chronic Illness (Chapter 7), we recommend further psychometric evaluation of this scale to strengthen the validation of this instrument. Comparisons across other neurological and non-neurological conditions will help evaluate the generalizability of the Stigma Scale for Chronic Illness to other chronic conditions. This would also be valuable when examining the sensitivity to change of the Stigma Scale for Chronic Illness because the effectiveness of many stigma reduction interventions is often not known.

## Conclusions

In conclusion, this thesis yielded three easy-to-apply, valid and reliable measurement instruments which are applicable across the range of NMD diagnoses. These measurement instruments offered a broad and unique insight into the consequences of NMD on the functioning of patients, and the impact of these consequences on their perceived QoL.

This insight may have great implications for multidisciplinary care and support for these patients and may give them a say in future decisions concerning their health.

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# Appendix



# Summary

The impact of neuromuscular diseases on functioning and quality of life

Neuromuscular diseases (NMDs) encompass many diseases which impair muscle function, either directly through pathologies of the muscles, or indirectly through pathologies of the nerves or neuromuscular junctions. NMDs are progressive diseases which can cause muscle weakness or spasticity, and increased and increasing need for supportive devices and medical and non-medical support. We developed two self-report instruments to measure disability in NMDs and examined the consequences of NMDs on functioning and quality of life. We also examined the prevalence and severity of stigmatization among NMD patients and the impact on quality of life.

In the introduction in **Chapter 1**, we described the central concepts in this thesis: the pathophysiology and epidemiology of the broad and extensive group of NMDs, and the consequences of NMDs on physical, mental and social functioning. We then introduced the International Classification of Functioning, Disability and Health (ICF) as a suitable classification method for the development of a measurement instrument for the assessment of disease-related functioning and disability. Stigmatization was introduced as a relevant consequence of physical, mental and social disabilities in NMDs. We then described the broad concept of quality of life (QoL) and what is known about the impact of having an NMD on QoL. Finally, we described the characteristics and importance of patient reported outcome measurements (PROMs) and how to examine their psychometric properties.
We concluded with the following research questions:

1 What is the content validity of the initial ICF Core Set for NMDs?

2 How should the prevalence and severity of NMD-related disabilities, using the ICF Core Set for NMDs, be assessed?

3 What is the impact of a broad range of NMD-related disabilities on QoL?

4 How should disability severity be assessed when focusing on extremity functioning in patients with an NMD?

5 What is the impact of stigma on the QoL of patients with an NMD?

In **Chapter 2** we described the validation of the initial ICF Core Set for NMDs. This initial Core Set was originally developed for three neurological diagnoses: Multiple Sclerosis, Parkinson's disease and Neuromuscular diseases. To examine the content validity of this initial ICF Core Set for NMDs, concepts in established and validated NMD quality of life measurement instruments were used. Concepts were linked to relevant ICF categories. Next these categories were compared with the ICF categories in the initial Core Set. The final NMD-ICF Core Set reflects a broad scope of NMD-related problems in functioning. In **Chapter 3** we described the development of the Neuromuscular Disease Impact Profile (NMDIP). The first step was to develop an initial questionnaire based on the NMD-ICF Core Set. The second step was to carry out a cross-sectional postal survey on NMD patients. We then constructed robust scales and examined the psychometric properties of these scales. The final NMDIP consists of 36 items divided into eight scales with satisfactory psychometric properties, and four single items. In **Chapter 4** we examined the stability over time and the Relative Validity of the NMDIP scales. The NMDIP is sensitive to detecting clinically important differences between relevant subgroups, and performed as well as or better than the concurrent measurement instruments.

In **Chapter 5** we reported on the prevalence and severity of a broad range of NMD-related disabilities and the impact of these disabilities on QoL. We found no differences in QoL between diagnosis-based subgroups. 'Impairments in muscle functions' had the highest prevalence and severity scores in the overall sample and diagnosis-based subgroups, while 'impairments in mental functions and pain' was the most important predictor of QoL, followed by 'restrictions in participation in life situations'. In **Chapter 6** we described the

adaptation and combination of two self-report measurement instruments for the assessment of disability-severity in NMD patients and examined the psychometric properties of this measurement instrument. The Extremity Functioning Index (EFI) proved to be a sound and easy to apply self-report disability-severity measurement instrument that was able to detect clinically important differences between relevant disability-severity subgroups.

In **Chapter 7** we reported on the influence of stigma on the QoL of patients with an NMD. We performed a postal survey among NMD patients and found that most patients (86%) reported self-stigma, while 64% reported enacted stigma. Self-stigma was a stronger predictor of poorer QoL compared with enacted stigma. In other words, patients suffered more from shame and fear of discrimination (self-stigma) than from actually experienced discrimination and exclusion (enacted stigma).

In **Chapter 8** we summarized and reflected on the thesis's main findings, including methodological considerations and implications for clinical practice and further research.

The aim of this thesis was to provide insight into the consequences of having an NMD on functioning and QoL. The main challenge in this study was to develop disease-specific measurement instruments for the evaluation of the consequences on functioning for all NMDs. We succeeded in developing two such measurement instruments. The NMDIP was primarily developed for organizing person-centred care and support for persons diagnosed with an NMD. The EFI was primarily developed as a disability-severity measure capable of discerning disease severity. We also translated a measurement instrument for the evaluation of the prevalence and severity of stigmatization, the Stigma Scale for Chronic Illness. We succeeded in providing a unique insight into the prevalence and severity of a broad range of NMD-related disabilities covering the large sample of NMDs. These findings underline the multidimensionality of the problems in functioning as a consequence of an NMD. We also found evidence of the differences in the severity of disease-related disabilities between NMD subgroups. To the best of our knowledge, this is the first time that such insight was obtained.

