# 2015•2016

master in de revalidatiewetenschappen en de kinesitherapie

# Masterproef

Validity and floor/ceiling effects of upper limb outcome measures in people with Multiple Sclerosis: an European RIMS multi-center study

Promotor : dr. IIse LAMERS dr. IIse BAERT

Tina Hendrickx Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie



Universiteit Hasselt | Campus Hasselt | Martelarenlaan 42 | BE-3500 Hasselt Universiteit Hasselt | Campus Diepenbeek | Agoralaan Gebouw D | BE-3590 Diepenbeek

# FACULTEIT GENEESKUNDE EN LEVENSWETENSCHAPPEN



# 2015•2016 FACULTEIT GENEESKUNDE EN LEVENSWETENSCHAPPEN

*master in de revalidatiewetenschappen en de kinesitherapie* 

# Masterproef

Validity and floor/ceiling effects of upper limb outcome measures in people with Multiple Sclerosis: an European RIMS multi-center study

Promotor : dr. IIse LAMERS dr. IIse BAERT

Tina Hendrickx

Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie



## Acknowledgement

I would first like to thank my promotor Dr. Ilse Lamers of the Hasselt University. She was always available when I had questions or ran into trouble with the statistics of my thesis. She allowed this paper to be my own work but steered me in the right direction whenever needed.

I would also like to thank Dr. Ilse Baert of the University of Hasselt as the second reader of this thesis, for her guidance and help with the data collection.

Finally, I really would like to thank my family and partner for their unfailing support and continuous encouragement throughout my years of study and through the process of researching and writing this thesis. This accomplishment would not have been possible without them. Thank you,

Hendrickx Tina

Hoeleden, 6/05/2016

## Content

Research context	1
Abstract	3
1. Introduction	5
2. Methods	7
2.1 Participants	7
2.2 Procedure	7
2.3 Outcome measures	8
Primary upper limb outcome measures	9
Secondary upper limb outcome measures	10
2.4 Data-analysis	11
3. Results	
3.1 Participant characteristics	
3.2 Construct validity	15
3.3 Floor effects	20
3.4 Ceiling effects	20
4. Discussion	23
4.1 Measures on body function and structure level	23
4.2 Measures on activity level	23
Capacity	23
Perceived performance	24
Capacity versus Perceived performance	25
4.3 Measures on body function and structure level and activity level	25
4.4 Study limitations	26
4.5 Recommendations for future research and conclusion	
5. References	27
Appendix	

#### Research context

This study is part of a multi-center study that took place within the European Rehabilitation In Multiple Sclerosis (RIMS) Network- Special Interest Group (SIG) on Occupation (www.eurims.org). RIMS aims to raise the profile of rehabilitation in MS with the best researchers and practitioners, improve the understanding of rehabilitation at every stage of MS, stimulate the implantation of new and existing evidence-based rehabilitation and to educate and train practitioners to integrate evidence into clinical practice. MS as a multifaceted disease requires multidisciplinary care and evidence-based rehabilitation. RIMS offers an international forum to share, discuss and develop such expertise.

The primary aim of this RIMS multi-center study was to investigate the psychometric properties (reliability, validity, responsiveness and floor/ ceiling effect) of upper limb outcome measures in persons with Multiple Sclerosis (PwMS). This master thesis will only report on the validity and possible floor/ ceiling effects. The research question of this research is composed in dialogue with Dr. Ilse Lamers and Dr. Ilse Baert.

#### Abstract

**Background:** A recent review on upper limb outcome measures highlighted the need for more studies investigating their psychometric properties.

**Objectives:** This study aimed to investigate the psychometric properties, in particular the construct validity and floor/ceiling effects in frequently used and new upper limb outcome measures in people with Multiple Sclerosis (PwMS).

Participants: 136 PwMS from 11 centers across Europe (RIMS network).

**Measurements:** Participants were assessed using different upper limb outcome measures on the three levels of the International Classification of Functioning (ICF). On body function and structures level, maximum isometric pinch, key, 3jaw grip strength and handgrip strength were evaluated using a dynamometer. Visual Analogue Scales (VAS) were used to evaluate the perceived presence of spasticity, muscle weakness, sensory impairment, coordination deficits and fatigability. On activity level, upper limb capacity was assessed by the nine-hole peg test (NHPT), box and blocks test (BBT), coin rotation test (CRT) and Action Research Arm Test (ARAT). The ABILHAND, Manual Ability Measure-36 (MAM-36) and Motor Activity Log (MAL) were used to evaluate the perceived performance. Pearson correlation coefficients were calculated to investigate the validity of the outcome measures. Descriptive statistics were used to examine possible floor and ceiling effects.

**Results:** The Pinch grip formations showed high correlation coefficients with each other (range R= 0.72-0.83, p<0.0001). Between the different VAS subscales low correlations were present (range R= -0.24-0.63, not significant). Low correlation coefficients were present between the different formations of the Pinch Grip and the several VAS subscales. NHPT, BBT and CRT were highly correlated with each other for both hands (range R= 0.65-0.87, p<0.0001). MAM-36 and ABILHAND were highly associated (R= 0.81, p<0.0001). ABILHAND and MAM-36 were low to moderately correlated with the NHPT, BBT and CRT for both hands. Low correlations were found between measures of body function and structure level and activity level.

Floor effects were found in the VAS Spasticity, VAS Sensory impairment and VAS Coordination deficits (>15% of the participants). The VAS Muscle weakness and VAS Fatigability were on the edge of a floor effect. Also the CRT showed a floor effect for both hands (>20% of the participants). Ceiling effects were present in the MAL total for the dominant hand (>15% of the participants). The ARAT was on the edge of a ceiling effect.

**Conclusion:** In future research, therapists should choose for one of the Pinch formations, taken into account the responsiveness of the measures in PwMS. We suggest to include objective measures instead of VAS scales to assess the level of impairment on body function and structure level. A decision should also be made between the NHPT or BBT and between the ABILHAND or MAM-36 on activity level, depending on other psychometric properties.

#### 1. Introduction

People with Multiple Sclerosis (PwMS) may present an impaired unilateral or bilateral upper limb function, even in people with a low Expanded Disability Status Scale (EDSS) score (1-3.5) (Johanssons S.2007). This upper limb dysfunction can be caused by sensory and/or motor deficits and negatively influences the performance of activities of daily living (ADL) (Yozbatiran N. 2006). The upper limbs are used to perform complex and multidimensional tasks such as reaching, stabilizing, grasping and manipulating objects which makes evaluating the upper limb function more complex in comparison with the lower limb function (Holper L. 2010).

To measure the upper limb function in PwMS, a range of reliable, valid and responsive tests are needed. Few studies describe the psychometric properties of upper limb outcome measures in PwMS (O'Dell M. et al, 2013; Mathiowetz V. et al 1985). In the review of Lamers et al, 2014 an overview of applied upper limb outcome measures in MS is given according to the Classification of Functioning, Disability and Health (ICF) levels and their psychometric properties in MS. This review concluded that the focus of the upper limb measure towards the upper limb disability level, the expected improvements on different ICF levels of the intervention and the psychometric properties should be taken into account when selecting upper limb outcome measures. Furthermore, they concluded that there was a lack of studies investigating the psychometric properties of currently used upper limb outcome measures in PwMS. In order to enable researchers to make evidence-based choices about the selection of appropriate outcome measures, knowledge of these psychometric properties is required.

In this masterthesis we focused on investigating the psychometric properties, validity and floor/ceiling effect. Construct validity is the extent to which a measure of one construct is less strongly related to measures of other constructs than measures of the same one. For example, we would expect measures of sensory function to be less strongly related to measures of muscle strength than other measures of sensory function. This can only be true, if our measure of sensory function is valid (Cramer D.; Howitt D. 2004). By using construct validity, researchers can eliminate outcome measures that investigate the same function, capacity or performance. When a scale or an instrument doesn't have a large enough range to accommodate the distribution of the data, participants can't be evaluate correctly and the effect of treatment will be interpreted incorrectly. To avoid these kind of errors, it is important to determine if certain measurements are sensitive for floor or ceiling effects.

