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Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

Upper Limb Dysfunction in Multiple Sclerosis: A Follow-up Study

Helena Gilson
Mats Hamaekers

Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie, afstudeerrichting revalidatiewetenschappen en kinesitherapie bij neurologische aandoeningen

PROMOTOR :
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Context

Our study investigates the long-term effects of MS, specifically on the upper limb (UL). Upper limb dysfunction has a crucial role in the daily functioning of people with MS (PwMS). There have not been a lot of longitudinal studies regarding this topic, therefore we set up this study in collaboration with dr. Lamers as a follow-up to an already existing study conducted by her and her team 10 years ago. By recruiting patients from the original study, an update and follow-up to the study 10 years ago could be set up with accurate follow-up data and by using the same methods of testing and assessing patients.

The objective of this study's protocol is to research the long-term effect of MS on the upper limb as well as to investigate specific predictors regarding disability to possibly assist in the creation of rehabilitation programs. This information can be very useful to set specific goals for rehabilitation and switch focus on different aspects of the disease in individual cases. The original study divided patients into groups, separated based on EDSS scores. This caused the sample and results to be more adaptable to the general population as groups became more homogeneous. Another specific differentiation was made in the outcome measures, grouping them according to their significant ICF-level. By sorting outcome measures this way conclusions could be made regarding which patients were more impaired on certain levels than others. The current study includes outcome measures on every level of the ICF to investigate which level(s) suffer(s) the biggest decrease in scores according to their significant outcome measures and which outcome measures remain relatively stable after 10 years.

The testing moments of this study were entirely conducted in the Noorderhart Rehabilitation and MS Center in Pelt, Belgium. As opposed to the original study, which was a multi-center study.

1. Abstract

1.1 Background A good upper limb (UL) function is crucial for daily functioning. There is a certain lack of studies regarding the longitudinal changes of UL functioning and predictors of upper limb disability on all ICF levels. Knowledge of these could help to better design specific rehabilitation programs tailored to individual patients and their goals.

1.2 Objectives: The objective of the study was to investigate long-term effects of MS on the upper limb on the different levels of the ICF and to determine possible predictors of disability.

1.3 Participants: 7 people participated in the study, they all had a form of Multiple Sclerosis with varying EDSS-scores.

1.4 Measurements: Outcome measures on all levels of the ICF were conducted. On the *Body functions and structures level* the Visual Analog Scale (VAS), Motricity Index (MI), Hand grip Strength, Modified Ashworth Scale (MAS), Active Range of Motion (AROM) for wrist extension and the Roylan Monofilaments Test (RMT) were conducted. Next, on the *Activity level* the Guy's Neurological Disability Scale (GNDS), Manual Ability Measure (MAM-36), Nine-Hole Peg Test (NHPT), Action Research Arm Test (ARAT) were completed by patients. Lastly, on the *Participation level* only the Community Integration Questionnaire (CIQ) was conducted. Additionally, the Hospital Anxiety and Depression Scale (HADS) and the Multiple Sclerosis Self-Management scale-revised (MSSM-r) were used to assess possible influencing factors.

1.5 Results: On group level, the mean CIQ score changed significantly compared to 10 years ago. A significant correlation between CIQ score and the MSSM-r was also found. Generally, all other outcome measures did not significantly change compared to baseline but individually, scores on the body structures and functions level decreased on almost all outcome measures.

1.6 Conclusion: The self-management of MS has an impact on the participation level of the disease. On the body structures and functions level, scores generally decreased after 10 years, but not significantly. On the activities level, outcome measures do not tend to decrease in score.

1.7 Keywords: Multiple Sclerosis; Upper Limb Dysfunction

2. Introduction

Multiple Sclerosis (MS) is known as one of the most prevalent chronic inflammatory diseases of the central nervous system[1]. According to Green et al. (2017), the symptom that contributes the most to the perception of health is pain, followed by gait dysfunction and fatigue[2]. In addition, the influence of upper limb dysfunctions cannot be overlooked. About 66% of people with MS (PwMS) have significant upper limb motor impairments that affect their performance of daily life activities (ADL activities)[3].