When comparing outcomes regarding the impact of an NMD on functioning between the two measurement instruments, the NMDIP and EFI, we found that 'loss of muscle strength' is more obvious in lower extremity function than in upper extremity function. We also found that the pain aspect had a stronger relationship with extremity function than expected. These findings underline the importance of the combination of both measurement instruments.

Another important challenge in this thesis was to provide a detailed insight into the consequences of having an NMD on perceived QoL. We succeeded in examining the relative impact of a broad range of NMD-related disabilities and their relative impact on QoL.

The main strength of this study is its large and broad sample of adult NMD patients, representing a large sample of NMDs, and the methods carefully selected and applied in the various studies. An important strength in the development of the NMDIP was the application of the ICF. This offered the opportunity to develop a measurement instrument which could provide a detailed insight into a broad spectrum of consequences of NMDs.

The NMDIP could contribute to a better understanding of patient problems in functioning when used as an assessment tool, especially in multidisciplinary rehabilitation teams. The EFI could also have important implications for clinical care and for patients. Clinicians now have an easy to apply and patient-friendly disability-severity instrument to measure changes in disability-severity over time. Both the NMDIP and the EFI could also have clinical implications for patient self-management.

We recommend further research to confirm the results found in this thesis, to assess its generalizability to other age-groups or cultural and social settings, and to explore further the psychometric properties of the EFI. Further research using the EFI should also focus on the applicability of this disability-severity measurement instrument.

To conclude, this thesis resulted in three easy to apply, valid and reliable measurement instruments which are applicable to a broad range of NMD diagnoses. These measurement instruments offer a broad and unique insight into the consequences of NMDs in adults in

functioning and QoL. This insight could have important implications for multidisciplinary care and support for these patients and help give them a say in future decisions concerning their health.

# Samenvatting

De impact van neuromusculaire aandoeningen op functioneren en kwaliteit van leven

Neuromusculaire aandoeningen (NMAs) omvatten vele aandoeningen die het functioneren van de spieren verstoren, hetzij direct door pathologie van de spieren, hetzij indirect door pathologie van de zenuwen of de neuromusculaire overgang. NMAs zijn progressieve aandoeningen die spierzwakte of spasticiteit kunnen veroorzaken en leiden tot een toenemende vraag naar ondersteunende hulpmiddelen en medische en niet-medische ondersteuning. We ontwikkelden twee zelfrapportage instrumenten voor het meten van functioneringsproblemen in NMAs en onderzochten de gevolgen van NMAs voor de kwaliteit van leven. Verder hebben we de prevalentie en ernst van stigmatisering onder mensen met een NMA onderzocht en het effect hiervan op de kwaliteit van leven.

In de inleiding in **Hoofdstuk 1**, beschrijven we de centrale concepten in deze thesis. Eerst de pathofysiologie en epidemiologie van een brede en omvangrijke groep NMAs en de gevolgen van NMAs voor het fysiek, mentaal en sociaal functioneren. Dan introduceren we de Internationale Classificatie van het menselijk functioneren (ICF) als een geschikte classificatie methode voor het ontwikkelen van een meetinstrument voor het in kaart brengen van ziekte gerelateerd functioneren en functioneringsproblemen. Stigmatisering werd geïntroduceerd als een relevant gevolg van fysieke, mentale en sociale functioneringsproblemen in NMAs. Vervolgens beschrijven we het brede concept van kwaliteit van leven (KvL) en wat bekend is over het effect van het hebben van een NMA op KvL. Ten slotte, beschrijven we de kenmerken en het belang van de meetinstrumenten met door de patiënt gerapporteerde uitkomstmetingen en hoe de psychometrische eigenschappen van deze meetinstrumenten te onderzoeken.

We besluiten met de volgende onderzoeksvragen:

1 Wat is de inhoudsvaliditeit van de initiële ICF Core Set voor NMAs?

2 Hoe moeten de prevalentie en ernst van NMA gerelateerde functioneringsproblemen met de ICF Core Set voor NMAs worden beoordeeld?

3 Wat zijn de effecten van NMA-gerelateerde functioneringsproblemen op KvL?

4 Hoe moet de ernst van functioneringsproblemen worden beoordeeld vanuit de focus op het functioneren van de extremiteiten bij patiënten met een NMA?