A ceiling effect is determined when scores on a variable are approaching the maximum value. Failure to recognize a ceiling effect may lead to the conclusion that an independent variable has no effect (Cramer D.; Howitt D. 2004). A floor effect is determined as when scores are so low that an experimental treatment cannot depress the scores any further. When a floor effect is not recognized, a part of the participants can't be measured and results will not be representative for the whole population. (Cramer D.; Howitt D. 2004).

With these needs in mind, we postulated that a large multi-center study with comprehensive upper limb assessment on different ICF levels in PwMS is warranted. Therefore, this European RIMS, multi-center study was conducted to investigate the psychometric properties (reliability, validity, responsiveness and floor/ ceiling effect) of new and frequently used upper limb outcome measures in PwMS. This masterthesis will only report on the validity and the possible floor/ ceiling effects of upper limb outcome measures in PwMS.

#### 2. Methods

PwMS were recruited in several rehabilitation centers across Europe within the RIMS network. Participating centers recruiting subjects were: University medical center Ljubljana (UMCL), Ljubiana, Slovenia; Eugenia Epalza Rehabilitation Center, Bilbao, Spain; Charles University and General Faculty Hospital, Prague, Czech Republic; MS hospitals, Hasley and Ry, Denmark; Italian Multiple Sclerosis Foundation (FISM), Scientific Research Area, Italy; Multiple Sclerosis Senteret Hakadal AS, Hakadal, Norway; John Paul II rehabilitation center for people with MS, Borne Sulinowo, Poland; Haukeland University hospital, Bergen, Poland; Barcelona day hospital CEMCAT, Barcelona, Spain; AZ Klina, de MICK, Brasschaat, Belgium and Rehabilitation and MS center, Overpelt, Belgium. The recruitment of participants took place from June 2015 until January 2016.

#### 2.1 Participants

Adult subjects (aged >25), diagnosed with MS (according to McDonald criteria (Polman, 2011)), who met the inclusion criteria were enrolled in the study. Inclusion criteria were: 1) receiving rehabilitation to maintain or improve upper limb function, 2) no relapse in the last month prior to the study, 3) no changes in disease modifying medication or no corticoid therapy in the last month prior to the study and 4) received at least ten sessions and maximum three months of upper limb rehabilitation.

Participants were excluded from the study if there were other medical conditions interfering with upper limb functioning (e.g. stroke, ...), if participants were not able to understand and to fulfill simple instructions. This study was approved by the central ethical committee UZ Leuven S56575(B322201421636; 31/07/2014) and the local ethical committees of the participating centers. A written informed consent of all included participants was obtained before enrollment in the study.

#### 2.2 Procedure

The upper limb outcome measures were assessed pre- and post-rehabilitation according to a standardized test protocol, including details on test procedures, verbal instructions and level of encouragement. Both arms of the participants were tested. The data of the PRE- testing were used to answer the research question of this manuscript. All outcome measurements were taken by qualified therapists.

To optimize inter-rater reliability between the therapists of each participating center and minimize bias, several precautions were taken: 1) A standardized instruction booklet was written with details on test procedures, order of testing, rest periods, level of encouragement, use of assistive device and possibility to divide testing in two visits (to avoid fatigue, fit the time schedule of the assessors). 2) Uniform scoring sheets and standardized data files were used for each test. 3) Time was provided for the therapists to familiarize with the measures. 4) Training session was held with demonstration and discussion about the correct use of measures during the annual RIMS conference in London-Brighton in June 2014. 5) All discussion points, questions and details on testing were always addressed to the coordinator of the project to define further internal agreements.

#### 2.3 Outcome measures

At pre and post-rehabilitation, the primary and secondary upper limb outcome measures were performed. Descriptive measures were assessed pre-rehabilitation.

#### Descriptive measures:

For each participant the age, gender, height, weight, type of MS, disease duration since diagnose, disability level (Expanded Disability Status Scale (EDSS), cognitive function: information processing speed (Symbol Digit Modalities Test (SDMT)) and severity of fatigue (Fatigue Scale for Motor and Cognitive functions (FSMC)) were measured at baseline (PRE). A short description of the descriptive measures is given below.

For measuring the disability level of each participant the Expanded Disability Status Scale (EDSS) was used. It is the golden standard for characterizing disability levels and determining disability progression in PwMS. The score ranges from 0.0 for normal to 10.0 for dead from MS. From the scores 0.0 to 4.0, people are able to walk without assistance. From the scores 7.5 to 10.0, the main determinant of EDSS is the person's ability to transfer from wheelchair to bed and to perform self-care. (Kurtzke JF. 1983)

The Symbol Digit Modalities Test (SDMT) evaluates processing speed of information and aspects of executive functioning. The test consists of single digits paired with abstract symbols. The participant is asked to match the number that corresponds with each symbol in 90 seconds. The longer it takes for a participant to match each number with the corresponding symbol, the lower the score will be. (Smith A. 1982)

For measuring MS-related cognitive and motor fatigue, the Fatigue Scale for Motor and Cognitive functions (FSMC) was used. A five-point scale ranging from "does not apply at all" to "applies completely" produces a score between one and five for each question. The minimum value is 20 and maximum is 100 (severest grade of fatigue). (Penner IK. 2009)

#### Primary upper limb outcome measures:

For each participant the upper limb function was measured by the primary and secondary upper limb outcome measures at PRE and POST-testing. Figure 1 gives an overview of the diverse outcome measures according to the International Classification of Functioning, Disability and Health (ICF).

#### Body function and structure level:

The maximal isometric pinch strength during different grip formation such as key, tripod, tip top tip was measured using a dynamometer (Chen CC. 2007). The perceived severity of spasticity was evaluated using the Spasticity 0-10 Numeric Rating Scale (NRS). Spasticity was defined as the muscle stiffness that the participant experienced, with anchors of 0 (no spasticity) and 10 (worst possible spasticity). (Farrar JT. 2008)

In this study a Visual analogue scale (VAS) was used to evaluate the perceived spasticity, muscle weakness, fatigability, sensory impairments and coordination deficits. Participants could score from zero (no impairment) to ten (most severe impaired). Participants specify their level of agreement of statement by indicating a position along a continuous line between two endpoints. (Boonstra AM. 2008)

#### Activity level - Capacity measures

Box and Block Test (BBT) assess unilateral gross manual dexterity. Participants were asked to transfer as many blocks as possible from one box to the other, one block at a time. The amount of blocks transferred in one minute is recorded. (Platz T. 2005)

For measuring motor speed, manual dexterity and in-hand manipulation the Coin Rotation Task (CRT) was used. Participants are asked to rotate a coin as quickly as possible between their thumb, index and middle finger. The time needed to perform 20 half turns (180 degrees) is measured for both hands (time limit = 60sec). If the subject was not able to perform 20 half turns in one minute, the number of turns was recoded. The number of turns per second were calculated and used in the data-analysis. (Kamm CP. 2012)

For measuring the unilateral fine manual dexterity the Nine Hole Peg Test (NHPT) was used. Participants were asked to place and remove nine pegs, one at a time and as quickly as possible (time limit of 300 seconds). Time needed to complete the task is recorded. The amount of pegs per second was calculated. (Cutter GR. 1999)

#### Activity level – Perceived performance

Manual Ability Measurement-36 (MAM-36) assesses the perceived difficulty that a person experience when performing activities in daily life (ADL). The participants are asked to rate 36 unilateral and bilateral ADL tasks using a four-point scale. The scores of all tasks are summed up and transformed using a Rasch-derived conversion table. A high score represents fewer limitations in a patient's ADL. (Chen CC. 2010)

For the ABILHAND participants had to rate 23 bilateral ADL tasks (performed in the last three months) using a three point ordinal scale. All the scores are summed up and transformed using a Rasch-derived conversion table. (Barrett L. 2012)

In the Motor Activity Log (MAL) participants are asked to score their amount of use of both arms (Amount Scale) and the quality of their movement (How Scale) during functional activities using an ordinal scale (zero to five). The sum of both scales results in a use score (score out of ten). A poor upper limb use results in a low score. (Mark VW. 2008; Taub et al. 2011)

#### Secondary upper limb outcome measures:

Some participating centers had time and resources to assess a few secondary measures. Hand grip strength (in kg) in general was measured by the JAMAR<sup>®</sup> hand-held dynamometer or Elink during three repeated trials for the dominant and non-dominant hand. The used procedure is recommended by the American Society of Hand Therapists. (Trampisch US. 2012) To assess speed and coordination of the upper limb the Plate tapping test was executed. Participants were asked to move one hand back and forward between two discs as fast as possible while the other hand is placed in the middle. The time that is needed to complete 25 cycles or 50 taps is recorded. (Kumar N. 2014)

Trunk Impairment Scale-modNV (TIS-modNV) is used to measure motor impairment of the trunk. Static, dynamic sitting balance and coordination of trunk movement is evaluated. Total score can range from zero to 16. How higher the score, how less trunk impairment is present. (Gjelsvik B. 2012).

