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FACULTEIT GENEESKUNDE EN LEVENSWETENSCHAPPEN
master in de revalidatiewetenschappen en de kinesitherapie

Masterproef

Insights in perceived manual ability performance in MS: a cross-sectional study

Promotor :
Prof. dr. Peter FEYS

Copromotor :
Mevrouw Ilse LAMERS

Silke Kelchtermans
Proefschrift ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie

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Silke Kelchtermans

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Research context

Seventy-five percent of the persons with MS (PwMS) experience upper limb dysfunction (unilateral or bilateral) during the course of the disease, affecting the performance of many activities of daily living (ADL) which further contributes to a decrease in participation in social/lifestyle activities and quality of life (QoL) (1-3). Despite the clinical relevance of upper limb function, research aiming to improve arm function in PwMS is limited while most available intervention studies in MS aim to improve the lower limb function (4;5). In the available intervention studies, different outcome measures on 'body function & structures' and 'activity' level of the International Classification of Functioning, Disability and Health (ICF) are used to demonstrate the effectiveness of their intervention. A systematic review of Lamers et al. (2014) offers an overview of all the outcome measures used to assess upper limb function in MS and, if investigated, their psychometric properties (4). It is clear that there are many different objective upper limb outcome measures on 'body function & structures' level and 'capacity scales' on activity level of the ICF, but recently also more subjective 'perceived performance scales' are used to evaluate unilateral and bilateral upper limb function (4;6-11). These perceived performance scales provide more information about the difficulties PwMS experience when performing upper limb ADL tasks. Both, the objective capacity scales and subjective perceived performance scales are important to get a complete picture of the upper limb function in PwMS since they both measure a different construct and have a different point of view on the multidimensional character of the upper limb function (4;12-14). So far, little is known about these perceived performance scales and further research is necessary. This cross-sectional study focuses on these perceived performance scales, more specific the Manual Ability Measure-36 (MAM-36), to better understand perceived manual ability while performing ADL tasks in PwMS.

The study presented in this master thesis is embedded within the research performed at REVAL, rehabilitation research center of Hasselt University. Research performed at REVAL focuses on investigating clinical and physiologic benefits of all different types of exercise therapy, as well as related immunological and neurophysiologic mechanisms. To realize this, a MS network Limburg was established in 2007, which facilitates the collaboration between REVAL, BIOMED and the Rehabilitation and MS Center Overpelt.

In recent years, Prof. Dr. Peter Feys (promoter of this master thesis) has developed a research line on assessment and rehabilitation of the upper limbs. Within this research line, different projects (INTERREG III & INTERREG IV entitled Rehabilitation Robotics II) were initiated. In 2010, Ilse Lamers (daily supervisor of this master thesis) started her PhD project entitled: 'Understanding upper limb function in multiple sclerosis: assessment and relationships between the levels of the International Classification of Functioning'. This PhD project aims to describe and investigate which clinical tests are able to predict upper limb capacity and performance in MS patients. Performance on unilateral and bilateral functional tasks are measured subjectively and objectively to identify the determinants and their relationship with the presence and severity of different types of impairments. The study presented in this master thesis fits within this PhD project and belongs therefore to the research field of neurological rehabilitation.

In my first year of my master in Rehabilitation Sciences and Physiotherapy, I worked together with Dra. Ilse Lamers on a systematic review about upper limb outcome measures and their psychometric properties, which was published in 'Archives of Physical Rehabilitation and Medicine' (4). During my last master year, we focused on the perceived upper limb performance of PwMS and tried to understand the impact of upper limb dysfunction on the ability to perform ADL.
The recruitment of de PwMS and the data-acquisition was done by student Nick Maesen and Dra. Ilse Lamers in collaboration with the Don Carlo Gnocchi Foundation in Italy from April 2012 till February 2013. During this master year, I helped other students with data acquisition and performed statistical analysis on the data collected by Nick Maesen and Dra. Ilse Lamers. Help and advice during this process was given by Prof. Dr Peter Feys and Dra. Ilse Lamers. The writing of this master thesis was conducted independently with feedback of Prof. Dr Peter Feys and Dra. Ilse Lamers.

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“Insights in perceived manual ability performance in MS: a cross-sectional study”

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Insights in perceived manual ability performance in MS: a cross-sectional study

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Abstract

Background: Little is known about perceived manual ability while performing ADL in persons with multiple sclerosis (PwMS).

Objectives: This study aimed to get more insight in PwMS with different levels of manual ability measured with the Manual ability Measure (MAM-36).

Methods: Hundred and five PwMS were included. Clinical scales on body function & structures- and activity level were conducted for both hands and perceived performance of manual ability in ADL was measured by the MAM-36. Descriptive statistics and Kruskall Wallis tests were performed to compare subgroups of manual ability levels.

Results: An almost normal score on clinical scales does not automatically mean that the PwMS experiences no limitations in the perception of their upper limb function and the performance of ADL tasks. Unilateral ADL tasks and tasks which require less accuracy are the easiest and bilateral tasks or tasks requiring fine motor control in combination with handling of sharp materials are the most difficult ADL tasks. Tasks critical for the personal hygiene and everyday care are the most important ADL tasks. A median score of 0.28pegs/s on the NHPT and 20kg on the Jamar is necessary in order to perform the different ADL tasks without any difficulties.

Conclusion: The MAM-36 is an important outcome measure to get a complete and accurate picture of the upper limb function in PwMS.

Key words: Multiple Sclerosis, Upper limb, Manual ability Measure (MAM-36), Activities of daily living (ADL)

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Introduction

Multiple Sclerosis (MS) is a chronic progressive inflammatory auto-immune disease of the central nervous system characterized by demyelination and axon degeneration. It is one of the most common neurological disorders among young and middle-aged adults (between 20 and 40 years old) in their most productive years of life (2). Depending on lesion distribution and degeneration, MS clinically presents with a variety of symptoms. The most common symptoms are spasticity, muscle weakness, sensory and visual deficits, loss of coordination, postural imbalance, fatigue, incontinence and affective and cognitive deficits (15).

Some of these symptoms may cause common unilateral or bilateral upper limb dysfunction in PwMS. Seventy-five percent of 219 PwMS (EDSS range 0-9.5) shows upper limb disability measured by the Nine Hole Peg Test (NHPT), an objective manual dexterity outcome measure (1). This high number of upper limb dysfunction has been confirmed by two other studies. Seventy-one percent of 205 PwMS (mean EDSS 3.5) report disabilities with hand and arm use and 67% specifically with fine hand use measured with a qualifier scale (0; no impairment to 4; complete impairment) (16). Seventy-five percent of 105 PwMS (mean EDSS 6,5) shows bilateral impaired manual dexterity evaluated with the NHPT and this bilateral involvement is even present in PwMS with an EDSS score below 3.5 (17). This upper limb dysfunction may present in an early stage of the disease: about 60% of the PwMS report to have impairment or restriction related to upper limb function in the first year of the disease with an increase to 70% after seven years, evaluated by a self-reported six-grade ordinal scale (18). It has been shown that manual dexterity (measured by the NHPT), is an important predictor of overall activity and participation within the community as assessed by the Katz activities of daily living (ADL) index and Frenchay activity index (19). Upper limb dysfunction not only causes limitations in ADL and participation, but also contributes to a decreased functional independence and self-related quality of life (2;3;20). For this reason, paying attention to the progression of upper limb dysfunction in PwMS and considering management strategies is very important, yet in the past only limited research was done toward understanding and improving upper limb function in PwMS (4;5).

Different outcome measures on ‘body function & structures’ and ‘activity’ level of the International Classification of Functioning, Disability and Health (ICF) are used to assess the impact of rehabilitation programs on the complex and multidimensional character of the upper limb. The outcome measures on ‘body function & structures level’ assess impairments as spasticity (e.g. modified asworth scale), muscle weakness (e.g. motricity index and jamar hand grip strength), loss of sensory (e.g semmes-weinstein monofilaments),… The ‘activity’ level of the ICF is divided into ‘capacity measures’ and ‘performance scales’. The capacity measures are objective measures e.g. the Nine Hole Peg test (NHPT) for manual dexterity, Action Research Arm test (ARAT) for handling different types of objects,... Capacity scales evaluate usually unilateral, only in few cases bilaterally, upper limb function making these scales of limited value for two reasons. Firstly, the results are strongly influenced by whether the dominant or non-dominant hand is affected and secondly persons uses their both hands predominantly together to perform tasks in their daily life (21).

Recently more attention is being paid towards performance scales and these can be either subjective (perceived performance) or objective (actual performance) which evaluates unilateral or bilateral upper limb function while performing ADL (4). These subjective perceived performance scales give more information about the difficulties PwMS experience when performing upper limb ADL tasks before and after a rehabilitation program. Lamers et al. (2014) indicates that the capacity measures and the perceived performance measures assess different aspects of upper limb function because of the variable correlation coefficients, suggesting the need to use both types of outcome measure to get an accurate and complete picture of the multidimensional character of the upper limb function in PwMS (4;12;13).

Several studies with perceived performance scales have been published in stroke and recently, also a limited number of studies use these scales in MS. The Motor Activity Log (MAL) (10;11;22), the ABILHAND (6;23;24), the Disabilities of the Arm, Shoulder and Hand Scale (DASH) (7) and the Manual Ability Measure-36 (MAM-36) (8;9) were used in PwMS. The MAL assesses the 'amount' and 'quality' of upper limb use during ADL performance, while the ABILHAND, the DASH and the MAM-36 assess the person's perceived ease/difficulty when performing ADL regardless of which upper limb is used. The ABILHAND assesses only bilateral tasks including many rather complex tasks such as peeling potatoes with a knife and shelling hazelnuts while the other performance scales measure both, unilateral and bilateral tasks. A conversion table to obtain a Rash-derived score is available for the ABILHAND and the MAM-36 while the MAL and the DASH used summed or calculated scores (9;25-27). The ABILHAND and MAM-36 appears to be reliable and valid in MS, in contrast to low psychometric properties that are found for the DASH and the lack of data for de MAL. Responsiveness to treatment has not yet been investigated for any of the perceived performance measures in MS (4). Recently there is a growing interest towards perceived upper limb function in MS, but until today there are few studies, mostly with a small population, using these performance scales.