5 Wat is de impact van stigma op de KvL van patiënten met een NMA?

In **Hoofdstuk 2** beschrijven we de validatie van de initiële ICF Core Set voor NMAs. Deze initiële Core Set werd oorspronkelijk ontwikkeld voor drie neurologische diagnosen: Multiple Sclerosis, Ziekte van Parkinson en Neuromusculaire aandoeningen. Voor het onderzoeken van de inhoudsvaliditeit van deze initiële ICF Core Set voor NMAs werden concepten in erkende en gevalideerde NMA specifieke kwaliteit van leven meetinstrumenten gebruikt. Concepten werden verbonden aan relevante ICF categorieën. Daarna werden deze categorieën vergeleken met de ICF-categorieën in de initiële Core Set. De definitieve NMA-ICF Core Set weerspiegelt een breed scala van NMA gerelateerde functioneringsproblemen. In **hoofdstuk 3** beschrijven we de ontwikkeling van de Neuromuscular Disease Impact Profile (NMDIP). De eerste stap was het ontwikkelen van een concept vragenlijst op basis van de NMA-ICF Core Set. De tweede stap was een transversaal onderzoek met deze vragenlijst (via de post) onder NMA patiënten. Vervolgens construeerden we robuuste schalen en onderzochten we de psychometrische eigenschappen van deze schalen. De definitieve NMDIP bestaat uit 36 items verdeeld over acht schalen met bevredigende psychometrische eigenschappen en vier afzonderlijke vragen. In **Hoofdstuk 4** hebben we de stabiliteit en de relatieve validiteit van de NMDIP-schalen onderzocht. De NMDIP is gevoelig voor het signaleren van klinisch belangrijke verschillen tussen relevante subgroepen en presteerde net zo goed, of beter, dan vergelijkbare meetinstrumenten.

In **hoofdstuk 5** rapporteren we over de prevalentie en ernst van de breed scala aan NMA-gerelateerde functioneringsproblemen en de impact van deze functioneringsproblemen op KvL. We vonden geen verschillen in KvL tussen diagnose gebaseerde subgroepen.

‘Stoornissen in spierfuncties’ had de hoogste prevalentie en ernst score in de totale steekproef en diagnose gebaseerde subgroepen, terwijl 'Stoornissen in de mentale functies en pijn' de belangrijkste voorspeller van KvL was, gevolgd door ‘Belemmeringen in Participatie in maatschappelijke situaties’. In **Hoofdstuk 6** beschrijven we de aanpassing en de combinatie van twee zelfrapportage meetschalen voor de beoordeling van de ernst van de functioneringsproblemen van patiënten met een NMA en onderzochten we de psychometrische eigenschappen van dit meetinstrument. De Extremity Function Index (EFI) bleek een goed en gemakkelijk toe te passen zelfrapportage meetinstrument voor de ernst van functioneringsproblemen dat in staat was klinisch belangrijke verschillen vast te stellentussen relevante subgroepen gebaseerd op ernst van functioneringsproblemen.

In **Hoofdstuk 7** rapporteren we over de invloed van stigma op de KvL van patiënten met een NMA. We hebben een onderzoek via de post uitgevoerd onder NMA patiënten en vonden dat de meeste patiënten (86%) zelfstigma rapporteerden, terwijl 64% interactioneel-stigma rapporteerde. Zelfstigma was een sterkere voorspeller voor lagere KvL vergeleken met interactioneel-stigma. Met andere woorden: patiënten leden meer onder schaamte en angst voor discriminatie (zelfstigma) dan van de werkelijk ervaren discriminatie en uitsluiting (interactioneel-stigma).

In **Hoofdstuk 8** vatten we de belangrijkste bevindingen in dit proefschrift samen en reflecteren we hierop, met inbegrip van de methodologische overwegingen en de implicaties voor de klinische praktijk en verder onderzoek.

Het doel van dit proefschrift was inzicht te bieden in de gevolgen van een NMA voor het functioneren en KvL. De belangrijkste uitdaging in deze studie was het ontwikkelen van ziekte specifieke meetinstrumenten voor de beoordeling van de gevolgen op het functioneren voor alle NMAs. We zijn erin geslaagd om twee dergelijke meetinstrumenten te ontwikkelen. De NMDIP is primair ontwikkeld voor het organiseren van persoonsgerichte zorg en ondersteuning voor mensen gediagnosticeerd met een NMA. De EFI werd primair ontwikkeld

als een meetinstrument voor het meten van de ernst van de functioneringsproblemen met de mogelijkheid om ziekte-ernst te verklaren. We hebben ook een meetinstrument vertaald voor de evaluatie van de prevalentie en de ernst van stigmatisering, de Stigma schaal voor Chronische Ziekte. We zijn erin geslaagd een uniek inzicht te geven in de prevalentie en ernst van een breed scala van NMA-gerelateerde functioneringsproblemen die relevant zijn voor het grote aantal NMAs. Deze bevindingen onderstrepen de veelzijdigheid van de functioneringsproblemen door een NMA.

We vonden ook bewijs voor de verschillen in de ernst van de ziekte gerelateerde functioneringsproblemen tussen de NMA-subgroepen. Voor zover we weten is dit de eerste keer dat een dergelijk inzicht werd verkregen. Bij het vergelijken van de resultaten tussen beide meetinstrumenten, de NMDIP en de EFI, vonden we dat 'verlies van spierkracht' duidelijker aanwezig is in de onderste extremiteiten dan in de bovenste extremiteiten. We vonden ook dat pijn een sterkere relatie had met het functioneren van de extremiteiten dan verwacht. Deze bevindingen onderstrepen het belang van de combinatie van beide meetinstrumenten.

Een andere belangrijke uitdaging in dit proefschrift was het geven van een gedetailleerd inzicht in de gevolgen van een NMA op ervaren QoL. We zijn erin geslaagd de relatieve impact van een breed scala van NMA-gerelateerde functioneringsproblemen te onderzoeken en hun relatieve impact op KvL. De belangrijkste kracht van deze studie is de grote en brede steekproef van volwassen NMA-patiënten die een grote verzameling van NMAs vertegenwoordigen, en de zorgvuldig geselecteerde en toegepaste methoden in de verschillende studies. Een belangrijk sterk punt in de ontwikkeling van de NMDIP was de toepassing van de ICF. Dit bood de mogelijkheid een meetinstrument te ontwikkelen dat een gedetailleerd inzicht geeft in een breed scala aan gevolgen van NMAs.