The unilateral ability to handle objects with different size, weight, shape and the gross upper limb movements is evaluated by the Action Research Arm Test (ARAT). 19 items can be scored divided in four subscales (grasp, grip, pinch and gross movement) by an ordinal scale from zero (no movement) to three (normal movement). Maximal score is 57. (Platz T. 2005)



Figure 1: Upper limb outcomes classified according to ICF

## 2.4 Data-analysis

Normal distribution was checked using the Kolmogorov-Smirnov test and by visual checking the normal quantile plots. Descriptive statistics (mean, standard deviation (SD), median, interquartile range (IQR)) were calculated for each upper limb outcome measure.

To investigate the construct validity, spearman correlations were first investigated between measures on each level of the ICF. Second, correlations were calculated between outcome measures on the different levels of the ICF. A correlations coefficient is defined as very high when the value was higher than 0.90. A high correlation reaches between the value of 0.70-0.89, a moderate correlation between 0.50 and 0.69 and a low correlation below the value of 0.49 (McDowell I.). JMP Pro 12 was used to perform following data-analyses.

Descriptive statistics and frequency analysis were used to investigate the presence of floor/ceiling effects. For all the measures, the number of participants that reached the highest or lowest score are calculated. A floor or ceiling effect is present when 15% or more of the participants reach the highest (ceiling effect) or lowest possible score (floor effect) (Arwert HJ. 2015; Terwee C.B. 2006). When participants present a maximum or minimum score on one outcome measure, the scores of all outcome measures were investigated in more detail. This is done in order to evaluate if these participants score general high (when a ceiling effect is present) or low (when a floor effect is present).

## 3. Results

### 3.1 Participant characteristics

136 participants met the inclusion criteria of the study. Descriptive data of the included participants can be found in Table 1. Table 2 presents the median score and interquartile range (IQR) for each measure classified according to the ICF. If appropriate, data were presented for the dominant and non-dominant hand. In Belgium, data were missing for the Pinch Grip and BBT (n=10). Secondary upper limb outcome measures were only conducted in 66 participants.

Tabel 1. Descriptive characteristics		Ν
	Median	IQR
Gender m/f	5	5/81
Age (years) mean (SD)*	51.0	(±11.9)
Disease duration (years)	14.0	9-20
EDSS	6.0	4.5-6.5
Primary progressive / Secondary progressive / Relapse Remitting	32,	/56/48
Right hand dominance / Left hand dominance / Ambidextrous	119	9/10/7
No assistance / Unilateral assistance / Bilateral assistance	48,	/19/14
Rollator/ Wheelchair dependent	2	6/28
Cognitive function (SDMT)	35.0	25-44
Fatigue scale: Motor function	37.0	31-41
Fatigue scale: Cognitive function	30.5	25-38
Fatigue scale: Total	67.0	56-77.75

IQR: interquantile range ; EDSS: Expanded Disability Status Scale; SDMT: Symbol Digit Modalities Test \*Age was normal distributed

	Domina	ant hand	Non-do	minant hand
	Median	(IQR)	Median	(IQR)
Body structures and functions				
Pinch grip Key (kg)*	5.75	(4.44-7.33)	5.33	(4.00-7.36)
Pinch grip Tripod (kg)*	5.00	(3.27-6.41)	4.50	(3.00-6.00)
Pinch grip Tip to tip (kg)*	3.83	(2.55-5.00)	3.33	(2.33-4.33)
VAS spasticity	0	(0-4)	2	(0-4.75)
VAS muscle weakness	2.85	(0.5-5.0)	3.40	(0.9-5.5)
VAS coordination deficits	2	(0.32-4.88)	3.4	(0.53-6.08)
VAS sensory impairment	2	(0.2-4.9)	3.4	(0.5-5.58)
VAS fatigue		4.5 (2.03-6.9	90)	
Handgrip strength (kg)	23	(15.08-29)	20.67	(13.33-25)
Plate tapping (sec)	26.87	(21.47-32.91)	28.82	(23.69-32.57)
Activity level				
CRT turns/s	0.60	(0.19-1.02)	0.45	(0.03-0.75)
NHPT pegs/s	0.30	(0.19-0.35)	0.24	(0.17-0.33)
BBT (number of blocks)*	41.5	(33-49)	39.5	(28-48)
ARAT	54	(45-56)	50	(29.25-55.75)
TIS-modNV		9.0 (6-13)		
Activity level Perceived perform	ance			
ABILHAND (logits)		2.25 (0.68-3.	46)	
MALamount	4.5	(3.13-5)	3	(2-5)
MALhow	4	(3-4.38)	3	(2-4)
MALtotal	8	(6.13-9)	6	(4.6-8)
MAM-36 (Rasch)		58.5 (51.13-	66)	

Tabel 2. Conducted tests for dominant and non-dominant hand

VAS: Visual Analogue Scale; CRT: Coin Rotation Task; NHPT: Nine Hole Peg Test; BBT: Box and Block Test; ARAT: Action Research Arm Test; TIS: Trunk Impairment Scale; MAL: Motor Activity Log; MAM-36: Manual Ability Measure -36; EDSS: Expanded Disability Status Scale; SDMT: Symbol Digit Modalities Test; IQR: interquantile range Secundary upper limb outcome measures (conducted in 66 participants)

\* Data of 10 Belgian participants were missing

#### 3.2 Construct validity

The correlation coefficients between the different outcome measures on body function and structure level are provided in Table 3a for the dominant hand and in Table 3b for the non-dominant hand. High correlation coefficients were found between the different Pinch Grip formations (range R= 0.72-0.83, p<0.0001), while low to moderate correlation coefficients were found between the different VAS subscales (range R= -0.24- 0.63, not significant). Low correlation coefficients were present between the different formations of the Pinch Grip and the several VAS subscales (range R = -0.47- -0.18, p<0.05).

Correlation coefficients between the measures on activity level are presented in Table 4a for the dominant hand and Table 4b for the non-dominant hand. On activity level Capacity, the NHPT was highly correlated with the BBT (R= 0.84 and 0.87 respectively for dominant and non-dominant hand, p<0.0001) and with the CRT (R= 0.76 and 0.78, p<0.0001). Moderate correlations were found between the CRT and BBT (R= 0.65 and 0.67, p<0.0001). On the activity level Perceived performance, the MAM-36 and ABILHAND were highly correlated with each other (R=0.81, p<0.0001).

When comparing measures on activity level Capacity with Perceived performance, the ABILHAND was low associated with the CRT, NHPT, BBT (range R= 0.35- 0.48, p<0.0001) for both hands. Low to moderate correlation coefficients were found for the MAM-36 with the CRT, NHPT and BBT (range R= 0.37-0.56, p<0.0001) for both hands. The MAL was moderately associated with the CRT, NHPT and BBT for both hands (range R= 0.41- 0.59, p<0.0001).

The correlations coefficients between outcome measures on body function and structure level and activity level are presented in Table 5a for the dominant and in Table 5b for the non-dominant hand. Low correlations were found for the CRT, BBT, NHPT and the different items of the Pinch Grip for both hands (range R= 0.31- 0.46, p<0.05). The VAS subscales showed low correlations coefficients with the CRT, BBT and NHPT (range R= -0.49- -0.003, not significant). Only low correlation coefficients were present when comparing the MAM-36 with the different items of the Pinch Grip (range R=0.11- 0.43, not significant) and the VAS subscales for both hands (range R= 0.34- -0.21, p<0.05). The same is true for the ABILHAND and MAL. Moderate correlation coefficients were found between the MAL and the VAS Muscle weakness and VAS Coordination deficits for the dominant hand (range R= -0.49- -0.64, p<0.0001). The MAL was also moderately associated with the Pinch Grip Tripod for the dominant hand (range R= -0.49- -0.64, p<0.0001).

