Functioning and ageing with late-onset sequelae of poliomyelitis

Janneke Stolwijk-Swüste
The cover design is based on a 3000 year old Egyptian hieroglyph depicting a Syrian boy named Ruma, who at 5 years old got very sick with pain in his head and his leg ached. His father carried the boy to the temple where they believed the priest would cure him with powerful magic. The story of Ruma is perhaps the earliest pictorial record of Polio. The stone tablet (stele) tells the story of Ruma, now a grown man and temple priest, with a withered right leg, holding a long stick to use as a crutch. He is shown with his wife and a gazelle for the goddess he believed saved his life.

The studies were part of the research programme Musculoskeletal Disorders of the Institute for Research in Extramural Medicine (EMGO).

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Functioning and ageing with late-onset sequelae of poliomyelitis

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Chapter 1

Introduction and outline of the thesis
The present thesis is part of the CARPA study ‘Co-morbidity and Ageing in Rehabilitation Patients: the influence on Activities’. This study investigates the course of functional status and the impact of physical impairments, co-morbidity and cognitive impairments on this course in elderly patients with late-onset sequelae of poliomyelitis, osteoarthritis and Parkinson’s disease. This thesis describes the results with regard to the patients with late-onset sequelae of poliomyelitis.

**Ageing and functioning**

In 2008 14.8% of the population in the Netherlands was aged 65 and over, and in 2050 it is expected that 24.5% of the population will be older than 65 years. This means that an increasing number of people will age in the twenty-first century. With ageing come ailments and increasing difficulties with daily life activities with increasing needs for health care services. The challenge for health care will be to reduce the burden of disease and to preserve functional independence in the elderly. Therefore, insight in how ageing affects functioning is required.

With ageing several physiologic functions decline such as muscle strength, cardiorespiratory fitness, basal metabolic rate, joint mobility, co-ordination and bone density. These increasing physical impairments may negatively affect the course of functional status.

In the Netherlands around two-thirds of all inhabitants aged 65 years or older have two or more chronic diseases, and this number increases with age. The presence of multiple co-existing conditions present in patients with a particular index disease, which are not directly related to that index disease, is called co-morbidity. Measuring co-morbidity is increasingly acknowledged as important, because it has been demonstrated that co-existing morbidities are negatively associated with quality of life and performing activities of daily life and lead to a higher use of healthcare services. Co-morbidity therefore, may be an important determinant of functioning in the elderly.

Eight percent of the senior Dutch population show mild cognitive impairments and 2% show severe cognitive impairments. The cognitive impairments may include problems with memory recall, orientation in time and organization of a household. Cognitive impairments have been shown to have an impact on disability, well-being and the use of healthcare services. Therefore cognitive impairments also may be a potential determinant of functioning in an ageing population.

The Health Council of the Netherlands reported in 2009 that physical impairments, co-morbidity and cognitive impairments are the most important causes of limitations in functioning in the elderly.

**Rehabilitation and ageing**

The profound increase in the number of senior people in the Netherlands in the future, will result in an increase in number of patients in need for rehabilitation care. In rehabilitation of elderly patients factors related to ageing, such as physical and cognitive impairments and co-morbidity need to be taken into account. These factors may modify the course of functional status and may have consequences for
rehabilitation of elderly.\textsuperscript{19,21} For the development of rehabilitation programs for an ageing population, knowledge of these determinants of the course of functioning is essential. In 1998 a survey of Dutch studies, focusing on elderly rehabilitation, showed that 59 studies were conducted in this field, but the lack of interest in specific aspects of ageing on rehabilitation was striking.\textsuperscript{22} Based on this survey it was concluded that the actual impact of specific aspects of ageing on the course of functional status was unknown. It was advised that future research focuses on the course of functioning in specific health conditions relevant for rehabilitation in relation to ageing and that the impact of physical impairments, co-morbidity and cognitive impairments on changes in functioning should be investigated.

**The CARPA study**

The CARPA study ‘Co-morbidity and Ageing in Rehabilitation Patients: the influence on Activities’ started in 2001 as a research program granted by the Netherlands organization for health research and development (ZonMw).\textsuperscript{23} In this study the course of functional status and the impact of physical impairments, co-morbidity and cognitive impairments on this course were studied in elderly patients with late-onset sequelae of poliomyelitis, osteoarthritis and Parkinson’s disease. These three patient groups were deliberately chosen because of the assumed differentiation in prevalence of physical impairments, co-morbidity and cognitive impairments. Patients with late-onset sequelae of poliomyelitis are characterized by a decline in physical functioning at midlife, due to decreasing muscle function and secondary degeneration of the locomotor system. As patients develop this decline in functioning at midlife, the prevalence of co-morbidity and cognitive impairments is likely to be relatively small. Therefore, the assumption in this patient group was that it would enable to study the effects of physical impairments on functional status in the relative absence of co-morbidity and cognitive impairments.

Osteoarthritis is a common chronic condition in the elderly,\textsuperscript{24} therefore supposed to result in a study population with physical impairments and a high prevalence of co-morbidity. It was assumed that in this group, the combined effect of physical impairments and co-morbidity on functioning could be studied.

The third diagnostic group is Parkinson’s disease: the second most prevalent neurodegenerative disease after Alzheimer’s disease.\textsuperscript{25,26} Apart from age-related co-morbidity, 24 – 36\% of newly diagnosed patients with Parkinson’s disease suffer from cognitive problems.\textsuperscript{27,28} This study population provides the opportunity to study the combined effects of physical impairments, co-morbidity and cognitive impairments on functioning.

This thesis encompasses the studies with regard to late-onset sequelae of poliomyelitis. Two other theses comprise the studies in osteoarthritis and Parkinson’s disease.\textsuperscript{29,30}

**Ageing with poliomyelitis**

Although poliomyelitis has become an almost forgotten disease in the Western world after the introduction of routine vaccination in the late 1950s, there are still many individuals with polio residuals (Table 1.1). The number of polio survivors is estimated
at 20 million by the World Health Organization.31 As these people are ageing, they are confronted with new neuromuscular symptoms 30 to 40 years after the original childhood disease.32-34 These symptoms include gradual or abrupt onset of progressive new weakness, abnormal muscle fatigability, with or without generalized fatigue, muscle atrophy, or pain.35 In population-based studies the prevalence of new neuromuscular symptoms ranges from 28.5 to 64.0%.36-38 The term used to describe these symptoms is post-polio syndrome (PPS) (Table 1.2). PPS requires the exclusion of other medical conditions that may also cause these symptoms.35 The gradual decline in muscle strength in PPS is due to isolated degeneration of enlarged motor units. After the acute poliomyelitis, some motor neurons survive and regain function. Denervated muscle fibers from permanently lost motor neurons are reinnervated by collateral sprouting from intact axons, resulting in motor units up to 10 times the regular size.39-41

In this thesis the more neutral term late-onset sequelae of poliomyelitis (LOSP) is being used instead of PPS. Late-onset sequelae refer to all new symptoms polio survivors may have, i.e. not only the symptoms as described in PPS, but also symptoms from secondary medical conditions related to the polio, co-morbidity and ageing. It may be very difficult to separate PPS symptoms, such as muscle weakness and fatigue, from symptoms related to ageing or co-morbidity. Taking into account that PPS is a diagnosis

**Table 1.1 Acute poliomyelitis**

Poliomyelitis is a highly infectious viral disease, which mainly affects children. Many infected people have no symptoms (90 – 95%) or influenza-like symptoms (4 – 8%). In only 0.1 – 2% of all infections, the disease results in an acute, usually asymmetrically distributed, flaccid paresis of a varying number of muscle groups.53 In these cases, the polio virus invades the central nervous system and predominantly destroys the spinal motor neurons. This acute stage of polio is followed for months to years by a muscle function recovery phase. Spinal motor neurons who survive regain function and denervated muscle fibres from lost motor neurons are reinnervated by collateral sprouting from intact axons, resulting in motor units up to 10 times the regular size.39-41

**Table 1.2 Diagnostic criteria of post-polio syndrome**

1. Prior episode of paralytic polio with residual motor neuron loss.
2. A period of neurological recovery followed by an interval (usually ≥ 15 years) of neurological and functional stability.
3. Gradual or abrupt onset of progressive new weakness with a duration of at least 12 months, or abnormal muscle fatigability, with or without generalized fatigue, muscle atrophy, or pain.
4. Exclusion of medical, orthopaedic, or neurological conditions that may be causing the symptoms mentioned above.
of exclusion and that this thesis focuses on the impact of age and co-morbidity on functioning of elderly patients with a history of poliomyelitis, the more neutral term LOSP was preferred.

The new late-onset neuromuscular symptoms cause increasing difficulties with physical functioning, such as walking, standing, climbing stairs and other mobility-related activities of daily life. Only few cross-sectional studies and prognostic studies have focused on functional independence and physical functioning in this patient group. In the studies that have focused on functioning, the recruitment of subjects differed from a random selection from the population to a selection of patients referred to a specialized post-poliomyelitis clinic. Some studies excluded patients above the age of 65 and excluded patients with co-morbidity, or did not assess or report the extent and nature of the co-morbidities or their influence on functioning. These differences in eligibility criteria limit the generalizability and may result in an underestimation of the functional problems and rate of decline in former polio patients. As the impact of age and co-morbidity on the course of functioning in patients with LOSP remains unresolved, this thesis focuses on patients in a broad age-range and investigates the effect of co-morbidity on functioning.

**Aim of the thesis**

The aim of this thesis is to describe the course of functional status of patients aged 45 – 85 years with late-onset sequelae of poliomyelitis over a period of 5 years and to explore the impact of age and co-morbidity on this course.

**Outline of the thesis**

This thesis focuses on the changes in functional independence, perceived physical functioning, muscle strength and walking capacity in a 5-year observational cohort study of 168 subjects with late-onset sequelae of poliomyelitis, aged 45 – 85 years, with specific interest in the impact of age and co-morbidity on this functioning. All patients had a consultation with a neurologist or a specialist in physical and rehabilitation medicine at a university hospital specialized in LOSP in the 5 years previous to inclusion.

Chapter 2 systematically reviews studies focussing on the course of functional status and muscle strength over time and prognostic factors of change in patients with LOSP based on a literature search.

Chapter 3 investigates the utility of the WOMAC physical functioning subscale in patients with LOSP and in patients with Parkinson’s disease. The WOMAC is an osteoarthritis-specific questionnaire used to establish the level of physical functioning. To answer the question whether the WOMAC physical functioning subscale can also be used to assess physical functioning in patients with LOSP and in patients with Parkinson’s disease, the WOMAC baseline measurements of the CARPA study (288 patients with osteoarthritis, 200 patients with Parkinson’s disease and 168 patients with LOSP) have been analyzed.

Chapter 4 compares reproducibility and mutual association of three questionnaires and
four walking capacity tests in order to decide which questionnaire and which walking
capacity test are to be used as core qualifiers of physical functioning in research and
clinical practice of subjects with LOSP. Physical functioning subscales from Short
Form-36, WOMAC and Nottingham Health Profile were compared as well as timed-
up-and-go test, time needed to walk 10 meter at self-preferred and maximum speed
and distance walked in 2 minutes at self-preferred speed.

Chapter 5 compares three age groups of patients with LOSP (45 – 54 years, 55 – 64
years and 65 – 85 years) with regard to functional independence, perceived physical
functioning, muscle strength and co-morbidity. The impact of age and co-morbidity
on functional independence and perceived physical functioning was also investigated
and discussed.

Chapter 6 presents the results of the 5-year observational cohort study with regard
to the impact of age and co-morbidity on the course of functional independence and
perceived physical functioning. The course of functional independence, perceived
physical functioning, co-morbidity, muscle strength and walking capacity tests is also
described and discussed.

The general discussion, in chapter 7, reflects on the main findings and discusses the
clinical implications. Finally, the study design and limitations of the study and future
research perspectives are considered.

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Introduction and outline of the thesis

Chapter 1
Chapter 2.1

The course of functional status and muscle strength in patients with late-onset sequelae of poliomyelitis: a systematic review

J.M. Stolwijk-Swüste, A. Beelen, G.J. Lankhorst, F. Nollet
On behalf of the CARPA study group

Arch Phys Med Rehabil
2005;86:1693-1701
Abstract

Objectives: To review systematically studies of late-onset polio sequelae on the course of functional status and muscle strength over time and to identify prognostic factors of change.

Data sources: We conducted a computerized literature search up to July 2004 in MEDLINE, EMBASE, CINAHL, Web of Science, Psychinfo and the Cochrane controlled trial register using the key words: postpolio, postpoliomyelitis, postpoliomyelitis syndrome, post poliomyelitis muscular atrophy and poliomyelitis.

Study selection: Reports were selected by 1 reviewer if the study involved subjects with a history of poliomyelitis, the outcome measures described functional status or muscle strength, and follow-up was for at least 6 months.

Data extraction: Studies were summarized with regard to population, design, sample size, outcome measures, results and methodological scores. Overlap in populations between studies was checked.

Data synthesis: Of 71 potentially relevant studies, 19 were included (2 on functional status, 15 on muscle strength, 2 on both muscle strength and functional status). Two studies on the course of functional status had sufficient quality and reported inconsistent results. Four studies on the course of muscle strength had sufficient quality. Two studies reported a decline in strength and 2 reported no change. Decline in strength was only reported in studies with a follow-up period longer than 2 years. One study reported extent of paresis as a prognostic factor for change in perceived physical mobility.

Conclusions: Conclusions cannot be drawn from the literature with regard to the functional course or prognostic factors in late-onset polio sequelae. The rate of decline in muscle strength is slow, and prognostic factors have not yet been identified. Long-term follow-up studies with unselected study populations and age-matched controls are needed, with specific focus on prognostic factors.
Introduction

Many people with a history of poliomyelitis report late-onset neuromuscular symptoms and a decline in functional abilities. These late symptoms are referred to as postpoliomyelitis syndrome (PPS) and include new or increased muscle weakness, fatigue, muscle and joint pain, muscle cramps and cold intolerance. The gradual decline in muscle strength results from isolated degeneration of enlarged motor units. The current pathophysiologic hypothesis is that this is caused by premature metabolic exhaustion of chronically overloaded motoneurons. The new symptoms cause increasing difficulties with physical functioning, such as walking, standing, climbing stairs and the mobility-related activities of daily life.

The number of polio survivors is estimated at 20 million by the World Health Organization (WHO). In population-based studies, the prevalence of new neuromuscular symptoms ranges from 28.5 to 64.0%. In contrast with the rapidly declining incidence of acute polio, PPS will remain an important problem for many years. In Western countries, where the large epidemics date back to the 1940s and 1950s, many polio survivors are now between 50 and 60 years old. It can be anticipated that because of ageing, their symptoms and functional decline will increase further in the coming decades. The future perspective is, therefore, the continued or even increased need for rehabilitation interventions in people with PPS. Research on the late-onset sequelae of poliomyelitis started in the late 1970s and early 1980s, and focused mainly on the pathophysiology of the increased muscle weakness observed in these patients. Several studies focused on the course of muscle strength, but reported conflicting results. Several narrative reviews on PPS have been published, but none has addressed the literature in a systematic way.

Knowledge about the rate of decline in muscle strength and functioning and prognostic factors of change for this patient group is important in clinical practice to provide patients with adequate information about the most likely course of their functional status. Health care providers need prognostic information to identify people at risk for increasing disabilities. A systematic review of the literature is a powerful tool with which to summarize the evidence and to critically evaluate the internal validity of studies. The objectives of this study were: 1) to review systematically studies on the course of functional status and muscle strength over time in subjects with late-onset sequelae of poliomyelitis; and 2) to identify prognostic factors of change in the functional status and muscle strength of those subjects.

Methods

Searching

A literature search up to July 2004 was conducted in the computerized bibliographic databases MEDLINE (1966 – 2004), EMBASE (1974 – 2004), CINAHL (1982 – 2004), Web of Science (1988 – 2004), Psychinfo (1887 – 2004) and the Cochrane controlled trial register (2004, issue 1). The following key words were used: *postpolio, postpoliomyelitis, postpoliomyelitis syndrome, post poliomyelitis muscular atrophy* and *poliomyelitis*. References from retrieved articles were also screened (citation tracking).
Selection
A study was included if it: (1) concerned subjects with a history of poliomyelitis; (2) reported 1 or more outcome measures of either (a) functional status in terms of activities and participation, according to the WHO's International Classification of Functioning Disability and Health\textsuperscript{16} or (b) muscle strength; (3) addressed a change in the level of functioning or muscle strength over a period longer than 6 months; (4) was written in English, German, Dutch or French; (5) was a full length article or a full written report. Randomized clinical trials were excluded.

To determine whether a study should be included, the article's abstract, identified by the initial search strategy, was assessed by 1 reviewer (JMS-S). If there was any doubt, the entire article was retrieved and discussed with a second reviewer (AB).

Quality assessment
Two reviewers (JMS-S and AB) independently scored the methodological quality of the articles according to 14 criteria, which were divided into 6 categories: study population, sample size, follow-up, outcome measure, prognostic factors, and analysis and data presentation (Table 2.1.1). The criterion of outcome measure concerning the course of functional status differed from that for studies focused on the course of muscle strength. Each criterion was rated as positive, negative or inconclusive (insufficient information presented). We used the quality assessment criteria list from Borghouts et al.\textsuperscript{17} The

Table 2.1.1 Criteria list for assessing the methodological quality of the studies with information on the course of functional status and the course of muscle strength in patients with late-onset sequelae of poliomyelitis

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1  Selection of study population</td>
<td>+/-/?</td>
</tr>
<tr>
<td>2  Description of inclusion and exclusion criteria</td>
<td>+/-/?</td>
</tr>
<tr>
<td>3  Study size</td>
<td>+/-?</td>
</tr>
<tr>
<td>4  Follow-up ≥ 24 months</td>
<td>+/-?</td>
</tr>
<tr>
<td>5  Drop-outs/loss to follow-up ≤ 15%</td>
<td>+/-?</td>
</tr>
<tr>
<td>6  Information on patients who completed follow-up versus drop-outs and loss to follow-up</td>
<td>+/-?</td>
</tr>
<tr>
<td>7a Relevance of outcome measures to the level of activities and participation</td>
<td>+/-?</td>
</tr>
<tr>
<td>7b Relevance of outcome measures to the level of muscle strength</td>
<td>+/-?</td>
</tr>
<tr>
<td>8  Validity of outcome measures</td>
<td>+/-/?</td>
</tr>
<tr>
<td>9  Reproducibility of outcome measures</td>
<td>+/-/?</td>
</tr>
<tr>
<td>10 Description of potential prognostic factors</td>
<td>+/-?</td>
</tr>
<tr>
<td>11 Descriptive statistics of most important outcome measures</td>
<td>+/-?</td>
</tr>
<tr>
<td>12 Descriptive statistics of most important prognostic factors</td>
<td>+/-?</td>
</tr>
<tr>
<td>13 Univariate technique</td>
<td>+/-/?</td>
</tr>
<tr>
<td>14 Multivariate technique</td>
<td>+/-/?</td>
</tr>
</tbody>
</table>
criteria were specified for the population studied and for the purpose of this review. The quality of the studies was judged on their internal validity, scored by 6 items of the methodological criteria list. A more detailed explanation of the criteria is given in Appendix 2.1.1. Disagreements between the 2 reviewers about whether a criterion was met were discussed and resolved by consensus.

A total score was obtained by summing the number of criteria rated as positive (range, 0 – 14 points). The score for internal validity was calculated by summing the scores on 6 criteria: selection of study population, study size, number of drop-outs or loss to follow-up, information reported on patients who completed the follow-up versus drop-outs or loss to follow-up, validity of outcome measures and reproducibility of outcome measures (range, 0 – 6 points). Articles with a score of 4 points for internal validity were considered to be of sufficient quality, and articles with a score of 5 or 6 points were considered to be of high quality. The results of all included articles are presented, but the conclusions are based on the results of articles with sufficient or high quality. To avoid double-counting the same patient data described in different articles, authors who published 2 or more articles that were included in this review were contacted for information about overlap between their study populations. In case of any overlap, we used only the article with the longest follow-up period in the conclusion. If 2 articles with partial overlap had the same follow-up period, the article with the most subjects was used in the conclusion.

Data extraction
Data from the included studies were summarized on a standardized form with regard to study population, study design, sample size, outcome measures, results, and methodological score. We describe the results of each outcome measure; a significant change is defined by a \( p \) value of less than .05. Effect sizes are described if reported by the authors. Furthermore, we have listed all factors analyzed by the authors as potential determinants of the course of functional status or muscle strength.

Results
Of the 71 potentially relevant studies identified through the search, 19 met the inclusion criteria: 2 articles reported on the course of functional status,18,19 15 on the course of muscle strength,2-3,20-32 and 2 on both functional status and muscle strength.33,34 One article on the course of muscle strength used 2 different study populations that were scored separately with regard to methodological quality.20

Quality assessment
The interrater agreement on the rating of the methodological criteria was good (overall agreement, 87.8%). There was disagreement on 34 items, mostly resulting from reading or interpretation errors. Most of the disagreement concerned the criteria: descriptive statistics of the most important outcome measures (24%), information on subjects who completed the follow-up versus drop-outs/loss to follow-up (18%) and descriptive statistics of the most important prognostic factors (age, gender, extent of paresis) (15%). All disagreements were resolved after discussion.
### Table 2.1.2 Characteristics and methodological scores of the studies with information on the course of functional status in subjects with sequelae of poliomyelitis

<table>
<thead>
<tr>
<th>Study</th>
<th>Study population</th>
<th>Study design</th>
<th>Sample size (N)</th>
<th>Outcome measure</th>
<th>Results</th>
<th>Total methodological score (max. 14)</th>
<th>Internal validity score (max. 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grimby &amp; Thoren Jonsson</td>
<td>Hospital registration and advertisements Co-morbidity not excluded</td>
<td>Retrospective Follow-up 4-5 y</td>
<td>59 70% PPS</td>
<td>KATZ ADL Index, WHO handicap classification: orientation, physical independence, mobility, occupation, social integration</td>
<td>2 additional persons developed dependency PPS ↓ non-PPS ↑ all</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Nollet et al.</td>
<td>Hospital registration and advertisements Co-morbidity excluded</td>
<td>Prospective Follow-up: 2 y performance 6 y questionnaires</td>
<td>103 74% PPS</td>
<td>NHP-I, NHP-II, Physical performance: standing up from lying supine, 10-m walk, rising from a chair, climbing/descending stairs, 75-m walk</td>
<td>NC in PPS and non-PPS in all scales, except energy: PPS* improvement and non-PPS* deterioration PPS* improvement in functioning, and NC in non-PPS; after 1 y improvement, after 2 and 6 y deterioration NC in PPS and non-PPS, ↑ 1.8 s/y in PPS</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>Stanghelle &amp; Festøe</td>
<td>Hospital registration Co-morbidity not excluded</td>
<td>Prospective Follow-up 3-5 y</td>
<td>68 100% PPS</td>
<td>Questionnaire: mobility, subjective rating of disability, use of aids, dependence in ADLs, employment status</td>
<td>60% reported this problem (SNM) ↑ report of severe and moderate disability (SNM) ↑ (SNM) ↑ from 2 to 6 persons (SNM) job full/part time ↓ from 59% to 27% (SNM)</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Windebank et al.</td>
<td>Unselected residents of a county Co-morbidity not excluded</td>
<td>Prospective Follow-up 5 y</td>
<td>50</td>
<td>30.6-m walking test, Upper limb function test: Minnesota Rate of Manipulation, Crawford Small Parts Dexterity test</td>
<td>* decrease in time, i.e. improvement in walking NC</td>
<td>10</td>
<td>5</td>
</tr>
</tbody>
</table>

**Note.** ADL = activities of daily living; ↓ = decrease; ↑ = increase; NC = no change; NHP = Nottingham Health Profile; SNM = significance not mentioned. *Significant (p < .05).*
In the articles on the course of functional status, the total methodological scores ranged from 3 to 11, with a mean of 7.8 points (Table 2.1.2). In the articles on the course of muscle strength, the total scores also ranged from 3 to 11, with a mean of 6.5 points (Table 2.1.3). In the 4 articles on the course of functional status, the internal validity scores ranged from 0 to 5, with a mean of 3.0 points. The reporting in 1 article was considered to be of sufficient quality (internal validity score, 4) and the reporting in another article was of high quality (internal validity score, 5). In the 17 articles on the course of muscle strength, the internal validity scores ranged from 0 to 5, with a mean of 2.7 points. Five articles were of sufficient quality (internal validity score, 4) and 1 article was considered to be of high quality (internal validity score, 5). Only 5 studies had study populations that consisted of a consecutive sample or a random sample. In all but 3 studies the inclusion and exclusion criteria were specified. The number of subjects in the studies ranged from 11 to 103, and the duration of follow-up varied from 0.7 years to 8.2 years, with a mean of 3.3 years. With regard to methodological quality, less frequently reported criteria were a description of potential prognostic factors, the descriptive statistics of the most important prognostic factors, and the appropriate multivariate analysis technique.

**Functional status**
The 4 articles concerning the course of functional status are summarized in Table 2.1.2. Different outcome measures were used in these studies. Their results were inconsistent and their internal validity varied. The retrospective study (low internal validity) reported that handicap deteriorated significantly over a period of 4 to 5 years. Stanghelle and Festvag (low internal validity) also described an increased subjective rating of disability and an increase in dependence on, and use of, aids by the patients in their study. Nollet et al. (sufficient internal validity) reported no change or initial improvement in any of the Nottingham Health Profile (NHP) categories after 1 year, followed by a deterioration after 5 years. In that study, the physical performance of patients with PPS improved slightly over 2 years, while on average the performance of those who did not have PPS remained unchanged. Windebank et al. (high internal validity) reported a decrease in the time taken to walk 30.6 m (i.e., improvement), but found no change in upper limb function over 5 years in a population with polio (with and without new neuromuscular symptoms).