MS causes impairments on the international classification of functioning, disability and health (ICF) body function and structure level, such as muscle weakness, impaired coordination, sensory dysfunction. These impairments lead to disability on ICF activity and participation level. A decline in manual dexterity is strongly associated with an overall deterioration of upper limb activity and a disuse of the upper limb during ADL activities in PwMS[4]. This decline of manual dexterity can be caused by a decrease in modularity and timing delay of activation in the wrist extensor muscles. In this research they also found that in advanced stages a decrease in modularity and timing delay of activation has been seen in the proximal muscles (anterior deltoid)[4]. On participation level, Cattaneo et al. (2017) described that pwMS may not always experience participation problems, and not in all domains of participation. The problems they experience are largely dependent on the severity of the disease. PwMS with an EDSS >7 experience participation restrictions in all domains, while persons with mild involvement reported no or only mild participation restrictions at home. Overall participation limitations were found to be more correlated with cognitive deficits than with balance and gait limitations, while hand dexterity was predominantly associated with participation restriction in home activities[5].

Almost 10 years ago, Lamers et al. (2015) and Bertoni et al. (2015) conducted a study investigating the associations of upper limb disability measures on different levels of the ICF in PwMS. The goal of their research was quantifying the relationships among different ICF levels so it may help clinicians to enhance upper limb rehabilitation strategies for people with MS[6,7]. Lamers et al. (2015), concluded that upper limb muscle strength is the most important impairment affecting capacity and perceived performance in daily life. Bertoni et al. (2015) found that uni-/bilateral upper limb abnormalities increased with overall disability at all levels of the ICF.

As has been concluded by Lamers et al. (2015) upper limb muscle strength is an important parameter in upper limb rehabilitation. An earlier longitudinal study in upper limb function in MS concluded that baseline grip strength and Nine-Hole Peg Test (NHPT) scores are good predictors for the change in their scores over a 2 year period[8]. The results showed that grip strength and NHPT scores worsened by 20% in 2 years' time. Newsome et al. (2019) also concluded that assessing hand dysfunction with a dynamometer and the NHPT could help improve the precision in detecting changes in hand function over time in PwMS[8]. This information might give us an insight in how to predict the evolution of hand function, so we can adjust the rehabilitation strategies as optimally as possible.

Another longitudinal study of Timmermans et al. (2020) investigated the evolution of hand function versus the evolution of walking capacity using the ARAT and NHPT. The results showed that only at a more advanced stage of the disease, patients start to experience progressive motor problems with their arm and hand function[9]. Timmermans et al. (2020) also reports that the NHPT changed significantly over 10 years' time. This is in line with the findings of Newsome et al. (2019). Up until now, there has been no exact research regarding the prediction of the evolution of hand function. Test procedures, such as the NHPT, seem to have an important clinical value regarding this subject[8,9].

The first objective of our current study is to investigate long-term effects of MS on the upper limb on the different levels of the ICF. This study will be trying to add to these findings using different measurements and a categorization based on the ICF. Secondly, prediction of upper limb disability can be a tremendous breakthrough in physical therapy rehabilitation strategies. If it is possible to predict the level of disability, then rehabilitation strategies can be adjusted when needed in order to have the best quality of life.

3. Methods

3.1 Participants

After getting permission from the METC to conduct the current study, the 50 subjects enrolled in the study of Lamers et al. (2015) and Bertoni et al. (2015)[6,7] were contacted and asked whether they were willing to participate in this follow-up study. Patients were only contacted by phone at the Noorderhart rehabilitation and MS center in Pelt to secure the patients contact details. If the subject had a MS relapse or treatment for a relapse in the last month prior to the data collection they were excluded. Subjects were also excluded if they suffered from other severe neurological, cognitive, orthopedic or rheumatic conditions that could possibly interfere with conducting the outcome measurements.

3.2 Study design

For this study, a cross-sectional study design was chosen. Different outcome measures on the different levels of the ICF were performed in 1 test session of 1.5 hours each. First general information about the patient was asked. Then all descriptive outcome measures were conducted. Subsequently all the remaining outcome measures were performed in a randomized order for both hands. All outcome measures were administered by the same investigator. To assess hand dominance of a person in everyday activities, the Edinburgh Handedness Inventory scale was used[10].