De NMDIP kan bijdragen aan een beter begrip van de functioneringsproblemen van een patiënt wanneer het wordt gebruikt als evaluatie-instrument, met name in

multidisciplinaire revalidatie teams. De EFI kan ook een belangrijke bijdrage leveren in de klinische zorg voor patiënten. Clinici hebben nu de beschikking over een gemakkelijk toe te passen en patiëntvriendelijk zelfrapportage meetinstrument voor het meten van de ernst van functioneringsproblemen en veranderingen in de tijd gezien. Zowel de NMDIP als de EFI kunnen klinische gevolgen hebben voor het zelfmanagement van patiënten.

We adviseren verder onderzoek om de gevonden resultaten in dit proefschrift te bevestigen en naar de generaliseerbaarheid naar andere leeftijdsgroepen, culturele en sociale omgevingen. Verder onderzoek zou zich ook moeten richten op de toepasbaarheid van de EFI als ziekte-ernst schaal.

Concluderend, resulteerde dit proefschrift in drie eenvoudig toe te passen, valide en betrouwbare meetinstrumenten die toepasbaar zijn voor de brede groep van NMAs. Deze meetinstrumenten bieden een breed en unieke inzicht in de gevolgen van NMAs bij volwassenen voor functioneren en QoL. Dit inzicht kan belangrijke gevolgen hebben voor de multidisciplinaire zorg en ondersteuning voor deze patiënten en hen helpen invloed uit te oefenen bij het maken van toekomstige beslissingen die hun gezondheid aangaan.

# Neuromuscular Disease Impact Profile (NMDIP)

English language version

## Neuromuscular Disease Impact Profile (NMDIP)

| NMDIP | | Body functioning questions |
|---|---|---|
| Scale | | Response options<br>0 = no, not at all<br>1 = yes, I have a slight impairment<br>2 = yes, I have a moderate impairment<br>3 = yes, I have a severe impairment<br>4 = yes, I have a complete impairment |
| MuF | B1 | Do you face loss of your **muscle power functions**? (b730) |
| MuF | B2 | Do you face loss of **muscle endurance functions**? (b740) |
| MoF | B3 | Do you face loss of **control of voluntary movements**? (b760) |
| MoF | B4 | Do you face **involuntary movements**? (e.g., tremors or tics) (b765) |
| MoF | B5 | Do you face **muscle stiffness or muscle spasm**? (b7800 / b7801) |
| SSF | B6 | Do you face impairment in your **speech functions**? (b320) |
| SSF | B7 | Do you face impairment in your **swallowing functions**? (b5105) |
| ERF | B8 | Do you face impairment in your **defecation functions**? (e.g., changes in frequency, constipation, incontinence) (b525) |
| ERF | B9 | Do you face impairment in your **urination functions**? (e.g., frequency of urination, incontinence, difficulties with urination) (b620) |
| ERF | B10 | Do you face limitations in **sexual functions**? (b640) |
| MFP | B11 | Do you face impairment in your **sleep functions**? (e.g., onset of sleep, the maintenance of sleep or the quality of sleep) (b134) |
| MFP | B12 | Do you experience **fatigue**? (b1300/b455) |
| MFP | B13 | Do you face **changes** in your **emotional functions**? (e.g., fear, depression, happiness) (b152) |
| MFP | B14 | Do you face **changes** in your **thought functions**? (e.g., the ability to think logically, the ability to memorize, the ability to concentrate) (b160) |
| MFP | B15 | Do you experience **sensation pain**? (b280) |
| single | B16 | Do you face impairment in your **seeing functions**? (With eyeglasses on or item lenses in) (b210) |

| NMDIP | | Activities questions |
|---|---|---|
| Scale | | Response options<br>0 = No<br>1 = Yes, but assistance devices and/or adaptations *are not* necessary<br>2 = Yes, and assistance devices and/or adaptations *are* necessary<br>3 = Yes, and assistance devices and/or adaptations *and* another person's help are necessary |
| AMA | A1 | Do you face limitations in **changing** your **body position**? (e.g., moving from lying down to standing up or from standing to sitting) (a410) |
| AMA | A2 | Do you face limitations in **maintaining** your **body position**? (e.g., maintaining kneeling, standing, and sitting postures) (a415) |
| AMA | A3 | Do you face limitations in **transferring** yourself? (e.g., moving from a chair into bed; from a wheelchair into a car) (a420) |
| AMA | A4 | Do you face limitations in **walking**? (a450) |
| AMA | A5 | Do you face limitations in **using transportation**? (a470) |
| AMA | A6 | Do you face limitations in activities you would like to undertake for **recreation and leisure**? (a920) |
| SDA | A7 | Do you face limitations in your **fine hand use**? (e.g., picking up small objects; manipulating a keyboard) (a440) |
| SDA | A8 | Do you face limitations in your **arm(s) and hand(s) use**? (e.g., pulling or pushing objects; turning or twisting knobs or handles; reaching for kitchen cupboard) (a445) |
| SDA | A9 | Do you face limitations in **washing yourself**? (a510) |