**Muscle strength**
Detailed information about the 17 articles that focused on the course of muscle strength is given in Table 2.1.3. Several methods were used to measure muscle strength. Nine studies used a fixed dynamometer, with the subject seated in an adjustable chair, to assess the muscle strength of the lower extremity. One study measured the strength of the elbow flexors with a dynamometer for the upper extremity. Six studies measured muscle strength by manual muscle testing (MMT) according to the Medical Research Council (MRC) scale, and 3 studies used a hand-held dynamometer (HHD), placed in a different position for each muscle tested. Twelve studies reported a decrease in muscle strength over time. There was no decline in muscle strength in 3 studies, and another 2 studies.
<table>
<thead>
<tr>
<th>Study</th>
<th>Study population</th>
<th>Study design</th>
<th>Sample size (N)</th>
<th>Outcome measures*</th>
<th>Results</th>
<th>Total methodological score (max. 14)</th>
<th>Internal validity score (max. 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Agre &amp; Rodríguez</strong></td>
<td>Advertisements</td>
<td>Prospective Follow-up 1 y</td>
<td>50 Controls: 41</td>
<td>KEIK</td>
<td>NC</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td><strong>Agre et al.</strong></td>
<td>Sweden: hospital registration and advertisements</td>
<td>Prospective Follow-up 4 y</td>
<td>Sweden: 41 60% PPS US: 37 68% PPS</td>
<td>KEIK KEIM</td>
<td>Total ↓ 9% *(SNM) ↓ 7% (NS)</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td><strong>Allen et al.</strong></td>
<td>Hospital registration and advertisements</td>
<td>Prospective Follow-up 2–3 y, mean 2.5 y</td>
<td>Co-morbidity excluded: 14, 79% PPS Co-morbidity not excluded: 40, Controls: n = 11</td>
<td>EFIM</td>
<td>Co-morbidity excluded NC</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td><strong>Bednarik &amp; Kadanka</strong></td>
<td>Recruitment not described</td>
<td>Prospective Follow-up 2 y</td>
<td>30 MMT: biceps brachii muscle (n = 9) tibialis anterior muscle (n = 21)</td>
<td>↓ 1 MRC grade in 11% (SNM) ↓ 1 MRC grade in 19% (SNM)</td>
<td>6</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Study</td>
<td>Methodology</td>
<td>Follow-up Duration</td>
<td>Patients</td>
<td>% PPS</td>
<td>Outcome Measures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------------</td>
<td>------------------------------------------------------------------------------</td>
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<td>----------</td>
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<td>----------------------------------------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dalakas et al.24</td>
<td>Referred by physician and co-morbidity excluded</td>
<td>4.5–20 y, mean 8.2 y</td>
<td>27</td>
<td>100%</td>
<td>MMT: sum score (range, 0-100) ↓ 11.8 points ↓ in 11.6 y follow-up, 4.1 points ↓ in 4.7 y follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grimby et al.29</td>
<td>Recruitment not described and co-morbidity not excluded</td>
<td>4 y</td>
<td>20</td>
<td>60%</td>
<td>KEIK 60/s KEIK 120/s KEIM KFIK 60/s KFIK 120/s KEIM</td>
<td>60% unstable (NC increase in muscle weakness at follow-up), 40% stable</td>
<td></td>
</tr>
<tr>
<td>Grimby et al.21</td>
<td>Hospital registration and advertisements and co-morbidity not excluded</td>
<td>4 y</td>
<td>18</td>
<td>50%</td>
<td>KEIM KFIIM</td>
<td>50% unstable (NC increase in muscle weakness at follow-up), 50% stable</td>
<td></td>
</tr>
<tr>
<td>Grimby et al.22</td>
<td>Recruitment not described and exclusion on co-morbidity not described</td>
<td>8 y</td>
<td>21</td>
<td>57%</td>
<td>KEIK60/s KEIK180/s KEIM</td>
<td>66% unstable (NC increase in muscle weakness at follow-up), 33% stable</td>
<td></td>
</tr>
<tr>
<td>Ivanyi et al.2</td>
<td>Recruitment not described and co-morbidity excluded</td>
<td>0.9–1.7 y, mean 1.3 y</td>
<td>11</td>
<td>45%</td>
<td>MMT: biceps brachii muscle or tibialis anterior muscle</td>
<td>5 PPS patients, 3 patients ↓ of 1 MRC grade (SNM), 6 stable patients: NC</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Study population</td>
<td>Study design</td>
<td>Sample size (N)</td>
<td>Outcome measures*</td>
<td>Results</td>
<td>Total methodological score (max. 14)</td>
<td>Internal validity score (max. 6)</td>
</tr>
<tr>
<td>-----------------------------</td>
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<td>-------------------------------------------------------------------------</td>
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<td>----------------------------------</td>
</tr>
<tr>
<td>Ivanyi et al.22</td>
<td>Hospital registration</td>
<td>Prospective Follow-up mean</td>
<td>120</td>
<td>HHD: 30 muscles</td>
<td>All subjects ↓*</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>and advertisements</td>
<td>2.0 y</td>
<td></td>
<td>Upper extremity</td>
<td>HHD sum score NC</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Co-morbidity excluded</td>
<td></td>
<td></td>
<td>(n = 71)</td>
<td>All subjects ↓*</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>96 in analysis</td>
<td>Lower extremity</td>
<td>Hip and knee extensors showed stable or slightly increasing strength</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(n = 65)</td>
<td>All subjects ↓*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Klein et al.26</td>
<td>Hospital registration</td>
<td>Prospective Follow-up 0.7 y</td>
<td>12</td>
<td>MMT sum score</td>
<td>NC or slightly ↑ (NS)</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>and advertisements</td>
<td></td>
<td></td>
<td>Symptomatic</td>
<td>Asymptomatic</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Co-morbidity excluded</td>
<td></td>
<td>96 in analysis</td>
<td>10/22 muscles</td>
<td>Symptomatic</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>↑*</td>
<td>Asymptomatic</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10/22 muscles</td>
<td>Sum score ↑*</td>
<td>Sum score NC</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>6</td>
<td>Sum score</td>
<td>NC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Munin et al.30</td>
<td>Advertisements</td>
<td>Prospective Follow-up:</td>
<td>77</td>
<td>KEIK60/s</td>
<td>Affected limb ↑*</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Co-morbidity excluded</td>
<td>n = 4: 2 y</td>
<td></td>
<td>KEIM</td>
<td>Unaffected limb ↑*</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>n = 1: 1.5 y</td>
<td></td>
<td></td>
<td>↑*</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>n = 2: 1.0 y</td>
<td></td>
<td></td>
<td>↑*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peach &amp; Olejnik21</td>
<td>Hospital registration</td>
<td>Prospective Follow-up 2.2 ±</td>
<td>77</td>
<td>MMT sum scores</td>
<td>Subgroups according to therapy compliance</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Co-morbidity excluded</td>
<td>1.2 y</td>
<td></td>
<td>Compl</td>
<td>↑ (NS) 1.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Partcompl</td>
<td>↓* 30%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Noncompl</td>
<td>↓* 4.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>All</td>
<td>↓* 1.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rodriguez et al.23</td>
<td>Advertisements</td>
<td>Prospective Follow-up 7 y</td>
<td>23</td>
<td>KEIM</td>
<td>48% unstable (NC, increase in quadriceps strength at follow-up),</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Co-morbidity excluded</td>
<td></td>
<td></td>
<td></td>
<td>52% stable</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>14</td>
<td></td>
<td>KEIM</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2.3 Continued

Review muscle strength and functioning | Chapter 2.1
<table>
<thead>
<tr>
<th>Study</th>
<th>Recruitment and Co-morbidity</th>
<th>Design and Follow-up</th>
<th>PPS KEIK</th>
<th>Unstable KEIK</th>
<th>Stable KEIK</th>
<th>All KEIK</th>
<th>KEIM</th>
<th>Unstable KEIM</th>
<th>Stable KEIM</th>
<th>All KEIM</th>
<th>KEIK 60/s KEIM KFIK</th>
<th>Unstable (SNM)</th>
<th>Stable (SNM)</th>
<th>All (SNM)</th>
<th>PPS MMT sum score HHD mean strength</th>
<th>Non-PPS</th>
<th>Unchanged (1.1 point)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stalberg &amp; Grimby&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Recruitment not described</td>
<td>Prospective Follow-up 4 y</td>
<td>61% PPS</td>
<td>↓* 13%</td>
<td>↓ (NS) 4%</td>
<td>↓* 7%</td>
<td>KEIK</td>
<td>KEIM</td>
<td>KEIM</td>
<td>KEIM</td>
<td>KEIK 60/s KEIM KFIK</td>
<td>↓* (SNM)</td>
<td>↓* (SNM)</td>
<td>↓* (SNM)</td>
<td>PPS MMT sum score HHD mean strength</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Grimby &amp; Thoren Jonsson&lt;sup&gt;33&lt;/sup&gt;</td>
<td>Hospital registration and advertisements Co-morbidity not excluded</td>
<td>Retrospective Follow-up 4–5 y</td>
<td>70% PPS</td>
<td>↓*</td>
<td>↓ (SNM)</td>
<td>↓ (SNM)</td>
<td>KEIK</td>
<td>KEIM</td>
<td>KEIM KFIK</td>
<td>KEIK 60/s KEIM KFIK</td>
<td>↓* (SNM)</td>
<td>↓* (SNM)</td>
<td>↓ (SNM)</td>
<td>PPS MMT sum score HHD mean strength</td>
<td>3</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Nollet et al.&lt;sup&gt;34&lt;/sup&gt;</td>
<td>Hospital registration and advertisements Co-morbidity excluded</td>
<td>Prospective Follow-up 2 y</td>
<td>74% PPS</td>
<td>↓* (1.1 point)</td>
<td>NC</td>
<td>NC</td>
<td>PPS</td>
<td>NC</td>
<td>Non-PPS</td>
<td>PPS MMT sum score HHD mean strength</td>
<td>↓* (1.1 point)</td>
<td>NC</td>
<td>NC</td>
<td>PPS MMT sum score HHD mean strength</td>
<td>11</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

*Note. Compl = compliers; EFIM = elbow flexion isometric; HHD = hand-held dynamometry; KEIK = knee extension isokinetic; KEIM = knee extension isometric; KFIK = knee flexion isokinetic; KFIM = knee flexion isometric; MMT = manual muscle testing; MRC = Medical Research Council scale; NS = not significant; ↓ = decrease; ↑ = increase; NC = no change. *Significant \( p < .05 \).*
described an increase in strength during the follow-up period. Four of the 6 studies that were considered to be of sufficient quality\textsuperscript{3,21-23} reported a deterioration in muscle strength, varying from 7\% in 4 years\textsuperscript{3} to 15\% in 8 years (there was a partial overlap in these studies).\textsuperscript{22} One study\textsuperscript{34} (sufficient internal validity) reported no change in HHD measurement and a slight deterioration in MMT (follow-up period, 2 y). The study that was of high methodological quality\textsuperscript{20} showed no change in muscle strength of the elbow flexors over a follow-up period with a mean of 1.7 years. Three authors (Agre, Nollet, Grimby) were contacted to gain information on double-counting in their articles that were selected for this review. The Agre group published 3 articles\textsuperscript{23,27,28} in which there was partial overlap, the Nollet and Ivanyi group published 3 articles\textsuperscript{2,32,34} with partial overlap, and the Grimby group published 6 articles\textsuperscript{3,21,22,27,29,33} with partial overlap.

**Prognostic factors**

Only 2 studies reported on prognostic factors: Nollet\textsuperscript{34} analyzed potential prognostic factors for the changes in NHP physical mobility score during a 6-year follow-up, and Klein et al.\textsuperscript{26} analyzed potential prognostic factors for changes in upper- and lower-extremity strength during an 8-month follow-up. In these studies, no comparisons were made with a population without a history of poliomyelitis.

The study carried out by Nollet\textsuperscript{34} was considered to be of sufficient quality. Age, sex, time since polio, symptom status, and history of residual weakness were investigated as potential prognostic factors in both studies. With regard to functional status, only the extent of paresis was a prognostic factor for changes in the NHP physical mobility score.\textsuperscript{34} No association was found between age, sex, time since polio, history of residual weakness, or number of clinically affected body sites and changes in the NHP Physical Mobility score. Klein\textsuperscript{26} (internal validity score, 2) reported an increasing rate of deterioration in upper-extremity strength with increasing age. No association was found between sex, time since polio, history of residual weakness, symptom status, or weight and change in muscle strength.\textsuperscript{26}

**Discussion**

**Functional status**

Because of the limited number of studies on the course of functional status that were of sufficient or high quality (2 studies\textsuperscript{18,34}), and the heterogeneity of these studies with respect to the outcome measures used, it was not possible to analyze quantitatively changes in functional status over time. Even within these 2 studies, further limitations must be considered. Nollet\textsuperscript{34} selected a study population by including patients with PPS and excluding co-morbidity, whereas Windebank\textsuperscript{18} studied an unselected population of polio survivors. Furthermore, the duration of follow-up should be considered: in the study by Nollet,\textsuperscript{34} the follow-up period was 2 years for performance tests and 6 years for questionnaires, and in the study by Windebank,\textsuperscript{18} the follow-up period was 5 years. Contrary to the expectation, the length of the follow-up period seemed to have little influence on the results with regard to the course of functional status. The results of these studies tend to indicate no change or improvement in the subjective outcomes (questionnaires). A possible explanation is that subjects may have over-
rated their health problems at the beginning of the study, and were reassured by the medical attention given them during the study. The objective physical performance tests also showed improvement or no change. This may be because of a learning effect, but it remains an unresolved issue. In the Nollet study, to avoid bias in performance tests, subjects used the same walking aids or orthosis during all test sessions. More research, with emphasis on physical performance tests, is necessary to interpret these findings correctly.

**Muscle strength**

With regard to the 4 studies with sufficient to high quality and no overlap in subjects, it was not possible to analyze quantitatively changes in muscle strength over time, because of the study population's heterogeneity, the duration of follow-up and insufficient data presentation.

The 2 articles that reported a decline in muscle strength had a follow-up duration of 7 and 8 years, respectively. This suggests that although muscle strength does deteriorate in people with late-onset sequelae of polio, the deterioration is slow and not detectable in a short follow-up period, because no decline in strength was found in studies with a follow-up of less than or equal to 2 years. In the 4-year follow-up reports of (partially) the same populations as the long-term studies, deterioration in muscle strength was found. This implies that the minimum follow-up period needed to detect a decline in strength is probably around 4 years.

The relevance of the outcome measure used in a study was rated according to criterion 7 in the list of methodological criteria: the use of a fixed dynamometer was scored as positive. The value of an HHD in detecting changes over time in the lower-extremity muscles of subjects with polio is limited. The value of MMT according to the MRC rating, is also limited in detecting changes in strength, and its interexaminer reliability is poor. Fixed dynamometers are more appropriate instruments with which to detect changes in strength, and their reproducibility is good. When considering only those studies that used dynamometry, the results remained the same: no change or an increase in muscle strength was reported only in studies with a maximum follow-up period of 2 years. The study populations differed with respect to the presence or absence of new neuromuscular symptoms, the description of these symptoms and the inclusion or exclusion of subjects with co-morbidity. Because different definitions of the new neuromuscular symptoms were used, it is impossible to evaluate the association between a decline in strength and the occurrence of new neuromuscular symptoms.

Four studies described in this review include groups of healthy controls, so as to compare the decline in muscle strength in subjects with polio with the decline in strength in healthy subjects. None of the studies showed a significant difference in change in muscle strength in time between polio subjects and healthy controls, but 3 of the 4 studies had a follow-up of less than 2 years. One study had a follow-up period of 7 years, but included only a small number of patients and controls. From these studies it can be concluded that muscle strength deteriorates slowly over the years in people with sequelae of poliomyelitis. However, deterioration in muscle strength cannot be detected with a follow-up period of less than 2 years.
Prognostic factors
The limited number of studies on prognostic factors of changes in functional status or muscle strength revealed only the extent of paresis as a prognostic factor for change in the NHP physical mobility score, that is, a weaker person declines more over time than does a stronger person.34

Review methodology
Six databases were used to identify relevant articles, and the reference lists of the selected articles were also examined; therefore, it seems unlikely that publications may have been missed because of, for instance, language restrictions or because they were published in nonindexed journals. The methodological criteria list was adapted from a list used to score the methodological quality of studies about the clinical course and prognostic factors of non-specific neck pain.17 The methodological criteria were specified for the population and the purpose of this review. The knowledge about prognostic methodological criteria is limited and few prognostic reviews have been published. The Borghouts criteria list17 has been developed to evaluate prognostic studies of musculoskeletal disorders and was therefore considered the best criteria list available for this review.

Some errors could have occurred in the methodological scoring, because in some studies it was not clear whether failure to meet the criterion was because of the study design or incomplete reporting. Furthermore, some studies did not report drop-outs or loss to follow-up; selection bias may be suspected only if those subjects who completed the follow-up are included.

We used arbitrarily chosen cutoff points to consider a study as of sufficient quality (internal validity score, 4 points) and of high quality (internal validity score, > 4 points). Although we did not do sensitivity analyses to assess the robustness of these cutoff points, it is unlikely that a change in cutoff point would have led to different conclusions.

Implications for future research
Given the limited evidence, further research is needed to inform subjects with polio residuals about their future perspectives with regard to functional decline and progression of weakness. This information is also valuable for clinicians managing patients with PPS and for targeting treatment programs to those people who are most at risk for functional decline. Because the population with late-onset sequelae of poliomyelitis is getting older, ageing and factors associated with ageing, such as co-morbidity must be considered. According to Nielsen et al.,42 people with a history of poliomyelitis have a slightly increased morbidity rate with regard to age-matched controls, as measured by hospitalizations, with a 1.2 to 1.3-fold increased risk of being hospitalized with pulmonary diseases, heart diseases, gastrointestinal tract disorders, or diseases of the locomotive apparatus. However, such subjects with co-morbidity have been excluded in most prospective studies, thereby introducing selection bias. Therefore, future studies should be conducted in an unselected study population that includes subjects with co-morbidity. Furthermore, it will be relevant to compare the
rate of decline in muscle strength in polio subjects with the rate of decline in muscle strength in age-matched controls with no history of poliomyelitis. Therefore, we recommend that a control group be included in future prognostic studies. The results of the studies reported in this systematic review indicate that future studies should have a sufficiently long follow-up period, preferably at least 4 years, in order to detect any change in muscle strength or functional status.

**Conclusion**

Due to the limited number of studies included in this review and their heterogeneity, it was not possible to draw a conclusion about the functional course of people with late-onset sequelae of poliomyelitis or the prognostic factors. Muscle strength deteriorates slowly over the years, and this was only reported in studies with a follow-up of at least 4 years. Because prognostic factors for change were not identified, and ageing and comorbidity may be assumed to aggravate the course of functional status and muscle strength in this large and still growing population of ageing survivors of poliomyelitis, long-term studies are urgently needed. These prospective studies should include age-matched controls and pay specific attention to prognostic factors.

**Acknowledgements**

Participants in the CARPA study group include: Janneke M. Stolwijk-Swüste, Anita Beelen, Frans Nollet, Guustaaaf J. Lankhorst, Joost Dekker, Gaby van Dijk, Els H. van den Ende, Bart Post, Maruschka Merkus, and Hans Speelman.
Appendix 2.1.1 Explanation of the methodological criteria from Table 2.1.1

1. Selection of study population. Positive if study population consists of a consecutive sample or random sample.

2. Description of inclusion and exclusion criteria. Positive if criterion is formulated for at least: history of paralytic poliomyelitis and a stable neurological period of at least 10 years.

3. Study size. Positive if the number of patients included in the study is ≥ 100.

4. Follow-up ≥ 24 months. Positive if the follow-up period is 24 months or more.

5. Drop-outs/loss to follow-up ≤ 15%. Positive if total number of drop-outs/loss to follow-up in a study ≤ 2 years is less than or equal to 15% or if total number of drop-outs/loss to follow-up in a study > 2 years is less than or equal to 20%.

6. Information on patients who completed follow-up versus drop-outs/loss to follow-up. Positive if reasons for drop-outs/loss to follow-up are given, or no drop-outs/loss to follow-up. Drop-outs/loss to follow-up: all patients in the assembled cohort minus the number of patients at the main moment of health status measurement for the main outcome measure, divided by all patients in the assembled cohort.

7a. Relevance of outcome measures to the level of activities and participation. Positive if at least 2 of the following 3 items are used as outcome measures: perceived disability in physical activities, performance in physical activities, quality of life.

7b. Relevance of outcome measures to the level of muscle strength. Positive if a fixed dynamometer is used.

8. Validity of outcome measures. Positive if the study tested the validity or referred to other studies in which validity was established.

9. Reproducibility of outcome measures. Positive if the study tested the reproducibility or referred to other studies in which reproducibility was established.

10. Description of potential prognostic factors. Positive if at least 6 of the following 11 items are reported at baseline: age (mean and standard deviation or CI), sex (number or percentage), clinical and disease characteristics, physical impairments, cognitive impairments, co-morbidity, coping and emotional status, social support/context, fatigue, treatments and use of rehabilitation services, use of aids and devices.

11. Descriptive statistics of most important outcome measures. Positive if frequency/percentage/mean(SD/CI/median)/range of at least 1 of the following 4 outcome measures are included in each follow-up measurement: perceived disability in physical activities, performance in physical activities, quality of life, strength.

12. Descriptive statistics of most important prognostic factors. Positive if frequency/percentage/mean(SD/CI/median)/range of the most important prognostic factors are included in each follow-up measurement.

Appropriate analysis techniques

13. Univariate technique. Positive if univariate crude estimates are provided and positive if criterion 14 is positive.

14. Multivariate technique. Positive if multivariate techniques are used to adjust for other prognostic factors and if the number of cases in the multivariate analysis is at least 10 times the number of independent variables in the analysis.
References


The course of functional status and muscle strength in patients with late-onset sequelae of poliomyelitis: an update of the literature (July 2004 – July 2009)

J.M. Stolwijk-Swüste,
A. Beelen, F. Nollet

Unpublished manuscript
Introduction

Polio survivors are often confronted with new neuromuscular symptoms 30 to 40 years after the acute polio, termed as the post-polio syndrome (PPS), which is characterized by progressive new weakness and/or abnormal muscle fatigability, with or without generalized fatigue, muscle atrophy, and pain in the absence of other medical conditions to explain the symptoms.1

In 2005 our systematic review, summarizing the available literature on the course of functional status and muscle strength in patients with late-onset sequelae of poliomyelitis (LOSP) until July 2004, was published.2 The systematic review reported that due to the limited number of studies and heterogeneity in outcome measures, it was not possible to draw a conclusion about the functional course of people with late-onset sequelae of poliomyelitis or prognostic factors. Literature on the course of muscle strength showed a slow deterioration over the years, but only in studies with a follow-up of at least 4 years.

The aim of this update is to provide an additional overview of the literature on the course of functional status and muscle strength in patients with LOSP, published between July 2004 and July 2009.

Methods

For this update a literature search from July 2004 up to July 2009 was conducted in MEDLINE, using the following keywords: postpolio, postpoliomyelitis, postpoliomyelitis syndrome, post poliomyelitis muscular atrophy, and poliomyelitis. The selection method was similar to the selection method used in the original systematic review.2 JMS-S and AB independently scored the methodological criteria of the articles that were identified according to the 14 criteria described in the review.2 The studies on both functional status and muscle strength, were scored twice with regard to methodological quality, because the outcomes of criterion 7, 8 and 9 could be different on the course of functional status or the course of muscle strength.

Results

Three articles meeting the inclusion criteria have been published since July 2004. In addition our own follow-up study was included.3 Four studies3-6 reported on the course of functional status of which 3 also studied the course of muscle strength.3,5,6 The total methodological scores of the 4 studies ranged from 5 to 12, with a mean of 8.6, and internal validity scores ranged from 1 to 5. The studies of Sorenson and Stolwijk were considered to be of sufficient and high quality (internal validity score, 4, 5 53). The data from the 4 articles are summarized in Table 2.2.1 with regard to study population, study design, sample size, outcome measures, results, and methodological scores.

Functional status

On the course of functional status, all included studies reported on the course of walking capacity, but different outcome measures were used. Klein et al. reported no change in a 10-m walking test at maximum speed,4 while Stolwijk et al. reported no
change in 10-m walking test at comfortable speed.\(^3\) The Stolwijk study though also described a significant decline in distance walked in 2 minutes over a period of 5 years.\(^3\) The 15-year follow-up study with sufficient quality\(^5\) reported an increase in time taken to walk 30-m of 2.5% and the 4-year follow-up study of low internal validity described an increase in time of 6–8% on the 30-m walking test.\(^6\) Per year, Sorenson described a decline of 0.2% in walking capacity, Willen of 1.5–2.0% and Stolwijk of 0.7%.\(^3,5,6\) Combining these 4 new studies with the studies reported in Chapter 2.1 results in 4 studies with sufficient to high quality on the course of functional status.\(^3,5,7,8\) Two of these 4 studies used the same population, for which the results were first reported at 5- and later on at 15-year follow-up.\(^5,7\)

**Muscle strength**

On the course of muscle strength 3 studies used a fixed dynamometer. Stolwijk et al. reported a decline in strength of the knee extensors of 8% over 5 years, i.e. a decline of 1.6% per year (high internal validity).\(^3\) Willen et al. (low internal validity) found a decline of 9.6% in knee flexion (isometric) and 19–20% in ankle dorsal flexion over 4 years, but no decline in knee extension, knee flexion (isokinetic) and ankle plantar flexion.\(^6\) Sorenson et al. (sufficient internal validity) measured a significant decline over 15 years in all muscle groups from the upper extremities, except for pronation, and a non-significant decline in strength for knee flexion, knee extension and ankle dorsal flexion of 0.2–1.4% per year and an increase in ankle plantar flexion of 0.4% per year.\(^5\)

**Prognostic factors**

One study reported on prognostic factors: Stolwijk et al. reported a small impact of co-morbidity on the course of functional independence, but no impact on the course of perceived physical functioning.\(^3\) Age had no impact on the course of functioning.\(^3\) Furthermore, the severity of paresis of the legs had a negative impact on the course of functional independence.\(^3\)

**Discussion**

**Functional status**

The total of 8 studies of low to high validity focussing on functional status used different outcome measures for perceived functioning and follow-up ranged from 1.4 to 15 years.\(^3,8,10,11\) All studies reported a deterioration in perceived functioning at their latest follow-up measurement. The heterogeneity of outcome measures, prevents a quantitative analysis of the changes in perceived functional status over time. This stresses the need for a uniform measurement instrument to assess perceived functioning in patients with LOSP. Recently, Stolwijk et al. have recommended the SF-36 physical functioning subscale as core qualifier to assess physical functioning in patients with a history of poliomyelitis.\(^11\) This update on the literature confirms the importance to implement such a common core qualifier.

Change over time in walking ability was detected in the 30-m and 2-minute walking test,
Table 2.2.1 Characteristics and methodological scores of the studies with information on the course of functional status and muscle strength in subjects with sequelae of poliomyelitis

<table>
<thead>
<tr>
<th>Study</th>
<th>Study population</th>
<th>Study design</th>
<th>Sample size (N)</th>
<th>Outcome measure</th>
<th>Results</th>
<th>Total methodological score (max. 14)</th>
<th>Internal validity score (max. 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Klein et al.</td>
<td>Local community</td>
<td>Prospective</td>
<td>96</td>
<td>Daily step activity</td>
<td>NC&lt;br&gt;↓ (SNM) in PPS</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Co-morbidity not excluded</td>
<td>Follow-up mean 1.4 ± 1.1 y</td>
<td>68% PPS Controls 112</td>
<td>Perceived activity PASE</td>
<td>↓ NC</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Maximum walking speed m/s</td>
<td>NC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sorenson et al</td>
<td>Unselected residents of a county</td>
<td>Prospective</td>
<td>50</td>
<td>30.6-m walking test</td>
<td>* 2.5% increase in time, i.e. decline in walking</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Co-morbidity not excluded</td>
<td>Follow-up 15 y</td>
<td></td>
<td>Object turning</td>
<td>↓ NC</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Object displacing</td>
<td>↑*</td>
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<td></td>
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<td></td>
<td></td>
<td>Pins and collars</td>
<td>↑* 24%</td>
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<td></td>
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<td></td>
<td></td>
<td>Screw manipulation</td>
<td>↑* 26%</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>EFIM</td>
<td>↑* 21%</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>EEIM</td>
<td>↑* 31%</td>
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<td></td>
<td></td>
<td>SUPIM</td>
<td>NC</td>
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<td></td>
<td>GripIM</td>
<td>NC</td>
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<td></td>
<td></td>
<td>PROM</td>
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<td></td>
<td>KFIM</td>
<td>NC</td>
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<td></td>
<td>KEIM</td>
<td>NC</td>
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<td>ADFIM</td>
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<td></td>
<td></td>
<td>APFIM</td>
<td>NC</td>
<td></td>
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<tr>
<td>Stolwijk et al</td>
<td>Hospital registration</td>
<td>Prospective</td>
<td>168</td>
<td>FIM total score</td>
<td>↓* 1.8%</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Co-morbidity not excluded</td>
<td>Follow-up 5 y</td>
<td></td>
<td>Short Form-36 physical functioning subscale</td>
<td>↓* 9.2%</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>2-minute walking test</td>
<td>↓* 3.6% in distance, i.e. decline in walking</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10-m walking test</td>
<td>↓* 10.6% in 3 years</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>KEIK</td>
<td>↑* 8% in 5 years in subgroup of n = 47</td>
<td></td>
<td></td>
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</tbody>
</table>
| Subscale physical mobility | Functional Status 2
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>↓, other subscales NC</td>
<td>Muscle Strength 3</td>
</tr>
<tr>
<td>Spontaneous walking *6–8% increase in time, i.e., decline in walking</td>
<td></td>
</tr>
<tr>
<td>Maximal walking NC</td>
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</tr>
</tbody>
</table>

Subscale physical mobility:
- KEIK
- KEIM
- KFIK
- KFIM

NHP-I: 30-m walking test

**Note.** ↓ = decrease; NC = no change; PASE = Physical Activity Scale for the Elderly; SNM = significance not mentioned; EFIM = elbow flexion isometric; EEIM = elbow extension isometric; SUPIM = supination isometric; gripIM = grip isometric; PROIM = pronation isometric; KFIM = knee extension isometric; KEIM = knee extension isokinetic; ADFIM = ankle dorsal flexion isometric; APFIM = ankle plantar flexion isometric; FIM = Functional Independence Measure; KEIK = knee extension isokinetic. NHP = Nottingham Health Profile; KFIM = knee flexion isokinetic.