The hand grip strength correlated low (range R= 0.01- 0.36, not significant) with the measures on activity level for both hands. The same was found in the Plate tapping test (range R=-0.32- 0.04, not significant).

	Pinch	Pinch	Pinch grip	VAS	VAS	VAS Sensorv	VAS	VAS	Handgrip
	grip	grip	Tip to tip	Spasticity	Muscle	impairment	Coordination	Fatigue	strength
	Кеу	Iripod	· ·	· · ·	weakness	•	deficits		
Pinch grip Key	1								
Pinch grip Tripod	0.76*	1	_						
Pinch grip Tip to tip	0.72*	0.83*	1						
VAS Spasticity	-0.32*	-0.34*	-0.31*	1					
VAS Muscle weakness	-0.47*	-0.42*	-0.40*	0.43*	1				
VAS Sensory impairment	-0.19°	-0.28°	-0.27°	0.36*	0.48*	1	_		
VAS Coordination deficits	-0.32°	-0.31°	-0.31°	0.38	0.63	0.51	1		
VAS Fatigue	-0.32°	-0.24°	-0.18	0.30°	0.36*	0.30°	0.29°	1	
Handgrip strength	0.07	0.08	0.05	-0.06	-0.10	-0.16	-0.24	-0.03	
Plate tapping	0.03	-0.03	-0.06	-0.002	0.12	0.008	0.15	0.05	-0.07
High correlation coefficier	nts	Moderate	e correlation	coefficients	Low correla	ation coefficients			

Table 3a. Spearman correlation coefficients between measures on body function and structures level for dominant he

Secondary upper limb outcome measures (in 66 participants)

#### °p<0.05

#### \*p<0.0001

Table 3b. Spearman correlation coefficient between measures on body function and structures level for non-dominant hand

	Pinch grip Key	Pinch grip Tripod	Pinch grip Tip to tip	VAS Spasticity	VAS Muscle weaknes	VAS Sensory impairment	VAS Coordination deficits	VAS Fatigue	Handgrip strength
Pinch grip Key	1								
Pinch grip Tripod	0.75*	1							
Pinch grip Tip to tip	0.70*	0.80*	1						
VAS Spasticity	-0.32°	-0.22°	-0.32°	1	_				
VAS Muscle weakness	-0.40*	-0.33°	-0.32°	0.50*	1				
VAS Sensory impairment	-0.20°	-0.17	-0.12	0.33*	0.48	1			
VAS Coordination deficits	-0.28°	-0.23°	-0.17	0.30°	0.58*	0.62*	1		
VAS Fatigue	-0.30°	-0.15	-0.14	0.26°	0.28°	0.12	0.24°	1	
Handgrip strength	0.24	0.19	0.18	-0.06	-0.10	-0.12	-0.20°	0.02	1
Plate tapping	0.07	-0.09	-0.06	0.019	-0.02	-0.25°	-0.02	0.15	-0.17

High correlation coefficients Moderate correlation coefficients Low correlation coefficients

Secondary upper limb outcome measures (in 66 participants)

#### °p<0.05

\*p<0.0001

	NHPT pegs/s	BBT	CRT turns/s	MALamount	MALhow	MAL total	MAM-36	ABILHAND
NHPT pegs/s	1							
BBT	0.87*	1						
CRT turns/s	0.78*	0.65*	1					
MALamount	0.41*	0.36*	0.34*	1				
MALhow	0.56*	0.46*	0.49*	0.70*	1			
MAL total	0.52*	0.44*	0.45*	0.93*	0.90*	1		
MAM-36	0.44*	0.40*	0.37*	0.31°	0.38*	0.36*	1	
ABILHAND	0.42*	0.35*	0.37*	0.29°	0.35*	0.34*	0.81*	1
ARAT	0.38°	0.30°	0.30°	0.10	0.30°	0.21	0.22	0.17

Table 4a. Spearman correlation coefficients between measures on activity level for dominant	han	a	r	r	I	г	lé	۱	h	ł		t	t	Ľ	า	r	ľ	a.	а	17	n	r	í	ıi	۱	ſ	n	n	r	n	r	)	С	C	10	ł	d	С	(	•	r	r	J	)	)	С	Э	С	fα	f	f	f	1	Ŀ	I	l	2	2	2	e	e	e	e	1	v	v	1	2	2	e	e	le	Ŀ		1	ı	ν		t١	t	it	'i	/	٧	i	t	t	С	٩f	ĉ	1	ſ	r	O		S	5	2	e	r	ır	J	u	L	51	S	S	15	а	а	а	2	22	2	e	e	16	h	n	γ	n	r	r	r	r	r	r	r	r	r	r	r	r	r	n	n	r	n	n	n	n	n	n	n	n	n
---	-----	---	---	---	---	---	----	---	---	---	--	---	---	---	---	---	---	----	---	----	---	---	---	----	---	---	---	---	---	---	---	---	---	---	----	---	---	---	---	---	---	---	---	---	---	---	---	---	----	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	----	---	--	---	---	---	--	----	---	----	----	---	---	---	---	---	---	----	---	---	---	---	---	--	---	---	---	---	---	----	---	---	---	----	---	---	----	---	---	---	---	----	---	---	---	----	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---

Very high correlation coefficient High correlation coefficient Moderate correlation coefficient Low correlation coefficient

Secondary upper limb outcome measures

#### °p<0.05

\*p<0.0001

#### Table 4b. Spearman correlation coefficients between measures on activity level for non-dominant hand

	NHPT pegs/s	BBT	CRT turns/s	MALamount	MALhow	MAL total	MAM-36	ABILHAND
NHPT pegs/s	1	_						
BBT	0.84*	1						
CRT turns/s	0.76*	0.67*	1					
MAL amount	0.56*	0.49*	0.53*	1				
MAL how	0.54*	0.41*	0.48*	0.66*	1			
MAL total	0.59*	0.48*	0.54*	0.88*	0.93*	1		
MAM-36	0.56*	0.46*	0.49*	0.46*	0.44*	0.49*	1	
ABILHAND	0.48*	0.36*	0.41*	0.37*	0.42*	0.43*	0.81*	1
ARAT	0.03	0.06	-0.02	0.03	0.08	0.08	0.05	-0.11

Very high correlation coefficient High correlation coefficient Moderate correlation coefficient Low correlation coefficient

Secondary upper limb outcome measures

°p<0.05

\*p<0.0001

Table 5a. Spearman correlation coefficients between measures on body function and structure level and activity level for the dominant hand

	CRT turns/s	BBT	NHPT	ARAT	MAM-36	5 ABILHAND	MALamount	MALhow	MAL total
Pinch grip Key	0.46*	0.32°	0.36*	-0.01	0.33°	0.37*	0.46*	0.42*	0.48*
Pinch grip Tripod	0.45*	0.40*	0.43*	-0.14	0.43*	0.42*	0.51*	0.49*	0.53*
Pinch grip Tip to tip	0.37*	0.32°	0.34°	-0.06	0.34°	0.30°	0.40*	0.37*	0.41*
VAS Spasticity	-0.18°	-0.23°	-0.24°	0.02	-0.33*	-0.26°	-0.48*	-0.39*	-0.47*
VAS Muscle weakness	-0.28°	-0.21°	-0.28°	-0.01	-0.31	-0.25°	-0.49*	-0.53*	-0.56*
VAS Sensory imp.	-0.26°	-0.08	-0.21°	0.04	-0.32*	-0.33*	-0.42*	-0.41*	-0.46*
VAS Coordination deficits	-0.33*	-0.31°	-0.39*	0.006	-0.29°	-0.27°	-0.51*	-0.64*	-0.64*
VAS Fatigue	-0.06	-0.003	-0.05	0.06	-0.26°	-0.21°	-0.24°	-0.17°	-0.24°
Handgrip strength	0.01	0.12	0.10	0.15	0.12	0.15	0.13	0.15	0.17
Plate tapping	-0.06	-0.02	-0.01	-0.32°	-0.05	0.01	-0.02	-0.15	-0.10
A A A A A A A A A A A A A A A A A A A									