In conclusion, detailed information is missing about the possibilities and limitations PwMS experience when performing ADL tasks and threshold values on capacity scales of the upper limb needed to carry out these ADL tasks. To gain more insight in this, perceived performance scales are important. However, for treatment planning, it is first important to know which upper limb ADL tasks are difficult for a PwMS. This is the starting point to determine realistic rehabilitation goals and a logical structure for a patient-oriented or client centered rehabilitation program but also the way to evaluate the effect of multiple intervention studies on the upper limb function afterwards.
For this reason, the first aim of this cross-sectional study is to understand how PwMS with different levels of perceived manual ability score on other objective clinical outcome measures assessing upper limb function. Secondly, we investigated a hierarchy in perceived difficulty and clinical importance of upper limb ADL tasks of the MAM for the PwMS. Finally, we gave insights in threshold values of upper limb capacity scales for different levels of manual ability to perform variable ADL tasks of the MAM-3.

Methods

Participants

A convenience sample of PwMS was recruited from the Rehabilitation and MS Center Overpelt (Belgium), the Mick Rehabilitation Center Brasschaat (Belgium) and LaRICE Don Gnocchi Foundation in Milan (Italy). Participants with a clinical definite diagnoses of MS (McDonald criteria (28)) and with a minimal ability to move the upper limb (able to touch their chin with one hand) were included. They were excluded if they had (a) a relapse or relapse-related treatment one month prior to the study, (b) a cognitive dysfunction hampering the execution of tests and (c) another orthopedic or rheumatoid impairment interfering with upper limb function. All subjects who signed the informed consent, after receiving information regarding the study, were included. The study was approved by the Ethics Committee of Hasselt University and local committees of the involved rehabilitation centers.

Study design and Procedure

In this cross-sectional study, descriptive outcome measures and outcome measures on 'body function & structures' and 'activity' level of the ICF were conducted during two separate test sessions, each lasting 90 minutes. The two tests sessions were performed at the same time of day, since the time of the day might have an effect on performance, and with a day in between to avoid excessive fatigue due to testing itself. During the test administration, a distinction was made between the dominant and non-dominant arm but both hands were tested in a random order.

Outcome measures

Descriptive measures

The Expanded Disability Scale Score (EDSS), disease duration and type of MS were determined by neurologists. The cognitive level was determined by the Symbol Digit Modalities Test (SDMT) (29). The Hauser Ambulation Index (AI) (30) was conducted to describe ambulation, scores ranges from 0 (asymptomatic) to 9 (wheelchair bounded). To determine the hand dominance they used the Edinburgh Handedness Inventory (31).

'Body function & structures' level

Overall upper limb muscle strength was assessed with the Motricity Index (MI). The upper limb section of the MI consists of three subtests: pinch grip, elbow flexion and shoulder abduction. Each movement is rated with a 6-point ordinal scale with scores between 0-33. A maximum score of 100 indicates a normal isometric muscle force in the upper limb (32). The JAMAR hand held dynamometer was used to measure the maximum isometric hand grip strength (Kg).The person was seated with the arm next to the body with the elbow in 90° flexion. After positioning, the person was asked to squeeze as hard as possible for three to five seconds. The average of three repeated trials was calculated and used as outcome of the hand grip strength (33). Active Range Of Motion (AROM) of wrist extension (°) was evaluated with a goniometer. The hands were placed with the palmar side on the table and the goniometer was positioned on the dorsal side of metacarpal three and the middle of de forearm. The median score (°) of 3 trials was calculated and used in this study. The maximums score is 85°-90°

(34). The Semmes-Weinstein monofilaments was used to test tactile sensitivity in the fingertips. In this study, five different monofilament diameters were used (2.83= normal sensation, 3.61= diminished light touch, 4.31= diminished protective sensation, 4.56= loss of protective sensation and 6.65= untestable). The monofilaments were randomly presented for approximately 1.5 seconds to the tip of the thumb, all filaments were tested three times. The filament with the smallest diameter, which was felt 3/3, was recorded as the score. For statistical analysis, we transformed scores (6.65, 4.56, 4.31, 3.61, 2.83) into categories (5,4,3,2,1) (35;36). Muscle tone (spasticity) in the shoulder adductors, elbow flexors and wrist flexors were evaluated with the Modified Ashworth Scale (MAS). This 5-point ordinal scale (0-4) is used to grade spasticity in the upper limb, a higher score indicates a higher amount of tone felt as a limb was moved passively through its arc of motion (32;37). Intention tremor and dysmetria during finger to nose test and also postural tremor were measured with the Fahn's Tremor Rating Scale (FTRS). It is a 5-point ordinal scale which grades tremor from 0-4, a higher score indicates a more marked tremor with a higher amplitude (38).

'Activity' level

Two capacity measures (Nine Hole Peg Test and Action Research Arm Test) and one perceived performance measure (Manual ability Measure-36) were included on activity level.

The Nine Hole Peg Test (NHPT) was used to measure fine manual dexterity. For each hand, the average time was measured based on two trials needed to place the nine pegs one by one using only one hand into the nine holes followed by removal of all the pegs. For statistical analysis, manual dexterity speed was calculated as pegs per second (pegs/s), a higher score indicates a better performance (2;32). The ability to handle objects differing in shapes, size and weight was evaluated with the Action Research Arm Test (ARAT). The test consists of 19 items organized in four subscales: grasp, grip, pinch and gross movements. Each item is scored using a 4-point ordinal scale and the time needed to complete the handling was noted. The maximum score is 57 with higher values indicating better performance (39;40). The Manual Ability Measure-36 (MAM-36) was used to assess perceived ease or difficulty that PwMS may experience when performing 36 common ADL tasks such as washing hands. Each task was rated for difficulty and clinical importance regardless of which hand they used and without the help of custom-ordered adaptive equipment. The difficulty of the task is scored from 0-4 (0= never do, 1= cannot do, 2= very hard, 3= little hard, 4= easy) with a higher score indicates a more easy task. The clinical importance of the task is also scored on a 0-4 ordinal scale, a higher score indicates greater importance of a task. The sum score of each subject was subsequently Rasch-calibrated and converted into a 'manual ability measure' from 0-100 (0= lowest and 100= perfect manual ability) (9).

Statistical analyses

For all statistical analyses, non-parametric statistics were applied, as most of the data was not normally distributed (Shapiro-Wilk Test). Differences between the dominant and non-dominant hand in upper limb capacity were investigated using the Wilcoxon Signed Rank test in the total sample.

For the first research question, descriptive statistics were calculated to provide scores on the clinical outcome measures assessing upper limb function for both the dominant and the non-dominant hand for the total sample and four manual ability subgroups, based on their score on the MAM-36 divided as

mildly (quartile 75-100), moderately (quartile 50-75), markedly (quartile 25-50) and severely impaired manual ability (quartile 0-25). A distinction between different levels of perceived manual ability provides much more information and determines whether the severity of limitations in ADL affects scores on other clinical outcome measures of the upper limb. A Kruskall Wallis test was applied to investigate the differences between the four subgroups with variable level of impaired manual ability ($p<0.05$) on the scores of the clinical outcome measures assessing upper limb function. If needed a Mann-Whitney Post Hoc test was performed with Bonferroni correction ($p<0.017$).
To investigate a hierarchy in the perceived difficulty in performing the variable ADL tasks of the MAM-36, percentages of the different scores for each ADL task were calculated with frequency analyses and plotted in a histogram. For the clinical importance of the various ADL tasks of the MAM-36, the same process was repeated not only for the total sample but also separately for the PwMS with mildly and severely impaired manual ability.
Finally, we gained insight into threshold values of upper limb capacity scales for different levels of manual ability to perform variable ADL tasks of the MAM-36. Descriptive statistics were calculated to provide scores on the Nine Hole Peg test and the JAMAR hand strength of the dominant and the non-dominant hand for three subgroups based on the individual score per ADL task of the MAM-36 in score 1+2 (can't do + very hard), score 3 (little hard) and score 4 (easy) to perform the ADL task. A Kruskall Wallis test was applied to investigate the differences between the three subgroups ($p<0.05$) on the scores on these two outcome measures of the upper limb function. If needed a Mann-Whitney Post Hoc test was performed with Bonferroni correction ($p<0.017$).
All analyses were conducted with IBM SPSS Statistics 22 with the significance level set at $p<0.05$.

Results

Participants

One hundred and ten PwMS were screened in the three different rehabilitation centers of whom 105 (62 females, mean age 53.7 (SD 11.1) years) met the required inclusion and exclusion criteria and participated in this study. Table 1 provides an overview of the descriptive characteristics of the total study sample and the four manual ability subgroups divided based on their score on the MAM-36 in mildly, moderately, markedly and severely impaired.

In the total sample, the majority (55,2%) of the included PwMS were diagnosed with secondary progressive MS. The mean disease duration and median EDSS score was 17.9 years (SD 11.2) and 6.5 (IQR 5-7.5) respectively. Twenty-five was the median score for the cognitive level. The median score for the Hauser Ambulation Index (AI) was five, which means they use bilateral support (canes, crutches or walker) but 27 (25.7%) PwMS were wheelchair bound. At the time of testing, 88 PwMS (83,8%) were right handed according the Edinburgh Handedness Inventory (EHI) and 8 PwMS (7.6%) had changed their hand dominance during the course of the disease.
In general, better descriptive characteristics were found for the PwMS with mildly and moderately impaired manual ability in comparison of those PwMS with markedly and severely impaired manual ability.