*Significant (p < .05).
but not in the shorter 10-m walking test. Apparently, short walking tests of 10 meters are less able to detect change over time in this population. This is in line with a recent study that a 2-minute walking test at comfortable speed showed the best clinimetric properties to detect change in comparison with 10-m walking tests at comfortable or maximal speed or the timed-up-and-go test.\textsuperscript{11} It was recommended to use the 2-minute walking test routinely as a common outcome measure in future studies to facilitate the comparison of results. The studies with sufficient to high quality reported a slow decline in walking capacity of 0.2 – 0.7\% per year.\textsuperscript{3,5} One study of low internal validity reported a decline of 1.5 – 2.0\% per year.\textsuperscript{6} Interestingly, the high quality study describing the intermediate results of the 15-year follow-up study population of Sorensen at 5 years follow-up showed no decline, but instead an improvement of 15\% on the 30-m walking test.\textsuperscript{7} At baseline measurement of the Sorenson study though only 66\% of the subjects reported symptoms of progressive weakness, at 5 year follow-up 76\% and at 15 year follow-up 82\%.\textsuperscript{5,7} This is a consequence of their study population, which consisted of an unselected population-based sample of persons with a history of poliomyelitis, and therefore not all experiencing LOSP at the start of the study. This may explain that a decline in walking capacity was only found in the longer follow-up as more subjects became symptomatic over time. Therefore the length of follow-up period needed to detect changes in walking capacity over time in polio survivors in the Sorenson study should be interpreted with caution.\textsuperscript{5} Based on the results of the sufficient to high quality studies and taking patients into account who already experience LOSP, we conclude that walking capacity deteriorates slowly over the years, ranging between 0.2 – 0.7\% per year, and require studies with at least 5 years of follow-up.

**Muscle strength**

The 2 extra studies identified in the update of the systematic review support the earlier conclusion that muscle strength deteriorates slowly over the years.\textsuperscript{3,5} The 6 sufficient to high quality studies reported a decline in muscle strength ranging between 0.2 and 1.9\% per year.\textsuperscript{3,5,8,12-14} This decline was only reported in studies with a follow-up of at least 4 years and already at 3 years in an older population with co-morbidity. This confirms the need for long term observational study designs in order to assess the course of muscle strength in subjects with a history of poliomyelitis.

**Prognostic factors**

In both the study by Nollet et al. and the study by Stolwijk et al. the extent of paresis at baseline, reflecting the severity of residual polio impairments, was a prognostic factor negatively affecting the course of functioning over time, although assessed with different outcome measures, respectively perceived physical functioning (Nottingham Health Profile) and functional independence (FIM\textsuperscript{TM}).\textsuperscript{3,8} These findings corroborate the hypothesis that in extensive paresis an insidious decline in strength may have a significant negative impact on functioning, since these subjects lack spare muscle capacity and their ability to adapt with new functional solutions by using other muscles is limited. Furthermore, to maintain certain daily life activities, polio survivors increasingly have to draw on their already reduced muscle mass. This supports the “overuse” hypothesis as an explanation for the new neuromuscular symptoms, such
as pain, fatigue and reduced endurance, in patients with a history of poliomyelitis. Stolwijk et al. was the only study who reported a small impact of co-morbidity on the course of functional independence. This finding is in line with studies in patients with stroke and multiple sclerosis. In their discussion, Stolwijk et al. questioned the sensitivity of the instrument used in their study, the Cumulative Illness Rating Scale, to measure co-morbidity in subjects with LOSP and recommended further research on the impact of co-morbidity on functioning in polio survivors with a co-morbidity measure which is sensitive to report co-morbidities especially in the musculoskeletal system.

Conclusions

The heterogeneity in outcome measures between studies precludes a quantitative analysis of the decline in perceived functional status over time. Nevertheless, all studies on perceived functioning report a deterioration over time. Walking ability, assessed with timed walking tests, deteriorates slowly, 0.2 – 0.7% per year, whereas muscle strength declines 1.5 – 1.9% per year. Factors that negatively affect the decline in functioning that have been reported in high-quality studies were the severity of polio residuals and co-morbidity, while age so far has not been shown to influence the decline in functioning over time. In general, studies require long term follow-up periods to observe a change in functioning with a minimum duration between 3 and 5 years depending on the outcome measures and study population. Uniformity in outcome measures between prognostic studies on all levels of functioning (impairments, activities and participation) is crucial to compare studies and to gain better insight in the course of functioning over time and in factors that may affect this course in polio survivors.

References


The WOMAC-PF as a measure of physical function in patients with Parkinson’s disease and late-onset sequelae of poliomyelitis: internal consistency and item behaviour

On behalf of the CARPA study group

Submitted for publication
Abstract

Background and aim: The WOMAC-PF is an osteoarthritis-specific questionnaire used to establish the level of physical functioning. The items of the WOMAC-PF are primarily related to activities involving the lower extremities. The question arises whether the WOMAC-PF can also be used to assess physical functioning in other diagnostic groups in which lower limb function is impaired. The aim of this study was to assess clinimetric properties of the WOMAC-PF in patients with late-onset sequelae of poliomyelitis (LOSP) and Parkinson’s disease (PD).

Methods: Unidimensionality (using Principal Component Analyses and item fit (using Rasch analyses) were separately established for three diagnostic groups: osteoarthritis (OA) \( n = 288 \), LOSP \( n = 168 \) and PD \( n = 200 \). Additionally, differential item functioning (DIF) between the 3 diagnostic groups was assessed using ordinal regression (PLUM) analyses.

Results: Unidimensionality was adequate, with all items loading on the first principal component. The Rasch analyses revealed that item fit was generally good. DIF was found to be present between the 3 diagnostic groups in 10 of 17 WOMAC-PF items.

Conclusion: The WOMAC-PF is a unidimensional measure of physical functioning in patients with LOSP and PD, in addition to its established use in OA. When making cross-diagnostic comparisons of the level of physical functioning, directly comparing WOMAC-PF scores may not be adequate due to the presence of DIF.
Introduction

Limitations in walking and other activities involving the lower extremities are common in musculoskeletal and neurological diseases. When assessing these limitations, generic measures—i.e., measures not focusing on a particular disease—potentially offer the advantage of a uniform interpretation of the scores across various diseases. Generic measures yield scores with a similar interpretation in various diseases: this allows comparison of scores across diseases.

Adequate generic measures of limitations involving the lower extremities are scarce, however. The physical function subscale of the Short-Form 36 (SF-36) is commonly used as a generic measure of limitations, but this questionnaire does not focus specifically on lower extremity function, resulting in a less focused assessment of lower extremity-related limitations. In osteoarthritis (OA) and joint replacement patients, this has resulted in worse responsiveness for the SF-36 than for the Western Ontario and MacMasters Universities Osteoarthritis Index (WOMAC).1,2

The WOMAC is commonly used as an outcome measure in OA research. This questionnaire was devised as an OA-specific instrument to assess the impact of OA on pain, stiffness and physical functioning.3 The physical functioning subscale (WOMAC-PF) comprises items which focus on daily activities primarily involving the lower extremities, such as walking, stair-climbing, and other transfers (seating oneself, reclining). In OA populations, the WOMAC-PF has shown excellent clinimetric properties: the reproducibility, validity and responsiveness of the WOMAC-PF have been extensively established for various language versions in different countries.1,4-24 Additionally, Wolfe and Kong reported on the internal consistency and unidimensionality of the WOMAC-PF in patients with rheumatoid arthritis and fibromyalgia.25 The question arises whether the WOMAC-PF can be used to measure loss of lower extremity function in patients with other musculoskeletal or neurological diseases.

Therefore, the aim of this study is to establish the internal consistency and individual item behaviour of the WOMAC-PF in patients with Parkinson’s disease (PD) and patients with late-onset sequelae of poliomyelitis (LOSP), additional to its established utility in OA. Two research questions were studied: 1) Is the WOMAC-PF a unidimensional and internally consistent measure of lower-extremity related physical functioning in patients with PD and LOSP, and 2) can the WOMAC-PF be used to directly compare the level of physical functioning between patients with PD, LOSP and OA (cross-diagnostic validity)? Clinimetical analyses were performed to assess unidimensionality, internal consistency, individual item fit and differential item functioning of the WOMAC-PF in patients with PD, LOSP and OA.

Patients and methods

Patients

For this study, data were used from the baseline measurements of the CARPA study. This is a large-scale prospective cohort study in patients with PD, LOSP and OA currently in progress within the Netherlands. The inclusion criteria for the CARPA
study are: Parkinson’s disease (PD): diagnosis of Parkinson’s disease as established with the Gelb criteria, age < 85 years, life expectancy > 1 year at the time of inclusion, sufficient control of the Dutch language.

Late-onset sequelae of poliomyelitis (LOSP): history of confirmed poliomyelitis anterior acuta including symptoms in at least one limb (muscle weakness, atrophy and areflexia with normal sensibility), a recorded visit to a neurologist or physiatrist within five years prior to inclusion, age 45 – 85 years, life expectancy > 1 year at the time of inclusion, sufficient control of the Dutch language.

Osteoarthritis (OA): diagnosis of uni- or bilateral OA of the knee and/or hip as established with the clinical or radiological ACR-criteria, a referral to a rheumatologist, orthopedic surgeon or physiatrist within one year prior to inclusion, Lequesne Algofunctional Index score > 2, age 50 – 85 years, life expectancy > 1 year at the time of inclusion, sufficient control of the Dutch language.

Data from all patients were used. In total, 200 PD patients, 168 LOSP patients and 288 patients with OA were included. This resulted in a total study population of N = 656.

WOMAC-PF

The WOMAC-PF consists of 17 items concerning daily activities with a dominant involvement of the lower extremities. These activities include ascending and descending stairs, standing, walking, bending, shopping, lying in bed, getting in and out of a bed, bath, chair or car seat, dressing, and doing household chores. All items are phrased as questions, asking the respondent how much difficulty is experienced while performing these activities as a consequence of OA. For the populations studied here, the phrasing of the questions was adjusted to indicate the correct diagnosis (either PD, LOSP or OA). Answers are provided on a 5-point scale ranging from 0 (no difficulty at all) to 4 (very much difficulty). All item responses are summed into a scale score ranging from 0 to 68, with a higher score indicating worse physical functioning.

Analyses

Unidimensionality and Internal consistency

To assess the unidimensionality of the WOMAC-PF in the 3 patient populations, a Principal Component Analysis (PCA) with a forced 1-component solution was performed. This analysis provides the fraction of variance in WOMAC-PF scores accounted for by the first principal component, and the loadings of the individual items on the first component. Component loadings were considered adequate if they exceeded 0.40. To assess the validity of limiting the PCA to a 1-component solution, scree plots were made showing the eigenvalues of all components. The number of components before the elbow of the plot is considered to be the adequate number of principal components for further analysis.

Subsequently, the internal consistency of the questionnaire was assessed by determining Cronbach’s alpha in the 3 patient groups. These analyses were performed in SPSS version 13.0.
Individual item fit

To assess the fit of all items within the scale, a Rasch analysis was performed.\textsuperscript{31,32} First, for every item an assessment was made of the most likely response given a specific level of physical functioning (‘threshold mapping’). The threshold map was considered adequate if no reverse thresholds were present within the item. This means that for low levels of physical functioning, the response category representing the worst ability is the most likely response and for high levels of physical functioning the response representing best ability is the most likely response, with a logical progression of most likely responses through the categories as functional ability increases. Reverse thresholds would mean this logical pattern is violated in the data.

Next, item difficulty and residual outfit statistics were estimated. Item fit was considered adequate if the outfit statistic’s value was between –2.5 and +2.5. A value below –2.5 indicates that the item is redundant (information provided by this item does not add sufficient unique information not provided by other items within the scale). A value over +2.5 represents a non-hierarchical item. This item cannot be assigned a fixed hierarchical position in the scale, within the tested population, indicating poor fit between expected and observed outcome.\textsuperscript{33,34} For every item, a Chi-square statistic indicated to what extent items fit over the whole range of the scale (i.e., does the item fit for both high-scoring and low-scoring patients). A significant $p$ value indicates poor fit in this Chi-square analysis. To control for the effects of multiple testing, the Bonferroni correction was used with the overall $\alpha$ set at 0.05 per scale analysis (i.e., per diagnostic group). All Rasch analyses were carried out using the Rumm2020 software.\textsuperscript{34}

Differential item functioning

The cross-diagnostic validity of the WOMAC-PF was determined by assessing differential item functioning (DIF) between the 3 patient populations. DIF is considered to be present when the difficulty of an item, as established with the Rasch analysis above, differs significantly between the 3 diagnostic groups. DIF can be further divided into uniform and non-uniform DIF. Uniform DIF is present when diagnostic group membership is a confounder of the relationship between the score on a single item and the overall scale score. Non-uniform DIF signifies that the association between a single item score and the overall scale score differs between diagnostic groups (i.e., diagnostic group membership is an effect-modifier of the relationship between single item score and overall scale score). To assess DIF, the analytical approach as described by Crane et al.\textsuperscript{35,36} and Zumbo and Gelin\textsuperscript{37,38} was used. In this approach, 3 different regression models are tested, with the WOMAC item score being used as the dependent variable in all 3 models. Three independent variables are used: trait level (i.e., WOMAC scale score), diagnostic group membership, and the interaction term of trait level and diagnostic group membership. The following 3 models were tested using ordinal regression (PLUM) analyses:

- Model 1: WOMAC item score = $B_1 \times$ trait level + $B_2 \times$ diagnostic group + $B_3 \times$ trait level $\times$ diagnostic group
- Model 2: WOMAC item score = $B_1 \times$ trait level + $B_2 \times$ diagnostic group
- Model 3: WOMAC item score = $B_1 \times$ trait level
Based on the outcomes of these 3 models, the presence of both uniform and non-uniform DIF can be established. In this paper, two different sets of criteria to establish DIF are used. According to Zumbo and Gelin, DIF can be identified by comparing Nagelkerke’s pseudo-$R^2$ between models. A change in $R^2$ of less than 0.035 signifies negligible DIF, between 0.035 and 0.07 shows moderate DIF, and 0.07 or greater indicates large DIF. Uniform DIF is assessed using the change in $R^2$ between Model 2 and Model 3 above. Non-uniform DIF is assessed by comparing $R^2$ between Model 1 and Model 2. The second set of criteria was presented by Crane et al. In their approach, first an overall assessment of DIF is made by comparing the $–2$ log likelihood ($–2$LL) difference between Model 1 and Model 3 with a Chi-square distribution with two degrees of freedom. A significant $p$ value denotes DIF. As a second step, uniform DIF is assessed by checking the regression coefficient for trait level (i.e., $B_1$ in the models above) in Models 2 and 3. If $B_1$ changes more than 5% in Model 3 as compared with Model 2, uniform DIF is considered to be present. Non-uniform DIF is established by analyzing the statistical significance of the difference in $–2$LL between Model 1 and Model 2.

Results
Characteristics of the 3 patient groups, including WOMAC-PF scale scores, are provided in Table 3.1. The percentage of patients with the lowest possible WOMAC-PF score (value 0) was 0.7% in OA, 6.7% in PD and 1.2% in LOSP. The maximum possible score of 68 was only reached by one OA patient. This indicates that no clear floor or ceiling effects were present in the WOMAC-PF sum scores for any of the diagnostic groups.

In the PCA to establish unidimensionality, all items of the WOMAC-PF loaded on the first principal components (component loadings $> 0.40$ for all items), in all 3 diagnostic groups. The fraction of variance accounted for by the first component was 55.6% in the OA group, 60.0% in the PD group and 50.5% in the LOSP group. Fraction of variance accounted for by the second component was 7.9% in OA, 7.3% in PD and 11.3% in LOSP respectively, indicating adequate unidimensionality of the WOMAC-PF in all 3 patient groups. Additionally, for all 3 populations the elbow of the scree plot was located at the second component, indicating that a 1-component solution is valid (see Figure 3.1). Internal consistency of the WOMAC-PF was excellent in both OA (Cronbach’s $\alpha = 0.95$), PD ($\alpha = 0.96$) and LOSP ($\alpha = 0.94$).

Table 3.2 features the results of the Rasch analyses. For the 3 patient groups, this table shows per item whether reversed thresholds were present (indicated with ‘Y’), the item difficulty with its standard error, the residual fit statistic, and the $p$ value of a Chi-

### Table 3.1 Correlations between questionnaires and walking capacity tests

<table>
<thead>
<tr>
<th></th>
<th>OA (n = 288)</th>
<th>PD (n = 191)</th>
<th>LOSP (n = 168)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (mean ± SD)</td>
<td>66.8 ± 8.8</td>
<td>66.8 ± 9.5</td>
<td>59.1 ± 7.9</td>
</tr>
<tr>
<td>Gender (% female)</td>
<td>71.2</td>
<td>42.9</td>
<td>60.1</td>
</tr>
<tr>
<td>WOMAC-PF (mean ± SD)</td>
<td>29.6 ± 13.5</td>
<td>17.3 ± 14.0</td>
<td>25.0 ± 13.1</td>
</tr>
</tbody>
</table>
Figure 3.1a–3.1c  Scree plots of the factor analyses
### Table 3.2 Results of the Rasch analyses

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. descending stairs</td>
<td>N</td>
<td>-0.27 ± 0.08</td>
<td>0.63</td>
<td>.886</td>
<td>N</td>
<td>0.33 ± 0.10</td>
<td>0.25</td>
<td>.928</td>
<td>N</td>
<td>-0.72 ± 0.09</td>
<td>3.28a</td>
<td>.024</td>
</tr>
<tr>
<td>2. ascending stairs</td>
<td>N</td>
<td>-0.47 ± 0.08</td>
<td>0.45</td>
<td>.404</td>
<td>N</td>
<td>-0.42 ± 0.10</td>
<td>1.71</td>
<td>.557</td>
<td>N</td>
<td>-1.58 ± 0.09</td>
<td>0.57</td>
<td>.589</td>
</tr>
<tr>
<td>3. rising from sitting</td>
<td>N</td>
<td>-0.50 ± 0.08</td>
<td>2.25</td>
<td>.025</td>
<td>N</td>
<td>-0.41 ± 0.10</td>
<td>-2.31</td>
<td>.161</td>
<td>N</td>
<td>-0.04 ± 0.09</td>
<td>-1.71</td>
<td>.023</td>
</tr>
<tr>
<td>4. standing</td>
<td>N</td>
<td>0.19 ± 0.08</td>
<td>0.28</td>
<td>.335</td>
<td>N</td>
<td>0.15 ± 0.10</td>
<td>0.29</td>
<td>.653</td>
<td>N</td>
<td>-0.65 ± 0.10</td>
<td>1.12</td>
<td>.457</td>
</tr>
<tr>
<td>5. bending to floor</td>
<td>N</td>
<td>-0.50 ± 0.08</td>
<td>1.08</td>
<td>.774</td>
<td>N</td>
<td>-0.41 ± 0.10</td>
<td>2.05</td>
<td>.186</td>
<td>N</td>
<td>-0.33 ± 0.09</td>
<td>-0.34</td>
<td>.815</td>
</tr>
<tr>
<td>6. walking on flat</td>
<td>N</td>
<td>0.64 ± 0.08</td>
<td>-1.14</td>
<td>.249</td>
<td>N</td>
<td>1.40 ± 0.12</td>
<td>0.84</td>
<td>.742</td>
<td>N</td>
<td>0.38 ± 0.10</td>
<td>-0.34</td>
<td>.535</td>
</tr>
<tr>
<td>7. getting in/out of car</td>
<td>N</td>
<td>-0.59 ± 0.08</td>
<td>1.06</td>
<td>.694</td>
<td>N</td>
<td>-0.75 ± 0.10</td>
<td>-0.26</td>
<td>.814</td>
<td>N</td>
<td>0.03 ± 0.11</td>
<td>-0.28</td>
<td>.298</td>
</tr>
<tr>
<td>8. going shopping</td>
<td>N</td>
<td>-0.69 ± 0.08</td>
<td>0.87</td>
<td>.180</td>
<td>N</td>
<td>-0.61 ± 0.10</td>
<td>-0.76</td>
<td>.282</td>
<td>N</td>
<td>-1.04 ± 0.10</td>
<td>2.12</td>
<td>.076</td>
</tr>
<tr>
<td>9. putting on socks</td>
<td>N</td>
<td>0.11 ± 0.08</td>
<td>1.91</td>
<td>.402</td>
<td>N</td>
<td>-0.50 ± 0.09</td>
<td>-1.64</td>
<td>.390</td>
<td>Y</td>
<td>0.78 ± 0.10</td>
<td>1.51</td>
<td>.649</td>
</tr>
<tr>
<td>10. rising from bed</td>
<td>N</td>
<td>0.11 ± 0.08</td>
<td>-1.35</td>
<td>.115</td>
<td>N</td>
<td>-0.48 ± 0.10</td>
<td>-1.38</td>
<td>.294</td>
<td>N</td>
<td>0.63 ± 0.10</td>
<td>-0.81</td>
<td>.008a</td>
</tr>
<tr>
<td>11. taking off socks</td>
<td>N</td>
<td>0.37 ± 0.08</td>
<td>-0.90</td>
<td>.614</td>
<td>N</td>
<td>-0.15 ± 0.10</td>
<td>-0.34</td>
<td>.944</td>
<td>Y</td>
<td>0.85 ± 0.11</td>
<td>0.68</td>
<td>.628</td>
</tr>
<tr>
<td>12. lying in bed</td>
<td>N</td>
<td>0.64 ± 0.08</td>
<td>2.62a</td>
<td>.050</td>
<td>N</td>
<td>0.45 ± 0.11</td>
<td>0.87</td>
<td>.257</td>
<td>Y</td>
<td>1.31 ± 0.11</td>
<td>0.67</td>
<td>.279</td>
</tr>
<tr>
<td>13. getting in/out of bath</td>
<td>N</td>
<td>0.05 ± 0.09</td>
<td>2.08</td>
<td>.130</td>
<td>Y</td>
<td>-0.16 ± 0.12</td>
<td>-0.51</td>
<td>.314</td>
<td>Y</td>
<td>-0.42 ± 0.09</td>
<td>0.49</td>
<td>.995</td>
</tr>
<tr>
<td>14. sitting</td>
<td>N</td>
<td>0.95 ± 0.09</td>
<td>0.36</td>
<td>.727</td>
<td>N</td>
<td>1.69 ± 0.13</td>
<td>1.31</td>
<td>.776</td>
<td>N</td>
<td>1.89 ± 0.11</td>
<td>0.85</td>
<td>.282</td>
</tr>
<tr>
<td>15. getting on/off toilet</td>
<td>N</td>
<td>0.43 ± 0.08</td>
<td>-1.73</td>
<td>.170</td>
<td>N</td>
<td>0.78 ± 0.11</td>
<td>-2.47</td>
<td>.053</td>
<td>N</td>
<td>1.11 ± 0.11</td>
<td>-1.83</td>
<td>.003a</td>
</tr>
<tr>
<td>16. heavy chores</td>
<td>N</td>
<td>-1.47 ± 0.08</td>
<td>1.59</td>
<td>.049</td>
<td>N</td>
<td>-1.55 ± 0.09</td>
<td>1.96</td>
<td>.028</td>
<td>N</td>
<td>-2.26 ± 0.11</td>
<td>-0.39</td>
<td>.258</td>
</tr>
<tr>
<td>17. light chores</td>
<td>N</td>
<td>1.00 ± 0.09</td>
<td>-0.35</td>
<td>.367</td>
<td>Y</td>
<td>0.19 ± 0.11</td>
<td>-0.83</td>
<td>.335</td>
<td>N</td>
<td>0.08 ± 0.10</td>
<td>-0.14</td>
<td>.859</td>
</tr>
</tbody>
</table>

Note. RT = reversed thresholds; SE = standard error; Sign. of Chi-sq. = p value of the Chi-square statistic. *non-hierarchical item; a poor item-fit over range of scale. For item difficulty, a lower value represents a more difficult item.
square statistic indicating the fit of the item over the range of the scale. No reversed thresholds were present in the OA group. In the PD group, 2 items showed reversed thresholds, and in the LOSP group 4. Residual fit statistics revealed that all items fit the scale in the PD group. In both the OA and LOSP group, one item did not fit the hierarchical pattern of the scale. No redundant items were present in the data of any of the 3 diagnostic groups. A significant Chi-square statistic was found for 2 items in the LOSP group, indicating poor fit of these items over the range of the scale. In both the OA and PD group, no significant Chi-square statistics were found.

In all 3 patient groups, the item concerning ‘heavy chores’ represented the most difficult activities (indicated by the most negative value for item difficulty in Table 3.2). ‘Going shopping’ was also among the 3 most difficult items in all 3 patient groups. ‘Getting in/out of a car’ was a difficult task for patients with OA and PD, but was of average difficulty in the LOSP population. At the opposite end of the scale, ‘sitting’ was among the easiest items in all 3 diagnostic groups, but there was a less consistent pattern over the groups for other items, indicating divergence in the hierarchical order of items between the 3 patient groups.

Based on Gelin and Zumbo’s guidelines for detecting DIF using Nagelkerke’s pseudo-$R^2$, moderate uniform DIF is present in the items on descending stairs, rising from bed, lying in bed and heavy chores. Large uniform DIF is present in the items on ascending stairs, putting on socks and taking off socks. In all other items, uniform DIF was negligible. No non-uniform DIF was detected in any item by this method.

Using the approach by Crane et al., the initial analyses for detecting DIF by looking at changes in $-2 \log$ likelihood between the full (including both main and interaction effects for diagnostic group membership as independent variables) and empty (comprising solely the trait level as independent variable) models suggests DIF is present in all 17 items. However, further analyses revealed uniform DIF (identified by a change in regression coefficient for trait level of at least 5% between a model including diagnostic group and a model without diagnostic group) to be present in 6 items: ascending stairs, standing, rising from bed, putting on socks, taking off socks, and heavy chores. Non-uniform DIF (identified by a significant change in $-2 \log$ likelihood between a model including the interaction term of trait level and diagnostic group membership, and a model without this interaction term) was present in 3 items when using $p = 0.01$ as cut-off point: rising from chair, bending to floor, and getting into/out of bath. Four additional items showed non-uniform DIF when applying $p = 0.05$ as cut-off point. No discernible DIF was detected in the remaining items.