The following descriptive variables were collected: age, gender, height, weight, type of MS and disease duration. Furthermore EDSS scores administered by the treating neurologist were extracted from the medical record.

3.3 Outcome measures

Body functions and structures level. The Motricity index (MI) was used to assess overall upper limb strength (pinch grip, elbow flexion and shoulder abduction) [11]. Average maximal isometric hand grip strength was measured with the Jamar handheld dynamometer, the average was

taken from 3 trials of maximal grip strength in a recommended arm position[12]. To determine the active range of motion (AROM) of wrist extension (in degrees), a goniometer was used. The axis of the goniometer was positioned perpendicular to the wrist joint (triquetrum). The fixed segment of the goniometer was aligned with the midline of the ulna, and the moving segment was aligned with the fifth metacarpal. The examiner stabilizes the proximal joint component and then carefully moves the distal component of the joint through its entire available range of motion until reaching the end feel[13]. In this study, the median score of 3 trials was used. Tactile sensitivity was assessed with the Semmes-Weinstein monofilament Test[14], it was measured in the fingertip of the thumb. Five monofilaments with varying diameters were used. Muscle spasticity in the upper limb (shoulder adductors, elbow flexors and wrist flexor muscles), was evaluated with the Modified Ashworth Scale[15]. A score of 0 (no increase in muscle tone) to 4 (affected part(s) rigid in flexion or extension) was given to each movement, the maximum achievable score was 15. The Fahn Tremor Rating Scale was used to assess the intention tremor during a finger to nose movement, it consists of a 5-point scale (0 meaning no tremor and 4 meaning severe amplitude) [16]. Pain was measured using the Visual Analogue Scale (VAS). Worst and best pain scores were conducted using a grading system (0 = no pain, 10 = worst pain).

Activity level. Fine manual dexterity was assessed using the Nine Hole Peg Test (NHPT)[17]. Subjects took two trials to place and remove the 9 pegs from the board and their average score was taken. Their manual dexterity was calculated as pegs per second. The Action Research Arm Test (ARAT) was used to measure manual ability to handle various objects[18], with an achievable score of 0-57 (low scores indicate lower levels of upper limb functioning). The Manual Ability Measure (MAM-36) was included as a measure of perceived performance, it inquires about 36 Activities of Daily Living (ADL tasks) and the subjects perceived difficulty with performing them. Participants were asked to rate these activities on a 4-point scale (4 easy, 3 a little difficult, 2 very hard, 1 cannot be performed)[19]. Afterwards a total score was calculated and was converted into a Rash Score. 2 extra scales were added in comparison to the baseline study, namely the Multiple Sclerosis Self-Management scale-Revised (MSSM-R). It measures the healthcare provider relationship and communication, treatment adherence/barriers, social/family support, Multiple Sclerosis knowledge and information and health maintenance behavior. It consists of 24 items total, each scored on a 5-point scale (1 I

disagree completely to 5 I agree completely)[20]. The other is the Hospital Anxiety and Depression Scale (HADS), it measures the risk of possible anxiety or depressive disorders. The HADS is divided into two subscales, depression and anxiety. A score of more than 7 out of 21 on one of these subscales indicates a possible disorder[21].

Participation level. The Community Integration Questionnaire was used to assess 3 levels of participation (home integration, social integration and productive activity), the questions in these 3 subdomains add up to a maximum achievable score of 29 (a high score indicates a high level of integration)[22].

3.4 Data Analysis

Normal distribution of data was checked using one-way ANOVA. In case of normal distribution of the data *mean ± standard deviation* were reported. In case of a skewed distribution of the data *median (interquartile range)* was reported. A paired t-test or Wilcoxon signed rank test was used to assess longitudinal changes in response variables. To investigate correlation between influencing factors associated with upper limb and participation decline and outcome measures a univariate logistic model was used. All factors were entered in a multivariate logistic model, a pearson test was used to assess correlation or a spearman's rho for nonparametric data. *P*-Values were deemed significant when they were smaller than 0.05 and very significant at >0.01. A 7-point Likert Scale was used to measure patients self-perceived change in general health and arm-hand function.