Significant differences between the dominant and the non-dominant hand were found for five outcome measures on 'body function & structures' level the MI (p=0.021), the FTRS postural tremor (p=0.016) and the JAMAR hand grip strength (p=0.000) and on 'activity' level the NHPT (p= 0.016) and ARAT subitem gross movement (p= 0.011). Based on these findings, further results were presented for the dominant and the non-dominant hand separately.

Table 1. Descriptive characteristics of the study sample.

		Manual ability subgroups based on the MAM-36			
	Total sample	Mildly impaired (quartile 75-100)	Moderately impaired (quartile 50-75)	Markedly impaired (quartile 25-50)	Severely impaired (quartile 0-25)
	n=105	n=26	n=26	n=27	n=26
Gender (m/f)	43/62	11/15	12/14	10/17	10/16
Age (years)	53.7 ± 11.1	51.5 ± 10.3	52.2 ± 11.8	52.8 ± 11.7	58.1 ± 9.5
Disease duration (years)	17.9 ± 11.2	12.4 ± 10.6	17.2 ± 10.8	18.4 ± 9.2	23.7 ± 11.6
Type of MS (RR/SP/PP)	34/58/13	14/8/4	7/17/2	9/16/2	4/17/5
EDSS	6.5 (5/7.5)	5.3 (3/6.5)	6 (4.4/6.6)	6.5 (5.5/7)	7.5 (6.4/8)
Cognition (SDMT)	25 (20/34)	28 (23/39.5)	28 (22/35.3)	22 (19/31)	20 (15.5/30)
Ambulation (AI: 0-9)	5 (3/8)	2.5 (1.8/6)	4 (2/5)	5 (4/8)	8 (6/9)
Hand dominance (EHI) (R/L/A)	88/9/8	23/2/1	23/2/1	23/1/3	19/4/3

Data are represented as number, median (1st/3rd quartile) and mean ± standard deviation; RR, relapsing remitting; SP, secondary progressive; PP, primary progressive; EDSS, Expanded Disability Status Scale; SDMT, Symbol Digit Modalities Test; AI, Hauser Ambulation Index; EHI, Edinburgh Handedness Inventory; R, right; L, left; A, ambidextrous

Scores on objective clinical outcome measures for PwMS with different levels of perceived manual ability

Table 2 presents the median, the interquartile range and p-values of the clinical outcome measures for the dominant and the non-dominant hand for the total sample and the four manual ability subgroups. Spasticity and tremor were hardly present in the total population (data not shown).

In the total sample, generally high scores were found on the capacity tests of the activity level. There were ceiling effects for the ARAT; the median scores of the ARAT achieved maximum scores on the grasp and gross subitems and almost maximum scores on the grip and pinch subitems of the ARAT. Lower scores compared to normal/maximum scores (34;41), with even weak scores for tactile sensitivity, were found on the outcome measures on body function & structures level.
In the groups with different levels of manual ability, these high scores and ceiling effects of the capacity tests were present in the PwMS with mildly and moderately impaired manual ability but drop very hard in the PwMS with markedly or severely impaired manual ability.

In general, relatively normal scores were found in PwMS with mildly impaired manual ability on the different capacity tests for upper limb function while they still reported upper limb disability affecting their ADL performance with the MAM-36. In addition, weak scores were showed in PwMS with severely impaired manual ability on the different capacity tests for upper limb function and yet still 50/100 on the perceived MAM-36.

The scores on all the different clinical outcome measures of the ICF were approximately the same for the PwMS with mildly and moderately impaired manual ability and were significantly better than those

scores for PwMS with markedly or severely impaired manual ability, except for tactile sensitivity. Tactile sensitivity seemed to be a problem for almost all the PwMS, independent of the degree of upper limb dysfunction.
More significant limitations were found only in the PwMS with severely impaired manual ability. These severely impaired PwMS had significant problems for the non-dominant hand with the Motricity Index, hand grip strength and Active ROM on the level of 'body function & structures' and on 'activity' level with the NHPT and ARAT (also the subitems) and for the dominant hand with the gross item of the ARAT. In addition, significantly decreased hand grip strength (JAMAR hand grip strength and grip item of the ARAT) was shown for the dominant hand for the PwMS with severely and markedly impaired manual ability which was no longer be significantly present in the PwMS with moderately impaired manual ability.

The scores of the dominant hand on the different clinical outcome measures assessing upper limb function were at least better than those of the non-dominant hand, except for the active range of motion wrist extension and some subitems of the ARAT. Yet there was clearly a bilateral upper limb involvement in all the PwMS.

Table 2: Scores on objective clinical outcome measures for PwMS with different levels of perceived manual ability

			Manual ability subgroups based on the MAM-36				p-value[a]	Post hoc[b]		
		Total sample	Mildly impaired (1)	Moderately impaired (2)	Markedly impaired (3)	Severely impaired (4)		1vs2	2vs3	3vs4
		n=105	n=26	n=26	n=27	n=26				
MAM-36		60.64 (52.28/73.35)	78.34 (75.43/92.33)	67.08 (64.22/69.69)	57.95 (55.04/60.11)	46.72 (43.60/49.13)				
Body function and structures level										
Motricity Index	D	91 (76/100)	100 (98/100)	100 (84.75/100)	83 (76/92)	69 (60/81)	<0.001	ns	0.005*	0.007*
(0-100)	ND	83 (70/100)	100 (84.5/100)	100 (77.5/100)	77 (72/92)	67.5 (49.25/80.75)	<0.001	ns	ns	0.005*
JAMAR hand grip strength	D	21.4 (14.73/32.95)	28.47 (20.53/34.59)	26.73 (19.03/38.13)	18 (13.33/23)	13.67 (4.5/24.18)	<0.001	ns	0.004*	ns
(kg)	ND	19 (10.67/29.28)	25.93 (17.62-31.61)	26.1 (15.13/32.81)	15.8 (10.53/27.33)	8.02 (1.52/19.35)	<0.001	ns	ns	0.012*
Active Range of Motion	D	58.5 (45/70)	60 (51.5/72.75)	65 (50/76)	60 (48/70)	45 (30.5/62.5)	0.017	ns	ns	ns
wrist extension (°)	ND	60 (48.5/70)	65.5 (56.5/74)	60 (50.5/75)	68 (57/70)	43.5 (10/61.25)	0.001	ns	ns	0.001*
Tactile sensitivity Thumb	D	3 (2/3)	2 (1.75/3)	3 (2/3)	3 (2/3)	3 (2/4)	0.239			
(1-5)	ND	2 (1/3)	2 (1/2)	3 (1/3)	2 (2/3)	3 (1.75/4.25)	0.067			
Activity level: Capacity measures										
Nine Hole Peg Test	D	0.28 (0.17/0.36)	0.36 (0.31/0.42)	0.32 (0.27/0.39)	0.20 (0.16/0.28)	0.14 (0.06/0.2)	<0.001	ns	0.000*	0.013*
(pegs/sec)	ND	0.27 (0.17/0.32)	0.31 (0.27/0.36)	0.28 (0.24/0.39)	0.20 (0.17/0.32)	0.10 (0.03/0.21)	<0.001	ns	ns	0.003*
Action Research Arm Test	D	54 (44.5/57)	57 (55/57)	56 (53.5/57)	49 (44/55)	41 (32.75/51.25)	<0.001	ns	0.000*	0.012*
(0-57)	ND	54 (43.5/57)	56 (54.75/57)	55 (49/57)	51 (44/56)	35.5 (4.75/45.25)	<0.001	ns	ns	0.001*
1) Grasp (0-18)	D	18 (15/18)	18 (18/18)	18 (17.75/18)	17 (13/18)	13 (9.75/17)	<0.001	ns	0.007*	0.014*
	ND	18 (14/18)	18 (18/18)	18 (17/18)	18 (14/18)	11.5 (0/17.25)	<0.001	ns	ns	0.000*
2) Grip (0-12)	D	11 (9/12)	12 (11/12)	12 (10.75/12)	11 (8/11)	8.5 (7.75/11)	<0.001	ns	0.002*	ns
	ND	11 (9/12)	12 (11/12)	12 (10/12)	11 (9/12)	6 (0/9.25)	<0.001	ns	ns	0.000*
3) Pinch (0-18)	D	17 (12/18)	18 (17.75/18)	18 (16.75/18)	14 (12/18	11.5 (9.5/16)	<0.001	ns	0.003*	0.008*
	ND	16 (12/18)	18 (16/18)	17.5 (15.75/18)	15 (13/17)	8.5 (0/12.75)	<0.001	ns	ns	0.000*
4) Gross (0-9)	D	9 (8/9)	9 (9/9)	9 (9/9)	9 (8/9)	7.5 (6/9)	<0.001	ns	0.316	0.006*
	ND	9 (8/9)	9 (9/9)	9 (9/9)	9 (8/9)	7 (3.75/9)	<0.001	ns	ns	0.001*

Data are represented as median (1st/3rd quartile); ND, non-dominant hand; D, dominant hand; grey, non-dominant hand; w hite, dominant hand; SWMT, Semmes-Weinstein Monofilament Test; aKruskall Wallis Test; bPost hoc Mann-Whitney test; *, significant p<0.017 (Bonferroni correction)

Hierarchy in the perceived difficulty and clinical importance of the different ADL tasks of the MAM-36

A hierarchical overview of the percentage of perceived difficulty of the various ADL tasks of the MAM-36 with the easiest ADL task on the bottom, is shown in figure 1. In grey if the person perceived the ADL task as 'easy' and further progression to red if the person assessed the task as 'almost never do'. There were both unilateral and bilateral ADL tasks and tasks that were performed sometimes unilaterally and sometimes bilaterally.