**Discussion**

The results of this study imply that the WOMAC-PF is an internally consistent and unidimensional measure of limitations in lower extremity-related physical functioning in patients with PD and LOSP, in addition to its accepted use in patients with OA. In all 3 patient groups, internal consistency was excellent and unidimensionality adequate. The Rasch analyses showed some imperfection in the scale, but in general it can be concluded that item hierarchy was satisfactory.
## Table 3.3 Results of the DIF analyses

<table>
<thead>
<tr>
<th>WOMAC item</th>
<th>Detection of DIF: Δ–2LL and ΔNagelkerke R² between Model 1a and Model 3c</th>
<th>Uniform DIF: %ΔB₁ and ΔNagelkerke R² between Model 2b and Model 3c</th>
<th>Non-uniform DIF: Δ–2LL and ΔNagelkerke R² between Model 1 and Model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Δ–2LL</td>
<td>ΔR²</td>
<td>%ΔB₁</td>
</tr>
<tr>
<td>1. descending stairs</td>
<td>252.695 (p = .000)</td>
<td>0.048</td>
<td>0.0</td>
</tr>
<tr>
<td>2. ascending stairs</td>
<td>201.689 (p = .000)</td>
<td>0.116</td>
<td>9.8</td>
</tr>
<tr>
<td>3. rising from chair</td>
<td>249.275 (p = .000)</td>
<td>0.020</td>
<td>3.4</td>
</tr>
<tr>
<td>4. standing</td>
<td>258.661 (p = .000)</td>
<td>0.032</td>
<td>6.2</td>
</tr>
<tr>
<td>5. bending to floor</td>
<td>310.975 (p = .000)</td>
<td>0.005</td>
<td>0.0</td>
</tr>
<tr>
<td>6. walking on flat</td>
<td>246.515 (p = .000)</td>
<td>0.016</td>
<td>0.7</td>
</tr>
<tr>
<td>7. getting in/out of car</td>
<td>242.329 (p = .000)</td>
<td>0.031</td>
<td>4.3</td>
</tr>
<tr>
<td>8. shopping</td>
<td>273.763 (p = .000)</td>
<td>0.023</td>
<td>0.0</td>
</tr>
<tr>
<td>9. putting on socks</td>
<td>204.881 (p = .000)</td>
<td>0.074</td>
<td>15.3</td>
</tr>
<tr>
<td>10. rising from bed</td>
<td>211.272 (p = .000)</td>
<td>0.044</td>
<td>11.7</td>
</tr>
<tr>
<td>11. taking off socks</td>
<td>201.176 (p = .000)</td>
<td>0.070</td>
<td>13.2</td>
</tr>
<tr>
<td>12. lying in bed</td>
<td>217.954 (p = .000)</td>
<td>0.042</td>
<td>0.8</td>
</tr>
<tr>
<td>13. getting into/out of bath</td>
<td>202.912 (p = .000)</td>
<td>0.014</td>
<td>2.6</td>
</tr>
<tr>
<td>14. sitting</td>
<td>205.142 (p = .000)</td>
<td>0.019</td>
<td>1.5</td>
</tr>
<tr>
<td>15. rising from toilet</td>
<td>186.565 (p = .000)</td>
<td>0.030</td>
<td>3.4</td>
</tr>
<tr>
<td>16. heavy chores</td>
<td>235.264 (p = .000)</td>
<td>0.064</td>
<td>8.6</td>
</tr>
<tr>
<td>17. light chores</td>
<td>220.007 (p = .000)</td>
<td>0.009</td>
<td>1.8</td>
</tr>
</tbody>
</table>

Note. aModel 1: WOMAC item score = B₁ * WOMAC scale score + B₂ * diagnostic group + B₃ * (WOMAC scale score * diagnostic group); bModel 2: WOMAC item score = B₁ * WOMAC scale score + B₂ * diagnostic group; cModel 3: WOMAC item score = B₁ * WOMAC scale score. 
Δ–2LL = change in –2 log likelihood statistic between the models; ΔNagelkerke R² = change in Nagelkerke pseudo-R² between the models; %ΔB₁ = percentual change in the regression coefficient for trait level (i.e., WOMAC scale score) between the models.
The WOMAC-PF was specifically designed as a measure of functional limitations in patients with OA of the hip or knee, focusing on daily activities involving the lower extremities, such as walking, stair climbing and other transfers.\textsuperscript{3,15} Although the WOMAC-PF is OA-specific, limitations in the activities included in the questionnaire are not specific to OA. Similar limitations are encountered in other musculoskeletal and neurological diseases such as PD and LOSP. The strong focus of the WOMAC-PF on these activities makes the questionnaire applicable to these other patient groups as well. The present study and previous work by Wolfe and Kong\textsuperscript{25} have shown that the WOMAC-PF performs well in patients with PD, LOSP, rheumatoid arthritis (RA) and fibromyalgia (FM).

Despite adequate clinimetric properties in both PD and LOSP, a direct comparison of the level of physical functioning between patients with different diseases based on the WOMAC-PF should be done with caution. The presence of DIF as established for a number of WOMAC-PF items in the present study means that the difficulty of a given activity varies depending on the diagnostic group. Due to specific symptoms and disease processes associated with OA, PD and LOSP respectively, different activities will become problematic. The item hierarchies found in analyses presented here may serve to identify specific disabilities relevant to specific disorders. In all 3 diagnostic groups, heavy chores and shopping were among the most problematic activities. In addition, specific activities were identified as problematic in specific populations. In LOSP patients, both ascending and descending stairs were high in the item hierarchy, indicating highly problematic activities. This is consistent with previous studies reporting disability in stair-climbing in LOSP patients.\textsuperscript{39,40} Similarly, for OA and PD patients getting into and out of a car represented difficult activities, as did rising from bed in PD and rising from sitting in OA. In OA, rising and sitting down have also been identified previously as activities susceptible to disability.\textsuperscript{41} These findings are consistent with a previous study by Wolfe and Kong.\textsuperscript{25} In their study, heavy chores was the most difficult WOMAC-PF item for patients with OA, RA and FM. Other difficult items for these 3 patient groups included going upstairs and getting in and out of bath. Item hierarchy over the different diagnostic groups was more consistent in Wolfe and Kong's study than in the present study, possibly due to the greater similarity of the 3 diagnoses studied.

These findings may represent an important stepping stone towards more precise and tailored assessment, or adaptive testing, of disabilities in musculoskeletal and neuromuscular disorders. However, in order to be able to adequately assess and identify the specific activities most problematic and relevant to patients from specific diagnostic groups, additional research and further input from the patient perspective is required. Based on the current results, cross-diagnostic comparisons of the level of physical functioning in patients with chronic musculoskeletal or neuromuscular disorders should be made with caution due to the possible presence of DIF. As the current study shows this to be present when comparing OA, LOSP and PD, it is likely that DIF will also be present when comparing other diagnostic groups using the WOMAC-PF.

In the DIF analyses, the initial test of comparing the \(-2LL\) statistic between the model comprising both the check for confounding and effect-modification (Model 1) and the
model comprising neither of the two (Model 3) suggested the presence of DIF in every single WOMAC-PF item. However, subsequent analyses showed that DIF was present in a maximum of 10 items. This can be explained through the criteria used to assess DIF. The initial check was based on the –2LL statistic, whereas the subsequent analysis for uniform DIF used the change in regression coefficient for trait level instead. In a number of items, diagnostic group membership was a strong independent predictor of item score, but not a confounder of the relationship between item score and trait level (i.e., scale score). This resulted in a significant change in –2LL but no change in the regression coefficient for trait level when diagnostic group was removed from the equation; hence the results suggesting presence of DIF when looking at the –2LL change, but not when comparing trait level regression coefficients.

A second methodological issue is that there are no established cut-off points to interpret the results of Rasch analyses as adequate or inadequate, with regard to the number of items within a scale not meeting all criteria for good item behaviour (no reversed thresholds, adequate residual fit, and adequate fit over the entire scale as expressed with the Chi-square statistic). In all 3 patient groups, there was at least one item not reaching the required standard on one of the criteria, but no items failing more than one criterion. In general, the analyses (including internal consistency and unidimensionality) show a consistent pattern indicating adequate clinimetric properties of the WOMAC-PF in both OA, LOSP and PD patients. We therefore feel our conclusion that this questionnaire can be used to assess physical functioning in these patient groups, is justified. However, it should be noted that the current study did not assess other clinimetric properties of the WOMAC-PF in PD and LOSP. Neither the validity nor the responsiveness of the WOMAC-PF have been established in these populations.

In this paper, the unidimensionality and item behaviour of the WOMAC-PF have been established for patients with PD and LOSP, providing a welcome addition to the assessment of specific disabilities in these patients. As such, this study serves as a first step towards a wider, generic application of the WOMAC-PF as a patient-reported outcome in medical outcome research.

References


SF-36 physical functioning scale and 2-minute walking test advocated as core qualifiers to evaluate physical functioning in patients with late-onset sequelae of poliomyelitis

J.M. Stolwijk-Swüste, A. Beelen, G.J. Lankhorst, F. Nollet
On behalf of the CARPA study group

Abstract

Objective: To select a questionnaire and walking capacity test based on comparison of clinimetric properties and mutual association to be used as ‘core’ qualifiers for physical functioning in patients with late-onset sequelae of poliomyelitis (LOSP).

Design: Repeated-measures at 3-week intervals.

Subjects: An unselected sample of 57 patients with late-onset sequelae of poliomyelitis from a prospective cohort study.

Methods: Physical functioning scales from Short Form-36 (SF36-PF), Western Ontario and McMaster Universities Osteoarthritis index (WOMAC-PF) and Nottingham Health Profile (NHP-PM). Timed-Up-and-Go test, 10 m walking at self-preferred and maximum speed, and 2-minute walking test.

Results: Test-retest reliability of SF36-PF and WOMAC-PF was good (intraclass correlation coefficient (ICC) 0.92 and 0.89, respectively), sufficient for NHP-PM (ICC 0.74) and excellent for walking tests (ICC 0.93 – 0.96). The smallest detectable changes were 18.4 and 16.5, respectively, for WOMAC-PF and SF36-PF, and 26.7 for NHP-PM. The smallest detectable change was best for the 2-minute walking test (22.9 m). Correlation coefficients between questionnaires and walking tests ranged from 0.32 to 0.69, with the highest correlation between the SF36-PF and 2-minute walking test.

Conclusions: The SF36-PF and 2-minute walking test are recommended as core qualifiers for physical functioning, the major increasing disability in late-onset sequelae of poliomyelitis, to assess perceived physical performance and walking capacity in research and clinical practice.
Introduction

Many individuals with a history of poliomyelitis suffer from post-poliomyelitis syndrome (PPS) and report increasing difficulties with physical functioning, such as walking, standing, climbing stairs and other mobility-related activities of daily life. The International Classification of Functioning, Disability and Health (ICF) is a framework that describes the functional consequences of a disease at the level of body function and structure and daily activities and participation. The qualifiers used for the activities and participation domain are performance and capacity. Performance describes what an individual does in his or her current environment, whereas capacity describes an individual’s ability to execute a task or action. Self-administered questionnaires about self-perceived physical functioning provide information about the appreciation of the performance of an individual in his or her own environment. Capacity can be measured in a standardized environment with time-scored walking capacity tests at self-preferred or maximum speed. In a clinical setting, walking at a comfortable speed is assumed to reflect walking capacity in daily life.

An essential requirement of all outcome measures is that they are valid and reproducible. In studies, group comparisons are usually made, but in clinical practice, measurements are often used for individual evaluation purposes and to detect changes over time in a patient. Therefore, parameters of measurement error or agreement are important.

Comparing the results of studies focusing on patients with late-onset sequelae of poliomyelitis is difficult, because many different instruments have been used to assess physical functioning. The aim of the present study was to prioritize one questionnaire and one walking test from a number of questionnaires and tests that are widely used in post-polio populations by comparing their reproducibility, measurement range and mutual associations, in order to advocate their use as core qualifiers of physical functioning in research and clinical practice.

Methods

Study population

The patients in this study formed an unselected subgroup consisting of a consecutive series of 57 patients from a cohort of 168 patients, which has already been described in detail elsewhere. The patients were recruited from 2 university hospitals that specialize in the treatment of late-onset sequelae of poliomyelitis. The inclusion criteria were: (i) history of poliomyelitis anterior acuta; (ii) presence of residual paresis in at least one extremity; (iii) consultation (not necessarily the first consultation) with a neurologist or physical medicine and rehabilitation specialist in the previous 5 years; (iv) age 45 to 85 years; (v) no medical condition indicating a life expectancy of less than one year. All patients gave their informed consent to participate in the study. The study has been approved by the medical ethics committee.
Core qualifiers physical functioning

Chapter 4

Measurement instruments

Perceived physical performance

Two questionnaires that are widely used were selected for this study: the Short Form 36\(^{11-13}\) (SF-36) and the Nottingham Health Profile (NHP).\(^{3,7,14-17}\) Furthermore the Western Ontario and McMaster Universities Osteoarthritis Index physical functioning scale (WOMAC-PF) was selected. The WOMAC was originally designed to assess osteoarthritis,\(^{18}\) but has recently been reported as a suitable instrument to measure physical functioning in patients with late-onset sequelae of poliomyelitis.\(^{19}\)

Short Form-36

The SF-36 is a self-administered questionnaire that measures generic health concepts, consisting of 9 multi-item scales: physical functioning, role limitations due to physical functioning, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional functioning, general mental health and change in health.\(^{11}\)

The SF-36 physical functioning subscale (SF36-PF) consists of 10 questions scored on a 3-point scale. A subscale score is calculated, and each scale is scored from 0 to 100, with higher scores indicating higher levels of functioning or well-being. The SF-36 has been translated and validated for the Dutch population.\(^{20}\)

Nottingham Health Profile

The NHP is a self-administered questionnaire that measures self-perceived health status, divided into 6 categories: physical mobility, energy, pain, social isolation, emotional reactions, and sleep. The physical mobility category (NHP-PM) consists of 9 questions, with a score ranging from 0 (no complaints) to 100 (answered yes to all questions). To compare the NHP with the SF-36 and the WOMAC, we transformed the score to 0 – 100, with higher scores indicating higher levels of functioning or well-being (no complaints). The Dutch version of the NHP-PM has been found to have satisfactory clinimetric properties in patients with chronic heart failure and myocardial infarction or stroke.\(^{14,21}\)

Western Ontario and McMaster Universities Osteoarthritis Index

The WOMAC is commonly used as an outcome measure in osteoarthritis (OA) research,\(^{18}\) but it has recently been reported to be an adequate questionnaire for the measurement of physical functioning in patients with late-onset sequelae of poliomyelitis.\(^{19}\) The physical functioning subscale (WOMAC-PF) consists of 17 items concerning daily activities that primarily involve the lower extremities, such as walking, stair-climbing, and other transfers (sitting down, reclining). The WOMAC-PF is scored on a 5-point scale, ranging from 0 (no difficulty at all) to 4 (very much difficulty). A subscale sum score is calculated, ranging from 0 to 100, with higher scores indicating higher levels of functioning or well-being. In OA populations the WOMAC-PF has been found to have excellent clinimetric properties.\(^{22}\) The Dutch version of the WOMAC makes valid international Dutch-English comparison possible after correction for differential item functioning.\(^{23}\)
Walking capacity

A wide range of walking tests has been used in this field of research to measure walking capacity.\textsuperscript{16,24,25} We selected 10 m walking at self-preferred and maximum speed, and the distance walked in 2 min at self-preferred speed. We chose the 2-minute walking test, and not the 6-minute walking test that is used in many other populations because we anticipated that a number of our patients would not be able to complete the 6-minute walking test, thereby introducing selection bias. We added the Timed-Up-and-Go test (TUG) which can easily be included in a routine medical examination and which measures basic mobility skills that are used in everyday life, besides walking itself, and therefore might have a higher correlation with physical functioning questionnaires.\textsuperscript{26} The walking tests were performed indoors on a marked path.

*Time needed to walk 10 m at self-preferred and maximum speed*

The time needed to walk 10 m at self-preferred and maximum speed was timed on a stopwatch. The 10-m walking test has been shown to be valid and reliable.\textsuperscript{27}

*Distance walked in 2 min at self-preferred speed*

The patients walked at a self-preferred speed for 2 min, and the distance they covered was measured. The 2 min were timed on a stopwatch.

*Timed-Up-and-Go test (TUG)*

The time needed to stand up from a sitting position, walk 3 m, turn around, walk 3 m back and sit down again in the chair, all at a self-preferred speed, was registered. This test has been shown to be valid and reliable.\textsuperscript{26,28}

**Assessment protocol**

Two test sessions were performed on 2 visits to the hospital that were scheduled with a 3-week interval. Prior to the visit to the hospital, the patients received the questionnaires and instructions on how to complete each questionnaire. They were asked to complete the questionnaires at home and to return them when they visited the hospital. At the hospital a physician interviewed the patients and administered the tests in a standard sequence.

**Data analysis**

Demographic data were analyzed with descriptive statistics. The test-retest reliability for the walking tests and questionnaires was assessed by calculating the intraclass correlation coefficient (ICC) and the 95% confidence interval (CI) of the ICC, using a one-way random effects analysis of variance.\textsuperscript{29} A lower CI limit of at least 0.75 is considered as good test-retest reliability.\textsuperscript{30} Systematic differences between visits were tested by Student's *t* tests and agreement of the results for all walking tests and questionnaires was analyzed according to the Bland-Altman method.\textsuperscript{31} The 95% limits of agreement (LOA) were calculated as mean (visit 2 – visit 1) ± 2 standard deviations (SD). The LOA represents the smallest detectable change (SDC) that can be detected within an individual. Normalized total scores on the first study visit were calculated to
compare total scores and floor and ceiling effects of the questionnaires. Correlations between the questionnaires and the walking tests were calculated with Pearson’s correlation coefficient. Furthermore the unstandardized residuals for the different walking tests were tested with a paired Wilcoxon signed-rank test. An $\alpha$ level of 0.05 was used for all tests of significance. The statistical analysis was performed in SPSS, version 12.0.1, statistical software package.

**Results**

The 57 patients (36 women, 21 men) had a mean age of 57.3 (7.2) years. Their age at the acute polio stage varied from newborn to 17 years, with a median age of 2.0 years. The mean duration of new neuromuscular symptoms was 10.3 (8.0) years.

**Questionnaires**

According to the ICCs the test-retest reliability of the SF36-PF and the WOMAC-PF scales was good (Table 4.1). The test-retest reliability of the NHP-PM scale was moderate (Table 4.1). There were no systematic differences between visits in the scores for all 3 questionnaires. The SDC within an individual was 16.5 for the WOMAC-PF, 18.4 for the SF36-PF (Figure 4.1a) and 26.7 for the NHP-PM. The normalized total

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**Table 4.1** Reproducibility results for questionnaires to assess physical functioning

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Visit 1</th>
<th>Visit 2</th>
<th>D*</th>
<th>p</th>
<th>95% LOA</th>
<th>ICC</th>
<th>95% CI ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF-36 physical functioning</td>
<td>44.4 (21.7)</td>
<td>45.2 (20.7)</td>
<td>0.8</td>
<td>0.5</td>
<td>-16.8, 18.4</td>
<td>0.92</td>
<td>0.86 – 0.95</td>
</tr>
<tr>
<td>WOMAC physical functioning</td>
<td>68.7 (16.9)</td>
<td>68.9 (17.5)</td>
<td>0.2</td>
<td>0.8</td>
<td>-16.1, 16.5</td>
<td>0.89</td>
<td>0.81 – 0.93</td>
</tr>
<tr>
<td>NHP physical mobility</td>
<td>67.3 (17.2)</td>
<td>68.2 (18.2)</td>
<td>-0.9</td>
<td>0.6</td>
<td>-26.7, 24.9</td>
<td>0.74</td>
<td>0.59 – 0.84</td>
</tr>
</tbody>
</table>

*Note: Values are means (standard deviation). LOA = limits of agreement; 95% CI = 95% confidence interval; ICC = intraclass correlation coefficient; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; NHP = Nottingham Health Profile.

*aMean difference between visits (second minus first visit).

**Table 4.2** Floor and ceiling effect for questionnaires on physical functioning

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Visit 1</th>
<th>P25</th>
<th>P50</th>
<th>P75</th>
<th>% floor</th>
<th>% ceiling</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF-36 physical functioning</td>
<td>44.4 (21.7)</td>
<td>30.0</td>
<td>40.0</td>
<td>57.5</td>
<td>0</td>
<td>1.8</td>
</tr>
<tr>
<td>WOMAC physical functioning</td>
<td>68.7 (16.9)</td>
<td>55.1</td>
<td>69.1</td>
<td>83.8</td>
<td>0</td>
<td>1.8</td>
</tr>
<tr>
<td>NHP physical mobility</td>
<td>67.3 (17.2)</td>
<td>62.5</td>
<td>62.5</td>
<td>75.0</td>
<td>0</td>
<td>3.5</td>
</tr>
</tbody>
</table>

*Note. Total scores are means (standard deviation) and 25th, 50th, 75th percentiles. % floor = % floor effect; % ceiling = % ceiling effect; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; NHP = Nottingham Health Profile.
Figure 4.1 Bland-Altman plots: (a) SF-36 physical functioning scale; and (b) distance walking in 2 min at self-preferred speed. The solid line represents the mean difference (second minus first visit) and the dotted lines represent the 95% LOA (limits of agreement).
scores and floor and ceiling effects of the questionnaires at the first visit are presented in Table 4.2. The mean normalized total score was highest for the WOMAC-PF (69 (SD 17)) and lowest for SF36-PF (44 (SD 22)); the NHP-PM total score was 67 (SD 17). None of the patients scored the lowest possible score on any of the 3 questionnaires. The maximum possible score was scored by one patient on the SF36-PF and the WOMAC-PF and by 2 patients on the NHP-PM.

### Walking capacity tests

According to the ICCs, the test-retest reliability of the 10-m walking test at self-preferred and maximum speed, the distance walked in 2 min at self-preferred speed, and the TUG test was excellent (Table 4.3). There were no systematic differences between visits in 10-m walking test at self-preferred speed, the distance walked in 2 min at self-preferred speed.

### Table 4.3 Reproducibility results for walking tests

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Visit 1 Mean (SD)</th>
<th>Visit 2 Mean (SD)</th>
<th>Δ</th>
<th>p Value</th>
<th>95% LOA (%) change from the mean</th>
<th>ICC</th>
<th>95% CI ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timed-Up-and-Go test (sec)</td>
<td>10.8 (3.8)</td>
<td>10.8 (4.1)</td>
<td>0.1</td>
<td>0.9</td>
<td>-2.4, 2.1</td>
<td>0.96</td>
<td>0.93 – 0.98</td>
</tr>
<tr>
<td>10 m self-preferred speed (sec)</td>
<td>9.7 (2.7)</td>
<td>9.7 (3.0)</td>
<td>0.1</td>
<td>0.6</td>
<td>-1.8, 1.9</td>
<td>0.95</td>
<td>0.91 – 0.97</td>
</tr>
<tr>
<td>10 m maximum speed (sec)</td>
<td>7.7 (2.3)</td>
<td>8.0 (2.4)</td>
<td>-0.2</td>
<td>0.03</td>
<td>-1.7, 1.2</td>
<td>0.95</td>
<td>0.92 – 0.97</td>
</tr>
<tr>
<td>Distance in 2 min walking at self-preferred speed (m)</td>
<td>136.0 (28.2)</td>
<td>136.8 (29.3)</td>
<td>0.9</td>
<td>0.6</td>
<td>-21.2, 22.9</td>
<td>0.93</td>
<td>0.88 – 0.96</td>
</tr>
</tbody>
</table>

**Note.** Values are means (standard deviation). LOA = limits of agreement; 95% CI = 95% confidence interval; ICC = intraclass correlation coefficient.

*Mean difference between visits (second minus first visit).

### Table 4.4 Correlations between questionnaires and walking capacity tests

<table>
<thead>
<tr>
<th>Outcome</th>
<th>SF-36 physical functioning</th>
<th>WOMAC physical functioning</th>
<th>NHP physical mobility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timed-Up-and-Go test (sec)</td>
<td>-0.58*</td>
<td>-0.41*</td>
<td>-0.36*</td>
</tr>
<tr>
<td>10 m self-preferred speed (sec)</td>
<td>-0.52*</td>
<td>-0.32*</td>
<td>-0.33*</td>
</tr>
<tr>
<td>10 m maximum speed (sec)</td>
<td>-0.58*</td>
<td>-0.37*</td>
<td>-0.40*</td>
</tr>
<tr>
<td>Distance in 2 min walking at self-preferred speed (m)</td>
<td>0.69*</td>
<td>0.45*</td>
<td>0.61*</td>
</tr>
</tbody>
</table>

**Note.** Pearson’s correlation coefficient. WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; NHP = Nottingham Health Profile.

*significant at 0.05 level.
speed and the TUG. However, there was a small systematic difference between visits in 10-m walking test at maximum speed (a reduced walking speed during the second visit). For the 10 m walking at self-preferred speed and maximum speed the SDC was 1.9 sec, and 1.7 sec. For the TUG, the SDC was 2.4 sec, and for the 2-minute walking test at self-preferred speed the SDC was 22.9 m (Figure 4.1b).

**Association between questionnaires and walking capacity tests**

The correlations between the questionnaires and the walking tests are shown in Table 4.4, with SF36-PF (Pearson’s correlation 0.52 – 0.69) showing the highest correlations with the walking tests. The unstandardized residuals for the different walking tests were tested with a paired Wilcoxon signed-rank test and showed no significant differences between walking tests.

**Discussion**

The aim of the present study was to select one physical functioning questionnaire and one walking capacity test from a number of frequently used valid instruments in patients with late-onset sequelae of poliomyelitis, as core qualifiers for the purpose of research and clinical evaluation. Based on the results, we would advocate the SF36-PF and the 2-minute walking test as the best options.

The population of this study is an unselected sample of a prospective cohort, based on a convenience sample from 2 university hospitals. Limitations to the cohort study are possible sampling biases, especially with the older patients. The 57 patients used in this study are an unselected sample of this cohort with no further bias and therefore results are in our opinion generalizable to the population of patients referred to a neurologist or physical medicine and rehabilitation specialist. The sample size of this study is adequate to answer the objectives of this study. Regarding reliability, a major criticism of the ICC is the influence of between-subjects variance on the ratio. In simple terms the ICC is the ratio of true score variance (between-subjects variance) to true score variance plus error. If the true score variance is sufficiently large, reliability will always appear high and vice versa. Therefore, for a group of subjects with a wide range of measurement scores, the ICC is likely to be greater than for a more homogeneous sample group with similar measurement scores. Although ICC’s are sensitive to variability between patients, this is of minor importance in this study since all the outcome measures are tested in the same population with the same patients with the same variability.

All the questionnaires showed good to sufficient test-retest reliability, in line with the findings reported in different diagnostic groups, such as multiple sclerosis. The limits of agreement indicate the ability to detect the smallest change in an individual’s self-perceived physical functioning. The SDCs of the SF36-PF and the WOMAC-PF scales were acceptable, with similar limited ability to detect change in an individual. Therefore, the 17 WOMAC-PF items scored on a 5-point scale are no more sensitive to detect change in an individual than the 10 SF36-PF items scored on a 3-point scale. The SDC for the NHP-PM was unacceptably large, and may be due to the limited number of items (9) and response options (yes/no), and the fact that one different response results in an 11% change in the total score. However, it is important to realize that,
for research purposes, groups will be compared, and the sensitivity to detect a group change is considerably better than the sensitivity to detect an individual change.

The normalized scores for the NHP-PM and the WOMAC-PF are in the same range, whereas the SF36-PF scores were markedly lower, suggesting a lower health status. The dichotomous items of the NHP-PM have a high threshold for positive scoring, and are not likely to detect minor illnesses. An explanation for the lower scores on the SF36-PF is that the majority of the SF36-PF items contain walking and climbing stairs, which are increasingly difficult for our population, whereas the WOMAC-PF also contains less difficult items, such as putting on/taking off socks, sitting, getting out of bed. For the SF36-PF, the NHP-PM, and the WOMAC-PF there was no ceiling or floor effect in our study population, and therefore this clinimetric characteristic does not limit the choice of questionnaires.