Moderate correlation Low correlation

Secondary upper limb outcome measures

°p<0.05

#### \*p<0.0001

Table 5b. Spearman correlation coefficients between measures on body function and structure level and activity level for the non-dominant hand

	CRT turns/	s BBT	NHPT	ARAT	MAM-36	ABILHAND	MALamount	MALhow	MAL total
Pinch grip Key	0.46*	0.37*	0.34*	0.33°	0.27°	0.36*	0.23°	0.28°	0.28°
Pinch grip Tripod	0.40*	0.35*	0.32°	0.38°	0.22°	0.29°	0.28°	0.28°	0.30°
Pinch grip Tip to tip	0.40*	0.35*	0.31°	0.30°	0.11	0.15	0.27°	0.24°	0.28°
VAS Spasticity	-0.29°	-0.40*	-0.32°	-0.28°	-0.32°	-0.35*	-0.35*	-0.43*	-0.43*
VAS Muscle weakness	-0.35*	-0.37*	-0.44*	-0.30°	-0.34*	-0.40*	-0.36*	-0.54*	-0.48*
VAS Sensory imp.	-0.20°	-0.20°	-0.25°	-0.17	-0.22°	-0.32°	-0.28°	-0.37*	-0.34*
VAS Coordination deficits	-0.37*	-0.39*	-0.49*	-0.18	-0.34*	-0.42*	-0.31°	-0.47*	-0.41*
VAS Fatigue	-0.07	-0.08	-0.03	0.02	-0.26°	-0.21°	-0.13	-0.19°	-0.17°
Handgrip strength	0.19	0.19	0.25°	0.36°	0.25°	0.35°	0.07	0.11	0.09
Plate tapping	0.04	-0.04	-0.03	-0.35°	-0.07	-0.03	-0.02	-0.07	-0.04

Moderate correlation Low correlation

Secondary upper limb outcome measures

#### °p<0.05

\*p<0.0001

#### 3.3 Floor effects

The maximum and minimum scores for each test and the number of participants reaching these score are given in Table 6. Possible floor effects were found in the VAS Spasticity, VAS Sensory impairment and VAS Coordination deficits, where more than 15% of the participants reached the lowest possible score of zero out of ten for both hands. The VAS Muscle weakness (12.5% D-hand and 11% ND-hand) and VAS Fatigability (11.8%) are on the edge of a floor effect. The scores on the NHPT, CRT and BBT of participants that reached a floor effect in the VAS Spasticity, VAS Sensory impairment and VAS Coordination deficits are presented in Table 7 in Appendix. For the dominant hand, the scores on the NHPT varied from 0.15 to 0.44 pegs/s with a median score of 0.325 pegs/s. The CRT scores ranged from 0.20 to 1.43 turns/s with a median score of 44 blocks in one minute. For the non-dominant hand, the scores on the NHPT varied from 0.17 to 0.47 pegs/s with a median score of 0.61 turns/s. The BBT presented scores from 27 to 67 blocks with a median of 37 blocks in one minute.

Another floor effect was present in the CRT for both hands (20.6% D-hand and 22.1% ND-hand). Scores on the NHPT and BBT of the participants with a minimum score on the CRT for both hands are presented in Table 8 in Appendix. For the dominant hand, the scores of the BBT ranged from 5 to 50 blocks with a median score of 25 blocks in one minute. The scores of the NHPT ranged from 0.03 to 0.32 pegs/s with a median score of 0.30 pegs/s. For the non-dominant hand, the scores of the BBT ranged from 0 to 47 blocks with a median score of 24 blocks in one minute. The NHPT scores ranged from 0.03 to 0.34 pegs/s with a median score of 0.24 pegs/s. EDSS scores ranged from 5 to 8.5 for the dominant hand and from 3.5 to 8.5 for the non-dominant hand with a median of 6.

#### 3.4 Ceiling effects

Ceiling effects were present in the MAL amount (46.3% of the participants), MAL how (17.6% of the participants) and in the MAL total (16.2% of the participants) only for the dominant hand. The ARAT is on the edge of a ceiling effect (12.1% D-hand and 10.6% ND-hand). Table 9 in Appendix presents the scores of the MAM-36 and ABILHAND from participants that reached a ceiling effect in the MAL subscales for the dominant hand. The scores for the MAM-36 ranged from 43 to 144 with a median score of 130.

The scores for the ABILHAND ranged from 7 to 52 with a median score of 41. The EDSS scores ranged from 1.5 to 8.5 with a median score of 6.

Test	Minimum score	n (D/ND)	% (D/ND)	Number participants scoring minimum with both hands	Maximum score	n (D/ND)	% (D/ND)	Number participants scoring maximum with both hands
VAS Spasticity	0	68 57	50 41.9	47	10	1 0	0.7 0	0
VAS Muscle weakness	0	17 15	12.5 11	6	10	2 4	1.5 2.9	0
VAS Sensory imp.	0	28 22	20.6 16.2	13	10	25	1.5 3.7	1
VAS Coordination deficits	0	27 21	19.9 15.4	9	10	47	2.9 5.1	2
VAS Fatigue	0	16	11.8		10	2	1.5	
NHPT pegs/s	0	0 0	0 0	0	*			
CRT turns/s	0	28 30	20.6 22.1	16	*			
MAM-36	0	0	0		144	3	2.2	
ABILHAND	0	0	0		52	1	0.7	
MAL amount	0	1 1	0.7 0.7	0	5	63 4	46.3 2.9	18
MAL how	0	0 1	0 0.7	0	5	24 3	17.6 2.2	4
MAL total	0	0 1	0 0.7	0	10	22 3	16.2 2.2	3
Plate tapping (sec)	0	1 1	1.5 1.5	1	*			
ARAT	0	3 5	4.5 7.5	3	57	87	12.1 10.6	6

Table 6. Floor and ceilings effects

D: Dominant hand; ND: Non-dominant hand

>15% of participants >10% and < 15% of participants

Secondary upper limb outcome measures

\* There is no defined upper limit for these measures. The higher the score, the better

#### 4. Discussion

The aim of this study was to investigate the validity and floor/ceiling effect of new and frequently used upper limb outcome measures in PwMS.

#### 4.1 Measures on body function and structure level

High correlation coefficients were found between the different Pinch grip formations (0.72-0.83, p<0.0001). The magnitude of these correlations suggest that when the score on one item is high, the scores on the other items will also be high and that they measure the same construct. Chen CC et al.,2007 found high correlations between the Pinch grip formations: Grip, Tip, Lateral and Palmar for both hands (range R= 0.70-0.82,  $p\le0.01$ ) in 44 patients with MS (EDSS score ranged from 2.5 to 8.5). It is possible that conducting one of the Pinch grip formations is enough to give an idea of the participant's pinch grip strength. Therapists should choose the Pinch grip formation which is most responsive to changes in PwMS.

Low correlation coefficients were found between the different Pinch Grip formations and VAS subscales (range R= -0.47- -0.12, not significant), this suggests that these measures focus on different constructs. The low correlation may be explained by the fact that the VAS is a subjective measure which is compared with an objective measure of strength. We expected to find higher correlations between the VAS muscle weakness and the strength measures. This could not be confirmed in our study, neither by other studies.

This study revealed a floor effect in the VAS Spasticity, VAS Sensory impairment and VAS Coordination deficits for both hands. The floor effect for the VAS can be explained by the fact that these scales are difficult for participants to judge. There is no guideline concerning what is actually meant by a score of four or seven out of ten (the meaning of a score of zero and ten is described). Paul-Dauphin et al. 1999, conducted six types of VAS with two orientations on 870 subjects and found that subjects with no symptoms are assumed to rate without mistakes. While subjects with weak symptoms are likely to wrongly rate zero.

We don't recommend to perform VAS subscales in PwMS in future research because of the presence of a floor effect. Instead, objective measures should be included.