In the hierarchy of perceived difficulty, unilateral and bilateral ADL tasks were partially mixed with each other, however in general the most easy ADL tasks were the unilateral tasks such as using a remote control, eating a sandwich, brushing teeth, turning a door knob,... Also the ADL tasks which require less fine motor control or accuracy such as washing hands, opening a previously opened jar,… were the easiest; more than 50-60% of the PwMS perceived these ADL tasks as 'easy'.

The most difficult ADL-tasks were the bilateral tasks or those tasks requiring fine motor control in combination with the handling of sharp materials like cutting nails, peeling fruits, cutting meat,… Using a hammer was the most difficult ADL task for PwMS and this task but also shuffling cards, folding clothes, carrying a shopping bag, cutting nails and fastening clothes snap were activities that the PwMS rarely or never perform.

This total figure of perceived ease or difficulty formed a kind of stair where multiple ADL tasks can be clustered into one step.

An overview of the percentage of perceived clinical importance of the various ADL tasks of the MAM-36 with the easiest ADL task at the bottom is shown in figure 2. In grey if the person perceived the ADL task 'really important' and further progression to red if the person assessed the task as 'not applicable'.

The hierarchy of perceived difficulty of the various ADL tasks appeared not to be the same as the hierarchy for perceived clinical importance of the ADL tasks, yet there is a partial overlap.

The unilateral ADL tasks, which are critical for personal hygiene and everyday care such as brushing teeth, using a spoon, eating a sandwich, drinking a glass of water,… were considered to be the most important in more than 50% of the PwMS. Tasks that do not have to be performed in terms of everyday care such as shuffling cards, wringing towels, folding clothes, handling CD/DVD,.. were rated in less than 50% as important and often these were not even applicable to them. In addition, the most difficult ADL tasks, which were rarely performed, were often regarded as unimportant, a lot of these difficult ADL tasks seemed 'not applicable' to different PwMS such as using a hammer, shuffling cards, folding clothes, carrying a shopping bag,…

An overview of the percentage of perceived clinical importance of the various ADL tasks of the MAM-36, separated according to the level of impaired manual ability is illustrated in appendix 1 and 2.

The score 'real important', was given in more than 60% on all the ADL tasks by the PwMS with mildly impaired manual ability, which is clearly a larger number compared to the scores of the total sample, especially for the more difficult mostly bilateral ADL-items of the MAM-36 such as peeling fruits, shuffling cards, cutting meat, wringing a towel, writing sentences, folding clothes and zipping a jacket

(appendix 1). Only a limited number of ADL tasks were graded ‘not applicable’ by the PwMS with mildly impaired manual ability such as using a hammer, cutting nails, shuffling cards, opening child-proof top, fastening clothes snap,…

Especially the unilateral ADL tasks which were critical for the personal hygiene and everyday care such as eating a sandwich, brushing teeth, drinking a glass of water, using a spoon,… were considered to be important by the PwMS with severely impaired manual ability while many other ADL tasks were ‘not important at all’ or even ‘not applicable’ to them (appendix 2).

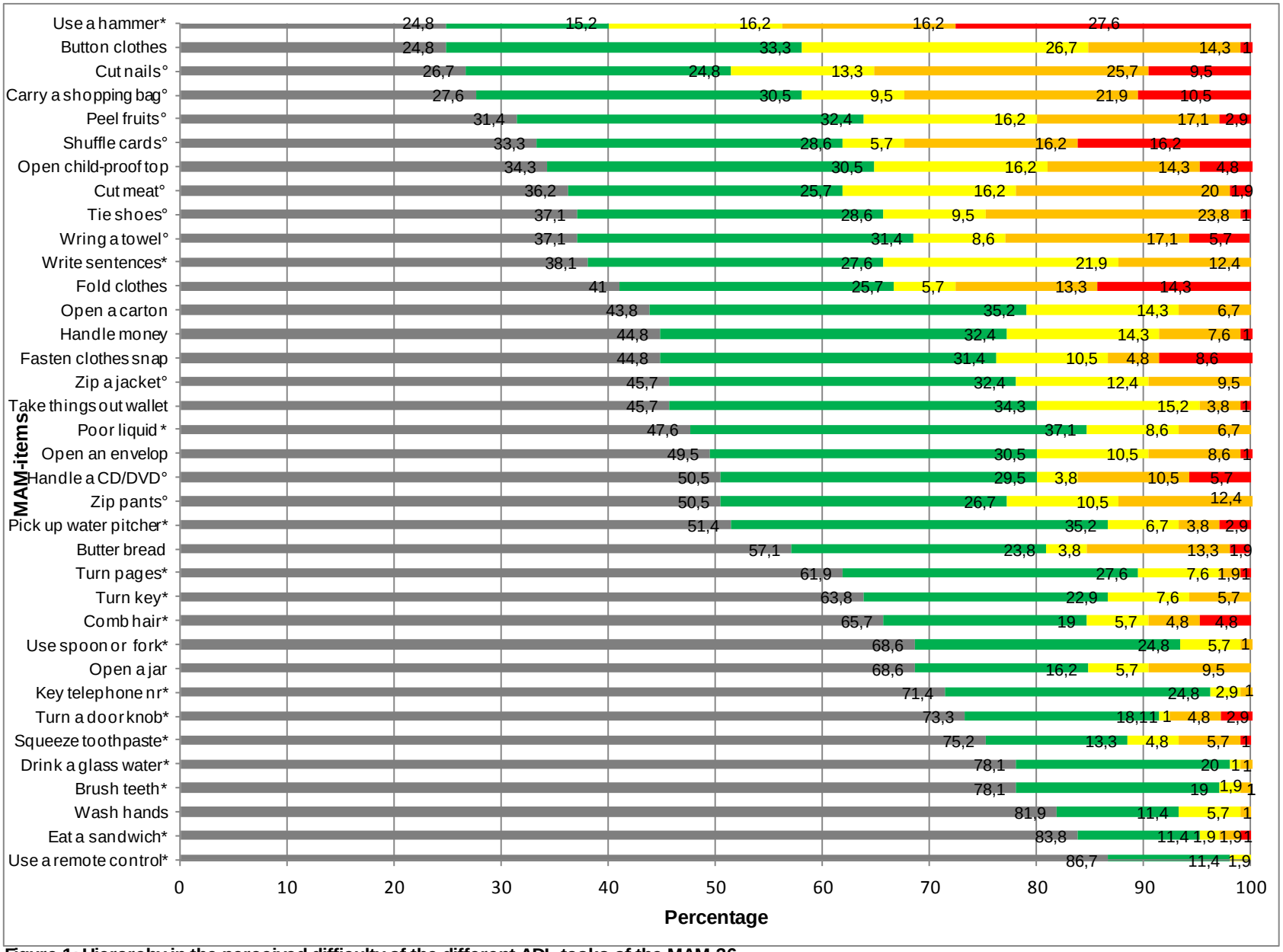

Figure 1: Hierarchy in the perceived difficulty of the different ADL-tasks of the MAM-36

Grey, easy; green, little hard; yellow , very hard; orange, can't do; red, almost never do; *, unilateral ADL-tasks; ° bilateral ADL-tasks