| | | |
|---|---|---|
| SDA | A10 | Do you face limitations in **caring for body parts**? (e.g., brushing teeth, clipping your nails, combing your hair, shaving) (a520) |
| SDA | A11 | Do you face limitations in **toileting**? (a530) |
| SDA | A12 | Do you face limitations in **dressing** yourself? (a540) |
| SDA | A13 | Do you face limitations in **preparing meals**? (a630) |
| SDA | A14 | Do you face limitations in **doing housework**? (a640) |
| **NMDIP** | | **Participation questions** |
| Scale | | Response options<br>0 = no<br>1 = Yes, as a consequence I have **some** trouble with ….<br>2 = Yes, as a consequence I have trouble with...<br>3 = Yes, as a consequence I have **a lot of** trouble with …<br>4 = Yes, as a consequence …. is (nearly) impossible |
| PLS | P1 | Are there **obstacles** in your **environment** that complicate your participation in **community, recreation, and leisure**? (e.g., accessibility of clubs or associations) (p910/p920) |
| PLS | P2 | Are there **obstacles** in your **environment** that complicate the **maintenance** of your **relationships with your closest family, friends, or relatives**? (e.g., the travel distance, the attitude of others) (p740-p760) |
| PLS | P3 | Are there **obstacles** in your **environment** that complicate your **mobility inside** or **outside** your home? (e.g., thresholds; curbs; absence of elevators) (p460 / 470) |
| **NMDIP** | | **Environmental factors questions** |
| Scale | | Response options<br>0 = Yes, very supportive;<br>1 = Yes, somewhat supportive;<br>2 = No, not supportive |
| Single item | E1 | Is your relationship with your **immediate family** supportive for you? (e.g., partner, children, parents, brothers, sisters) (e310) |
| Single item | E2 | Are the **social security services** supportive for you? (e.g., income support) (e570) |
| Single item | E3 | Are the **health services** supportive for you? (e.g., medical and nursing care) (e580) |

MuF = Muscle Functions; MoF=Movement Functions; SSF = Swallowing and Speech Functions; ERF = Excretion and Reproductive Functions; MFP = Mental Functions and Pain; AMA = Activities of Moving Around; SDA = Self-care and Domestic Activities; PLS = Participation in Life Situations.

# Neuromuscular Disease Impact Profile (NMDIP)

Nederlandse versie

## Neuromusculair Disease Impact Profile (NMDIP)

| NMDIP | | functie vragen |
|---|---|---|
| schaal | | antwoord mogelijkheden<br>0 = nee, helemaal niet<br>1 = ja, een beetje<br>2 = ja, behoorlijk<br>3 = ja, ernstig<br>4 = ja, zeer ernstig |
| SF | F1 | Is er bij u sprake van **krachtsverlies** in de spieren? (b730) |
| SF | F2 | Is er bij u sprake van verminderd uithoudingsvermogen van de spieren? (b740) |
| BF | F3 | Is er bij u sprake van een **verminderde controle van willekeurige bewegingen**? (b760) |
| BF | F4 | Is er bij u sprake van **onwillekeurige bewegingen**? (bijvoorbeeld tremoren of tics) (b765) |
| BF | F5 | Is er bij u sprake van **spierstijfheid** of **spierspasmen**? (b7800/7801) |
| SSF | F6 | Is er bij u sprake van een stoornis in het **spreken**? (b320) |
| SSF | F7 | Is er bij u sprake van een stoornis in het **slikken?** (b5105) |
| URF | F8 | Is er bij u sprake van een afwijkend **ontlastingspatroon**? (bijv. verandering in frequentie, obstipatie, incontinentie) (b525) |
| URF | F9 | Is er bij u sprake van een afwijkend **patroon van urineren**? (bijv. verandering in frequentie, incontinentie, moeilijk kunnen plassen) (b620) |
| URF | F10 | Zijn er voor u beperkingen op **seksueel gebied**? (b640) |
| MFP | F11 | Is er bij u sprake van een afwijkend **slaappatroon**? (bijv. het inslapen, doorslapen of de kwaliteit van de slaap (b134) |
| MFP | F12 | Is er bij u sprake van **vermoeidheid**? (bijv. verminderde energie en uithoudingsvermogen) (b1300/b455) |
| MFP | F13 | Is er bij u sprake van een verandering in uw **stemming**? (bijv. angst, somberheid, vreugde) (b152) |
| MFP | F14 | Is er bij u sprake van een verandering in uw **verstandelijke vermogens**? (bijv. in het logisch kunnen denken, het onthouden van dingen, het kunnen concentreren) (b160) |
| MFP | F15 | Heeft u **pijn**? (b280) |
| Single item | F16 | Is er bij u sprake van een stoornis in het **zien**? (met bril op of contactlenzen in) (b134) |