4. Results

4.1 Recruitment

Out of 50 participants of the study 10 years ago, only seven participated again. The other participants dropped out due to loss of contact details (n=5), inability to participate because of pain or disability (n=4), unwillingness to participate again without particular reason (n=18) or unresponsiveness to invitation by phone calls or emails (n=10). Six patients from the original study are also deceased.

4.2 Patient characteristics

Table 1 shows the patient characteristics for every single participant and a group mean for both moments. Currently the oldest person with MS included in the study was 71 years old, while the youngest was only 43 years old. Disease duration ranges from 12 to 40 years. Where the EDSS score of 4 out of 7 participants (pt. 2,3,4,5) remained stable, the scores of only 2 patients (pt. 1,6) increased, and this with 2 points or more. Remarkably, the EDSS score of one participant (pt. 7) dropped by half a point after 10 years. All patients, except Pt. 7 progressed from relapsing-remitting MS to a secondary progressive form.

Table 1: **Patient baseline characteristics and demographics**

	Gender (F/M)		Age (years)		EDSS		Hand dominance (R/L/A)		Disease duration (years)		Type of MS (RR/SP/PP)		SDMT		Ambulation index	
	Baseline	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**
Pt. 1	F	F	59	69	4	6	R	R	2	12	SP	SP	32	46	2	4
Pt. 2	F	F	61	71	3	3	A	R	30	40	SP	SP	35	35	1	4
Pt. 3	F	F	55	65	6.5	6.5	R	R	25	35	SP	SP	30	40	5	6
Pt. 4	F	F	38	48	8	8	R	R	17	26	SP	SP	15	12	9	9
Pt. 5	M	M	33	43	3	3	L	L	8	18	RR	SP	31	53	0	2
Pt. 6	M	M	58	67	3	6.5	R	R	13	22	RR	SP	26	31	1	2
Pt . 7	F	F	42	52	3	2.5	R	R	9	19	RR	RR	52	50	0	2
Mean	5/2	5/2	49.42 ± 11.44	59.29 ± 11.32	3 (3/6.5)	5.07 ± 2.19	5/1/1	6/1/0	14.86 ± 9.89	25.80 ± 9.23	3/4/0	1/6/0	31.57 ± 11.08	38.14 ± 13.97	1 (0/5)	4.14 ± 2.61

Pt.: Patient F: Female; M: Male; EDSS: Expanded Disability Status Scale; R: Right; L: Left; A: Ambidextrous; MS: Multiple Sclerosis; RR: Relapsing-Remitting; SP: Secondary Progressive; PP: Primary Progressive; SMDT: Symbol Digit Modalities Test

* Values presented are: mean standard deviation ±, median + interquartile range ( ) or total sum of values / /

4.3 Experimental Measures

Tables 2, 3 and 4 show the scores on the different outcome measures for baseline and 10 years later arranged according to the different levels of the ICF. Table 2 contains scores for general outcomes table 3 contains outcome measures specifically for the dominant hand and table contains outcome measures for the non-dominant hand respectively.

Four patients (pt. 3,5,6,7) scored the maximum score of 100 on the Motricity index with their dominant hand at baseline and their scores did not decrease compared to 10 years ago. At baseline, 5 out of 7 patients (Pt. 1,3,4,5,7) had a better grip strength with their dominant hand. 10 years later only pt. 3 and pt. 5 have a better grip strength with their dominant hand compared with the non-dominant hand. Overall spasticity only slightly increased, with three participants (pt. 1,3,4) going from no spasticity in either hand to a slight increase in muscle tone (score 1) in one of both hands, the rest scored 0. Active Range Of Motion for wrist extension increased in all patients except for pt. 4, who lost 21-30 degrees of motion but follow-up data is missing for 3 of the participants (pt. 1,6,7). Follow-up data for the Roylan Monofilaments Test was also missing for 2 patients (pt. 6, 7). 3 out of the 5 remaining patients (pt. 2, 4, 5) kept their original scores for the RMT on the dominant hand. Only pt. 4 and 5 also kept their original score on the non-dominant hand. Lastly, VAS scores during the measuring moments changed drastically for 4 out of 7 participants (pt. 1,3,4,7), changing with a minimum of 6 compared to the previous testing moment. These drastic changes become very apparent in the graph (figure 5).