The test-retest reliability of all the walking capacity tests was good, and comparable to those reported in other studies. A significant difference between the first and the second visit was found for the 10-m walking test at maximum speed, i.e. a slower walking speed at the second visit. In the literature, findings on systematic retest differences are diverse: some studies have reported (a tendency towards) learning effects, whereas other studies reported no learning effect. However, the significant difference in walking at maximum speed, i.e. slower at the second visit, was of little clinical importance, because the mean difference between the 2 visits was only 0.3 seconds.

In our study population, the SDC of the distance covered in the 2-minute walking test was greater than the SDC reported by Horemans et al. The Bland-Altman plot (Figure 4.1b) clearly shows 3 outliers with large differences between the 2 study visits in the distance walked. Omitting these outliers from the analysis results in an SDC of 14.0 m which is comparable to the SDC reported by Horemans et al.

A comparison of the SDCs of the 4 walking tests, with different measurement units (m and sec) and scale ranges, can only be made by expressing them as a percentage of the group mean scores for the test (Table 4.3). This comparison suggests that the 2-minute walking test has the best SDC.

The SF36-PF scale showed the highest correlation with all the walking tests, and the 2-minute walking test showed the highest correlation with all questionnaires, both without statistic significant differences. The TUG test, which measures the basic mobility skills required for everyday life activities, did not show the highest correlation with physical functioning. The correlation of the SF36-PF with the walking capacity tests is in line with the findings of Noonan et al. in patients with late-onset sequelae of poliomyelitis. The correlations found in the present study between physical functioning questionnaires and capacity measures are comparable with the correlations found in patients with fibromyalgia and higher than in patients with total hip and knee arthroplasty. The SF36-PF and the WOMAC-PF showed similar reliability and ability to detect individual change, but because the correlations with the walking capacity tests were higher for the SF36-PF, we recommend the SF36-PF scale for the assessment of physical functioning.
In conclusion, the SF-36 physical functioning scale and the 2-minute walking test are recommended as core qualifiers to assess physical functioning in patients with late-onset sequelae of poliomyelitis. These should routinely be applied in research to facilitate the comparison of results, although cross-cultural differences in responses must be taken into account. They are also the most appropriate for use in clinical practice, because they have the greatest ability to detect individual changes. However, this does not exclude the addition of other outcome measures for specific research questions or evaluation purposes.

Acknowledgements
We wish to thank all those who participated in the study for their time and efforts. The study was supported by a grant from ZonMw, the Netherlands.


References


Impact of age and co-morbidity on the functioning of patients with sequelae of poliomyelitis: a cross-sectional study

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On behalf of the CARPA study group

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2007;39:56-62
Abstract

Objective: To investigate the impact of age and co-morbidity on the functional independence and perceived physical functioning of patients with sequelae of poliomyelitis.

Design: Cross-sectional study.

Subjects: A convenience sample of 168 patients with sequelae of poliomyelitis, aged 45 – 85 years, recruited from two university hospitals.

Methods: Outcome measures were Functional Independence Measure (FIM™) for functional independence, Short Form-36 (SF-36) for physical functioning and general mental health, Cumulative Illness Rating Scale (CIRS) for co-morbidity.

Results: FIM™ scores were significantly lower for the 65 – 85 year age group than for the 45 – 54 year age group. No differences in the SF-36 were found between the age groups, except that the SF-36 general mental health subscale score was significantly better in the 65 – 85 year age group than in the 45 – 54 year age group. The CIRS score increased significantly with age. Linear regression showed that age, gender, polio severity, and 4 co-morbidity scores (“cardiac”, “vascular”, “endocrine, metabolic” and “muscle, bone, skin”) were significantly and inversely associated with functional independence and physical functioning.

Conclusion: The level of functional independence of elderly former poliomyelitis patients is lower than that of younger patients. Specific attention should be paid to co-morbidity and ageing in this increasingly older population of polio survivors, since they negatively affect functional independence and perceived functioning.
Introduction

Poliomyelitis is a viral infection of the motor neurons in the spinal cord, resulting in an acute flaccid paresis of a varying number of muscle groups. Nowadays, the incidence of acute poliomyelitis in the western world is low, but many individuals with a history of poliomyelitis report late onset neuromuscular symptoms and a decline in functional abilities. These late symptoms are referred to as the post-poliomyelitis syndrome, and include a gradual or sudden onset of progressive and persistent new muscle weakness or abnormal muscle fatigueability (decreased endurance), with or without generalized fatigue, muscle atrophy, or muscle and joint pain. The new symptoms cause increasing difficulties with physical functioning, such as walking, standing, climbing stairs and other mobility-related activities of daily life.

Few cross-sectional and prognostic studies have focused on functional independence and physical functioning in subjects with sequelae of poliomyelitis. In those that have, the recruitment of subjects differed from a random selection from the population to a selection of patients referred to a specialized post-poliomyelitis clinic. Furthermore, different outcome measures were used, and the follow-up periods ranged from 2 to 15 years. The results were inconsistent, sometimes even between different outcome measures in the same study and ranged from deterioration to no change and to improvement in functioning. One study, with a 15-year follow-up period, a randomly selected population with and without post-poliomyelitis and good methodological quality, reported a modest, but significant, decline in the performance of a 100-foot walking test and a decline in upper limb functioning.

Measuring co-morbidity is acknowledged to be increasingly important in research, because it has been demonstrated that co-existing morbidities are associated with quality of life and the activities of daily living. However, few studies have yet investigated co-morbidity in patients with sequelae of poliomyelitis. Nielsen et al. reported that people with a history of poliomyelitis have a slightly increased morbidity rate compared to age-matched controls, and have a 1.2 to 1.3-fold increased risk of being hospitalized with pulmonary, heart, gastrointestinal tract and locomotor apparatus diseases. Nielsen et al. also reported an increased risk of Parkinson's disease, multiple sclerosis and female breast cancer. Gawne et al. focussed on risk factors, and reported that the post-poliomyelitis population carries a high prevalence of two or more coronary heart disease risk factors, partly because of their sedentary lifestyle, controversy about the safety of exercise, and their age.

Some studies which focussed on functional independence and physical functioning in patients with sequelae of poliomyelitis excluded subjects with co-morbidity, did not include elderly patients (above the age of 65 years), or did not assess or report the extent and nature of the co-morbidities or their influence on functioning. These differences in eligibility criteria limit the generalizability (or external validity) and may result in an underestimation of the functional problems and rate of decline in former polio patients. Therefore, the present study focuses on patients in a broad age-range, without excluding co-morbidity.

The objectives of this study were (1) to evaluate functional independence and perceived
functioning, specifically physical functioning, and (2) to explore the impact of age and co-morbidity on functional independence and perceived physical functioning in patients aged 45 – 85 years with sequelae of poliomyelitis.

**Methods**

**Study population**
The patients were recruited from two university hospitals that specialize in the treatment of sequelae of poliomyelitis. To compare outcome measures according to age, the aim was to assemble three equally large age groups: 45 – 54 years, 55 – 64 years and 65 – 85 years with 60 subjects in each group. The inclusion criteria were: (i) history of poliomyelitis anterior acuta; (ii) presence of residual paresis in at least one extremity; (iii) consultation (not necessarily the first consultation) of a neurologist or physical medicine and rehabilitation specialist in the previous 5 years; (iv) age 45 to 85 years; (v) no medical condition indicating a life-expectancy of less than one year. All patients gave their informed consent to participate in the study.

A total of 258 subjects were invited to participate in the study by means of a letter that was sent to their last known address. Eighteen letters were returned by mail because of an incorrect address. Eighteen subjects (73%) volunteered to participate, 75% in the 45 – 54 year age group, 72% in the 55 – 64 year age group and 72% in the 65 – 85 year age group. Two subjects were excluded, one because of language problems (45 – 54 year age group) and one because the diagnosis of poliomyelitis anterior acuta was not confirmed (55 – 64 year age group). Five other subjects were not included in the study because there were already enough subjects in their age group by the time they volunteered to participate (3 in the 45 – 54 year age group, 2 in the 55 – 64 year age group).

**Measurement instruments**

**Functional Independence Measure™**
The FIM™ is a generic tool, that can be used to measure functional independence in functioning in patients undergoing rehabilitation. The FIM™ consists of 18 activities, each scored on a 7-point scale, with a score of 1 indicating total assistance and 7 indicating complete independence. A total score, ranging from 18 to 126, is calculated by summing up all the 18 activities. The FIM motor score is calculated by summing up 11 activities, the FIM bowel/bladder score is calculated by summing up 2 activities and the FIM cognitive score is calculated by summing up 5 activities. The FIM™ has been found to have good validity and reproducibility.

**Short Form-36**
The Short Form-36 (SF-36) is a self-administered questionnaire measuring generic health concepts, composed of 36 questions and standardized response choices, grouped into 9 multi-item scales: physical functioning, role limitations due to physical functioning, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional functioning, general mental health and change in health. The SF-36 physical functioning subscale consists of 10 questions on a 3-point scale. A
subscale score is calculated by adding the raw item scores, minus the lowest possible raw score and dividing this by the possible raw score range. Each scale is scored from 0 to 100, with higher scores indicating higher levels of functioning or well-being. The SF-36 has been translated and validated for the population of the Netherlands.  

Muscle strength

Residual paresis in patients with sequelae of poliomyelitis varies from local paresis in one extremity to extensive paresis involving all four extremities, trunk and bulbar muscles. To quantify the degree of residual impairment of poliomyelitis, muscle strength of all extremities was measured manually (manual muscle testing, MMT) according to the Medical Research Council scale, with each muscle group receiving a score ranging from 0 to 5. The following muscle groups were measured: shoulder abductors, elbow flexors, elbow extensors, wrist dorsal flexors, wrist palmar flexors, hip flexors, hip extensors, hip abductors, hip adductors, knee flexors, knee extensors, ankle dorsal flexors, ankle plantar flexors. A legs strength sum score was obtained by adding the MMT-scores of all 16 leg muscle groups tested (range 0 – 80) and an arms strength sum score was obtained by adding the MMT-scores of all 10 arm muscle groups tested (range 0 – 50).  

Cumulative Illness Rating Scale

The Cumulative Illness Rating Scale (CIRS) is a short, physician-rated, comprehensive and reliable instrument for assessing the burden of chronic medical illness. The scale consists of 13 relatively independent categories grouped under body systems. Ratings are made on a 5-point “degree of severity” scale, ranging from “none” to “extremely severe”. Only co-morbidity is rated in this scale, and not the index disease in question, i.e. poliomyelitis and resulting orthopaedic interventions (e.g. ankle arthrodesis) in early childhood. The total score is calculated by summing up the category scores. The CIRS has been found to have good validity and good inter-rater and test-retest reliability.  

Assessment protocol

Prior to the visit to the hospital, the patients received a questionnaire with instructions, which they returned during their visit to the hospital. At the hospital, a physician interviewed the patients and administered the tests in a standard sequence.  

Data analysis

Demographic data were analyzed by using descriptive statistics. The means of all the outcome measures were compared according to age group by applying one-way analysis of variance (ANOVA) with a post hoc Bonferroni test. Associations between the variables of interest and the outcome measures (FIM total score and SF-36 physical functioning) were assessed with multivariate linear regression analysis. A forward stepwise selection method, with a p value of less than 0.05, was used as the selection criterion, with a probability of F-to-enter < 0.10. The statistical analysis was performed in SPSS, version 12.0.1, statistical software package. An α level of 0.05 was used for all tests of significance.
Results

A total of 168 patients (101 women, 67 men) were included in three age groups: 45 – 54 years \((n = 60)\), 55 – 64 years \((n = 60)\) and 65 – 85 years \((n = 48)\). Their age at the acute polio stage varied from newborn to 27 years, with a median of 3.0. There was no difference between the age groups in the number of affected body sites during acute polio infection or the number of affected body sites with residual paresis. The mean duration of new neuromuscular symptoms was 12.5 ± 8.9 years. General fatigue was reported more frequently by the 45 – 54 year age group compared with the older age groups \((p < 0.01)\) (Table 5.1).

FIM™

The 65 – 85 year age group scored significantly lower than the 45 – 54 year age group on the FIM total score \((p = 0.0015)\), the FIM motor score \((p = 0.033)\), and the FIM bowel/bladder score \((p = 0.033)\), i.e. the oldest age group was more functionally dependent in

<table>
<thead>
<tr>
<th>Table 5.1 Subject characteristics</th>
<th>Age groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristics</td>
<td>45 – 54 years</td>
</tr>
<tr>
<td><strong>n</strong></td>
<td>60</td>
</tr>
<tr>
<td>Age in years, mean ((SD)) (range)</td>
<td>50.8 (2.5) (45 – 54)</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>25/35</td>
</tr>
<tr>
<td>Age in years at acute polio median (range)</td>
<td>2.5 (0 – 17)</td>
</tr>
<tr>
<td>Body sites with residual paresis,(^a) median (IQ 25 – 75%)</td>
<td>1 (1;2)</td>
</tr>
<tr>
<td>New symptoms (yes/no)</td>
<td>59/1</td>
</tr>
<tr>
<td>Mean duration of new symptoms (in years) ((SD))</td>
<td>11.5 (7.2)</td>
</tr>
<tr>
<td>New muscle weakness (yes/no)</td>
<td>48/12</td>
</tr>
<tr>
<td>New muscle pain (yes/no)</td>
<td>32/28</td>
</tr>
<tr>
<td>New muscle fatigue (yes/no)</td>
<td>42/18</td>
</tr>
<tr>
<td>New muscle atrophy (yes/no)</td>
<td>21/39</td>
</tr>
<tr>
<td>General fatigue (yes/no)</td>
<td>59/1**</td>
</tr>
</tbody>
</table>

*\(p < 0.01\) \((\chi^2)\) compared with 45 – 54 year age group; **\(p < 0.01\) \((\chi^2)\) compared to 55 – 64 age group; \(^a\) range 0 – 8 (four extremities, trunk, neck, face, throat).
these areas than the youngest age group. The 45 – 54 year age group and the 55 – 64 year age group did not differ in any of the scores for functional independence. There was no difference between any of the age groups in the FIM cognitive score. It must be taken into account, however, that there was a profound ceiling effect on the FIM bowel/bladder score and the FIM cognitive score in this population (Table 5.2).

**SF-36**

No significant differences were found between the age groups in any of the subscales except general mental health, i.e. the 65 – 85 year age group experienced a better mental health compared with the 45 – 54 year age group \((p = .021)\) (Table 5.3).

**Table 5.2** FIM total score, FIM motor score, FIM bowel/bladder score, FIM cognitive score and Manual Muscle Testing (MMT)

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Age groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>45 – 54 years</td>
</tr>
<tr>
<td>FIM total score (range 18 – 126)</td>
<td>121.9 ± 3.3</td>
</tr>
<tr>
<td>FIM motor score (range 11 – 77)</td>
<td>73.0 ± 3.2</td>
</tr>
<tr>
<td>FIM bowel/bladder score (range 2 – 14)</td>
<td>13.9 ± 0.3</td>
</tr>
<tr>
<td>FIM cognitive score (range 5 – 35)</td>
<td>35.0 ± 0.0</td>
</tr>
<tr>
<td>Manual muscle testing legs strength sum score</td>
<td>65.9 (49.1 – 71.2)</td>
</tr>
<tr>
<td>Manual muscle testing arms strength sum score</td>
<td>50.0 (49.0 – 50.0)</td>
</tr>
</tbody>
</table>

*Note.* Values are medians (25 and 75 percentile scores). \(* p < 0.05\) compared with 45 – 54 year age group. Sum scores for the muscle strength of the legs and arms were calculated by adding 16 and 10 muscle groups, respectively. Each muscle group had a score between 0 and 5. MMT legs strength sum score ranged from 0 to 80 and MMT arms strength sum score ranged from 0 to 50.

**Table 5.3** SF-36 subscales

<table>
<thead>
<tr>
<th>SF-36 subscale</th>
<th>Age groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>45 – 54 years</td>
</tr>
<tr>
<td>Physical functioning</td>
<td>40.8 ± 22.1</td>
</tr>
<tr>
<td>Role limitations due to physical functioning</td>
<td>45.0 ± 41.9</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>55.5 ± 21.6</td>
</tr>
<tr>
<td>General health perception</td>
<td>55.5 ± 20.1</td>
</tr>
<tr>
<td>Energy vitality</td>
<td>50.8 ± 15.8</td>
</tr>
<tr>
<td>Social functioning</td>
<td>64.6 ± 23.9</td>
</tr>
<tr>
<td>Role limitation due to emotional problems</td>
<td>75.0 ± 38.6</td>
</tr>
<tr>
<td>Mental health</td>
<td>70.0 ± 17.0</td>
</tr>
<tr>
<td>Change in health</td>
<td>43.8 ± 18.8</td>
</tr>
</tbody>
</table>

*Note.* Values are means (SD). \(* p < 0.05\) compared with 45 – 54 year age group.
Table 5.4 CIRS category scores

<table>
<thead>
<tr>
<th>CIRS category score</th>
<th>45 – 54 years</th>
<th>55 – 64 years</th>
<th>65 – 85 years</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 60</td>
<td>n = 60</td>
<td>n = 48</td>
<td>n = 168</td>
</tr>
<tr>
<td>CIRS total score</td>
<td>4 (0 – 13)</td>
<td>6 (0 – 14)*</td>
<td>8 (2 – 21)*</td>
<td>6 (0 – 21)</td>
</tr>
<tr>
<td>Cardiac</td>
<td>0 (0 – 2)</td>
<td>0 (0 – 3)</td>
<td>0 (0 – 3)*</td>
<td>0 (0 – 3)</td>
</tr>
<tr>
<td>Vascular</td>
<td>0 (0 – 2)</td>
<td>0 (0 – 3)</td>
<td>0 (0 – 3)*</td>
<td>0 (0 – 3)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>0 (0 – 3)</td>
<td>0 (0 – 3)</td>
<td>0 (0 – 3)</td>
<td>0 (0 – 3)</td>
</tr>
<tr>
<td>Eye, ear, nose, throat</td>
<td>1 (0 – 2)</td>
<td>1 (0 – 3)</td>
<td>1 (0 – 3)*</td>
<td>1 (0 – 3)</td>
</tr>
<tr>
<td>Upper GI</td>
<td>0 (0 – 2)</td>
<td>0 (0 – 3)*</td>
<td>0 (0 – 3)</td>
<td>0 (0 – 3)</td>
</tr>
<tr>
<td>Lower GI</td>
<td>0 (0 – 2)</td>
<td>0 (0 – 2)</td>
<td>0 (0 – 2)</td>
<td>0 (0 – 2)</td>
</tr>
<tr>
<td>Hepatic</td>
<td>0 (0)</td>
<td>0 (0 – 2)</td>
<td>0 (0 – 3)</td>
<td>0 (0 – 3)</td>
</tr>
<tr>
<td>Renal</td>
<td>0 (0 – 3)</td>
<td>0 (0 – 1)</td>
<td>0 (0)</td>
<td>0 (0 – 3)</td>
</tr>
<tr>
<td>Other urogenital</td>
<td>0 (0 – 2)</td>
<td>0 (0 – 2)</td>
<td>0 (0 – 3)*</td>
<td>0 (0 – 3)</td>
</tr>
<tr>
<td>Muscle, bone, skin</td>
<td>2 (0 – 3)</td>
<td>2 (0 – 3)</td>
<td>2 (0 – 3)</td>
<td>2 (0 – 3)</td>
</tr>
<tr>
<td>Neurologic</td>
<td>0 (0 – 2)</td>
<td>0 (0 – 3)</td>
<td>0 (0 – 3)</td>
<td>0 (0 – 3)</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>0 (0 – 3)</td>
<td>0 (0 – 3)</td>
<td>0 (0 – 2)</td>
<td>0 (0 – 3)</td>
</tr>
<tr>
<td>Endocrine, metabolic</td>
<td>0 (0 – 2)</td>
<td>0 (0 – 2)</td>
<td>0 (0 – 3)*</td>
<td>0 (0 – 3)</td>
</tr>
</tbody>
</table>

Note. Values are medians (range). * p < 0.05 compared with 45 – 54 year age group; † p < 0.05 compared with 55 – 64 year age group. GI = gastro-intestinal tract; CIRS = Cumulative Illness Rating Scale.

Table 5.5 Multivariate linear regression model for FIM total score and SF-36 subscale physical functioning

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>B (95% CI)</th>
<th>p</th>
<th>Adjusted R²</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FIM total score</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>113.3 (105.6 to 121.0)</td>
<td>.000</td>
<td>0.14</td>
</tr>
<tr>
<td>Legs strength sum score</td>
<td>0.11 (0.07 to 0.14)</td>
<td>.000</td>
<td>0.21</td>
</tr>
<tr>
<td>CIRS ‘cardiac’ score</td>
<td>−0.96 (−1.63 to −0.28)</td>
<td>.006</td>
<td>0.26</td>
</tr>
<tr>
<td>Arms strength sum score</td>
<td>0.20 (0.08 to 0.33)</td>
<td>.002</td>
<td>0.26</td>
</tr>
<tr>
<td>CIRS muscle, bone, skin’ score</td>
<td>−0.60 (−1.13 to −0.70)</td>
<td>.027</td>
<td>0.29</td>
</tr>
<tr>
<td>Age</td>
<td>−0.77 (−0.15 to 0.00)</td>
<td>.042</td>
<td>0.31</td>
</tr>
<tr>
<td>Gender</td>
<td>−1.32 (−2.44 to −0.19)</td>
<td>.022</td>
<td>0.32</td>
</tr>
<tr>
<td>CIRS ‘vascular’ score</td>
<td>−0.62 (−1.21 to −0.03)</td>
<td>.041</td>
<td>0.34</td>
</tr>
<tr>
<td><strong>SF-36 physical functioning</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>18.3 (4.3 to 32.3)</td>
<td>.000</td>
<td></td>
</tr>
<tr>
<td>Legs strength sum score</td>
<td>0.77 (0.60 to 0.93)</td>
<td>.000</td>
<td>0.27</td>
</tr>
<tr>
<td>CIRS ‘endocrine, metabolic’ score</td>
<td>−5.63 (−8.95 to −2.31)</td>
<td>.002</td>
<td>0.33</td>
</tr>
<tr>
<td>Gender</td>
<td>−10.06 (−15.80 to −4.33)</td>
<td>.015</td>
<td>0.37</td>
</tr>
<tr>
<td>CIRS ‘vascular’ score</td>
<td>−3.80 (−6.68 to −0.91)</td>
<td>.078</td>
<td>0.39</td>
</tr>
<tr>
<td>CIRS muscle, bone, skin’ score</td>
<td>−3.32 (−6.01 to 0.62)</td>
<td>.073</td>
<td>0.41</td>
</tr>
</tbody>
</table>

Note. Factors included in regression analysis were age (years), gender (male = 1; female = 2), legs strength sum score, arms strength sum score, CIRS categories. B = beta, regression coefficient; CIRS = Cumulative Illness Rating Scale.
Chapter 5

Muscle strength

The median value of the MMT legs strength sum score was 2.6 points higher in the 55 – 64 year age group compared with the 45 – 54 year age group, and 1.4 points higher compared with the 65 – 85 year age group. The differences in the MMT legs strength sum score between the age groups were not significant, but it must be noted that there was a large variability in the legs strength sum score among participants in every age group (Table 5.2). The MMT arms strength sum scores had a much smaller range, and there was no significant difference between the age groups (Table 5.2).

CIRS

The 65 – 85 year age group had a significantly higher CIRS total score compared with the younger age groups. The 55 – 64 year age group had a significantly higher CIRS total score, compared to the 45 – 54 year age group (Table 5.4). The body systems “ear, nose, throat, eye (including glasses and hearing aids)” and “muscle, bone, skin” were most frequently scored as positive (136 and 128 positive scores, respectively). The CIRS “cardiac” score consisted of 44% heart failure, 26% myocardial infarction, 18% cardiac arrhythmias and 12% valvular heart diseases. The CIRS vascular score consisted of 88% hypertension and 12% other diseases. The CIRS “endocrine, metabolic” score consisted of 37% hypercholesterolemia, 27% osteoporosis, 15% thyroid diseases, 12% diabetes mellitus and 10% other diseases. The CIRS “muscle, bone, skin” score consisted of 43% lower extremity problems, 23% upper extremity problems, 19% back problems, 6% skin-related problems, and others (9%).

Impact of age and co-morbidity on functional independence and perceived physical functioning

Two multivariate linear regression models were constructed to investigate the impact of age and co-morbidity on the dependent variables FIM total score and SF-36 subscale physical functioning. The associated factors that were analyzed were age, gender, legs strength sum score, arms strength sum score and CIRS category scores. Thirty-four percent of the variation in the FIM total score could be attributed to legs strength sum score, CIRS “cardiac” score, arms strength sum score, CIRS “muscle, bone, skin” score, age, gender and CIRS “vascular” score (Table 5.5). The co-morbidity scores added 11.4% in explaining the variance in the FIM total score after the legs strength sum score had been added to the model, and age added 3%. Forty-one percent of the variation in the SF-36 subscale physical functioning could be attributed to the presence of legs strength sum score, CIRS “endocrine, metabolic” score, gender, CIRS “vascular” score, and CIRS “muscle, bone, skin” score (Table 5.5). The co-morbidity scores added 9.2% in explaining the variance in SF-36 subscale physical functioning after the legs strength sum score had been added to the model and when age was not included in the model.

Discussion

This study evaluated the level of functioning and the impact of age and co-morbidity on functioning in patients aged 45 – 85 years with sequelae of poliomyelitis. The study population was older than that of most earlier studies and co-morbidity was
not excluded. However, sampling bias may have occurred, especially in the oldest group, i.e. 65 – 85 years of age, rendering the findings less generalizable. In line with the recent literature, our population reported new physical complaints, with muscle weakness and fatigue being the most frequently reported symptoms. The youngest age group reported fatigue most frequently and this may be due to a more (physically) active lifestyle, because they are more involved in working and raising a family.

Functional independence, based on a FIM total score, FIM motor score and FIM bowel/bladder score, was significantly lower in the 65 – 85 year age group compared with the 45 – 54 year age group. The difference in median value of the FIM total score between the youngest and the oldest age group was only 1.5 points, indicating only a small difference in functional independence. Farbu et al. interviewed patients about daily functioning and reported a reduction in mobility daily functioning, but not in functions concerning personal care. Within the FIM motor score, the elderly group scored significantly lower on the items “climbing stairs” and “transfer to bath/shower”, and therefore these findings confirm the results of the study carried out by Farbu et al.

The SF-36 score for perceived physical functioning did not differ significantly between the age groups and perceived general mental health was even better in the older age group. Two explanations can be given for these findings. Elderly people probably experience less physical and mental stress as they are less (physically) active. Secondly, elderly patients might have adapted to their physical limitations and rate their current health status against the background of newly adapted standards. This phenomenon is called response shift, and refers to a change in the meaning of one's self-evaluation of a target construct. Response shift is a result of a change in the respondent's internal standards of measurement, a redefinition of the target construct or a change in the respondent's values (the importance of component domains constituting the target construct).

Functional independence (FIM™) was assessed by an investigator, whereas the SF-36 physical functioning subscale was measured with a self-administered questionnaire and is therefore a person's perception of his or her own physical functioning. It appears that the subjective experience of physical functioning can vary widely between patients with the same high level of functional independence (FIM™ ≥ 120) (Figure 5.1). Therefore functional independence and perceived physical functioning measure two different constructs.