| NMDIP | | activiteiten vragen |
|---|---|---|
| schaal | | antwoord mogelijkheden<br>0 = nee<br>1 = ja, maar hulpmiddelen en/of aanpassingen zijn niet nodig<br>2 = ja, hulpmiddelen en/of aanpassingen zijn wel nodig<br>3 = ja, maar hulpmiddelen en/of aanpassingen én hulp van anderen zijn nodig. |
| BBA | A1 | Zijn er voor u beperkingen in het **veranderen van uw lichaamshouding**? (bijv. van liggen gaan zitten of vanuit staan gaan zitten) (a410) |
| BBA | A2 | Zijn er voor u beperkingen in het **handhaven van uw lichaamshouding**? (bijv. het kunnen blijven staan of zitten) (a415) |
| BBA | A3 | Zijn er voor u beperkingen in het kunnen **verplaatsen van uzelf**? (bijv. van stoel naar bed of van rolstoel in de autostoel) (a420) |
| BBA | A4 | Zijn er voor u beperkingen in het **lopen**? (a450) |
| BBA | A5 | Zijn er voor u beperkingen in het gebruik kunnen maken van (openbaar) **vervoermiddelen**? (a470) |
| BBA | A6 | Zijn er voor u beperkingen bij wat u **in uw vrije tijd** graag zou willen doen? (a920) |
| ADL | A7 | Zijn er voor u beperkingen in het nauwkeurig kunnen **gebruiken van uw hand(en)**? (bijv. het oppakken van kleine voorwerpen of het gebruiken van een toetsenbord) (a440) |
| ADL | A8 | Zijn er voor u beperkingen in het **gebruiken van uw arm(en) én hand(en)**? (bijv. trekken of duwen van voorwerpen, omhoog of omlaag drukken van knoppen, reiken naar keukenkastje) (a445) |
| ADL | A9 | Zijn er voor u beperkingen in het **wassen** van uzelf? (a510) |
| ADL | A10 | Zijn er voor u beperkingen in het **verzorgen van lichaamsdelen**? (bijv. tanden poetsen, nagels knippen, haren kammen, scheren) (a520) |

| | | |
|---|---|---|
| ADL | A11 | Zijn er voor u beperkingen in de **toiletgang**? (a530) |
| ADL | A12 | Zijn er voor u beperkingen in het **aan- en uitkleden**? (a540) |
| ADL | A13 | Zijn er voor u beperkingen in het **bereiden van maaltijden**? (a630) |
| ADL | A14 | Zijn er voor u beperkingen in het **doen van het huishouden**? (a640) |
| **NMDIP** | | **participatie vragen** |
| Schaal | | antwoord mogelijkheden<br>0 = nee<br>1 = ja, hierdoor heb ik enige moeite met ….<br>2 = ja, …. kost mij hierdoor moeite<br>3 = ja, …. kost mij hierdoor veel moeite<br>4 = ja, …. Is hierdoor (vrijwel) niet mogelijk. |
| PML | P1 | Zijn er voor u **belemmeringen in uw omgeving** die **vrijetijdsbesteding** bemoeilijken? (bijv. bereikbaarheid van clubs of verenigingen) (p910/p920) |
| PML | P2 | Zijn er **belemmeringen in uw omgeving** die het **onderhouden van uw relaties** met uw **naaste familie, vrienden of bekenden** bemoeilijken? (bijv. reisafstand, de houding van anderen) (p740-p760) |
| PML | P3 | Zijn er **belemmeringen in uw omgeving** die uw **mobiliteit binnen- en buitenshuis** bemoeilijken? (bijv. drempels, stoepranden, afwezigheid van liften) (p460/p470) |
| **NMDIP** | | **externe factoren vragen** |
| Scale | | antwoord mogelijkheden<br>0 = ja, (zeer) ondersteunend<br>1 = ja, enigszins ondersteunend<br>2 = nee, niet ondersteunend |
| Single item | E1 | Is uw **naaste** familie ondersteunend voor u? (partner, kinderen, ouders, broers en zusters, enz.) (e310) |
| Single item | E2 | Zijn de **voorzieningen op het gebied van de sociale zekerheid** ondersteunend voor u? (bijv. inkomenssteun, uitkeringen en uitkerende instanties) (e570) |
| Single item | E3 | Zijn de **gezondheidszorgvoorzieningen** ondersteunend voor u? (bijv. medische en verpleegkundige zorg) (e580) |

SF = Spier functies; BF = Bewegingsfuncties; URF = Uitscheidings- en Reproductie Functies; MFP = Mentale Functies en Pijn; BBA = Basale Bewegingsactiviteiten; ADL = Activiteiten van het Dagelijkse Leven; PML = Participatie aan het Maatschappelijke Leven; EF = Externe Factoren.

# Extremity Function Index (EFI)

English language version

## The Extremity Function Index (EFI)

Response options
0 = not difficult
1 = slightly difficult
2 = moderately difficult
3 = quite difficult
4 = extremely difficult or impossible

### Upper Extremity Function Index (UEFI)

We are interested in whether the upper-limb problem for which you are seeking help is causing you any difficulty with the activities listed below.

**Please indicate how difficult each of the following activities is or would be for you today:**

1. Any of the activities involved in your usual work, housework, or schoolwork
2. Your usual hobbies, recreational or sporting activities
3. Lifting a bag of groceries to waist level
4. Lifting a bag of groceries above your head
5. Grooming your hair
6. Pushing up on your hands (e.g., from a bathtub or chair)
7. Preparing food (e.g., peeling, cutting)
8. Driving
9. Vacuuming, sweeping, or raking
10. Dressing
11. Buttoning your clothing
12. Using tools or appliances
13. Opening doors
14. Cleaning
15. Tying or lacing shoes
16. Sleeping
17. Laundering clothes (e.g., washing, ironing, folding)
18. Opening a jar
19. Throwing a ball
20. Carrying a small suitcase (with your affected limb)

### Lower Extremity Function Index (LEFI)

We are interested in whether the lower-limb problem for which you are seeking help is causing you any difficulty with the activities listed below.