On the activity level of the ICF we found no large changes in NHPT or ARAT (Table 6). The baseline mean NHPT score (pegs/sec) for the total group was 0.34 ± 0.16, dropping slightly to 0.33 ± 0.16 after 10 years. ARAT score for the baseline total was 57 (55/57), median and interquartile range respectively. Looking at the specific trend lines (figure 1.1, 1.2) for the NHPT we see that mean pegs/sec did not increase for all patients after 10 years, because for some patients scores decreased, the mean score for the whole group remained relatively unchanged. Looking at the graphs for the ARAT (figure 2.1,2.2) we can see that the relatively small change in score after 10 years can be addressed to a ceiling effect being reached, as multiple patients achieved the maximum score of 57 for at least one of their hands (pt. 2,5,6,7) For the GNDS, data was missing for 3 patients (pt. 3,6,7), making it difficult to draw an overall conclusion. Therefore, this outcome measure is described in more detail in the *individual case*

results. The last test on the activity level is the MAM-36 (figure 6), mean score at baseline for the entire group was 69.07 ± 18.69, this dropped to 65.14 ± 20.12

The only test at the participation level of the ICF was the CIQ (figure 7), mean scores dropped over the course of 10 years from 16.07 ± 5.43 to 12.71 ± 4.31. Only Pt. 1 improved in her CIQ score, all other CIQ scores decreased after 10 years.

Table 5, 6 and 7 contain the results of the matched pairs test, this test was conducted to determine any significant changes in the overall scores on outcome measures. As for some tests follow-up or baseline data was missing, each time only all patients with scores for both baseline and follow-up were concluded in the analysis of a specific outcome measure (cf. AROM: n=4). The matched pairs test resulted in a significant change in scores on the Mobility GNDS, according to the Wilcoxon signed rank test. Scores for the CIQ also significantly changed when comparing baseline to 10 years later, but only according to the Wilcoxon signed rank test and not the paired t-test (both were conducted as the data for the CIQ was normally distributed). For all outcome measures specifically investigating the dominant or non-dominant hand, no significant differences were found between baseline and 10 years later.

To investigate possible influencing factors of disease evolution, the HADS and the MSSM-R were conducted (see Table 8). Both tests were only included in the current study so baseline test scores are unknown. Mean scores are 5 ± 3.70 and 6.86 ± 5.05 for the HADS subscales, scores above 7 suggest a possible anxiety or depression disorder. While mean scores are under 7, there are four outliers when we look at individual scores, who score more than 7 on at least one subscale. The MSSM-r mean score is 76.34 ± 3.89 for the group total. After using a multivariate method to determine correlations between outcome measurements and the possibly influencing factors (Table 9), a significant pearson correlation was found between MSSM-r score and the CIQ score. This result suggests that self-management of MS might have an influence on community integration, respectively. No other significant correlations were found.

Table 2: **Scores on general outcome measures for individual patients**

	Body functions and structures Level		**Activity Level**						**Participation Level**	
	VAS current pain level		GNDS-UL Total (0-10)		GNDS-MOB Total (0-5)		MAM-36 (0-100)		CIQ Total (0-29)	
	Baseline	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**
Pt. 1	7	1	6	9	5	4	76.5	50.5	11	12
Pt. 2	3	2	8	4	5	4	51.5	57	19.5	10
Pt. 3	0	8	/	5	/	4	60.5	64.5	17	15
Pt. 4	8	2	9	6	4	3	44.5	37	9	8
Pt. 5	0	0	4	0	4	2	72	73.5	21	13
Pt. 6	0	0	0	/	4	2	100	100	12	10
Pt. 7	0	6	0	/	4	2	78.5	73.5	23	21

Pt.: Patient; VAS: Visual Analog Scale; GNDS: Guy's Neurological Disability Scale; UL: Upper Limb; MOB: Mobility; MAM: Manual Ability Measure; HADS: Hospital Anxiety and Depression Scale; CIQ: Community Integration Questionnaire

/ missing value for this outcome measure

Table 3: **Scores on outcome measures of individual patients for the dominant hand**