In the past few years the importance of co-morbidity for functional prognosis in rehabilitation medicine is increasingly recognized. The present study focussed on the relationship of age and co-morbidity with functional independence and perceived physical functioning. Age was a factor that was significantly associated with functional independence, but not with perceived physical functioning. This corroborates an age-related shift in the perception of physical limitations. In line with the expectation, the level of co-morbidity increased significantly with age. The body systems “cardiac”, “vascular”, “endocrine, metabolic” and “muscle, bone, skin” appeared to be significantly associated with both outcomes. Gawne et al. advised screening for dyslipidemia and providing education on controllable risk factors in former polio patients. This seems to
be even more important because co-morbidity involving these body systems appears to be an important factor in explaining the functioning of these patients.

The three age groups appeared to have a similar level of polio impairments, because no significant differences were found in MMT. In the model explaining functional independence, both the leg and arms strength sum score were significantly associated factors, whereas in the perceived physical functioning model only the legs strength sum score was a significant factor. A possible explanation is that the FIM total score consists of 6 items involving the use of the arms, whereas the SF-36 physical functioning subscale consists of 10 items, with only 2 items specifically involving the use of the arms.

The female sex was a negative associated factor with both functional independence and perceived physical functioning. Women with sequelae of poliomyelitis are known to report a lower level of perceived physical functioning than men. In line with this finding it may be that women are more likely to report a lower level of functional independence.

In conclusion, the level of functional independence of elderly former poliomyelitis patients is lower than that of younger patients. Co-morbidity negatively affects the functional independence and perceived physical functioning. Prospective studies
with unselected study populations, without the exclusion of co-morbidity or elderly patients, but including age-matched controls and measures to record co-morbidity are needed to investigate the influence of co-morbidity on the course of functioning in this population.

Acknowledgements
We wish to thank all those who participated in the study for their time and efforts. The study was supported by a grant from ZonMw, the Netherlands.


References
Chapter 6

The impact of age and co-morbidity on the progression of disability in late-onset sequelae of poliomyelitis

J.M. Stolwijk-Swüste, I. Tersteeg, A. Beelen,
G.J. Lankhorst, F. Nollet
On behalf of the CARPA study group

Submitted for publication
Abstract

Objectives: To describe the functional course over 5 years in patients aged 45 – 85 years with late-onset sequelae of poliomyelitis (LOSP) and to explore the impact of age and co-morbidity.

Methods: Prospective cohort study of 168 subjects with LOSP taking five measurements over 5 years. Outcome measures were the functional independence measure (FIM™), short form-36 for physical functioning (SF36-PF), walking test, isokinetic quadriceps strength, and cumulative illness rating scale (CIRS) for co-morbidity.

Results: The FIM™ score (mean baseline 121, SD 4) and SF36-PF (mean baseline 39.5, SD 24) decreased 2.2 and 3.7 points, respectively, over 5 years independent of age. The distance walked in 2 minutes (mean baseline 126.2 m, SD 34) decreased 4.5 m, quadriceps strength (mean baseline 88.0 Nm, SD 42.2) declined 7 Nm (8%), and CIRS (median baseline 6, range 0 – 21) increased 1.5 points. A higher CIRS score was correlated with a lower FIM total score and faster decrease in the FIM™. A longitudinal model of factors associated with the FIM™ included gender, age, legs strength sum score, arms strength sum score, and CIRS score. The interaction of CIRS and legs strength sum score with follow-up time was significant. A model of factors associated with SF36-PF included gender, age, legs strength sum score, and CIRS score.

Conclusions: Despite a reduction in muscle strength, disability increased little in patients with LOSP. Increased age and co-morbidity has a negative effect on disability. Co-morbidity and the severity of leg paresis impacted the course of functional independence but not the course of perceived physical functioning.
Introduction

Acute poliomyelitis has disappeared from Western countries, but many people who contracted polio in the past are ageing. Polio survivors are often confronted with new neuromuscular symptoms 30 to 40 years after experiencing acute polio, termed post-poliomyelitis syndrome (PPS). The syndrome is characterized by progressive new weakness and/or abnormal muscle fatigability, with or without generalized fatigue, muscle atrophy, and pain in the absence of other medical conditions that explain the symptoms. At present, the mainstay of treatment for PPS is low intensity exercise to prevent further muscle function decline; pharmacological agents have not been proven effective.

In older age, individuals with polio residuals are assumed to develop morbidities in line with the increasing prevalence of co-morbidity in the general ageing population. Former polio patients have an increased rate of morbidity compared to age-matched controls and a 1.2 to 1.3-fold increased risk of being hospitalized with pulmonary, heart, gastrointestinal tract, or locomotor apparatus disease. Measuring co-morbidity is acknowledged as being increasingly important because co-existing morbidities are negatively associated with quality of life and performing the activities of daily life and associated with increased use of healthcare services. Co-morbidity may be an important determinant of disability and may have consequences in the rehabilitation of the elderly, including patients with late-onset sequelae of poliomyelitis (LOSP).

Physical activities, such as walking, climbing stairs, and daily life-related activities, become increasingly difficult for polio survivors with late-onset neuromuscular symptoms. A systematic review found that it is not possible to draw conclusions about prognostic factors and the course of functioning over time in this patient group, though muscle strength deteriorates slowly. More recently, three follow-up studies of 15 years (50 subjects), 4 years (106 subjects), and 1 week to 3 years (96 subjects) reported minor to modest changes in walking tests, perceived physical mobility, upper limb functioning, and muscle strength. None of the studies on the course of functioning or muscle strength in patients with polio residuals reported the impact of age or co-morbidity. The studies excluded individuals over the age of 65 years and subjects with co-morbidity, or they did not assess or report the extent and nature of the co-morbidities or their influence on functioning. These differences in the eligibility criteria between studies limit the generalizability of the results to elderly patients with LOSP and co-morbidity and may result in underestimating their disability and rate of decline.

Because the impact of age and co-morbidity on the course of functioning in patients with a history of poliomyelitis remains unresolved, the aim of the present 5-year follow-up study was to describe the course of functioning and to explore the impact of age and co-morbidity on this course in patients with LOSP, without excluding elderly patients and patients with co-morbidity.
Methods

Study population

The study included patients with LOSP because, according to its definition, PPS would imply the exclusion of patients with certain co-morbidities and of an older age, which might also cause symptoms of muscle weakness and fatigue. In total, 168 subjects were recruited from two university hospitals and followed for 5 years. The study participants were described previously. All subjects provided informed consent. The study was approved by the medical ethics committee of VU University Medical Centre.

Measurement instruments

Functional Independence Measure™

The functional independence measure (FIM™) instrument is a valid and reproducible generic tool to measure independence in functioning. The FIM™ consists of 18 activities, each scored on a 7-point scale with 1 indicating total assistance and 7 indicating complete independence. The total score is calculated by summing all activities, resulting in a total score of 18 to 126. The FIM motor score is calculated by summing 11 activities.

Short Form-36 physical functioning subscale

Short Form-36 (SF-36) is a self-administered questionnaire consisting of 9 subscales that measure generic health. The SF-36 physical functioning subscale (SF36-PF) consists of 10 questions scored on a 3-point scale. A subscale score is calculated by adding the raw item scores, subtracting the lowest possible raw score, and dividing by the scale range. Each subscale ranges between 0 and 100 with higher scores indicating higher levels of perceived functioning. The SF-36 has been translated and validated for the Dutch population. The reliability of SF36-PF in patients with LOSP is good.

Walking capacity test: distance walked in 2 minutes

The 2-minute walking test has excellent test-retest reliability and an acceptable smallest detectable change in this patient group. The patients walked an indoor 50-meter track at a self-preferred speed for 2 minutes, and the distance covered was measured.

Maximal quadriceps strength

Maximal quadriceps strength was measured using a chair dynamometer. Each subject performed three maximal isokinetic contractions of the quadriceps at a velocity of 30°/s, with each leg if possible. The mean score per quadriceps was calculated. Scores for the strongest and weakest leg were used in the analysis. The quadriceps with the highest strength at baseline was regarded as the strongest throughout all follow-up measurements. The reliability of the isokinetic strength measurements in patients with LOSP is good.

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*a Kinetic Communicator; Chattecx Corp, Chattanooga Group, 4717 Adams Rd, Hixson, TN 37343.
Severity of polio paresis
The severity of polio paresis was assessed by manual muscle testing (MMT) at baseline according to the Medical Research Council scale. Based on the methods described by Nollet et al., legs strength and arms strength sum scores were calculated. These sum scores are considered to be potential determinants in the longitudinal models of functioning, representing polio paresis severity.

Extent of co-morbidity
The extent of co-morbidity was assessed by the cumulative illness rating scale (CIRS), which is a short, physician-rated, comprehensive, and reliable instrument for assessing the burden of chronic medical illness with good validity and good inter-rater and test-retest reliability. The scale consists of 13 relatively independent categories grouped by body system. Ratings are made on a 5-point “degree of severity” scale ranging from “none” to “extremely severe”. Only co-morbidity is rated on this scale, not the index disease in question, (i.e. poliomyelitis) or resulting orthopaedic interventions (e.g., ankle arthrodesis) in early childhood. The total score is the sum of the category scores.

Assessment protocol
Measurements were conducted at baseline (time of enrollment) and after 1, 2, 3, and 5 years. Subjects completed questionnaires at home and were interviewed and tested at the hospital. Some patients were unable to visit the hospital during follow-up and were tested at their homes in order to minimize loss to follow-up.

Data analysis
Demographic data were analyzed using descriptive statistics. Statistical analyses were performed using the SPSS statistical software package (version 12.0.1 and 16.0). An α level of 0.05 was used for all statistical analyses. Longitudinal analyses were performed with linear general estimated equations (GEE) using the STATA software package (version 9.0).

GEE analysis is a linear regression analysis which takes into account the dependency of the observations within one patient, and which allows all longitudinal data to be used, and not only the data on complete cases. The correlation structure was set at exchangeable (i.e., correlation coefficients between the first and successive measurements are approximately equal). Time was modelled as a continuous variable expressed in years in all regression models. Two multivariable repeated measures models were constructed to investigate the impact of potential determinants on the dependent variables: FIM total score and SF36-PF. The potential determinants considered were gender, age, co-morbidity (CIRS total score), and extent of polio paresis (legs and arms strength sum scores). Impact of potential determinants on the time course of functioning was tested using interaction terms time by determinant. The significance level for time, determinants and interaction terms time by determinant was set at 0.05. Secondary analyses compared the course of the FIM total score and SF36-PF between subjects complaining of new muscle weakness or new fatigue and...
subjects without complaints. In addition, analyses were performed to check for bias caused by the large drop-out at the 5-year measurement of quadriceps strength.

**Results**

The baseline characteristics of the 168 subjects are summarized in Table 6.1. The severity of polio paresis at baseline was $61.7 \pm 16.7$ points for the legs strength sum score and $47.6 \pm 4.1$ points for the arms strength sum score. During the 5-year follow-up, five patients died: two 45 – 54 years old, one 55 – 64 years old, and two 65 – 85 years old. Fourteen individuals were lost to follow-up over a period of 5 years (8.3%): 5 patients in the 45 – 54

### Table 6.1 Subject characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>45 – 54 years</th>
<th>55 – 64 years</th>
<th>65 – 85 years</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>60</td>
<td>60</td>
<td>48</td>
<td>168</td>
</tr>
<tr>
<td>Age in years, mean (SD) (range)</td>
<td>50.8 (2.5) (45 – 54)</td>
<td>59.6 (2.5) (55 – 64)</td>
<td>69.1 (4.3) (65 – 81)</td>
<td>59.1 (7.9) (45 – 81)</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>25/35</td>
<td>25/35</td>
<td>17/31</td>
<td>67/101</td>
</tr>
<tr>
<td>Age in years at acute polio median (range)</td>
<td>2.5 (0 – 17)</td>
<td>2.0 (0 – 27)</td>
<td>4.0 (0 – 21)</td>
<td>3.0 (0 – 27)</td>
</tr>
<tr>
<td>Body sites with residual paresis* (IQ 25 – 75%)</td>
<td>1 (1;2)</td>
<td>2 (1;2)</td>
<td>1.5 (1;2)</td>
<td>1.5 (1;2)</td>
</tr>
<tr>
<td>New symptoms (yes/no)</td>
<td>59/1</td>
<td>57/3</td>
<td>46/2</td>
<td>162/6</td>
</tr>
<tr>
<td>Mean duration of new symptoms (in years) (SD)</td>
<td>11.5 (7.2)</td>
<td>12.0 (9.2)</td>
<td>14.4 (10.4)</td>
<td>12.5 (8.9)</td>
</tr>
<tr>
<td>New muscle weakness (yes/no)</td>
<td>48/12</td>
<td>51/9</td>
<td>39/9</td>
<td>138/30</td>
</tr>
<tr>
<td>New muscle pain (yes/no)</td>
<td>32/28</td>
<td>35/25</td>
<td>24/24</td>
<td>91/77</td>
</tr>
<tr>
<td>New muscle fatigue (yes/no)</td>
<td>42/18</td>
<td>40/20</td>
<td>32/16</td>
<td>114/54</td>
</tr>
<tr>
<td>New muscle atrophy (yes/no)</td>
<td>21/39</td>
<td>18/42</td>
<td>14/34</td>
<td>53/115</td>
</tr>
<tr>
<td>General fatigue (yes/no)</td>
<td>59/1</td>
<td>48/12</td>
<td>40/8</td>
<td>147/21</td>
</tr>
<tr>
<td>Manual muscle testing legs strength sum score (range)</td>
<td>65.9 (49.1 – 71.2)</td>
<td>68.5 (58.1 – 75.9)</td>
<td>67.1 (54.2 – 74.6)</td>
<td>61.7 ± 16.7</td>
</tr>
<tr>
<td>Manual muscle testing arms strength sum score (range)</td>
<td>50.0 (49.0 – 50.0)</td>
<td>50.0 (45.6 – 50.0)</td>
<td>50.0 (47.1 – 50.0)</td>
<td>47.6 ± 4.1</td>
</tr>
</tbody>
</table>

*Note. Values are means $\pm$ SD or median (25th and 75th percentiles). Median (range) for age at acute polio and range for age. * range 0 – 8 (four extremities, trunk, neck, face, throat). Sum scores for muscle strength for the legs and arms were calculated by adding 16 and 10 muscle groups respectively. Each muscle group had a score between 0 and 5, MMT legs strength sum score ranged from 0 to 80 and MMT arms strength sum score ranged from 0 to 50.
years age group, 7 in the 55 – 64 years age group, and 2 in the 65 – 85 years age group. Three patients emigrated, 2 could not be retrieved, and 9 refused further participation, of whom three refused for medical reasons. At the 5-year follow-up, 25 subjects were unable to visit the hospital and were tested at their homes (four in the 45 – 54 group, 11 in the 55 – 64 group, and 10 in the 65 – 85 age group). The numbers of available data for each outcome measure and determinant at each measurement point are shown in Table 6.2. At the 5-year follow-up, only 47 patients performed the quadriceps strength test due to technical problems with the dynamometer. As a consequence, patients had to make an additional visit for the isokinetic test, and no more than 47 patients were willing to do so.

**FIM**

All age groups showed a significant decrease in the FIM total score (mean baseline 121, SD 4) with 0.44 (SE 0.09) points per year, which was 1.8% over 5 years, independent of sex or age (Table 6.2). The FIM motor score declined (mean baseline 72.3, SD 4.2) 0.40 points per year, which was 2.6% over 5 years. A higher CIRS score correlated with a lower FIM total score (0.35 point reduction per point increase on the CIRS) and a faster decrease in the FIM over time (additional 0.06 FIM point decrease per CIRS score point each year).

**Table 6.2** Course of FIM total score, SF-36 physical functioning, CIRS total score, walking capacity tests and maximal quadriceps strength at baseline and follow-up and number of available data

<table>
<thead>
<tr>
<th>Outcome measure / determinant</th>
<th>Baseline</th>
<th>1 year</th>
<th>2 years</th>
<th>3 years</th>
<th>5 years</th>
<th>B (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIM total score</td>
<td>121.0 (4.3)</td>
<td>120.4 (5.0)</td>
<td>120.0 (5.4)</td>
<td>119.1 (5.8)</td>
<td>118.8 (7.4)</td>
<td>−0.44 (0.09)*</td>
</tr>
<tr>
<td></td>
<td>n = 168</td>
<td>n = 158</td>
<td>n = 157</td>
<td>n = 157</td>
<td>n = 149</td>
<td></td>
</tr>
<tr>
<td>SF-36 physical functioning</td>
<td>39.5 (23.5)</td>
<td>38.1 (23.7)</td>
<td>37.2 (23.8)</td>
<td>35.3 (24.0)</td>
<td>36.1 (25.6)</td>
<td>−0.73 (0.27)*</td>
</tr>
<tr>
<td></td>
<td>n = 167</td>
<td>n = 159</td>
<td>n = 155</td>
<td>n = 149</td>
<td>n = 148</td>
<td></td>
</tr>
<tr>
<td>Distance in 2 minutes walking at self-preferred speed (m)</td>
<td>126.2 (33.6)</td>
<td>124.0 (33.3)</td>
<td>127.4 (33.8)</td>
<td>127.3 (34.1)</td>
<td>123.9 (33.0)</td>
<td>−0.86 (0.3)*</td>
</tr>
<tr>
<td></td>
<td>n = 152</td>
<td>n = 144</td>
<td>n = 139</td>
<td>n = 131</td>
<td>n = 113</td>
<td></td>
</tr>
<tr>
<td>Maximal quadriceps strength strongest leg (Nm)</td>
<td>88.0 (42.2)</td>
<td>81.5 (39.1)</td>
<td>83.3 (40.2)</td>
<td>79.6 (39.4)</td>
<td>92.7 (48.9)</td>
<td>At 3 years: −3.1 (0.6)*</td>
</tr>
<tr>
<td></td>
<td>n = 143</td>
<td>n = 130</td>
<td>n = 127</td>
<td>n = 116</td>
<td>n = 47</td>
<td></td>
</tr>
<tr>
<td>Maximal quadriceps strength weakest leg (Nm)</td>
<td>62.6 (36.8)</td>
<td>59.2 (37.3)</td>
<td>60.5 (34.1)</td>
<td>57.9 (33.3)</td>
<td>72.6 (52.3)</td>
<td>At 3 years: −1.5 (0.7)</td>
</tr>
<tr>
<td></td>
<td>n = 92</td>
<td>n = 86</td>
<td>n = 82</td>
<td>n = 79</td>
<td>n = 36</td>
<td></td>
</tr>
<tr>
<td>CIRS total score</td>
<td>6.5 (3.7)</td>
<td>6.9 (3.9)</td>
<td>7.0 (3.8)</td>
<td>7.7 (4.0)</td>
<td>8.1 (4.2)</td>
<td>0.30 (0.04)*</td>
</tr>
<tr>
<td></td>
<td>n = 168</td>
<td>n = 158</td>
<td>n = 157</td>
<td>n = 158</td>
<td>n = 149</td>
<td></td>
</tr>
</tbody>
</table>

*Note. Values are means (SD). B = coefficient in GEE analysis; SE = standard error of B. *p < 0.05.
SF36-PF
All age groups showed a significant decrease (mean baseline 39.5, SD 24) of 0.73 (SE 0.27) points per year on the SF36-PF, which was 9.2% over 5 years, independent of sex or age (Table 6.2).

Walking capacity test
The distance walked in 2 minutes at a self-preferred speed (mean baseline 126.2, SD 34) decreased 0.9 m (SE 0.3) (p = 0.008) each year, which was 3.6% over 5 years (Table 6.2). The subjective rating scale for perceived exertion showed no change over the years.

Maximal quadriceps strength
Maximal quadriceps strength of the strongest leg declined over the 5 years by 1.4 (0.5) N/m per year (mean baseline 88, SD 42; Table 6.2), but there was no significant decline (0.04, SE 0.6) in the weakest leg (mean baseline 62.6, SD 36.8). Over 5 years, the decline in muscle strength was 8% for the strongest leg and 0.3% for the weakest leg.

Secondary analyses
At baseline, 138 subjects reported new muscle weakness and 114 reported new muscle fatigue. In total, 147 patients reported new muscle weakness or new muscle fatigue. These individuals exhibited the same decline in functional independence and maximal quadriceps strength over time as the 21 patients who reported no new muscle weakness or muscle fatigue.

At the 5-year follow-up, only 47 patients performed the isokinetic strength test compared to 143 at baseline and 116 at 3 years. Quadriceps strength declined 3.1 (0.6) N/m per year in the strongest leg and 1.5 (0.7) N/m per year in the weakest leg in the first 3 years, which was 10.6% and 7.2%, respectively. The subgroup of 47 subjects who performed the isokinetic strength test at the 5-year follow-up had a significantly higher score at baseline for the FIM total score (3 points), SF36-PF (17 points), and legs strength sum score (10 points). Age did not differ between the groups, but the subgroup had a significantly lower CIRS total score at baseline (2 points). The isokinetic quadriceps strength did not significantly differ between the subgroup and the entire study sample at baseline, though the 47 subjects scored 9 Nm higher. The FIM total score declined 0.20 points each year in this subgroup (p < 0.05) but declined 0.44 points in the entire study sample. The SF36-PF (0.66 points per year, p = 0.08) and distance walked in 2 minutes (0.8 m per year, p = 0.08) did not decrease significantly in this subgroup over the 5 years.

CIRS
The CIRS total score (median baseline 6, range 0 – 21) significantly increased 0.30 (0.04) points per year over the 5-year course, independent of age (Table 6.2).
Progression of disability

Chapter 6

Longitudinal models

Two repeated measures models were constructed to investigate the impact of age and co-morbidity on the dependent variables FIM total score and SF36-PF. Significant factors associated with the FIM\textsuperscript{TM} included gender, age, legs strength sum score, arms strength sum score, and CIRS with a significant interaction between CIRS and legs strength sum score and the follow-up time (Table 6.3). This model explained 34% of the FIM total score variance. The model of factors associated with SF36-PF included gender, age, legs strength sum score, and CIRS, and it explained 35% of the SF36-PF variance (Table 6.3).

Discussion

Disability increased little in our cohort over the 5 years despite a pronounced reduction in muscle strength. Age did not affect the progression of disability and co-morbidity, and the severity of paresis in the legs impacted the course of functional independence.

### Table 6.3  Longitudinal model for FIM total score and SF-36 physical functioning subscale

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Total FIM score</th>
<th>SF-36 physical functioning</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model</strong></td>
<td><strong>B</strong></td>
<td><strong>SE</strong></td>
</tr>
<tr>
<td>Constant</td>
<td>114.866</td>
<td>4.339</td>
</tr>
<tr>
<td>Follow-up time</td>
<td>−0.572</td>
<td>0.256</td>
</tr>
<tr>
<td>Gender</td>
<td>−1.586</td>
<td>0.575</td>
</tr>
<tr>
<td>Age at baseline</td>
<td>−0.159</td>
<td>0.040</td>
</tr>
<tr>
<td>CIRS total score</td>
<td>−0.123</td>
<td>0.073</td>
</tr>
<tr>
<td>CIRS total score * follow-up time</td>
<td>−0.056</td>
<td>0.024</td>
</tr>
<tr>
<td>Arms strength sum score</td>
<td>0.237</td>
<td>0.079</td>
</tr>
<tr>
<td>Legs strength sum score</td>
<td>0.118</td>
<td>0.025</td>
</tr>
<tr>
<td>Legs strength sum score * follow-up time</td>
<td>0.010</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Note: Factors included in General Estimated Equations analysis were gender (male 1/female 2), age at baseline (years), arms strength sum score, legs strength sum score, follow-up time (years), CIRS total score. B = beta, coefficient; SE = standard error of B; CIRS = Cumulative Illness Rating Scale.

Longitudinal models

Two repeated measures models were constructed to investigate the impact of age and co-morbidity on the dependent variables FIM total score and SF36-PF. Significant factors associated with the FIM\textsuperscript{TM} included gender, age, legs strength sum score, arms strength sum score, and CIRS with a significant interaction between CIRS and legs strength sum score and the follow-up time (Table 6.3). This model explained 34% of the FIM total score variance. The model of factors associated with SF36-PF included gender, age, legs strength sum score, and CIRS, and it explained 35% of the SF36-PF variance (Table 6.3).

Discussion

Disability increased little in our cohort over the 5 years despite a pronounced reduction in muscle strength. Age did not affect the progression of disability and co-morbidity, and the severity of paresis in the legs impacted the course of functional independence.
The course of functioning

The decline in functional independence, as measured by the FIM™ (1.8% over 5 years), occurred in the motor items of the instrument. This finding is in line with earlier studies that reported a reduction in daily mobility functioning, but not personal care, and the development of additional dependency in daily living activities in only 2 of 59 persons over 4 – 5 years. The FIM™ (range 18 – 126 points) may not be a responsive tool in this patient group as our cohort had a mean score of 118.8 (SD 7.4) at the fifth year, indicating that all our patients scored in the upper range.

The moderate change in the SF36-PF (9.2% over 5 years) is in accordance with Willen et al., who reported a small deterioration in physical mobility as assessed with the Nottingham Health Profile (NHP) over 4 years. Nollet et al. reported no change in physical mobility (NHP) in a 6-year follow-up study, mainly due to improvements after 1 year. The moderate change in perceived functioning may underestimate the decline in functional abilities and could be due to a ‘response shift’; patients may have adapted to their physical limitations and rate their current functioning against the background of newly adapted standards. On the other hand, functional capacities decreased only slightly over time; therefore, a response shift is debatable and patients may have maintained functioning.

The distance walked in 2 minutes at a self-preferred speed decreased only 3.6% over 5 years. Comparing the walking tests results with other studies of polio survivors is difficult because different walking tests were used. Therefore, Stolwijk et al. recommended the use of one walking test, the 2-minute walking test, as a core qualifier of physical functioning to assess walking capacity in research and clinical practice. The modest change in the 2-minute walking test observed in our cohort is in line with Sorenson, who reported a 2% decline on a 100-feet walking test over 15 years, and Willen, who reported a change of 6 – 8% over 4 years on a 30-meter walking test.

In a systematic review, we concluded that muscle strength deteriorates slowly and requires a follow-up of at least 4 years. In our cohort, isokinetic quadriceps strength declined 8% over 5 years (1.6% per year). However, selective drop-out at the fifth measurement must be assumed. The 47 subjects who performed the 5-year follow-up isokinetic quadriceps test performed better at baseline on all outcome measures and had less co-morbidity compared to the other subjects. Judging from the decline in muscle strength in 116 subjects at the 3-year follow-up (10.6% or 3.5% per year), adding the fifth year strength measurement from these 47 subjects to the longitudinal model probably underestimates the real decline in strength. The results of the subgroup are in line with results from Grimby et al., who showed a 9 – 15% decrease in isokinetic quadriceps strength over 8 years in 21 subjects with a mean age of 48 ± 2 years. Ageing and co-morbidity may explain the steeper decline in muscle strength of our cohort at the 3-year follow-up. The 3.5% per year decline in strength over this period may better reflect the true decline in ageing polio survivors. In further follow-up, specific attention will be paid to obtaining muscle strength data from a larger number of patients in this cohort to obtain non-biased long-term data and gain insight into the real decline in muscle strength in this population.

In line with the study by Nollet et al., the extent of paresis at baseline, which reflects
the severity of polio impairment, was a prognostic factor that negatively affected the course of functioning over time. This finding corroborates the hypothesis that, in extensive paresis, an insidious decline in strength may have a significant negative impact on functioning because these subjects lack spare muscle capacity, and their ability to adapt with new functional solutions using other muscles is limited. Furthermore, to maintain certain daily life activities, polio survivors have to increasingly utilize their already reduced muscle mass. This idea supports the “overuse” hypothesis as an explanation for the new neuromuscular symptoms, such as pain, fatigue, and reduced endurance, in patients with a history of poliomyelitis.