**Please indicate how difficult each of the following activities is or would be for you today:**

1. Any of the activities involved in your usual work, housework, or schoolwork
2. Your usual hobbies, recreational or sporting activities
3. Getting into or out of the bathtub
4. Walking between rooms
5. Putting on your shoes or socks
6. Squatting
7. Lifting an object (e.g., a bag of groceries) from the floor
8. Performing light activities around your home
9. Performing heavy activities around your home
10. Getting into or out of a car
11. Walking 10 yards
12. Walking 200 yards
13. Going up or down 10 steps (about 1 flight of stairs)
14. Standing for 10 minutes
15. Sitting for 1 hour
16. Walking on even ground
17. Walking on uneven ground
18. Making sharp turns while walking quickly
19. Jumping
20. Rolling over in bed

# Extremity Function Index (EFI)

Nederlandse versie

# De Extremity Function Index (EFI)

Antwoord opties
0 = geen moeite
1 = weinig moeite
2 = matige moeite
3 = veel moeite
4 = extreme moeite/onmogelijk

## Upper Extremity Function Index (UEFI)

We willen graag weten hoeveel moeite u door de NMA heeft met het uitvoeren van de hieronder genoemde activiteiten. Het zijn activiteiten waarbij u uw armen moet gebruiken.
Wilt u bij elke activiteit het best passende hokje aankruisen?

**Had u vandaag en/of de afgelopen dagen moeite met de volgende activiteiten?**

1 Uw dagelijkse werk, huishouden of schoolactiviteiten
2 Uw hobby's, recreatieve of sport activiteiten
3 Optillen van een boodschappentas tot uw middel
4 Optillen van een boodschappentas boven uw hoofd
5 Verzorgen van uw haar
6 Uzelf omhoog duwen met de handen. (bv. uit het bad of de stoel)
7 Eten klaar maken (bv. schillen, snijden)
8 Autorijden
9 Stofzuigen, vegen of harken
10 Aankleden
11 Dichtknopen van kleding
12 Gebruik van gereedschap of hulpmiddelen
13 Openen van deuren
14 Schoonmaken
15 Schoenveters strikken
16 Slapen
17 Kleding wassen (bv. wassen, strijken, vouwen)
18 Een pot openmaken
19 Gooien van een bal
20 Dragen van een koffertje (met uw aangedane arm)

## Lower Extremity Function Index (LEFI)

We willen graag weten hoeveel moeite u door de NMA heeft met het uitvoeren van de hieronder genoemde activiteiten. Het zijn activiteiten waarbij u uw benen moet gebruiken.
Wilt u bij elke activiteit het best passende hokje aankruisen?

**Hebt u vandaag en/of de afgelopen dagen moeite met de volgende activiteiten?**

1 Uw dagelijkse werk, huishouden of schoolactiviteiten
2 Uw hobby's, recreatieve of sport activiteiten
3 In of uit bad gaan
4 Het lopen van de ene naar de andere kamer
5 Uw schoenen of sokken aantrekken
6 Hurken
7 Een voorwerp optillen, bv. een boodschappentas van de vloer
8 Uitvoeren van lichte activiteiten rondom uw huis
9 Uitvoeren van zware activiteiten rondom uw huis
10 In of uitstappen van een auto
11 10 meter lopen
12 200 meter lopen
13 10 traptreden naar boven of beneden lopen (ongeveer 1 trap)
14 10 minuten staan
15 1 uur zitten
16 Lopen over een vlakke ondergrond
17 Lopen over een oneffen ondergrond
18 Scherpe bochten maken terwijl u hard loopt
19 Springen
20 Omdraaien in bed

# Stigma Scale for Chronic Illness (SSCI)

English language version

## Stigma Scale for Chronic Illness

Response options
0 = never
1 = rarely
2 = often
3 = sometimes
4 = always

**Your experience of the consequences of your illness**
**T**he following propositions are about possible consequences of your illness and your experience of it.
In the **past seven days** how often you experience the proposition? Please tick the box of your choice

| | |
|---|---|
| 1 | Because of my illness, I felt emotionally distant from other people |
| 2 | Because of my illness, I felt left out of things |
| 3 | Because of my illness, I felt embarrassed in social situations |
| 4 | Because of my illness, I worried about other people's attitudes towards me |
| 5 | I was unhappy about how my illness affected my appearance |
| 6 | Because of my illness, it was hard for me to stay neat and clean |
| 7 | Because of my illness, I worried that I was a burden to others |
| 8 | I felt embarrassed about my illness |
| 9 | I felt embarrassed because of my physical limitations |
| 10 | I felt embarrassed about my speech |
| 11 | Because of my illness, I felt different from others |
| 12 | I tended to blame myself for my problems |
| 13 | I avoided making new friends to avoid telling others about my illness |
| 14 | Because of my illness, some people seemed uncomfortable with me |
| 15 | Because of my illness, some people avoided me |
| 16 | Because of my illness, people were unkind to me |
| 17 | Because of my illness, people made fun of me |
| 18 | Because of my illness, people avoided looking at me |
| 19 | Because of my illness, strangers tended to stare at me |
| 20 | Because of my illness, I was treated unfairly by others |
| 21 | Because of my illness, people tended to ignore my good points |
| 22 | Some people acted as though it was my fault I have this illness |
| 23 | People with my illness lost their jobs when their employers found out about it |
| 24 | I lost friends by telling them that I have this illness |