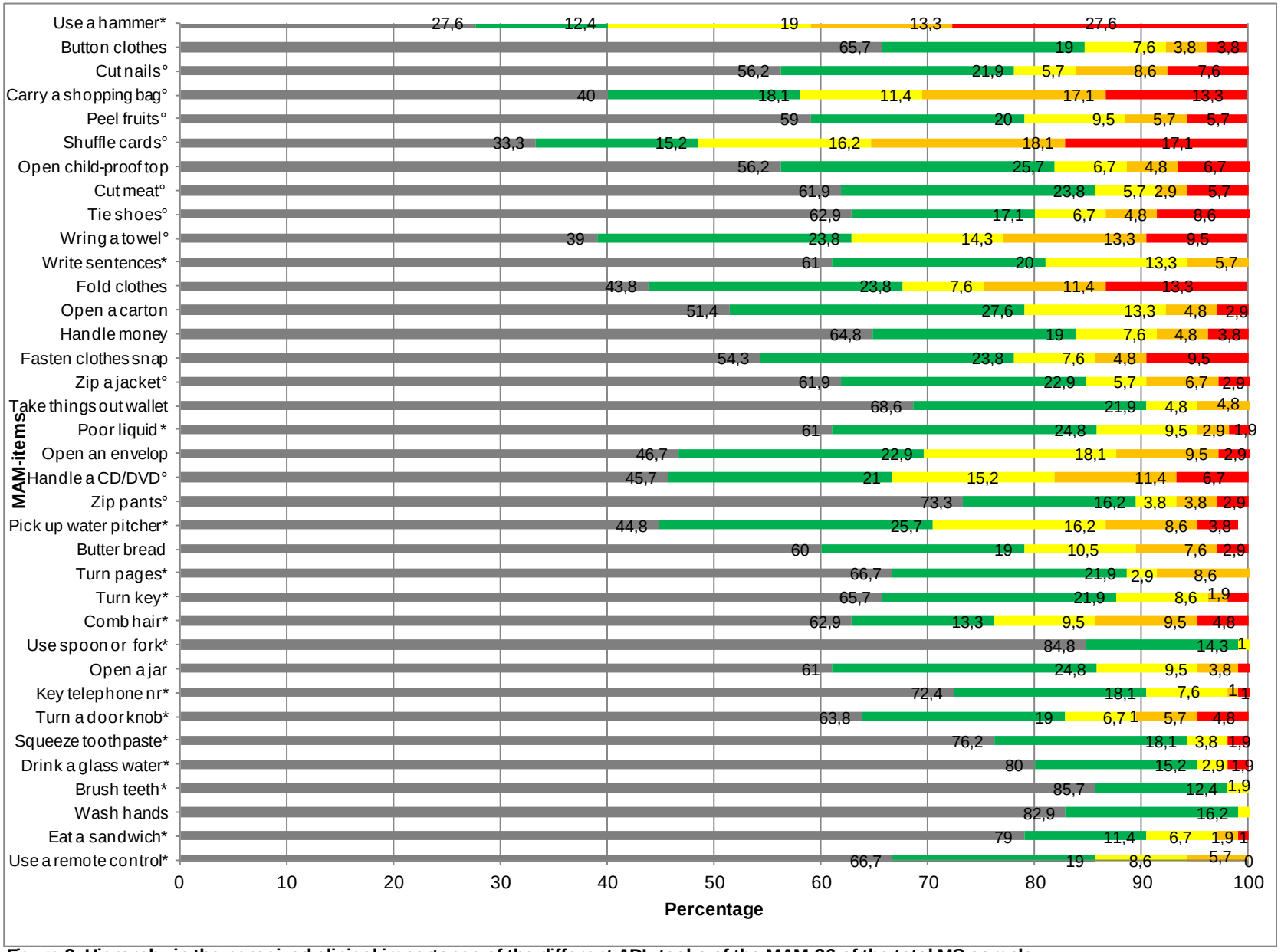

Figure 2: Hierarchy in the perceived clinical importance of the different ADL-tasks of the MAM-36 of the total MS sample

Grey, real important; green,important; yellow , not really important; orange, not important at all; red, not applicable; *, unilateral ADL-tasks; ° bilateral ADL-tasks

Threshold values of upper limb capacity tests for different levels of manual ability to perform variable ADL tasks.

Figure 3-6 provides more insight into how PwMS scored on the capacity tests when they reported difficulties when performing a specific ADL task. Six ADL tasks were chosen which were thought to represent the 36 ADL tasks of the MAM as well as possible. The six ADL tasks were ranked from easy tot difficult on the X-axis. Also the number of PwMS that determine the median score of the associated bar was shown on the X-axis.

Better scores with their dominant hand than their non-dominant hand were found for the NHPT and JAMAR hand grip strength. Additionally, more difficult ADL tasks were associated with a higher score on the clinical tests than the easier ADL task for the dominant hand.

Figure 3 illustrates that for the easier ADL tasks, PwMS with ‘very hard’ and ‘little hard’ perceived difficulty had lower scores on the NHPT compared to those with no perceived difficulty (easy) while for the more difficult ADL tasks, the PwMS with great difficulty (very hard) still perform poorly while those with moderate difficulty (little hard) had scores more in line with the PwMS without problems (easy). The ADL tasks which require a lot of dexterity such as handling money and buttoning clothes, showed definite contrasts between the groups in their scores on the NHPT.
In general, a median score of 0.28 pegs/s on the NHPT (corresponding to 32-33 seconds) was necessary in order to perform the different ADL tasks without any difficulties.

For the non-dominant hand, shown in figure 4, the scores on the NHPT for the ADL tasks which require a lot of dexterity were approximately the same for the PwMS with ‘little hard ‘or ‘no difficulties’ to perform the task.

Figure 5 and 6 showed for the various ADL tasks, except for using a remote control, a nice hierarchy in the strength score of the JAMAR in relation to the perceived difficulty.
For the dominant hand, the scores on the JAMAR of the PwMS which had ‘very hard’ and ‘little hard’ difficulties to perform the task were closer together than the scores of the PwMS which had no difficulties to perform the ADL tasks.
Generally a median score of 20 kg on the JAMAR with both the dominant and non-dominant hand, were necessary in order to perform the different ADL tasks without any difficulties.

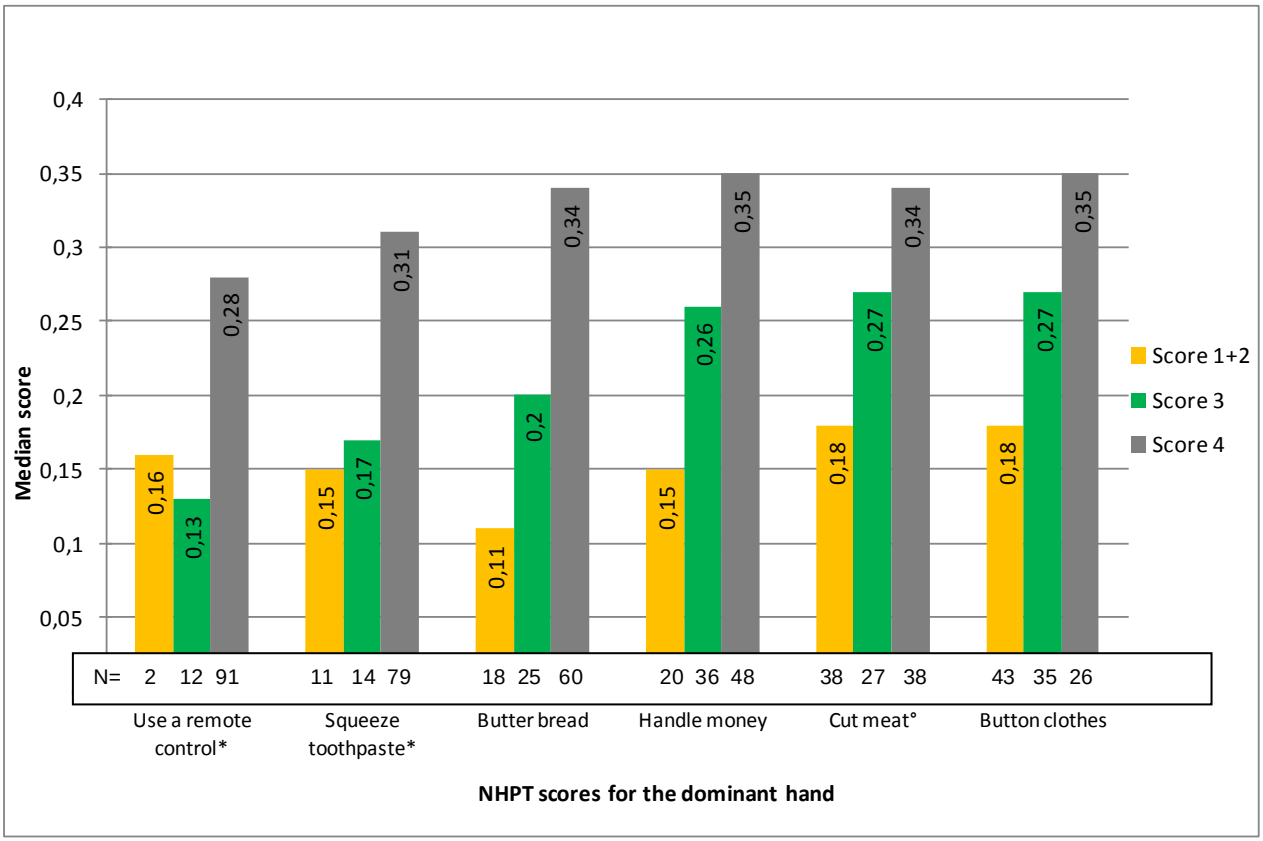

Figure 3: NHPT scores for the dominant hand for different levels of manual ability for 6 ADL-tasks ot the MAM-36

Score 1 + 2: Can't do + very hard; score 3: little hard; score 4: easy; *: unilateral ADL-tasks; °: bilateral ADL-tasks