	Body functions and structures Level										**Activity Level**					
	MI (0/100)		Hand Grip Strength (kg.)		MAS (0-4)		AROM Wrist extension (degrees)		RMT Thumb (1.65-6.65)		NHPT (seconds)		NHPT (pegs/sec)		ARAT Total (0-57)	
	Baseline	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**
Pt. 1	76	84	20.60	19.33	0	1	65	/	3.61	4.56	44.53	33.2	0.2	0.27	55	55
Pt. 2	92	76	24.03	14.67	0	0	45	49.33	4.31	4.31	22.10	20.78	0.41	0.43	57	56
Pt. 3	100	100	33.20	32.67	0	0	70	73.3	4.31	3.61	20.58	23.57	0.44	0.38	57	57
Pt. 4	64	84	8.53	11	0	1	40	39.33	4.31	4.31	150.40	/	0.06	0	32	29
Pt. 5	100	100	43.70	45.33	0	0	50	37.33	2.83	2.83	25.26	22.63	0.36	0.40	57	57
Pt. 6	100	100	51.60	35	0	0	55	/	3.61	/	24.19	26.4	0.37	0.34	57	55
Pt. 7	100	100	29.17	23.67	0	0	52	/	2.83	/	16.67	18.72	0.54	0.48	57	57

Pt.: Patient; MI: Motricity Index; kg.: Kilograms; MAS: Modified Ashworth Scale; AROM: Active Range Of Motion; RMT: Roylan Monofilaments Test; NHPT: Nine-Hole Peg Test; ARAT: Action Research Arm Test; / missing value for this outcome measure

Table 4: **Scores on outcome measures of individual patients for the non-dominant hand**

	Body functions and structures Level										**Activity Level**					
	MI (0/100)		Hand Grip Strength (kg.)		MAS (0-4)		AROM Wrist extension (degrees)		RMT Thumb (1.65-6.65)		NHPT (seconds)		NHPT (pegs/sec)		ARAT Total (0-57)	
	Baseline	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**	**Baseline**	**10 years later**
Pt. 1	83	100	20.00	19.6	0	0	70	/	4.31	2.83	28.26	21.41	0.32	0.42	56	57
Pt. 2	100	100	26.97	22.67	0	0	70	47.3	4.31	3.61	19.65	19.97	0.46	0.45	57	57
Pt. 3	91	92	32.90	30.33	0	1	72	80	6.65	4.31	33.89	38.52	0.27	0.23	56	56
Pt. 4	70	92	7.23	10.33	0	0	80	59	4.31	4.31	95.18	/	0.1	0.0	36	29
Pt. 5	100	100	34.73	37.33	0	0	52	40.33	2.83	2.83	37.67	29.3	0.24	0.31	54	57
Pt. 6	100	100	52.49	39.00	0	0	60	/	3.61	/	26.89	32.48	0.33	0.28	57	57
Pt. 7	100	100	24.40	24.00	0	0	42	/	2.83	/	19.30	20.92	0.47	0.43	57	57

Pt.: Patient; MI: Motricity Index; kg.: Kilograms; MAS: Modified Ashworth Scale; AROM: Active Range Of Motion; RMT: Roylan Monofilaments Test; NHPT: Nine-Hole Peg Test; ARAT: Action Research Arm Test; / missing value for this outcome measure

Table 5: **Changes in scores on general outcome measures after 10 years**

	Baseline	After 10 years	Wilcoxon Signed Rank Test	Paired t-Test
Body functions and structures Level				
VAS Current pain level (0-10) (n=7)	0 (0/7)	2.71 ± 3.09	$P = 1.000$	
Activity Level				
GNDS-UL Total (0-10) (n=4)	6.75 ± 2.22	4.75 ± 3.77	$P = 0.3750$	$P = 0.3203$
GNDS-Mob Total (0-5) (n=6)	4 (4/5)	2.5 (2/4)	$P = 0.0313$*	
MAM-36 (0-100) (n=7)	69.07 ± 18.69	65.14 ± 20.12	$P = 0.5625$	$P = 0.3723$
Participation Level				
CIQ Total (0-29) (n=7)	16.07 ± 5.43	12.71 ± 4.31	$P = 0.0469$*	$P = 0.0610$

n: number of patients; VAS: Visual Analog Scale; GNDS: Guy's Neurological Disability Scale; UL: Upper Limb; Mob: Mobility; MAM: Manual Ability Measure; CIQ: Community Integration Questionnaire
*: significant *P*-value → $P < 0.0500$