# Stigma Scale for Chronic Illness (SSCI)

Nederlandse versie

## Stigma schaal voor chronische aandoeningen

Antwoord opties
0 = nooit
1 = zelden
2 = soms
3 = vaak
4 = altijd

**Uw beleving van de gevolgen van uw ziekte**
De volgende stellingen gaan over mogelijke gevolgen van uw ziekte en uw beleving daarvan. Wilt u de bij iedere stelling aankruisen hoe vaak deze voor u de **afgelopen 7 dagen** van toepassing was?

| | |
|---|---|
| 1 | Door mijn ziekte voelde ik een emotionele afstand tot andere mensen |
| 2 | Door mijn ziekte voelde ik mij bij activiteiten buitengesloten |
| 3 | Door mijn ziekte schaamde ik mij in sociale situaties |
| 4 | Door mijn ziekte maakte ik mij zorgen over de houding van andere mensen naar mij toe |
| 5 | Ik voelde mij ongelukkig over hoe mijn ziekte mijn uiterlijk veranderde |
| 6 | Door mijn ziekte was het voor mij moeilijk schoon en verzorgd te blijven |
| 7 | Door mijn ziekte was ik bezorgd dat ik anderen tot last zou zijn |
| 8 | Ik schaamde mij voor mijn ziekte |
| 9 | Ik schaamde mij voor mijn fysieke beperkingen |
| 10 | Ik schaamde mij voor mijn spraak |
| 11 | Door mijn ziekte voelde ik mij anders dan anderen |
| 12 | Ik had de neiging mijzelf de schuld te geven voor mijn problemen |
| 13 | Ik vermeed het aangaan van nieuwe vriendschappen om te voorkomen dat ik over mijn ziekte moest vertellen |
| 14 | Door mijn ziekte leken sommige mensen zich niet op hun gemak te voelen bij mij |
| 15 | Door mijn ziekte vermeden sommige mensen mij |
| 16 | Door mijn ziekte waren mensen onvriendelijk tegen mij |
| 17 | Door mijn ziekte maakten mensen grappen over mij |
| 18 | Door mijn ziekte vermeden mensen het om naar mij te kijken |
| 19 | Door mijn ziekte hadden vreemden de neiging om naar mij te staren |
| 20 | Door mijn ziekte werd ik door anderen oneerlijk behandeld |
| 21 | Door mijn ziekte neigden mensen ernaar mijn goede punten te negeren |
| 22 | Sommige mensen deden alsof het mijn schuld was dat ik deze ziekte heb |
| 23 | Mensen met dezelfde ziekte als ik verloren hun baan nadat hun werkgevers er achter kwamen |
| 24 | Ik heb vrienden verloren door ze te vertellen dat ik deze ziekte heb |

# Dankwoord

Het is algemeen bekend dat een promotieonderzoek een samenwerkingstraject is en dat betekent ook dat meerdere mensen zich hiermee hebben bezig gehouden. Deze mensen wil ik in het bijzonder bedanken voor hun inbreng.

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Henriette-**mijn** paranimf, wij samen zijn één en jouw aandeel is enerverend harmonieus. Samen huishouden, een serie kijken of reizen gaat ons goed af. Je was blij dat ik wat om handen had maar niet minder nu meer tijd beschikbaar is voor gezamenlijke uitdagingen.

# Curriculum vitae

Isaäc Bos werd geboren op 30 januari 1952 in Treebeek, gemeente Heerlen. Hij startte zijn verpleegkundige beroepsopleiding eind 1969 in het toenmalige De Weever ziekenhuis te Heerlen. Hij volgde daarna de Kinderaantekening en Anesthesie-opleiding in het Scheper ziekenhuis te Emmen. Daarna volgde hij de opleiding psychiatrisch verpleegkundige in Dennenoord te Zuidlaren, waarna hij een jaar werkervaring opdeed in het Martiniziekenhuis te Groningen. Augustus 1981 zette hij zijn carrière voort op de Medium care afdeling van de afdelingen Kinderchirurgie en Intensive Care Chirurgie in het toenmalige Academisch Ziekenhuis Groningen (AZG), nu Universitair Medisch Centrum Groningen (UMCG). Hier volgde hij met succes de Intensive Care opleiding, de Midden Management opleiding en de studie Verplegingswetenschap. Na de Intensive Care afdeling was hij voor een periode van vijf jaar hoofdverpleegkundige van de Kinder Intensive Care. In 1997 vervolgde hij zijn loopbaan bij de afdeling Neurologie als verpleegkundig consulent neuromusculaire aandoeningen. Deze functie combineerde hij met het projectleiderschap van zorgvernieuwingsprojecten bij het Coördinatiecentrum Chronisch Zieken - Noord Nederland Dit Coördinatiecentrum werd gesubsidieerd tot 2005 waarna het werd gesloten. In plaats van het projectleiderschap kreeg hij een deeltijdfunctie aan de Faculteit voor Medische Wetenschappen als onderwijscoördinator voor het ‘Master1 blok Beweging’ van de opleiding geneeskunde. In november 2009 startte hij zijn promotieonderzoek naar de impact van neuromusculaire aandoeningen op het functioneren en de kwaliteit van leven.
Op 31 oktober 2017 bereikte hij de pensioengerechtigde leeftijd en is hij gestopt met werken.