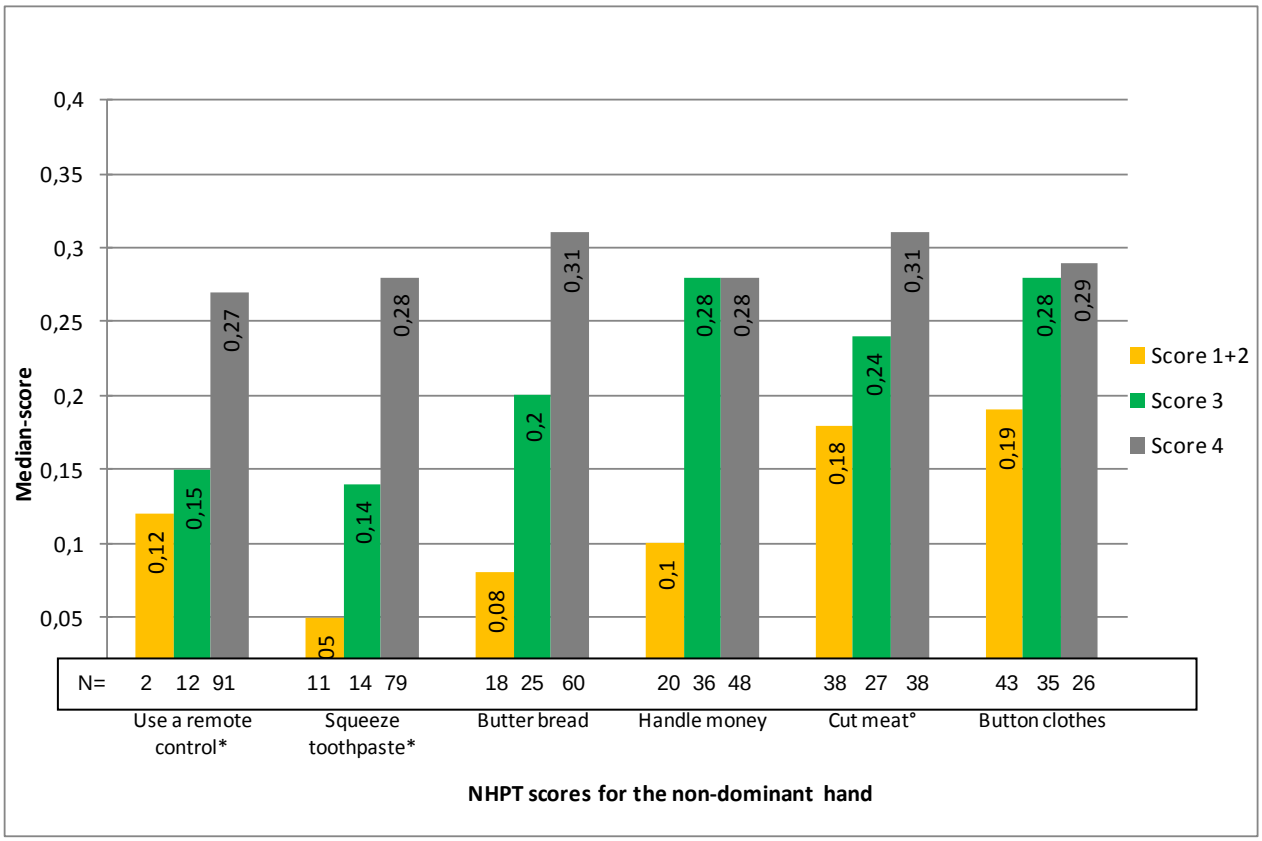

Figure 4: NHPT scores for the non-dominant hand for different levels of manual ability for 6 ADL-tasks ot the MAM-36

Score 1 + 2: Can't do + very hard; score 3: little hard; score 4: easy; *:unilateral ADL-tasks; °:bilateral ADL-tasks

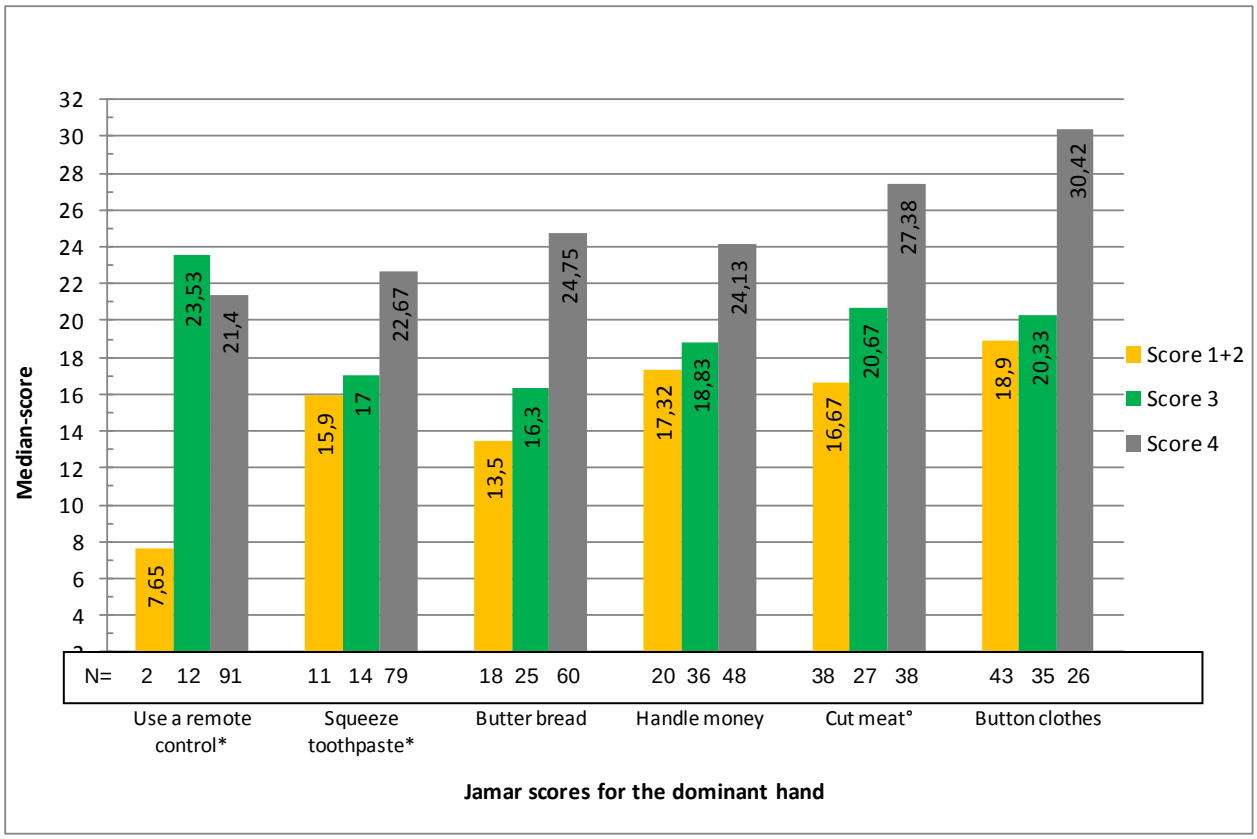

Figure 5: Jamar scores for the dominant hand for different levels of manual ability for 6 ADL-tasks ot the MAM-36

Score 1 + 2: Can't do + very hard; score 3: little hard; score 4: easy; *: unilateral ADL-tasks; °: bilateral ADL-tasks

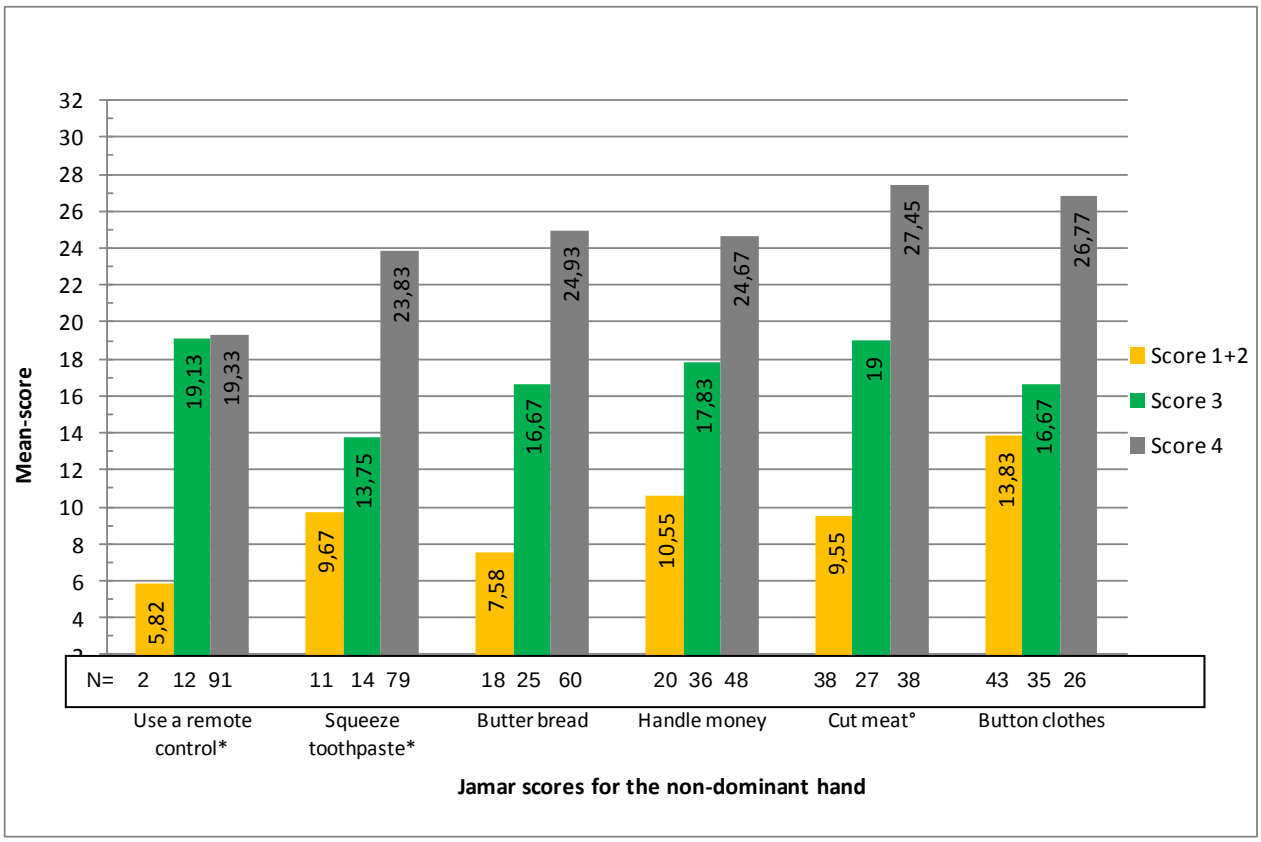

Figure 6: Jamar scores for the non-dominant hand for different levels of manual ability for 6 ADL-tasks ot the MAM-36

Score 1 + 2: Can't do + very hard; score 3: little hard; score 4: easy; *: unilateral ADL-tasks; °: bilateral ADL-tasks

Discussion

The present study aimed to understand how 105 PwMS with different levels of perceived manual ability score on other objective clinical outcome measures assessing upper limb function for both, the dominant and non-dominant hand. Descriptive statistics showed an overview of perceived difficulty and clinical importance of the different ADL tasks of the MAM-36. The last aim was to gain insights in threshold values of upper limb capacity scales for different levels of manual ability to perform variable ADL tasks of the MAM-36.

Scores on objective clinical outcome measures for PwMS with different levels of perceived manual ability

In order to understand how PwMS with different levels of perceived manual ability score on other objective clinical outcome measures, the total sample was divided into four different levels of manual ability based on their score on the perceived performance manual ability measure (MAM-36) since this scale explicitly evaluates upper limb function and can be subdivided into unilateral and bilateral ADL tasks.