#### 4.2 Measures on activity level

#### Capacity

On activity level Capacity, high correlation coefficients were found between the NHPT and the BBT (R= 0.87 D-hand and R=0.84 ND-hand, p<0.0001) and between the NHPT and the CRT

(R= 0.78 D-hand and R=0.76 ND-hand, p<0.0001). CRT and BBT were moderately correlated (R= 0.65 D-hand and R= 0.67 ND-hand, p<0.0001). Goodkin DE. et al 1988, found similar correlations between the NHPT and BBT (R= -0.70) in PwMS. Although these results suggest that the NHPT and BBT may be interchangeable, the study of Goodkin DE et al. 1988 revealed that each measure (NHPT or BBT) was able to detect changes that the other test failed to detect. Therefore, Goodkin DE et al. 1988, recommends to administer both tests, since neither is as sensitive as the combined results. They also found that the prevalence of upper extremity functional impairment in MS is significantly higher, when measured by the NHPT and BBT then when using the EDSS as an indicator of disability. This can be explained by the fact that the EDSS mostly focus on lower limb function in daily living. Disturbances in the upper limb function is only mentioned from a score of 8.5 in the EDSS (Kurtzke JF. 1983).

The measures on Capacity assess the manual dexterity and require manipulation of an object (peg, coin or block), this was performed unilaterally with the dominant and non-dominant hand. These measures can be difficult to perform in patients with severe upper limb dysfunction, especially if they have an impaired distal upper limb function. The CRT presented a floor effect (20.6% D-hand and 22.1% ND-hand), which suggests that the measure was too difficult to perform for more than 20% of the included participants. The CRT measures rapid precise coordinated finger movements that are needed to manipulate small objects. While the NHPT and BBT, mainly assess precision of arm movements, motor grasp and release skills of the hand (Heldner et al 2014 and Yancosek et al 2009). Because of the presence of a floor effect in the CRT, we suggest that NHPT or BBT should be conducted in PwMS on activity level Capacity. A choice between NHPT or BBT should be made dependent on their responsiveness in PwMS.

#### Perceived performance

On activity level Perceived performance, a high correlation coefficient was found between the MAM-36 and ABILHAND (R=0.81 p<0.0001). The high correlation between these measures can be explained by the fact that there is an overlap between the items these measures use to evaluate the manual ability (e.g. cutting one's nails, fastening a zipper, spreading butter on a slice of bread). This study is, according to our knowledge, the first one to review the construct validity between the ABILHAND and the MAM-36. Ceiling effects were found in the MAL amount, (46.3% of the participants), MAL how (17.6%) and in the MAL total (16.2%) for the dominant hand. Barrett et al. 2013, found a floor effect in the ABILHAND in 300 PwMS.

The difference in the findings between Barret et al. 2013 and our study can be allocated to the use of different percentages for determination of a floor effect. Barret et al. 2013 used a cut-off value of 3% for a floor effect while our study used a cut-off of 15%. Based on the findings of this study, we suggest to conduct the ABILHAND or the MAM-36 on activity level Perceived performance in future research. However, therapists should choose between these measures considering the responsiveness in PwMS.

#### Capacity versus Perceived performance

When comparing Capacity (NHPT, BBT, CRT and ARAT) with Perceived performance measures (ABILHAND, MAM-36, MAL), moderate correlation coefficients were found between MAL subscores and the NHPT for both hands. The results of our study are in line with the results of Lamers I. et al 2014, where moderate to high correlation coefficients were found between the NHPT and MAL (range R= -0.81- -0.51, p<0.01) in 30 wheelchair-bound MS patients. The MAM-36 showed low to moderate correlation coefficients with NHPT, CRT and BBT for both hands. This finding corresponds with the finding of Lamers et al. 2015, where a moderate correlation coefficient was found for the total group between the NHPT and the MAM-36 in 105 patients with MS. The ABILHAND was low correlated with the NHPT, BBT and CRT for both hands. The low correlations could be explained by the fact that the ABILHAND includes bilateral task in contrast to the NHPT and that NHPT mainly assesses precision of arm movements, while the ABILHAND assesses manual ability in daily activities. Based on the correlation coefficients between Capacity and Perceived performance, we may conclude that measures of these sublevels are concentrated on other aspects of the upper limb function. We suggest that measures of both levels should be conducted to fully understand the upper limb function on activity level in PwMS.

#### 4.3 Measures on body function and structure level and activity level

When comparing outcome measures on body function and structure level and activity level Capacity, only low correlations were found between the different measures. According to our knowledge, these findings could not be confirmed by literature. After comparing outcome measures on body function and structure level and activity level Perceived performance, we found moderate correlation coefficients for the Pinch Tripod and the MAL subscores for the dominant hand. The VAS Muscle weakness was moderately correlated with the MAL how for both hands and the MAL total for the dominant hand. The VAS Coordination deficits showed moderate correlation coefficients with the MAL subscores for the dominant hand.

According to our knowledge, none of these findings could be confirmed by other studies. Handgrip strength and Plate tapping correlated low with the measures on activity level for both hands. The study of Chen CC. et al 2007, also found low correlations between the handgrip strength and MAM-36 for both hands (range R= 0.33-0.36, p≤0.05) in 44 community-dwelling PwMS. A possible explanation for these low correlations could be that the MAM-36 requires finger strength and dexterity, while the Handgrip strength only measures strength. In contrast to our results, the study of Lamers I. et al, 2014 found moderate correlations between the handgrip strength and MAL subscales (range R= 0.51-0.67, p<0.01) for both hands in 30 wheelchair-bound MS. The correlations found between body function and structure level and activity level suggests that measures on activity level. We suggest that measures of body function and structure level and activity level (Capacity and Perceived performance) should be included in further research in PwMS.

#### 4.4 Study limitations

First, the secondary upper limb outcome measures (ARAT, Plate tapping and Handgrip strength) were only conducted in 66 PwMS, while the primary upper limb outcome measures were conducted in 136 PwMS. The lower number of participants performing the secondary outcome measures could make these results less representative. Second, this study included data of different participating centers across Europe which could lead to little differences. These differences are kept to a minimum by using a standardized instruction booklet and uniform scoring sheets.

#### 4.5 Recommendations for future research and conclusion

In future research, therapists should choose for the Pinch grip formation which is more responsive to change in PwMS. We suggest to include objective measures instead of VAS scales to assess the level of impairment on body function and structure level. A decision should also be made between the NHPT or BBT and between the ABILHAND or MAM-36 on activity level, depending on other psychometric properties. In research in PwMS, it is important to include upper limb outcome measures on different levels of the ICF, with a distinction between Capacity and Perceived performance on activity level, to fully understand the upper limb function. Which measures should be conducted on each level is dependent on their psychometric properties, the upper limb disability level of the participants and the clinical utility of these measures.

#### 5. References

- Arwert HJ, Keizer S, Kromme C, Thea P.M, Vlieland V, Meesters J. The validity of the Michigan Hand Outcomes Questionnaire in stroke participants. *Archives of physical medicine and rehabilitation* 2015 September, 10.1016/j.apmer.2015.09.018
- Barrett L, Cano S, Zajicek J, Hobart J. Can the ABILHAND handle manual ability in MS? *Mult Scler* 2013 May; 19(6): 806-15.
- Bertoni MA, Sakel M, Hojjattoleslami A, Bertoni IV, Ratnarajah N. Neuroimaging assessment of spasticity developed after acquired brain injuries and Multiple Sclerosis. *The Neuroradiology Journal* 2012; 25: 311-317.
- Boonstra AM, SchiphorstPreuper H.R., Reneman M.F., Posthumus, J.B., Stewart R.E., Reliability and validity of the visual analogue scale for disability in participants with chronic musculoskeletal pain. *J Rehabil Res* 2008: 165-69.
- Chen CC, Bode RK. Psychometric validation of the Manual Ability Measure-36 (MAM-36) in participants with neurologic and musculoskeletal disorders. *Arch Phys Med Rehabil* 2010 March;91(3):414-20.
- Chen CC, Kasven N, Karpatkin HI, Sylvester A. Hand strength and perceived manual ability among participants with multiple sclerosi-s. *Arch Phys Med Rehabil* 2007 June;88(6):794-7.
- Connell LA, Tyson SF. Clinical reality of measuring upper-limb ability in neurologic conditions: a systematic review. *Arch Phys Med Rehabil* 2012 February;93(2):221-8.