Table 6: **Changes in scores on different outcome measures for the dominant hand after 10 years**

	Baseline	After 10 years	Wilcoxon Signed Rank Test	Paired t-Test
Body functions and structures Level				
MI (0-100) (n= 7)	100 (76/100)	100 (84/100)	$P = 0.7500$	
Hand Grip Strength (kg.) (n= 7)	30.12 ± 14.43	25.95 ± 12.26	$P = 0.2969$	$P = 0.1594$
MAS (0-4) (n=7)	0 (0/0)	0 (0/1)	$P = 0.5000$	
AROM Wrist Extension (degrees) (n = 4)	51.25 ± 13.15	49.82 ± 16.50	$P = 1.000$	$P = 0.7386$
RMT Thumb (1.65 – 6.65) (n=5)	4.31 (3.22/4.31)	3.92 ± 0.71	$P = 1.000$	
Activity Level				
NHPT (seconds) (n=6)	23.15 (19.60/13.07)	24.22 ± 5.11	$P = 1.000$	
NHPT (pegs/sec) (n=7)	0.34 ± 0.16	0.33 ± 0.16	$P = 0.6875$	$P = 0.5977$
ARAT Total (0-57) (n=7)	57 (55/57)	56 (55/57)	$P = 0.2500$	

MI: Motricity Index; n: number of patients kg.: Kilograms; MAS: Modified Ashworth Scale; AROM: Active Range Of Motion; RMT: Roylan Monofilaments Test; NHPT: Nine-Hole Peg Test; ARAT: Action Research Arm Test
*: significant *P*-value → $P < 0.0500$

Table 7: **Changes in scores on different outcome measures for the non-dominant hand after 10 years**

	Baseline	After 10 years	Wilcoxon Signed Rank Test	Paired t-Test
Body functions and structures Level				
MI (0-100) (n= 7)	100 (83/100)	100 (92/100)	$P = 0.2500$	
Hand Grip Strength (kg.) (n= 7)	28.39 ± 14.01	26.19 ± 10.14	$P = 0.4688$	$P = 0.3409$
MAS (0-4) (n=7)	0 (0/0)	0 (0/0)	$P = 1.000$	
AROM Wrist Extension (degrees) (n = 4)	63.25 ± 9.43	50.74 ± 20.11	$P = 0.2500$	$P = 0.1877$
RMT Thumb (1.65 – 6.65) (n=5)	4.48 ± 1.37	3.63 ± 0.81	$P = 0.25000$	$P = 0.1071$
Activity Level				
NHPT (seconds)	27.61 ± 7.04	27.1 ± 7.56	$P = 1.000$	$P = 0.8398$
NHPT (pegs/sec) (n=7)	0.31 ± 0.13	0.30 ± 0.16	$P = 0.7500$	$P = 0.7211$
ARAT Total (0-57) (n=7)	56 (54/57)	57 (56/57)	$P = 1.000$	

MI: Motricity Index; n: number of patients kg.: Kilograms; MAS: Modified Ashworth Scale; AROM: Active Range Of Motion; RMT: Roylan Monofilaments Test; NHPT: Nine-Hole Peg Test; ARAT: Action Research Arm Test

*: significant *P*-value → $P < 0.0500$

Table 8: **Outcome measures regarding possible influencing factors of disease evolution**

	Pt. 1	Pt. 2	Pt. 3	Pt. 4	Pt. 5	Pt. 6	Pt. 7	Total
Activity Level								
HADS Total Depression (0-21)	0	7	3	11	7	2	5	5 ± 3.70
HADS Total Anxiety (0-21)	2	8	8	15	5	0	10	6.86 ± 5.05
MSSM-R Total (0-100)	76.04	73.96	75	79.17	79.17	81.25	69.79	76.34 ± 3.89