The results showed generally high scores for the PwMS with mildly and moderately impaired manual ability with ceiling effects on the capacity tests and somewhat lower scores on the outcome measures on body function & structures level which both drop very hard in the PwMS with markedly or severely impaired manual ability. Striking was that the PwMS which scored almost normal on these clinical outcome measure, still experienced limitations in the perception of their upper limb function and the performance of ADL tasks which was visible in the low median score of the MAM-36[1]. Therefore the MAM-36 differentiated more in level of upper limb dysfunction in PwMS with mild disease severity than other clinical outcome measures that often reach ceiling effects because of their ordinal scoring system. The MAM-36 was also more functional as it offers insights into which ADL tasks are difficult. This demonstrated the surplus value of the MAM-36 to detect problems if there is little objectifiable upper limb dysfunction. The MAM-36 seemed to be less useful in PwMS with marked disease severity because the other clinical outcome measures already clearly demonstrated the impaired manual ability. This study confirmed the findings of Lamers et al. (2014) that capacity measures and perceived performance measures assess different aspect of upper limb function and both types of outcome measures are necessary to get an accurate and complete picture of the multidimensional character of the upper limb function in PwMS (4;12;13).

This study showed that the more serious the impaired manual ability revealed by the MAM-36, the worse the score on other clinical motor but not sensory tests. Decreased arm capacity and performance were proportional with disease progression. With the exception of tactile sensitivity, which may be presented during the onset of the disease in PwMS with mildly upper limb disability and did not increase together with the overall disability level. These findings are in line with an earlier study of the natural history of MS symptoms: about 60% of the PwMS reported to have impairment or

[1] Give a short comment on this, to our knowledge no studies reported norm scores for the MAM-36 in healthy persons or any other patient population in the past. Therefore it is difficult to compare our results and to know which scores are bad or good because even healthy persons scores sometimes ‘alsmost never do’ because they never performed that task so they get no maximum score of 100.

restrictions related to upper limb function in the first year of the disease evaluated by a self-reported six-grade ordinal scale (42). Other studies in PwMS confirm this affected tactile sensitivity in the earlier stage of the disease. Guclu-Gunduz et al. (2012) (22 MS patients, median EDSS 2) indicates that hand sensation had decreased in MS patients who had mild to moderate disability (43). Also Cuypers et al. (2010) (26 MS patients, EDSS 3-6.5) showed that light touch-pressure (35.26%) and protective sensation (40/38%) had diminished in MS patients measured with the Semmes-Weinstein monofilaments (35). All these studies provide evidence of an early involvement of somatosensory pathways. However, it seems to have no impact on the perceived ease or difficulty to perform the different ADL tasks which may indicate that PwMS probably have developed compensation strategies to perform their ADL such as visual compensation.

Distinction between both hands is necessary, the scores of the dominant hand on the different clinical outcome measures are at least better than those of the non-dominant hand, except for the active range of motion wrist extension and some subitems of the ARAT. These higher scores for the dominant hand were confirmed by Krishnan et al. (2008) (12 MS patients, EDSS 2.5-5.5) for the NHPT (44) and by Lamers et al. (2013) (30 MS patients, median EDSS 7.5) for the JAMAR, the motricity index, the NHPT and the ARAT (10). These results were contradicted by Yozbatiran et al. (2006) (31 MS patients, mean EDSS 2.56 (± 1.91)) (2) and Marwaha et al. (2006) (13 MS patients, EDSS 1.5-4) (45) for the NHPT. So it is only contradicted for the NHPT by studies with a small study population. To our knowledge, there is no explanation why the non-dominant hand in PwMS has better active range of motion wrist extension than the dominant hand; we suspected it was coincidence.
There was clearly a bilateral arm involvement in all the PwMS, even in these with mildly impaired manual ability, which is in contrast to patients with stroke. Bilateral involvement of the different outcome measures of the upper limb function such as handgrip strength, muscle strength, tactile sensitivity, the NHPT and ARAT was also presented in a study of Lamers et al. (2014) (17). These results indicate the importance of addressing both upper limbs in rehabilitation programs.

Hierarchy in the perceived difficulty and clinical importance of the different ADL tasks of the MAM-36

A hierarchical view of the perceived ease or difficulty showed that unilateral ADL tasks and tasks that require less fine motor control or accuracy are the easiest. Bilateral tasks or those tasks requiring fine motor control in combination with handling of sharp materials were the most difficult. The overview of the perceived clinical importance revealed that unilateral tasks, which are critical for the personal hygiene and everyday care, were considered to be the most important. Using a hammer, shuffling cards, folding clothes, carrying a shopping bag, cutting nails and fastening clothes snap were activities that the PwMS rarely perform and were not important at all for the PwMS.
To our knowledge, there is no other study available in MS that displays overall information about the upper limb function in relation to ADL in such a way; the already available studies use outcome measures that assess more specific parts of the overall upper limb function like the NHPT for manual dexterity (13), the Functional Independence Measure (FIM) (46) and the difference between unilateral

or bilateral involvement to determine the degree of severity (17).
Fortunately, recently more attention has been paid to performance scales which give more information about the difficulties PwMS experience when performing ADL. Many perceived performance scales are available. We chose the MAM-36 above other perceived performance scales since this scale comprises different ADL tasks which were representative of the overall activities of ADL for various reasons. The MAM-36 contains a variety of tasks regarding degree of difficulty (e.g easy to wash hands but difficult to cut nails), this scale uses a mix of unilateral and bilateral tasks (e.g turning a key with one hand and washing hands with both hands) and it includes a variety in tasks specific for male and female (e.g using a hammer typical for male and folding clothes for female). There is also a mix in clinical importance of the tasks; independence in performing personal hygiene and daily care is very important for all MS patients and in this way can increase their quality of life.
These results are in line with an earlier study of Edmonds et al. (2007) which identified in PwMS (physical disabilities ranged from mild to severe) that independence is important for them since this answer was given to the open-ended question 'What issues are important in living with MS?' (47). Finally, many ADL tasks of the MAM-36 for example writing, carrying out daily routine, fine hand use, hand and arm use,…are similar to the Comprehensive ICF Core Set for Multiple Sclerosis (48).

The use of a hammer was the most difficult task. This is surprising because using a hammer is not very difficult but according to the guidelines of the MAM-36, this item includes also the use of a screwdriver in which both hands performed precision work making, it a difficult task. According to the guidelines of the MAM-36, this task is considered as an unilateral task with which we want to show that the labeling of a unilateral or bilateral task is debatable and not always easy.

The level of impaired manual ability affects the perceived importance of an ADL task. PwMS with severely impaired manual ability (appendix 2) assessed much more ADL tasks as 'not important at all' or even 'not applicable' than the PwMS with mildly impaired manual ability (appendix 1). It is important to have less high expectations of their ability to perform different ADL tasks and to consider many more tasks as irrelevant if they are severed impaired in order to deal with the progression of the disease. Adjustments of the targets for rehabilitation by the physiotherapist based on this information is very important. This makes sense, but to our knowledge, no other studies reported this information.

In conclusion, both figures provide a lot of information for a PwMS and the integration of this information forms the basis for the selection of an appropriate patient-oriented rehabilitation approach. This way, one can see where the individual problems lie, and for which items you can expect improvement after a tailored rehabilitation program based on the difficulty and the importance of the ADL tasks for the patient.

Threshold values of upper limb capacity tests for different levels of manual ability to perform variable ADL tasks

The NHPT and the JAMAR hand grip strength were selected as capacity tests because dexterity and strength are very important skills to execute many ADL tasks, and moreover, these are continuous

scales which are more sensitive to change and give more information than ordinal scales.
Ideally, all the 36 tasks were shown because each task includes various characteristics on 'body function & structures' and 'activity' level. This was not realistic nor clear so we chose six ADL tasks which represent ADL tasks of different difficulty level of the MAM-36 as well as possible. Although we acknowledge that this may seem arbitrary, we have considered the different groups in the degree of perceived difficulty, the perceived importance and the variation of unilateral and bilateral ADL tasks for the selection of these six tasks. For example to use a remote control, the individual needs a certain amount of strength, manual dexterity and correct tactile sensitivity and limited tremor and spasticity. In addition we also know that other characteristics, which were not measured, for example position sense, play an important role in using a remote control. If any of these characteristics is affected, other characteristics or compensation strategies can make sure that the task can be, possibly with problems, carried out. Therefore it is impossible to set general scores that must be achieved to perform ADL since they are different from individual to individual and from ADL task to ADL task.

Better scores with their dominant hand than their non-dominant hand were found for the NHPT and JAMAR hand grip strength. For the dominant hand, more difficult ADL tasks were associated with a higher score on the clinical tests than the easier ADL task. This is necessary to ultimately perform these difficult tasks. Clear is the low number of PwMS in the 'very hard' group of the easiest ADL task 'using a remote control' making that one should be careful with the interpretation of these data. Even the severely impaired PwMS experience fewer problems with such a very easy ADL task and shift from the 'very hard' to 'little hard' score group.