**Age and co-morbidity**

Age at baseline was a factor in the longitudinal model of both functional independence and perceived physical functioning but did not affect the time course of either model. The question still remains of whether or not age affects the long-term course of functioning in LOSP. This 5-year follow-up study may have been too short to find an effect of age on functioning even though we included an ageing population. The absence of an age-matched control group for comparison is a principal limitation of this study. It is difficult to say whether the small changes in functioning over 5 years that we described in this study are due to normal ageing or are specific to LOSP. Therefore, future long-term follow-up studies should be conducted with age-matched controls without a history of poliomyelitis to compare the rate of decline in both groups.

In line with studies of patients with stroke or multiple sclerosis, an impact of co-morbidity on the course of functioning was found. Patients with multiple sclerosis and specific musculoskeletal system co-morbidity exhibited a greater decline in physical functioning compared to patients without these conditions. Kriegsman et al. reported that combinations of diseases that influence physical functioning through different mechanisms (locomotor symptoms vs. decreased endurance capacity) may be more detrimental to perceived physical functioning than other combinations. The course of perceived physical functioning in our cohort was, contrary to our expectation, not affected by co-morbidity. This observation may reflect a true finding but could also be due to the method used to quantify co-morbidity. A sum score of the ordinal rating scores for the different body systems was calculated in the CIRS, resulting in a total score. Whether this total score was a good parameter of co-morbidity in this population is questionable. In future research of LOSP, different outcome measures of co-morbidity need to be critically reviewed and assessed for their sensitivity to report co-morbidities, especially in the musculoskeletal system.

**Methodological aspects**

Because this study used the more neutral term LOSP instead of the diagnosis of PPS, the question of whether the results of this study can be generalized to PPS patients exists. The subgroup of 87.5% who reported key symptoms of PPS did not show a different course for disability and muscle strength compared to the group who reported no key symptoms of PPS at baseline. This finding is in line with the 6-year follow-up study of Nollet et al. As there are still no long-term follow-up studies available with large sample sizes analyzing symptomatic and asymptomatic patients, our study results...
should be considered of value for PPS patients as well.

A limitation of this study is possible sampling bias, especially in the oldest age group, 65 – 85 years of age, rendering the findings less generalizable. The non-responders could have been individuals with a low level of functioning who did not want to participate because of their impairments and limitations in activities; therefore, we cannot exclude an underestimation of functional problems and decline in functioning over time in the elderly age group. The loss to follow-up was limited to 8% over 5 years, equally distributed over the age groups. For the relatively long follow-up duration of 5 years, this is a small drop-out rate. Furthermore, the loss to follow-up did not create a selection for age because it was equally distributed over the age groups.

In conclusion, despite a considerable reduction in muscle strength, disability increased little in this cohort of former polio patients of various ages and including co-morbidity. The decline in muscle strength was probably underestimated due to selective drop-out. Apparently, LOSP patients maintain functioning by compensating for their progressive loss of muscle capacity. Although age, co-morbidity, and extent of paresis negatively affect disability, co-morbidity and the extent of paresis only negatively influence the course of functional independence, not the course of perceived physical functioning.

Acknowledgements

We wish to thank all those who participated in the study for their time and efforts. The study was supported by a grant from ZonMw, the Netherlands.


References


Chapter 7

General discussion
The aim of this thesis was to describe the course of functional status of patients, aged 45 – 85 years, with late-onset sequelae of poliomyelitis over a period of 5 years and to examine the impact of age and co-morbidity. To date, studies on the course of functioning of people with a history of poliomyelitis have almost always excluded subjects above the age of 65 and those with co-morbidities, or co-morbidities were not assessed or reported. Therefore, functional problems and the rate of decline may have been underestimated in ageing patients. The present chapter summarizes the main findings of this thesis and discusses the clinical implications. Furthermore, methodological limitations of the study are critically addressed and recommendations for future research are made.

**The course of functioning**

**Decline in physical functioning**

The 5-year follow-up study described in Chapter 6 found functioning, measured as functional independence, perceived physical functioning, and walking capacity, declined little in our cohort; whereas, muscle strength decreased somewhat more. The moderate decline in physical functioning, measured with the Short Form-36 (SF-36), is in agreement with earlier studies of post-polio syndrome (PPS).\(^1\,^2\) The perceived decrease in physical functioning may have underestimated the true decline in functioning in ageing polio survivors due to a ‘response shift’, i.e. patients adapt to their gradually increasing physical limitations and evaluate their level of activities and participation against adapted standards.\(^3\,^4\) However, a response shift is debatable as the declines in time-tested walking and functional independence were small and mainly accounted for by the motor items of the Functional Independence Measure (FIM\(^\text{Tm}\)).

**Decline in walking capacity**

Walking capacity at a self-chosen speed declined modestly at 0.7% per year in our cohort; this lies between the 0.2% annual decline reported by Sorenson et al. in their study with sufficient methodological quality and the 1.5 – 2.0% decline reported by Willen et al. in a study with insufficient methodological quality.\(^1\,^5\) Our study population was older and reported more late-onset neuromuscular symptoms at baseline compared to Sorenson’s study sample.\(^5\) Therefore, the decline in our cohort is considered a valid assessment of the rate of decline in walking ability over time in people with late-onset sequelae of poliomyelitis (LOSP).

**Decline in muscle strength**

Several physiologic functions decline with age such as muscle strength, cardio respiratory fitness, basal metabolic rate, joint mobility, co-ordination and bone density.\(^6\,^9\) The normal age-related decline in muscle strength varies between muscle groups and between studies. The estimated rates of decline in muscle strength derived from cross-sectional studies range from 1.5 to 3% per year,\(^10\,^12\) but these rates may not correspond with true age-related declines in strength. Longitudinal studies of isometric or isokinetic muscle strength of knee extensors are limited in number.
Hughes et al. described a 1.4% loss of isokinetic muscle strength per year, based on a 10-year follow-up of 120 subjects aged 46 – 78 years; whereas, Aniansson et al. reported a decline of 2.3 – 3.2% per year based on an 11-year follow-up of a population of only 9 men with a mean age of 70 years. From the age of 30, muscle strength is already reduced due to atrophy, deterioration of mechanical properties, and motor unit loss. After the age of 60, a progressive loss of motor neurons occurs. On top of the age-related decline, muscle function declines in people with PPS as a result of isolated degeneration of enlarged motor units. In our cohort, isokinetic strength of the quadriceps declined 8% in 5 years or 1.6% annually. This decline is in agreement with the study by Grimby et al., who reported a 1.1 – 1.9% deterioration of muscle strength per year in middle-aged polio survivors. Unfortunately, selective drop-out at the 5-year isokinetic strength measurement in our cohort is likely. The 47 subjects who performed the 5-year maximal strength quadriceps test had better strength, did significantly better at the level of activities and participation, and suffered from less co-morbidity at baseline. Therefore, the decline in strength is likely underestimated for the whole cohort. At the 3-year follow-up measurement, involving a much larger number of subjects, a more distinct reduction in muscle strength of 3.5% per year was found; perhaps this better reflects the true decline in ageing patients with LOSP and co-morbidity. Further follow-up measurements of muscle strength in this cohort are required to answer this question.

Muscle overuse and functioning

A systematic review of the literature published up to July 2004 (Chapter 2.1), did not allow conclusions to be drawn on the course of functioning over time in patients with LOSP. Muscle strength appeared to deteriorate slowly in studies with a least 4 years follow-up. This review was updated (Chapter 2.2) and 4 new studies published between July 2004 and July 2009 were retrieved, including our own follow-up study. It was determined that, depending on outcome measures and study population, follow-up durations of at least 3 to 5 years are needed to demonstrate declines in functioning over time. Although a quantitative analysis could not be performed due to heterogeneity in outcome measures, all studies on perceived functioning reported a decline over time. Timed walking tests showed a slow deterioration of 0.2 – 0.7% per year, while muscle strength declined faster (1.5 – 1.9% per year). Two studies, including our own, reported the severity of polio residuals was a prognostic factor of functioning (Chapter 6). The difference in deterioration rates between walking capacity and muscle strength supports the concept of ‘overuse’ of muscles in daily life. To maintain their functioning over the years, patients are forced to use their weakening muscles at increasing relative loads. Overuse of muscles may contribute to or partially explain symptoms such as weakness, increased muscle fatigability, general fatigue, and pain.

Impact of age and co-morbidity on functioning

People with polio residuals are assumed to develop morbidities in accordance with the increasing prevalence seen in the general ageing population. Co-morbidity and age may be important determinants of functioning in an ageing population and may have consequences for rehabilitation of the elderly, including people with a history
of poliomyelitis. No studies are presently available in literature on the impact of age and co-morbidity on functioning in polio survivors.

**Impact of age on functioning**

In our prognostic study, age at baseline was significantly associated with both functional independence and perceived physical functioning; yet, contrary to expectation, age did not impact on the course of either of them. However, the increase in disability was small. From our review, we concluded studies require at least 3 to 5 years follow-up to demonstrate a slow decline in functioning. It may be that even longer follow-up is needed to identify the impact of prognostic factors, such as age, on the course of functioning. Therefore, further continuation of this cohort study is important.

**Impact of co-morbidity on functioning**

In this cohort, co-morbidity, measured with the Cumulative Illness Rating Scale (CIRS), appeared to be significantly associated with functional independence (FIM total score) and perceived physical functioning (SF36-PF) at baseline (Chapter 5). This was the case for the CIRS total score and the CIRS body systems: 'cardiac', 'vascular', 'endocrine, metabolic', and 'muscle, bone, skin'. In the longitudinal models, the CIRS total score impacted the course of the FIMTM, but not the SF36-PF (Chapter 6). None of the CIRS body systems were found to affect the course of the FIMTM or SF36-PF. Some studies reported an impact of co-morbidity on the course of functioning in stroke patients, while co-morbidity had no effect on the course of functioning in another study. In two other patient groups of the CARPA study, co-morbidity also influenced the course of functioning. Co-morbidities, especially cardiac diseases and vision problems, turned out to have a large impact on patients with osteoarthritis, resulting in increased limitations in activities after 3 years of follow-up. In patients with Parkinson’s disease, co-morbidity contributed to increasing disability and worsening of quality of life over time.

In conclusion, disability increased little in our cohort in 5 years despite a more pronounced reduction in muscle strength. Age did not affect the progression of disability, and co-morbidity and the severity of paresis of the legs had limited impacts on the course of functional independence.

**Clinical implications**

**Can future functioning be predicted for LOSP patients?**

Age, co-morbidity, and extent of paresis were factors associated with functional independence; while co-morbidity and extent of paresis of the legs were prognostic factors for the course of functional independence over time. To translate the prognostic model to patients, imagine 4 fictitious patients (Table 7.1). Patient 1 is male, 50 years old, has no paresis of the arms, limited paresis of the legs, and is completely healthy, i.e. has no co-morbidity. According to our longitudinal model (Chapter 6), this patient’s FIM total score will not change and he will still be independent in 5 years time. Patient 2 is a female of 50 years with moderate paresis of the arms and severe paresis of the legs,
but otherwise healthy. In 5 years, she will decrease one point on the FIM total score and still function independently with either extra time or an occasional assistive device needed to complete tasks. Patient 3, a 75 year old male with the same limited paresis as patient 1, suffers from an extensive co-morbidity. In 5 years, the combination of his age and extensive co-morbidity will result in a decrease in functioning of 4 points, i.e. some extra time and assistive devices will be needed for some activities. The last patient, patient 4, is a 75 year old female with moderate to severe paresis similar to patient 3 and abundant co-morbidity. Her FIM total score will decrease 5 points and she will need some physical help to function, in addition to the assistive aids and extra time she already needed to do daily activities. This longitudinal model needs validation in another sample of polio survivors and the confidence limits of the model need to be considered. Yet, these 4 patients give some idea of the differences in progression of disability in terms of functional independence and the importance in considering age, co-morbidity, and paresis for the functional prognosis of individuals with LOSP.

**Table 7.1** Prediction of total FIM score over 5 years of 4 fictitious patients based on the longitudinal model for total FIM score

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender (M/F)</th>
<th>Age (years)</th>
<th>Arm strength sum score</th>
<th>Leg strength sum score</th>
<th>CIRS total score</th>
<th>Total FIM score after 5 yrs</th>
<th>Δ total FIM score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>M</td>
<td>50</td>
<td>50</td>
<td>70</td>
<td>0</td>
<td>126</td>
<td>0</td>
</tr>
<tr>
<td>Patient 2</td>
<td>F</td>
<td>50</td>
<td>42</td>
<td>45</td>
<td>0</td>
<td>118</td>
<td>1</td>
</tr>
<tr>
<td>Patient 3</td>
<td>M</td>
<td>75</td>
<td>50</td>
<td>70</td>
<td>15</td>
<td>116</td>
<td>4</td>
</tr>
<tr>
<td>Patient 4</td>
<td>F</td>
<td>75</td>
<td>42</td>
<td>45</td>
<td>15</td>
<td>108</td>
<td>5</td>
</tr>
</tbody>
</table>

*Note: Δ = change in total FIM score over 5 years.*

**Therapeutic interventions**

Our longitudinal study confirms patients with LOSP are largely able to maintain their daily life functioning, at the cost of overloading their progressively weakening muscles. This may impact the appropriateness of rehabilitation interventions for specific patients. Two aims within multidisciplinary rehabilitation therapy can be distinguished (1) preservation or improvement of muscular capacity (muscle function and cardio respiratory function) and (2) the reduction of physical demands in daily life activities.

**Preservation of muscular capacity**

Patients with PPS have traditionally been advised to avoid muscular overuse and intensive training as this may worsen their symptoms. However, PPS patients who were regularly physically active did function better and had less symptoms in comparison with those who were inactive. Furthermore, several studies of moderate quality have reported beneficial effects of exercise on muscle strength and aerobic capacity without adverse effects. Based on these studies, the EFNS guideline of 2006 concluded (recommendation level B) that supervised, aerobic muscular training is a safe and effective way to prevent further decline. In connection with our study results,
patients, especially those with limited polio residuals and a favourable prognosis, may benefit from muscle training to maintain their functioning over the years. It can be questioned whether in patients with severe polio residuals exercise is able to maintain functioning.

Reduction of physical demands

To reduce the physical demands of daily life, energy conservation measures are advocated. Individual or group multidisciplinary treatment programs provide education in energy conservation skills, environmental adaptations at home or work, transportation aids, braces, and assistive devices and are tailored to the individual's needs and lifestyle. Changes can help patients reduce their daily physical workload. The EFNS guidelines of 2006 recommends group training, regular follow-ups, patient education, and adjustment of properly fitted assistive devices as described above. Research on the benefit of such multidisciplinary treatment programs is currently underway. Above all, patients with a poor functional prognosis may benefit from these multidisciplinary treatment programs because they are less able to train their diminished and overused muscles.

Methodological considerations

Sampling bias and selective drop-out

A strength of this cohort is the inclusion of 48 subjects aged 65 years and older. A particular concern is the possibility of sampling bias in the elderly subjects, although non-responses for participation in the study were equally divided between younger and older patients. If the non-responders had a lower level of functioning, more co-morbidity, or more severe pareses compared to the subjects participating in the study, the decrease in functioning over time may have been underestimated.

Due to efforts to visit subjects at home and to consult with them by phone if they were not able to visit the hospital, only 14 patients were lost to follow-up. Selective drop-out probably occurred at the 5-year measurement of isokinetic strength because, unfortunately, the dynamometer was out of order for some time. To minimize the consequences of missing data, GEE analyses were used, a longitudinal data analysis technique that uses all longitudinal data, not only data on complete cases. The use of GEE analyses does not prevent bias due to selective drop-out at the last measurement point. Therefore, an underestimation of the increase in disability and decline in muscle strength cannot be excluded and should be considered especially in the older subjects of this cohort.

Main outcome measures

Functional Independence Measure

The Functional Independence Measure (FIM™) was chosen in the CARPA study to assess functional independence because it has been proven a valid, reproducible generic tool in patients undergoing rehabilitation. The polio cohort declined very little in functioning over 5 years according to the FIM™. As our subjects scored in
the upper range of the FIM™, it may be questioned whether this is an appropriate outcome measure to assess functioning with respect to its measurement range and responsiveness to detect change in functioning in polio survivors. No other studies using the FIM™ in patients with polio residuals have been published. In other patient groups, the FIM™ did not show a ceiling effect.46,47 The responsiveness of the FIM™ has been assessed in patients with stroke and multiple sclerosis in comparison with other disability evaluating outcome measures, such as the Barthel Index, and similar responsiveness was shown.46,47 Lacking better alternatives, the FIM™ was considered a satisfactory, observation based outcome measure to assess functional independence in this cohort.

Short Form-36 physical functioning

The physical functioning subscale of the Short Form-36 (SF36-PF), the Western Ontario and MacMaster Universities Osteoarthritis Index (WOMAC-PF), and the physical mobility category of the Nottingham Health Profile (NHP-PM) were used to assess perceived physical functioning. The clinimetric properties of the WOMAC-PF, an osteoarthritis specific questionnaire focusing on activities involving the lower extremities, were assessed in our population of patients with LOSP. The results from Chapter 3 showed the WOMAC-PF was an internally consistent, unidimensional measure of limitations in lower extremity related physical functioning in polio survivors. The test-retest reliability and smallest detectable change of these 3 questionnaires in our specific population were described in Chapter 4. As the SF36-PF showed good test-retest reliability, an acceptable smallest detectable change, and the highest correlation with walking capacity tests, it was a core qualifier for physical functioning.

Determinants

Age

Age was, to our surprise, not a prognostic factor for change in functioning. Further follow-up of this cohort should confirm or invalidate this finding over long-term. The addition of age-matched controls to this cohort would enable the comparison of functional decline over time in polio survivors with LOSP and peers without a history of poliomyelitis. This would allow age-related decline in functioning to be distinguished from LOSP-related decline in functioning.

Co-morbidity

Based on a systematic review of measurement instruments to assess co-morbidity, the Cumulative Illness Rating Scale (CIRS)48 was selected to measure co-morbidity because of its good clinimetric properties with respect to validity49 and its inter-rater and test-retest reliability.48,50,51 Furthermore, the CIRS is structured according to clinically relevant body systems and the severity ranking is clinically sound and clear, which makes it a useful co-morbidity measure in clinical research.52 Another important advantage of the CIRS is that it can easily be applied to different populations; this is an important criterion as the research carried out in this thesis was part of the CARPA study, also involving patients with osteoarthritis and Parkinson’s disease.
In the longitudinal analyses, co-morbidity only slightly impacted the course of functional independence and did not impact perceived physical functioning. The question arises whether this reflects a true finding and co-morbidity indeed plays a minor role in the course of functioning, or that this result was due to inappropriateness of the outcome measure or required even longer follow-up. The CIRS distinguishes 13 body systems which can be scored on a 5-point scale. Three co-morbidity scores can be derived from the CIRS: the total score, a sum of all the 13 category scores; the morbidity count, a sum of the number of categories that scored a level of morbidity in their category; and the severity index, the total score divided by the morbidity count. The CIRS total score was used to measure the severity of co-morbidities, as it was assumed to be the most sensitive to changes in co-morbidity. However, a limitation of the CIRS is its restricted ability to classify the severity of co-morbidities in cases of multiple co-morbidities within the same category. For patients with LOSP, a variety of secondary medical conditions related to polio, such as degenerative arthritis and compression neuropathies due to the use of crutches, are frequent co-morbidities. However, they are all reduced to one score in the category ‘muscle/bone/skin’ of the CIRS. To our knowledge, no specific co-morbidity measure for musculoskeletal conditions exists; for future polio research studies, a more extensive classification of musculoskeletal co-morbidities would be valuable to determine their influence on functional status.

**Measuring muscle strength**

In this cohort, a fixed dynamometer was used to assess the course of maximal strength of the quadriceps, and manual muscle testing was used to measure the extent of paresis of the legs as a potential prognostic determinant. Manual muscle testing is known to be limited in its measurement range, especially in lower extremities, as it has poor inter-rater reliability and limited ability to detect change. Although, in this cohort, manual muscle testing to assess the severity of polio at baseline was considered an acceptable method as all tests were performed by the same physician. Apart from fixed dynamometry of the knee extensors, it would have been desirable to measure the decline in other muscle groups as well. Muscle groups such as knee flexors and ankle plantar and dorsal flexors could also have been measured with fixed dynamometry. However, this is very time consuming. Since the measurement sessions already took about 2 hours, additional dynamometry was not considered feasible for the patients. Unfortunately, easily applicable and reliable alternatives to measure strength in a larger number of muscle groups are lacking. Hand-held dynamometry has poor reproducibility and a limited measurement range with a ceiling effect at about 200 – 250 N. It is also unable to detect small changes, especially in larger lower extremity muscle groups. Even a fixed dynamometer has its limitations in polio survivors. Horemans et al. found fixed dynamometry was unable to detect small changes in strength in symptomatic muscles of patients with PPS, due to larger intra-individual variability in strength compared to healthy control subjects. This may have partially resulted from PPS patients being less able to fully activate their muscles. However, Horemans et al. did conclude the reproducibility of fixed dynamometry was sufficient to evaluate changes in groups of subjects in follow-up studies.
Core qualifiers for physical functioning
The ICF Research Branch of the WHO puts great effort in the development of internationally agreed ICF Core Sets for outcome assessments in patient care and research.60 These Core Sets are based on the International Classification of Functioning, Disability, and Health (ICF), which is a framework that describes the functional consequences of a disease at the levels of body function and structure, and daily activities and participation.61 There is currently no ICF Core Set for patients with LOSP. In Chapter 4, 2 outcome measures were postulated as core qualifiers to assess physical functioning in patients with LOSP; it was recommended to routinely apply the measures worldwide in research and clinical practice to facilitate comparisons of results. The SF-36 physical functioning scale and 2-minute walking test have been proposed to be included as outcome measures in the development of an ICF Core Set for polio survivors (and possibly for similar slowly progressive neuromuscular diseases). These tests would measure the performance and capacity domains related to activities and participation.

Future research
Recommendations for future research can be made based on this prospective study and new insights in the pathophysiology and treatment of PPS. First, the future of the CARPA study, in which this study is embedded, will be discussed.

CARPA
Overall analyses of the 3 cohorts included in the CARPA study are necessary to gain insight into the differences and similarities between patients with LOSP, osteoarthritis, and Parkinson’s disease with regard to the influence of physical impairments, co-morbidity, and cognitive impairments on the course of functional status over time. Continuation of the CARPA study is important and will provide unique data to study the long-term effects of these determinants in a large cohort of 656 patients.

Continuation of this cohort
The present cohort of patients with late-onset sequelae of polio should be studied further to achieve a better understanding of the long-term course of functioning and the impact of prognostic factors. As LOSP is characterized by a slow progression rate, the patient’s disability will likely increase with longer follow-up, and will most likely reveal a more pronounced reduction in functioning and muscle strength over time. Furthermore, it can be assumed that with longer follow-up the course of functioning between subjects will become more diverse due to differences in patients’ characteristics with respect to the severity of residual paresis, co-morbidities, age, and perhaps other factors. This will provide the opportunity to improve the longitudinal models on functioning.

The challenge in continuing this cohort study will be to assure complete data collection with regard to the different outcome measures. To avoid selection bias, especially in the older age group, subjects should be encouraged and assisted to visit the hospital for testing. Patients should only be visited at home if they are unable to
reach the hospital. To maximize data collection for the most accurate and reproducible strength measurements, hospital visits remain crucial because they require fixed dynamometry.

Although the impact of age and co-morbidity on the functional course appeared to be absent or small, their impact on functioning in polio survivors in longer follow-up remains to be determined. Age-matched controls must be included in further follow-up of this cohort to separate LOSP-related decline in functioning from age-related decline. Also, co-morbidity measures need to be critically reviewed and comprehensive measures of co-morbidities of the musculoskeletal system are required and may need to be developed.

**Additional outcome measures for this cohort**

New insights in LOSP may lead to adding new outcome measures and determinants to this study. Perceived fatigue is a major complaint in post-polio syndrome.²,⁶²,⁶³ Fatigue may be related to muscle overuse in daily functioning. Presently, the longitudinal data of this cohort are being analyzed to investigate factors associated with perceived fatigue. Depending on these findings, questionnaires on fatigue and the impact of fatigue on functioning may be added to this cohort.

Due to the difference in deterioration rates between walking capacity and muscle strength, the concept of muscle overuse needs further evaluation. Physical activity in daily life should be measured with an activity monitor over several consecutive days. The long-term changes in muscle function in LOSP will be investigated on the level of motor unit size with High Density-EMG measurements in another cohort of 65 patients with PPS, in collaboration with the neurophysiology department of the University Medical Centre St Radboud in Nijmegen, the Netherlands. This may result in more sensitive measures to monitor changes in muscle function over time, in addition to measurements of muscle strength.

Ideally, the number of participants in an observational study should be very large to assess the impact of many determinants, without being limited to the number of determinants that can be applied in longitudinal models. A larger study sample can be acquired by international collaborations with other research groups with interests in polio.

The latest insights suggest immunologic factors may play a role in the pathophysiology of PPS. Several studies have reported increased levels of pro-inflammatory cytokines in the serum and cerebrospinal fluid of patients with PPS.⁶⁴-⁶⁷ Based on these findings, the effect of immune modulating therapies have been investigated.⁶⁸-⁷⁰ These studies indicate that intravenous immunoglobulins (IVIGs) could have a beneficial effect in PPS, but this needs further investigation. At present IVIG are not recommended as treatment for PPS.⁷¹ It would be interesting to start collecting blood samples from our cohort to investigate the presence of elevated pro-inflammatory cytokine levels and their effect on the course of functional status.
**Therapeutic interventions**

Cognitive behavioural therapy (CBT) is a new approach in rehabilitation that has been proven effective in reducing fatigue and functional impairment in chronic fatigue syndrome and post-cancer fatigue. The evidence for CBT in PPS is currently limited to results from an unpublished, uncontrolled pilot study, which found an increase in health-related quality of life. Furthermore, 2 uncontrolled follow-up studies of multidisciplinary rehabilitation, including some aspects of CBT, reported a positive effect on fatigue and physical capacity up to one year after the intervention. A randomized clinical trial has recently started in our research group to study the efficacy of exercise therapy and CBT for reducing fatigue and improving activities and health-related quality of life in patients with PPS. The cost-effectiveness of each intervention compared to standard care will also be investigated. This study will use the core qualifiers, SF-36 physical functioning subscale and 2-minute walking test at a comfortable speed, to assess disability.

Knowledge on the course of functional status and muscle strength in ageing patients with late-onset sequelae of poliomyelitis and co-morbidities will probably increase in the near future. Ongoing intervention studies aim to reduce neuromuscular symptoms and optimize quality of life. Step by step, the pathophysiology and successful treatment of late-onset sequelae of poliomyelitis will hopefully be solved like pieces of a puzzle. A large effort has focused on eliminating acute polio worldwide, and low incidence rates have been achieved over the past decades. The present challenge is to eradicate acute polio, but the ultimate goal for polio survivors, estimated to be at least 20 million individuals worldwide, is rehabilitation based care to retain their functioning as they age.