Cramer D.; Howitt D. The SAGE Dictionary of Statistics, 2004.

- Cutter GR, Baier ML, Rudick RA, Cookfair DL, Fischer JS, Petkau J, Syndulko K, Weinshenker BG, Antel JP, Confavreux C, Ellison GW, Lublin F, Miller AE, Rao SM, Reingold S, Thompson A, Willoughby E. Development of a multiple sclerosis functional composite as a clinical trial outcome measure. *Brain* 1999 May;122 (Pt 5):871-82.
- Farrar JT, Troxel AB, Stott C, Duncombe P, Jensen MP. Validity, reliability, and clinical importance of change in a 0-10 numeric rating scale measure of spasticity: a post hoc analysis of a randomized, double-blind, placebo-controlled trial. *Clin Ther* 2008 May;30(5):974-85.

- Gjelsvik B, Breivik K, Verheyden G, Smedal T, Hofstad H, Strand LI. The Trunk Impairment Scale modified to ordinal scales in the Norwegian version. *Disabil Rehabil* 2012;34(16):1385-95.
- Goodkin DE, Hertsgaard D, Seminary J. Upper extremity function in multiple sclerosis: improving assessment sensitivity with box-andblock and nine-hole peg tests. Arch Phys Med Rehabil 1988;69:850-4.
- Heldner MR., Vanbellingen T., Bohlhalter S., Mattle HP., Müri RM., Kamm CP., Coin rotation task: a valid test for manual dexterity in multiple sclerosis. *Phys. Ther.* 2014 November; 94 (11):1655-51.
- Holper L, Coenen M, Weise A, Stucki G, Cieza A, Kesselring J. Characterization of functioning in multiple sclerosis using the ICF. *J Neurol* 2010 January;257(1):103-13.
- Johansson S, Ytterberg C, Claesson IM, Lindberg J, Hillert J, Andersson M, Widen HL, von KL. High concurrent presence of disability in multiple sclerosis. Associations with perceived health. *J Neurol* 2007 June;254(6):767-73.
- Kamm CP, Heldner MR, Vanbellingen T, Mattle HP, Muri R, Bohlhalter S. Limb apraxia in multiple sclerosis: prevalence and impact on manual dexterity and activities of daily living. *Arch Phys Med Rehabil* 2012 June;93(6):1081-5.
- Kheder A., NAIR KPS. Spasticity: pathofysiology, evaluation and management. *Practical Neurology* 2012 October; 12(5): 289
- Kumar N, Khan M, Singh N, Singh S. Impact of smoking on speed and coordination of upper limb movement. *Addict Health* 2014 Summer-Autumn; 6 (3-4): 155-58.
- Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology* 1983 November;33(11):1444-52.
- Lamers I, Cattanea D, Chen CC, Bertoni R, Van Wijmeersch B, Feys P. Associations of Upper Limb
   Disability Measures on Different Levels of the International Classification of Functioning,
   Disability and Healt in People With Multiple Sclerosis. *Physical Therapy*, 2015; Vol 95 (1):
   65-75.

- Lamers I, Kelchtermans S, Baert I, Feys P. Upper limb assessment in multiple sclerosis: a systematic review of outcome measures and their psychometric properties. *Arch Phys Med Rehabil* 2013;accepted.
- Lamers I, Kerkhofs L, Raats J, Kos D, Van Wijmeersch B, Feys P. Perceived and actual arm performance in multiple sclerosis: relationship with clinical tests according to hand dominance. *Mult Scler.*, 2014.
- Learmonth YC, Motl RW, Sandroff BM, Pula JH, Cadavid D. Validation of participant determined disease steps (PDDS) scale scores in persons with multiple sclerosis. *BMC Neurol* 2013 April 25;13(1):37.
- Lemmens RJ, Timmermans AA, Janssen-Potten YJ, Smeets RJ, Seelen HA. Valid and reliable instruments for arm-hand assessment at ICF activity level in persons with hemiplegia: a systematic review. *BMC Neurol* 2012;12:21.
- Mark VW, Taub E, Bashir K, Uswatte G, Delgado A, Bowman MH, Bryson CC, McKay S, Cutter GR. Constraint-Induced Movement therapy can improve hemiparetic progressive multiple sclerosis. Preliminary findings. *Mult Scler* 2008 August;14(7):992-4.
- Marrie RA, Goldman M. Validity of performance scales for disability assessment in multiple sclerosis. *Mult Scler* 2007 November;13(9):1176-82.
- Mathiowetz V, Volland G, et al. Adults norms for the Box and Block Test of manual dexterity. *J* OccupTher 1985: 386-91.
- McDowell I. Measuring health: a guide to rating scales and questionnaires. New York: Oxford Univ. Pr; 2006.
- O'Dell M, Grace K, Rivera L, Fieo R, Christos P, Polistena C, Fitzgerald K, Gorga D. A psychometric evaluation of the arm motor ability test. *J Rehabil Med* 2013 June; 45(6): 519-27.
- Paternostro-Sluga T., Grim-Stieger M., Posch M., Schuhfried O., Vacariu G., Mittermaier C., Bittner
  C., Fialka-Moser V. Reliability and validity of the Medical Research Council (MRC) scale and
  a modified scale for testing muscle strength in patients with radial palsy. *Rehabil. Med.*2008; 40: 665-671.

- Paul-Dauphin A., Guillemin F., Virion JM., Braincon S., Bias and precision in Visual Analogue Scales:
   A Randomised Controlled Trail. *American Journal od Epidemiology* 1999 Vol 150 (10): 1117-1127.
- Penner IK, Raselli C, Stocklin M, Opwis K, Kappos L, Calabrese P. The Fatigue Scale for Motor and Cognitive Functions (FSMC): validation of a new instrument to assess multiple sclerosisrelated fatigue. *Mult Scler* 2009 December;15(12):1509-17.
- Platz T, Pinkowski C, van WF, Kim IH, di BP, Johnson G. Reliability and validity of arm function assessment with standardized guidelines for the Fugl-Meyer Test, Action Research Arm Test and Box and Block Test: a multicentre study. *Clin Rehabil* 2005 June;19(4):404-11.
- Simone A., Rota V., Tesio L., Perucca L., Generic ABILHAND Questionnaire can measures manual ability across a variety of motor impairments. *International Journal of Rehabilitation Research*, 2011, Vol.34(2), p.131-140.
- Smith A. Symbol digit modalities test: Manual. 1982.

Taub E., McCulloch K., Uswatte G., Morris D. Motor Activity Log (MAL) Manual. 2011

- Terwee C, Bot S, de Boer M, van der Windt D, Knol D, Dekker J, Bouter L, de Vet H. Quality criteria were proposed for measurement properties of health status questionnaires. *J Clinical Epidemiology* 2006 March; 29; (60): 34-42.
- Trampisch US, Franke J, Jedamzik N, Hinrichs T, Platen P. Optimal Jamar dynamometer handle position to assess maximal isometric hand grip strength in epidemiological studies. *J Hand Surg Am* 2012 November;37(11):2368-73.
- Velstra IM, Ballert CS, Cieza A. A systematic literature review of outcome measures for upper extremity function using the international classification of functioning, disability, and health as reference. *PM R* 2011 September;3(9):846-60.
- Yancosek KA., Howell D. A narrative review of dexterity assessments. *Journal of hand therapy* 2009, 22: 258-70.

Yozbatiran N, Baskurt F, Baskurt Z, Ozakbas S, Idiman E. Motor assessment of upper extremity function and its relation with fatigue, cognitive function and quality of life in multiple sclerosis participants. *J Neurol Sci* 2006 July 15;246(1-2):117-22.