The scores on the NHPT for the non-dominant hand for the unilateral ADL tasks which require a lot of dexterity (handle money and button clothes) were approximately the same for the PwMS with the scores 'little hard' and 'easy' to perform the task. This is due to the fact they perform these unilateral ADL tasks with the dominant hand unless the person with MS has changed hand dominance due to the disease of MS, which was the case in 7.6% of the PwMS in this sample.
In general, a median score of 0.28 pegs/s on the NHPT was necessary in order to perform the different ADL tasks without any difficulties. These findings are in line with the study of Lamers et al. (2014) which proposed 0.28 pegs/s on the NHPT as cut-off value to differentiate between PwMS with different level of impaired manual dexterity (13). Conflicting with our results, is the 0.50 pegs/s on the NHPT as proposed by Kierkegaard et al. (2012) (19). This latter cut-off value is quite broad and can only be used to differentiate between PwMS with no and severely impaired upper limb dysfunction. Generally a median score of 20kg on the JAMAR with both the dominant and non-dominant hand, were necessary in order to perform the different ADL tasks without any difficulties, which is relatively low in comparison with the norm values for healthy persons (41).

Study limitations and future research

A number of considerations need to be made when interpreting the results of this study. Firstly, we recruited the MS sample from three rehabilitation centers leading to an overrepresentation of subjects having an EDSS higher than 5.5. However, these results are representative for most of the PwMS

enrolled in a rehabilitation program. Also, we think we had a nice spread of severity of arm dysfunction across our sample. Secondly, the perceived performance scale, the MAM-36, has drawbacks as these results may be influenced by the honesty of the patients.

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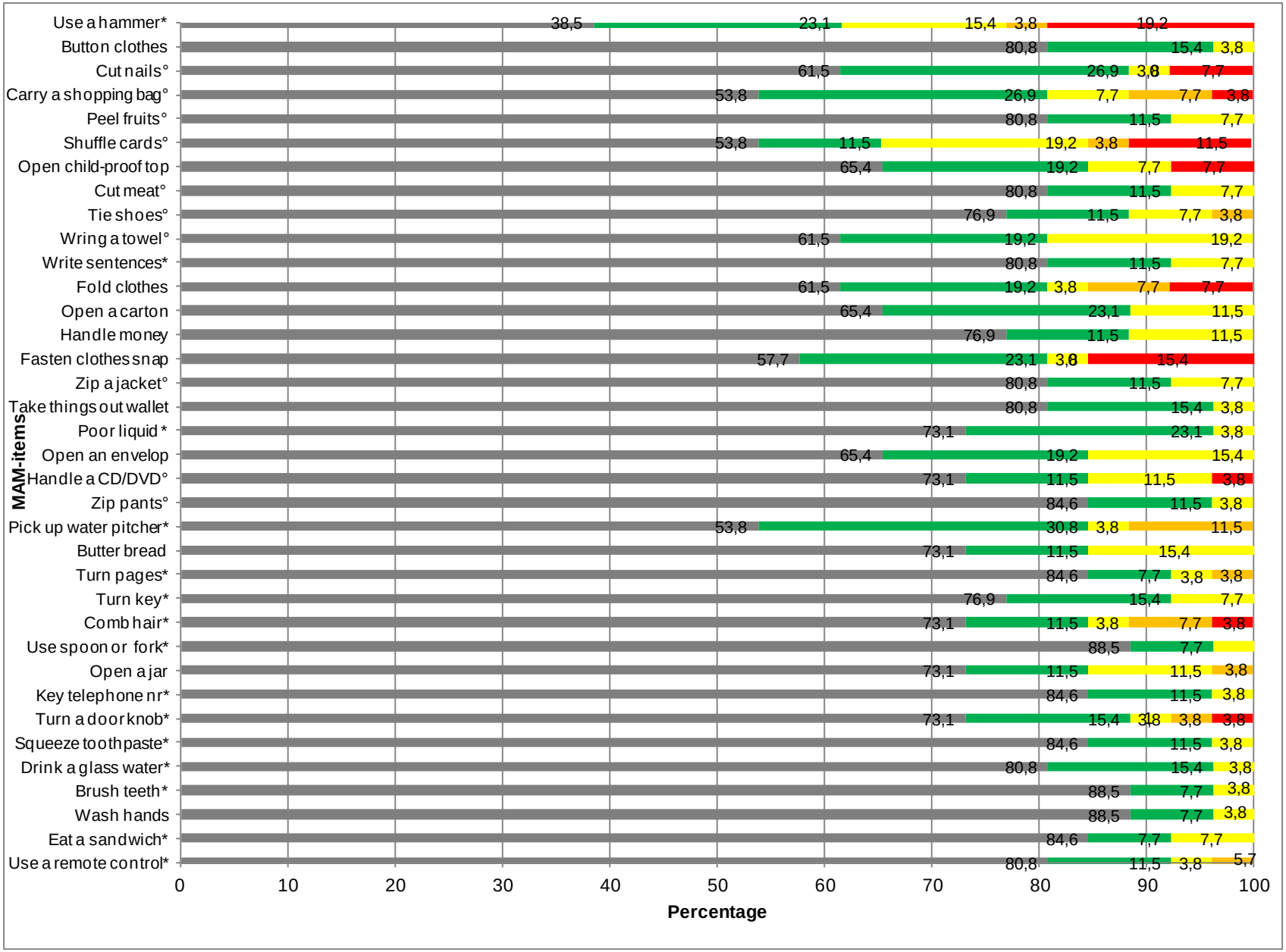
Appendix

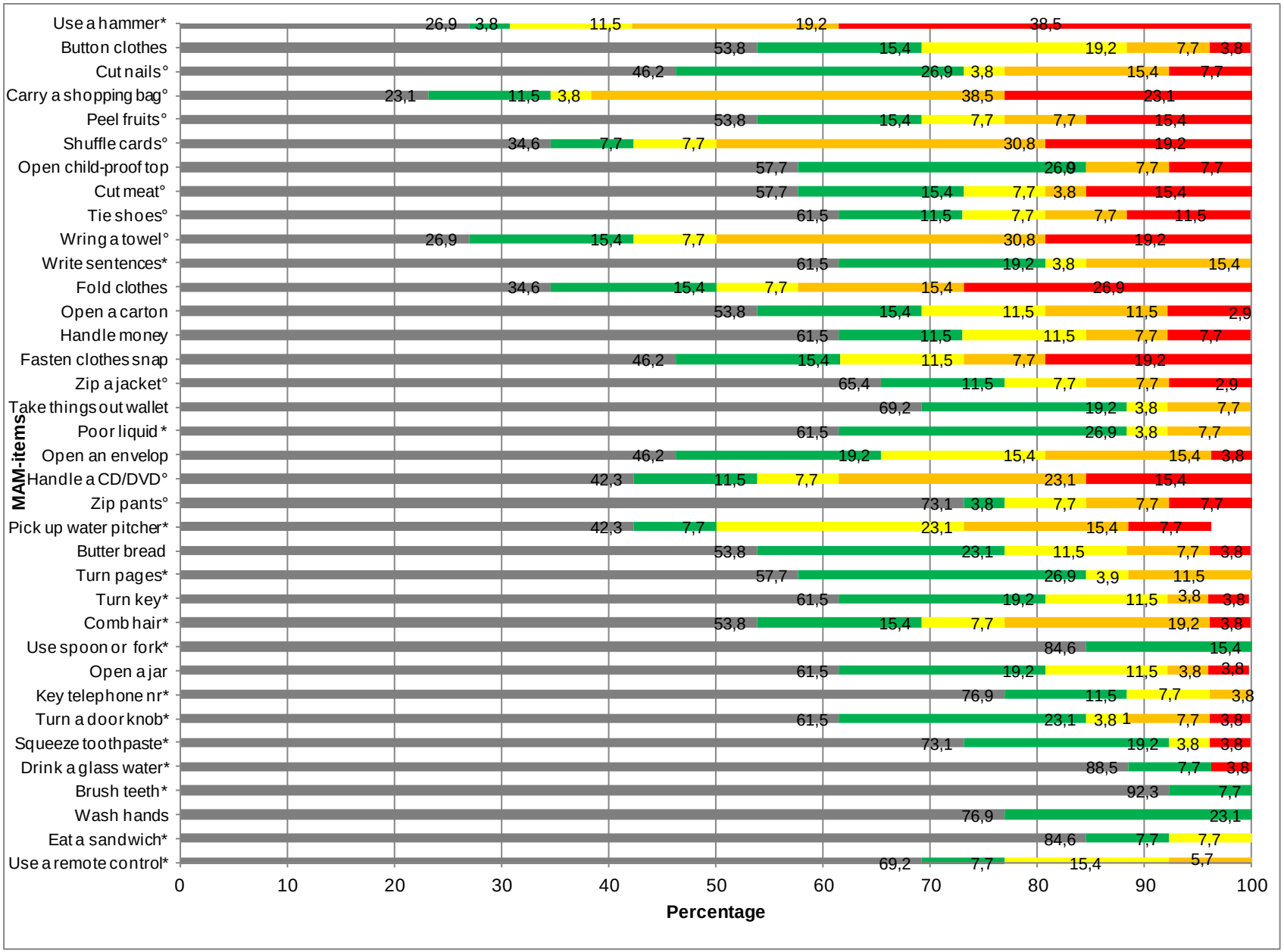
Appendix 1



Appendix 1: Hierarchy in the perceived importance of the different ADL-tasks of the MAM-36 for the PwMS with mild impaired manual ability

Grey, real important; green,important; yellow , not really important; orange, not important at all; red, not applicable; *, unilateral ADL-tasks; ° bilateral ADL-tasks; mild impaired manual ability: quartile 75-100 of the MAM-36

Appendix 2



Appendix 2 Hierarchy in the perceived importance of the different ADL-tasks of the MAM-36 for the PwMS with severe impaired manual ability

Grey, real important; green,important; yellow , not really important; orange, not important at all; red, not applicable; *, unilateral ADL-tasks; ° bilateral ADL-tasks; severe impaired manual ability: quartile 0-25 of the MAM-36

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Richting: **master in de revalidatiewetenschappen en de kinesitherapie-revalidatiewetenschappen en kinesitherapie bij musculoskeletale aandoeningen**
Jaar: **2014**

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