**References**


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76. FACTS-2-PPS study: Exercise therapy and cognitive behavioural therapy in Postpoliomyelitis Syndrome: effects on fatigue, activities and quality of life. A randomized controlled trial. Registered in de Dutch Trial Register, Trial ID NTR1371.
Summary
The profound increase in the number of elderly people in the Netherlands in the future, will result in an increase in number of patients in need for rehabilitation care. With ageing several physiologic functions decline and the resulting physical impairments may negatively affect the course of functional status. At older age, people may develop multiple morbidities, which have been demonstrated to be negatively associated with quality of life, and performance of activities in daily life, and, lead to a higher use of healthcare services. Cognitive impairments may also increase with age, and have been shown to impact on disability, well-being and the use of healthcare services. Physical impairments, multiple morbidities and cognitive impairments are the most important causes of limitations in functioning in the elderly. For the development of rehabilitation programs for an ageing population, knowledge of these determinants on the course of functioning is essential.

The present thesis is part of the CARPA study ‘Co-morbidity and Ageing in Rehabilitation Patients: the influence on Activities’. This study investigates the course of functional status and the impact of physical impairments, co-morbidity and cognitive impairments on this course in elderly patients with late-onset sequelae of poliomyelitis, osteoarthritis and Parkinson’s disease. This thesis encompasses the studies with regard to late-onset sequelae of poliomyelitis.

Although poliomyelitis has become an almost forgotten disease in the Western world after the introduction of routine vaccination in the late 1950s, there are still many individuals with polio residuals. As these people are ageing, they are confronted with new neuromuscular symptoms 30 to 40 years after the original childhood disease. These symptoms include a gradual or, less frequent, abrupt onset of progressive new weakness, abnormal muscle fatigability, with or without generalized fatigue, muscle atrophy, or pain. The denominator for these late-onset symptoms is post-polio syndrome (PPS). Taking into account that PPS is a diagnosis by exclusion and that this thesis focused on the impact of age and co-morbidity on functioning of elderly patients with a history of poliomyelitis, the more neutral term late-onset sequelae of poliomyelitis (LOSP) was preferred.

The new late-onset neuromuscular symptoms cause increasing difficulties with physical functioning, such as walking, standing, climbing stairs and other mobility-related activities of daily life. To date, studies on the course of functioning of people with a history of poliomyelitis have almost always excluded subjects above the age of 65 and subjects with co-morbidity, or co-morbidities were not assessed or not reported. Therefore, these studies may have underestimated the functional problems and rate of decline in ageing former polio patients. As the impact of age and co-morbidity on the course of functioning in patients with LOSP remains unresolved, this thesis aims to describe the course of functional status of patients aged 45 – 85 years with late-onset sequelae of poliomyelitis over a period of 5 years and to explore the impact of age and co-morbidity.

Chapter 2 systematically reviewed studies focusing on the course of functional status and muscle strength over time and prognostic factors of change in patients with LOSP based on a literature search. A computerized literature search up to July 2004 was conducted and these results were published (chapter 2.1). An unpublished update of
the literature from July 2004 to July 2009 was added in Chapter 2.2. The original review comprised 2 studies on the course of functional status and 4 studies on the course of muscle strength with sufficient methodological quality. In Chapter 2.2, 2 additional articles with sufficient or high quality on the course of functional status (including the 5-year longitudinal CARPA study (Chapter 6)), and the course of muscle strength, were summarized. Adding the results of these studies to the original systematic review gave better insight in the course of functioning and muscle strength in patients with LOSP. The heterogeneity in outcome measures between studies, prevented a quantitative analysis of the decline in perceived functional status over time. Nevertheless, all studies on perceived functioning reported a deterioration over time. Walking ability, assessed with timed walking tests, deteriorates slowly, 0.2 – 0.7% per year. Muscle strength declines approximately 3 times faster (1.5 – 1.9% per year). Factors that negatively affect the decline in functioning that have been reported in high-quality studies were the severity of polio residuals and co-morbidity, while age so far has not been shown to influence the decline in functioning. In general, studies require long term follow-up periods to observe a change in functioning with a minimum between 3 and 5 years depending on the outcome measures and study population. Furthermore it was concluded that uniformity in outcome measures between prognostic studies on all levels of functioning (impairments, activities and participation) is crucial to compare studies and to gain better insight in the course of functioning over time and factors that may affect this course in polio survivors.

In Chapter 3, the baseline data of the entire CARPA study with regard to the Western Ontario and MacMasters Universities Osteoarthritis Index (WOMAC) have been used to investigate whether its physical functioning subscale can be used to assess physical functioning in patients with LOSP and in patients with Parkinson's Disease (PD). The WOMAC originally is an osteoarthritis-specific questionnaire to establish the level of physical functioning. The baseline data of the WOMAC physical functioning subscale (WOMAC-PF) of 288 patients with osteoarthritis, 200 patients with Parkinson's disease and 168 patients with LOSP have been analyzed. Unidimensionality was adequate and item fit was generally good. Differential item functioning was found to be present between the 3 diagnostic groups in 10 of 17 WOMAC-PF items. Therefore it was concluded that the WOMAC-PF is an unidimensional measure of physical functioning in patients with LOSP and PD, in addition to its established use in OA. When making cross-diagnostic comparisons of the level of physical functioning, directly comparing WOMAC-PF scores may not be adequate due to the presence of differential item functioning.

Chapter 4, 5 and 6 reported on the data derived from the 5-year follow-up study of 168 patients with late-onset sequelae of poliomyelitis, aged 45 – 85 years.

Heterogeneity in outcome measures used in studies focusing on patients with late-onset sequelae of poliomyelitis prevents summarizing the evidence in an effective way. The aim of Chapter 4 therefore was to prioritize one questionnaire and one walking test from a number of questionnaires and tests that are widely used in post-polio populations by comparing their reproducibility, measurement range and mutual associations, in order to advocate their use as core qualifiers of physical functioning in research and clinical practice.
Physical functioning subscales from Short Form-36 (SF36-PF), WOMAC and Nottingham Health Profile were compared as well as timed-up-and-go test, time needed to walk 10 meter at self-preferred and maximum speed and distance walked in 2 minutes at self-preferred speed. The results showed that the test-retest reliability of all questionnaires was sufficient to excellent. The smallest detectable changes were best for SF36-PF and WOMAC-PF and the 2-minute walking test. SF-36 physical functioning scale and 2-minute walking test showed the highest correlation. Based on these results, the SF36-PF and 2-minute walking test were recommended as core qualifiers for physical functioning, to assess the perceived physical performance and walking capacity in research and clinical practice.

In chapter 5 functional independence and perceived physical functioning of patients with LOSP in 3 age groups (45 – 54 years, 55 – 64 years and 65 – 85 years) were compared and the impact of age and co-morbidity on these outcome measures was investigated. Elderly patients showed a lower level of functional independence, whereas no difference in perceived physical functioning was found. The co-morbidity score increased with age. Age was independently associated with functional independence, but not with perceived physical functioning. This may corroborate an age-related shift in the perception of physical limitations. The co-morbidity categories ‘cardiac’, ‘vascular’, ‘endocrine, metabolic’ and ‘muscle, bone, skin’ appeared to be associated with both functional independence and perceived physical functioning. It was concluded that co-morbidity negatively affects functional independence and perceived physical functioning. Prospective studies with unselected study populations, without exclusion of co-morbidity or elderly subjects, but including age-matched controls and measures to record co-morbidity were advised to investigate the influence of co-morbidity on the course of functioning in this population.

Chapter 6 presented the results of the 5-year observational cohort study with regard to the course of functioning and muscle strength and the impact of age and co-morbidity on the course of functional independence and perceived physical functioning. Disability, measured as functional independence, walking capacity and perceived physical functioning, declined little. The rate of decline in functioning was in line with other studies on polio survivors. Muscle strength, assessed as maximal quadriceps strength on a fixed dynamometer, decreased somewhat more. Unfortunately selective drop-out, resulting in a functionally better group with less co-morbidity, must be assumed at the fifth measurement due to temporary malfunction of the dynamometer. Judging from the decline in muscle strength at the 3-year follow-up, the 5-year measurements probably underestimate the real decline in muscle strength and the decline measured at 3-year follow-up may better reflect the true decline in ageing polio survivors. Co-morbidity increased over the years and a higher level of co-morbidity correlated with a lower score in functional independence and faster decrease in functional independence. For functional independence and perceived physical functioning prognostic models were constructed. Legs strength sum score and co-morbidity total score were prognostic factors for functional independence, whereas age was not. The prognostic model for perceived physical functioning included gender, age, legs strength sum score and co-morbidity total score, but no prognostic determinants were identified. To our surprise, age did not impact on functioning and future long-term follow-up studies should be
conducted with age-matched controls to compare the rate of decline in subjects with and without a history of poliomyelitis. Long-term follow-up with a sensitive outcome measure for musculoskeletal co-morbidities should determine whether the impact of co-morbidity will increase over the years.

Finally, chapter 7 discussed the main findings and clinical implications, critically focused on the methodology and gave recommendations for future research.

Four imaginary patients who differ in age, gender, extent of paresis of the legs and rate of co-morbidity were discussed to give some idea of the difference in the progression of disability in terms of functional independence between patients and the importance to consider age, co-morbidity and paresis for the functional prognosis of individuals with LOSP.

The longitudinal data showed that walking measured with walking tests deteriorates slowly, whereas muscle strength declined faster. Furthermore 2 studies, including our own, reported that the severity of polio residuals was a prognostic factor of functioning. The difference in deterioration rate between walking capacity and muscle strength supports the concept of ‘overuse’ of muscles in daily life. To maintain functioning over the years, patients are forced to use their weakening muscles at increasing relative loads.

In rehabilitation therapy, 2 approaches, that can be complementary to each other, can be distinguished: (1) preservation or improvement of muscular capacity and (2) the reduction of physical demands of daily life activities. Especially patients with relative good functional prognosis and muscle strength should be considered to use preservation of muscular capacity as an appropriate mean of therapy, because these patients still have a muscle status that can be trained. Patients with a worse functional prognosis should be considered to benefit from multidisciplinary treatment programs focusing on the reduction of physical demands, necessitating life style changes, because these patients are likely less able to train their limited and overused muscles.

An important methodological limitation to this study is the fact that sampling bias and selective drop-out might have occurred in our cohort. Therefore, an underestimation of the increase in disability and decline in muscle strength cannot be excluded and should be considered in especially the older subjects.

In future research this cohort should be followed further to gain insight in the long-term course of functioning and the impact of prognostic factors. The challenge will be to assure complete data collection with regard to the different outcome measures, especially muscle strength. Age-matched controls must be included to separate LOSP-related decline in functioning from age-related decline. A comprehensive measure of co-morbidities of the musculoskeletal system should be added to the outcome measures. Based on new insights, questionnaires on fatigue, activity monitoring and the collection of blood samples to assess the level of cytokines are to be added to the measurements.

The goal for the future with respect to rehabilitation must be that the millions of polio survivors can retain their functioning at the highest achievable levels as they age.
Functioneren en ouder worden met de late gevolgen van poliomyelitis

(Summary in Dutch)
Door de vergrijzing in Nederland zal het aantal patiënten dat revalidatiezorg behoeft toenemen. Bij het ouder worden gaan diverse fysiologische functies achteruit en de daaruit voortvloeiende fysieke stoornissen kunnen een negatieve invloed hebben op het beloop van functioneren (hoofdstuk 1). Met toename van de leeftijd kunnen mensen meerdere ziektes tegelijk ontwikkelen, oftewel co-morbidity. Het is aangetoond dat co-morbidity een negatieve invloed heeft op de kwaliteit van leven en het uitvoeren van dagelijkse activiteiten en leidt tot een hoger zorggebruik. Cognitieve stoornissen kunnen ook toenemen bij veroudering en zijn van invloed op beperkingen in dagelijks functioneren, welbevinden en gebruik van zorg. Fysieke stoornissen passend bij veroudering, het bestaan van meerdere ziektes naast elkaar en cognitieve stoornissen zijn de belangrijkste oorzaken van beperkingen in het functioneren van ouderen. Voor het ontwikkelen van revalidatiebehandelprogramma’s voor ouderen is kennis over de invloed van deze factoren op het beloop van functioneren essentieel.

Dit proefschrift is onderdeel van de CARPA-studie “Co-morbidity en veroudering in revalidatiepatiënten: de invloed op activiteiten”. Deze studie onderzoekt het beloop van functioneren en de invloed van fysieke stoornissen, co-morbidity en cognitieve stoornissen op het beloop van functioneren bij ouderen met late gevolgen van poliomyelitis, artrose en de ziekte van Parkinson. Dit proefschrift beperkt zich tot de resultaten met betrekking tot de late gevolgen van poliomyelitis.

Alhoewel poliomyelitis, kinderverlamming, in de Westerse wereld bijna in de vergetelheid is geraakt na de invoering van vaccinaties eind jaren 50, zijn er nog veel mensen met restverschijnselen van polio. Deze mensen worden, 30 tot 40 jaar na de oorspronkelijke kinderziekte, geconfronteerd met nieuwe neuromusculaire symptomen. Deze symptomen omvatten een geleidelijk of, minder frequent, abrupt begin van progressieve nieuwe spierzwakte, abnormale spiervermoeidheid, met of zonder algehele vermoeidheid, afname van spiermassa en pijn. Deze klachten worden gevatt onder de term post-polio syndroom (PPS), nadat andere aandoeningen die de klachten kunnen verklaren zijn uitgesloten. Aangezien dit proefschrift zich richt op de invloed van leeftijd en co-morbidity op het functioneren van oudere patiënten die polio hebben doorgemaakt, is voor de meer neutrale term ‘late gevolgen van poliomyelitis’ (LGVP) gekozen.

De nieuwe neuromusculaire symptomen veroorzaken een toename van problemen in het fysieke functioneren, zoals lopen, staan, traplopen en andere aan mobiliteit gerelateerde activiteiten van het dagelijks leven. Tot nu toe hebben studies met betrekking tot het beloop van functioneren bij mensen met een status na polio de invloed van co-morbidity niet onderzocht. Veelal werden proefpersonen boven 65 jaar of met co-morbidity geëxcludeerd. Het is daardoor mogelijk dat de ernst van functionele problemen en de mate van achteruitgang bij oudere poliopathiënten op grond van deze studies onderschat worden. Omdat de invloed van leeftijd en co-morbidity op het beloop van functioneren bij ouder worden de patiënten met LGVP nog steeds onbekend is, is dit proefschrift gericht op het beschrijven van het beloop van functionele status van patiënten in de leeftijd van 45 – 85 jaar met late gevolgen van poliomyelitis over een periode van 5 jaar en het bestuderen van de invloed van leeftijd en co-morbidity hierop.
Hoofdstuk 2 beoordeelde, op basis van systematisch literatuuronderzoek, studies gericht op het beloop van functionele status en spierkracht en prognostische factoren voor verandering hierin bij patiënten met LGVP. De resultaten van dit literatuuronderzoek, waarin publicaties zijn opgenomen die zijn verschenen voor juli 2004, werden gepubliceerd (hoofdstuk 2.1). Een niet-gepubliceerde update van de literatuur die is verschenen tussen juli 2004 tot juli 2009 werd toegevoegd in hoofdstuk 2.2. Het originele literatuuronderzoek beschreef twee studies over het beloop van functionele status en vier studies over het beloop van spierkracht die een voldoende methodologische kwaliteit hadden. Hoofdstuk 2.2 voegde daar nog twee studies van voldoende tot goede kwaliteit aan toe met betrekking tot het beloop van functioneren en het beloop van spierkracht (waaronder de 5-jaars CARPA-beloopstudie (hoofdstuk 6)). Door toevoging van de resultaten van deze recente studies ontstond een beter inzicht in het beloop van functioneren en spierkracht bij patiënten met LGVP. Het was niet mogelijk een kwantitatieve analyse van de achteruitgang in beloop van ervaren functioneren te maken door de heterogeniteit van uitkomstmaten. Desalniettemin rapporteerden alle studies een achteruitgang in ervaren functioneren in de tijd. Loopvaardigheid, gemeten via tijdgescoorde testen, ging langzaam achteruit met 0.2 – 0.7% per jaar. De ernst van de poliorestverschijnselen en co-morbiditeit, zoals gerapporteerd in studies van goede kwaliteit, waren factoren die de achteruitgang in functioneren negatief beïnvloedden, terwijl leeftijd geen invloed op deze achteruitgang leek te hebben. In het algemeen kan gesteld worden dat studies een lange follow-upperiode nodig hebben om de achteruitgang vast te stellen, variërend van 3 tot 5 jaar, afhankelijk van gebruikte uitkomstmaten en studiepopulatie. Verder werd er geconcludeerd dat uniformiteit in de gebruikte uitkomstmaten onontbeerlijk is in prognostische studies bij poliopatiënten om zo studies te kunnen vergelijken en beter inzicht te krijgen in het beloop van functioneren in de tijd en in factoren die dit beloop kunnen beïnvloeden.

In hoofdstuk 3 zijn gegevens van de vragenlijst Western Ontario and MacMasters Universities Osteoarthritis Index (WOMAC) van de gehele CARPA-studie gebruikt met als doel om te onderzoeken of de subschaal fysiek functioneren gebruikt kan worden om fysiek functioneren bij patiënten met LGVP en patiënten met de ziekte van Parkinson te bepalen. Oorspronkelijk is de WOMAC een vragenlijst specifiek gericht op het vaststellen van het niveau van fysiek functioneren bij patiënten met artrose. De gegevens van de eerste meting (op baseline) van de WOMAC fysiek functioneren subschaal (WOMAC-PF) van 288 patiënten met artrose, 200 patiënten met de ziekte van Parkinson en 168 patiënten met LGVP werden geanalyseerd. De unidimensionaliteit, oftewel de mate waarin de onderliggende vragen (items) hetzelfde begrip meten, was bevredigend en de item fit (de mate waarin het gekozen IRT-model de antwoorden op een bepaalde vraag of item verklaart) was in het algemeen goed. Differential item functioning was aanwezig tussen de drie diagnosegroepen in 10 van de 17 WOMAC-PF items. Dit betekent dat de moeilijkheidsgraad van het uitvoeren van bepaalde activiteiten verschillend is voor de drie diagnosegroepen. Zodoende werd geconcludeerd dat de WOMAC-PF een unidimensionele maat is voor het meten van fysiek functioneren bij patiënten met LGVP en de ziekte van Parkinson, naast het bestaande gebruik bij artrose. Het vergelijken van het fysiek functioneren van patiënten
met verschillende diagnoses is echter op basis van WOMAC-PF scores niet mogelijk door het bestaan van differential item functioning in 10 items.

**Hoofdstuk 4, 5 en 6** beschrijven de resultaten van de 5-jaars beloopstudie van 168 patiënten met late gevolgen van poliomyelitis in de leeftijd van 45 – 85 jaar.

De synthese van beschikbare kennis uit studies over patiënten met LGVP wordt belemmerd door de heterogeniteit van gebruikte uitkomstmaten. Het doel van **hoofdstuk 4** was dan ook om één vragenlijst en één looptest te selecteren uit een aantal vragenlijsten en looptests, gebaseerd op vergelijking van reproduceerbaarheid, meetbereik en onderlinge associatie, om deze meetinstrumenten te kunnen aanbevelen als ‘core qualifiers’ van fysiek functioneren in onderzoek en klinische praktijk. De fysiek functioneren subschalen van Short Form-36 (SF36-PF), WOMAC en Nottingham Health Profile werden met elkaar vergeleken en de timed-up-and-go test, tijd nodig om 10 meter op comfortabele en maximale snelheid te lopen en afstand afgelegd in 2 minuten lopen op comfortabele snelheid werden met elkaar vergeleken. De resultaten lieten zien dat de test-hertestbetrouwbaarheid van alle vragenlijsten voldoende tot excellent was. De kleinst detecteerbare veranderingen waren het best voor de SF36-PF, de WOMAC-PF en de 2 minuten looptest. De SF36-PF en de 2 minuten looptest laten de hoogste correlatie zien. Gebaseerd op deze resultaten werden het gebruik van de SF36-PF en de 2 minuten looptest geadviseerd als core qualifiers voor fysiek functioneren om ervaren fysiek functioneren en loopcapaciteit te meten in onderzoek en klinische praktijk.

In **hoofdstuk 5** werd het zelfstandig functioneren en ervaren fysiek functioneren van patiënten met LGVP in drie leeftijdsgroepen (45 – 54 jaar, 55 – 64 jaar en 65 – 85 jaar) vergeleken en werd de invloed van leeftijd en co-morbiditeit op deze uitkomstmaten onderzocht. De oudere patiënten lieten een lager niveau van zelfstandig functioneren zien, terwijl er geen verschil in ervaren fysiek functioneren gevonden werd. Co-morbiditeit nam toe met de leeftijd. Leeftijd was onafhankelijk geassocieerd met zelfstandig functioneren, maar niet met ervaren fysiek functioneren. Dit zou een leeftijdsgeregelateerde verschuiving in de perceptie van fysieke beperkingen kunnen onderschrijven. De co-morbiditeitscategorieën ‘cardiaal’, ‘vasculair’, ‘endocrien, metabool’ en ‘spier, bot, huid’ bleken geassocieerd te zijn met zelfstandig functioneren en ervaren fysiek functioneren. Geconcludeerd werd dat co-morbiditeit zelfstandig functioneren en ervaren fysiek functioneren negatief beïnvloedt. Om de invloed van co-morbiditeit op het beloop van functioneren in deze populatie nader te onderzoeken werden prospectieve studies aanbevolen met ongeselecteerde studiepopulaties, zonder exclusie van ouderen of patiënten met co-morbiditeit, en met een controlegroep bestaande uit leeftijdgenoten die geen polio hebben doorgemaakt.

In **hoofdstuk 6** worden de resultaten beschreven van de 5-jaars beloopstudie met aandacht voor het beloop van functioneren en spierkracht en de invloed van leeftijd en co-morbiditeit op dit beloop. Zelfstandigheid in functioneren, loopvaardigheid gemeten met looptests en ervaren fysiek functioneren gingen iets achteruit. Deze mate van achteruitgang was in overeenstemming met resultaten van eerdere studies betreffende poliopatiënten. De afname in spierkracht van de bovenbeenspieren (quadriceps), gemeten met een vaste dynamometer, was iets groter. Helaas moet
uitgegaan worden van selectieve uitval bij de 5-jaarsmeting omdat we tijdelijk geen gebruik konden maken van de dynamometer. Hierbij is de krachtsmeting bij een beter functionerende subgroep uitgevoerd. Uitgaande van de achteruitgang in spierkracht zoals gemeten na 3 jaar follow-up zou de 5-jaarsmeting waarschijnlijk de werkelijke achteruitgang in spierkracht onderschatten. De achteruitgang zoals gemeten na 3 jaar beloop geeft waarschijnlijk een betere schatting van de werkelijke achteruitgang bij ouder wordende polio-patiënten. Co-morbiditeit nam toe over de jaren en meer co-morbiditeit was geassocieerd met een lager niveau van zelfstandig functioneren en een snellere achteruitgang in zelfstandig functioneren. Voor zelfstandig functioneren en ervaren fysiek functioneren werden prognostische modellen gemaakt. Spierkracht in de benen (somscore van verschillende beenspiergroepen) en co-morbiditeit totaalscore bleken prognostische factoren voor zelfstandig functioneren, terwijl leeftijd dit niet was. Voor ervaren fysiek functioneren bleken geslacht, leeftijd, somscore spierkracht benen en co-morbiditeit totaalscore geen prognostische betekenis te hebben. Leeftijd bleek niet van invloed op het beloop van functioneren in 5 jaar. Toekomstige beloopstudies zullen patiënten onder een langere periode moeten volgen waarbij tevens een controlegroep bestudeerd wordt van leeftijdgenoten die geen polio hebben doorgemaakt, om zo de mate van achteruitgang in personen met en zonder status na polio te kunnen vergelijken. Follow-upstudies met een lang beloop en een gevoelige uitkomstmaat voor het meten van co-morbiditeit rond spieren en botten zullen moeten uitwijzen of de invloed van co-morbiditeit in het algemeen en invloed van co-morbiditeit rond spieren en botten op het beloop van functioneren zal toenemen in de tijd.

Ten slotte worden in hoofdstuk 7 de belangrijkste bevindingen, de implicaties voor de klinische praktijk en de methodologie bediscussieerd en worden aanbevelingen gedaan voor toekomstig onderzoek. Vier fictieve patiënten, die verschillen wat betreft leeftijd, geslacht, paresis in de benen en co-morbiditeit, worden hierin besproken om inzicht te geven in het verschil van achteruitgang van zelfstandigheid in functioneren. Het belang van het overwegen van leeftijd, co-morbiditeit en mate van paresis bij het stellen van een functionele prognose werd op deze manier naar voren gebracht.

De longitudinale data lieten zien dat lopen, gemeten via looptesten, langzaam achteruit ging, terwijl spierkracht sneller achteruit ging. Twee studies (inclusief de CARPA-studie) rapporteerden dat de ernst van restverschijnselen een prognostische factor voor functioneren was. Het verschil in achteruitgang tussen looptesten en spierkracht bevestigt het concept van overbelasting van spieren in het dagelijkse leven. Om gedurende de jaren te kunnen blijven functioneren zijn patiënten genoodzaakt om hun zwakker wordende spieren relatief meer te belasten.

Binnen de revalidatiegeneeskunde bestaan er twee benaderingen die complementair kunnen zijn: (1) behoud of verbetering van spiercapaciteit en (2) reductie van fysieke eisen in het dagelijks leven. Met name bij patiënten met een goede functionele prognose en spierkracht zou behoud of verbetering van spiercapaciteit overwogen moeten worden met adequate therapie, aangezien deze patiënten nog over voldoende spiermassa beschikken welke trainbaar is. Patiënten met een slechte functionele prognose zouden meer profijt hebben van een multidisciplinair behandelprogramma gericht op reductie van fysieke eisen en het belang van verandering in leefstijl, omdat
Deze patiënten minder mogelijkheden hebben om hun overbelaste en beperkte spierkracht te trainen.

Een belangrijke methodologische beperking van deze studie is het feit dat er mogelijk een selectiebias bij inclusie en selectieve uitval gedurende de studie is opgetreden. Hierdoor kan een onderschatting van de toename van beperkingen en achteruitgang in spierkracht niet uitgesloten worden, met name bij de oudere patiënten.

In toekomstig onderzoek zou dit cohort langer vervolgd moeten worden om inzicht te krijgen in het beloop van functioneren op de lange termijn en de invloed van prognostische factoren. De uitdaging zal liggen in het zo compleet mogelijk verzamelen van alle data, met name de spierkracht. Leeftijd-gematchte controles moeten worden toegevoegd om te kunnen differentiëren in achteruitgang als gevolg van LGVP en achteruitgang op basis van veroudering. Een gespecificeerde classificatie van co-morbiditeit met betrekking tot spieren en botten zou moeten worden toegevoegd. Op basis van nieuwe inzichten zouden vragenlijsten over vermoeidheid, het meten van dagelijkse activiteiten en bloedafname met als doel het bepalen van de waarde van cytokines in het bloed kunnen worden toegevoegd.

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About the author
Janneke Stolwijk-Swüste was born on October 14th, 1973 in Capelle aan den IJssel, the Netherlands. In 1992 she graduated from secondary school at Murmellius Gymnasium in Alkmaar. Between 1992 and 2000 she studied Movement Sciences at the faculty of Health Sciences at Maastricht University. Between 1995 and 2000 she studied Medicine at Maastricht University. After she received her medical degree, she worked as a resident in internal medicine in a hospital in Apeldoorn for one year. Between October 2001 and June 2007 she worked as a Medical Trainee for Clinical Research (AGIKO) at the department of rehabilitation medicine at the VU University Medical Center and at Heliomare rehabilitation center in Wijk aan Zee. During this time the research for this thesis was carried out, while being trained to be a physiatrist. From July 2007 she works as a physiatrist at the clinical spinal cord injury ward of the Rehabilitation Center of Amsterdam (RCA).

Janneke is married to Frederik Stolwijk and they have a daughter, Marieke (2008).