## Appendix

	Minimu	ım scores (dom	inant hand)	Scores on a	ctivity level	(Capacity)
	VAS Spasticity	VAS Coordination	VAS Sensory impairments	NHPT pegs/s	CRT turns/s	BBT
Participant 1	0	0	0	0.31	0.73	
Participant 2	0	0	0	0.15	0.20	31
Participant 3	0	0	0	0.38	1.06	45
Participant 4	0	0	0	0.38	0.66	47
Participant 5	0	0	0	0.42	1.42	49
Participant 6	0	0	0	0.30	0.69	47
Participant 7	0	0	0	0.30	1.12	39
Participant 8	0	0	0	0.32	1.10	43
Participant 9	0	0	0	0.35	0.65	44
Participant 10	0	0	0	0.31	0.33	37
Participant 11	0	0	0	0.24	0.92	43
Participant 12	0	0	0	0.33	0.89	41
Participant 13	0	0	0	0.44	1.43	64
Participant 14	0	0	0	0.23	0.60	39
Participant 15	0	0	0	0.21	0.48	33
Participant 16	0	0	0	0.44	0.67	66
Participant 17	0	0	0	0.44	1.10	56
Participant 18	0	0	0	0.40	1.10	49
Median	0	0	0	0.325	0.810	44

Table 7. Scores on activity level (Capacity) after reaching minimum scores for VAS
Spasticity, VAS Coordination defecits and VAS Sensory impairments.

	Minimum	scores (non-do	ominant hand)	Scores on activity level (Capacity)		
	VAS Spasticity	VAS Coordination	VAS Sensory impairments	NHPT pegs/s	CRT turns/s	BBT
Participant 2	0	0	0	0.21	0.17	37
Participant 14	0	0	0	0.28	0.74	41
Participant 15	0	0	0	0.24	0.60	33
Participant 19	0	0	0	0.34	0.84	48
Participant 20	0	0	0	0.47	0.75	67
Participant 21	0	0	0	0.31	1.16	45
Participant 22	0	0	0	0.17	0.36	34
Participant 23	0	0	0	0.20	0.49	33
Participant 26	0	0	0	0.22	0.61	27
Median	0	0	0	0.24	0.61	37

Note: participant 2, 14 and 15 were the same participants for the dominant and nondominant hand.

Dominant nand			-	11011-0	omman	t Hallu			
	CRT	BBT	NHPT	EDSS		CRT	BBT	NHPT	EDSS
Participant 1	0		0.17	7	Participant 1	0		0.04	7
Participant 2	0		0.22	8.5	Participant 2	0		0.03	8.5
Participant 3	0		0.21	8.5	Participant 3	0		0.03	8.5
Participant 4	0	18	0.03	7	Participant 5	0	44	0.24	6
Participant 5	0	37	0.26	6	Participant 7	0	37	0.34	7
Participant 6	0	52	0.32	6	Participant 9	0	6	0.03	7.5
Participant 7	0	25	0.08	6.5	Participant 10	0	32	0.21	8
Participant 8	0	30	0.13	7	Participant 11	0	6	0.04	8
Participant 9	0	37	0.30	7.5	Participant 17	0	32	0.15	8
Participant 10	0	33	0.14	8	Participant 19	0	19	0.10	8
Participant 11	0	25	0.13	8	Participant 20	0	40	0.24	5
Participant 12	0	17	0.13	6.5	Participant 23	0	17	0.03	6
Participant 13	0	21	0.09	7.5	Participant 24	0	20	0.12	7.5
Participant 14	0	50	0.29	6.5	Participant 25	0	29	0.06	6.5
Participant 15	0	5	0.03	8	Participant 26	0	25	0.13	7
Participant 16	0	30	0.14	4.5	Participant 27	0		0.03	8.5
Participant 17	0	25	0.09	8	Participant 28	0		0.11	6.5
Participant 18	0	33	0.19	6.5	Participant 29	0	47	0.30	7
Participant 19	0	22	0.06	8	Participant 30	0	24	0.07	6.5
Participant 20	0	43	0.24	5	Participant 31	0	24	0.05	6.5
Participant 21	0	16	0.04	6.5	Participant 32	0	0	0.03	7.5
Participant 22	0	16	0.09	6.5	Participant 33	0	17	0.04	5
Participant 23	0	20	0.03	6	Participant 34	0	12	0.03	7.5
Participant 24	0	19	0.08	7.5	Participant 35	0	25	0.18	3.5
Participant 25	0	24	0.08	6.5	Participant 36	0	24	0.03	6
Participant 26	0	38	0.16	7	Participant 37	0	17	0.03	6.5
Median	0	25	0.30	6	Participant 38	0	36	0.19	6.5
					Participant 39	0	28	0.19	7.5
					Participant 40	0	33	0.13	4.5
					Participant 41	0	12	0.03	7
					Participant 42	0	0	0.03	7
					Participant 43	0	36	0.22	6.5
					Median	0	24	0.24	6

 Table 8. Scores on BBT and NHPT after reaching minimum scores for CRT for both hands

 Dominant hand
 Non-dominant hand

Note: participant 1, 2, 3, 5, 7, 8, 9, 10, 11, 17, 19, 20, 23, 24, 25 and 26 were the same for dominant and non-dominant hand

	Maximu	ım scores (domi	inant hand)	Scores on MAM-36, ABILHAND (dominant hand)			
	MAL how	MALamount	MAL total	MAM-36	ABILHAND	EDSS	
Participant 1	5	5	10	80	13	8.5	
Participant 2	5	5	10	43	7	8.5	
Participant 3	5	5	10	126	41	6.5	
Participant 4	5	5	10	134	39	6.5	
Participant 5	5	5	10	70	29	6.5	
Participant 6	5	5	10	132	45	6	
Participant 7	5	5	10	132	45	6	
Participant 8	5	5	10	104	37	6.5	
Participant 9	5	5	10	132	51	6.5	
Participant 10	5	5	10	128	41	6.5	
Participant 11	5	5	10	126	33	6.5	
Participant 12	5	5	10	102	34	7.5	
Participant 13	5	5	10	132	46	7	
Participant 14	5	5	10	142	47	5.5	
Participant 15	5	5	10	140	50	6	
Participant 16	5	5	10	124	41	5	
Participant 17	5	5	10	134	47	6	
Participant 18	5	5	10	139	51	6	
Participant 19	5	5	10	125	42	4	
Participant 20	5	5	10	126	39	4	
Participant 21	5	5	10	144	50	1.5	
Participant 22	5	5	10	121	26	4.5	
Participant 23	5	5	10	143	52	2	
Participant 24	5	5	10	117	30	4	
Participant 25	5	5	10	103	33	4.5	
Median	5	5	10	130	41	6	

Table 9. Scores on MAM-36 and ABILHAND after reaching maximum scores for MAL how, MAL amount and MAL Total

# Auteursrechtelijke overeenkomst

Ik/wij verlenen het wereldwijde auteursrecht voor de ingediende eindverhandeling: Validity and floor/ceiling effects of upper limb outcome measures in people with Multiple Sclerosis: an European RIMS multi-center study

Richting: master in de revalidatiewetenschappen en de kinesitherapie-revalidatiewetenschappen en kinesitherapie bij inwendige aandoeningen Jaar: 2016

in alle mogelijke mediaformaten, - bestaande en in de toekomst te ontwikkelen - , aan de Universiteit Hasselt.

Niet tegenstaand deze toekenning van het auteursrecht aan de Universiteit Hasselt behoud ik als auteur het recht om de eindverhandeling, - in zijn geheel of gedeeltelijk -, vrij te reproduceren, (her)publiceren of distribueren zonder de toelating te moeten verkrijgen van de Universiteit Hasselt.

Ik bevestig dat de eindverhandeling mijn origineel werk is, en dat ik het recht heb om de rechten te verlenen die in deze overeenkomst worden beschreven. Ik verklaar tevens dat de eindverhandeling, naar mijn weten, het auteursrecht van anderen niet overtreedt.

Ik verklaar tevens dat ik voor het materiaal in de eindverhandeling dat beschermd wordt door het auteursrecht, de nodige toelatingen heb verkregen zodat ik deze ook aan de Universiteit Hasselt kan overdragen en dat dit duidelijk in de tekst en inhoud van de eindverhandeling werd genotificeerd.

Universiteit Hasselt zal mij als auteur(s) van de eindverhandeling identificeren en zal geen wijzigingen aanbrengen aan de eindverhandeling, uitgezonderd deze toegelaten door deze overeenkomst.

Voor akkoord,

Hendrickx, Tina