Pt.: Patient; HADS: Hospital Anxiety and Depression Scale; MSSM-R: Multiple Sclerosis Self-Management Scale-Revised

*: Values presented are: mean standard deviation ±, median + interquartile range ( )

Table 9: **Correlation of possible influencing factors and outcome measures current study**

	HADS Depression		**HADS Anxiety**		**MSSM-R**	
Body functions and structures Level						
MI (n=7)	R= -0.2714	*P*= 0.5561	R= -0.2111	*P*= 0.6496	R= 0.1809	*P*= 0.6979
Hand Grip Strength (n=7)	R= -0.2977	*P*= 0.5167	R= -0.5385	*P*= 02124	R= 0.3209	*P*= 0.4828
MAS (n=7)	R= 0.0000	*P*= 1.000	R= 0.1595	*P*= 0.7326	R= 0.2393	*P*= 0.6053
AROM Wrist Extension (n=4)	R= -0.8401	*P*= 0.1599	R= -0.1710	*P*= 0.8290	R= -0.7012	*P*= 0.2988
RMT Thumb (n=5)	R= -0.1385	*P*= 0.8242	R= 0.1589	*P*= 0.7986	R= -0.3967	*P*= 0.5084
VAS Current pain level (n=7)	R= -0.0729	*P*= 0.8766	R= 0.4452	*P*= 0.3168	R= -0.6852	*P*= 0.0893
Activity Level						
GNDS-UL (n=5)	R= -0.4601	*P*= 0.4355	R= -0.0380	*P*= 0.9516	R= -0.3121	*P*= 0.6092
GNDS-Mob (n=6)	R= -0.1557	*P*= 0.7389	R= 0.0778	*P*= 0.8682	R= -0.3503	*P*= 0.4411
NHPT (n=7)	R= -0.4157	*P*= 0.3536	R= -0.4042	*P*= 0.3685	R= -0.5263	*P*= 0.2250
ARAT (n=7)	R= -0.0189	*P*= 0.9680	R= 0.0566	*P*= 0.9040	R= -0.5287	*P*= 0.2225
MAM-36 (n=7)	R= -0.4449	*P*= 0.3172	R= -0.6506	*P*= 0.1135	R= 0.1816	*P*= 0.6968
Participation Level						
CIQ Total (n=7)	R= -0.2720	*P*= 0.5551	R= 0.0668	*P*= 0.8869	R= -0.7616	*P*= 0.0467*

MI: Motricity Index; n: number of patients; MAS: Modified Ashworth Scale; AROM: Active Range Of Motion; RMT: Roylan Monofilaments Test; VAS: Visual Analog Scale; GNDS: Guy's Neurological Disability Scale; UL: Upper Limb; Mob: Mobility; NHPT: Nine-Hole Peg Test; ARAT: Action Research Arm Test; MAM: Manual Ability Measure; CIQ: Community Integration Questionnaire
*: significant *P*-value → $P < 0.0500$

Table 10: **GRS: a 7-point Likert scale comparing overall arm-hand function with 10 years ago**

	Very much worse	**Much worse**	**Minimally worse**	**No change**	**Minimally better**	**Much better**	**Very much better**
Pt. 1	X						
Pt. 2			X				
Pt. 3				X			
Pt. 4	X						
Pt. 5			X				
Pt. 6				X			
Pt. 7				X			

GRS: Global Rating Scale; Pt: Patient

Table 10: **GRS: a 7-point Likert scale comparing overall general health with 10 years ago**

	Very much worse	Much worse	Minimally worse	No change	Minimally better	Much better	Very much better
Pt. 1		X					
Pt. 2			X				
Pt. 3			X				
Pt. 4			X				
Pt. 5			X				
Pt. 6				X			
Pt. 7			X				

GRS: Global Rating Scale; Pt: Patient

4.4 Individual case results

Patient 1. A female patient with the age of 69. This patient did not change in hand dominance or type of MS. Her disease duration at baseline was only 2 years where it has now been 12 years since diagnosis, the shortest duration in the entire sample. EDSS score increased from 4 to 6 meaning she now requires a walking aid where she did not 10 years ago. This corresponds with the ambulation index score which went up to a 4. Her motricity index score increased from 76 to 84 as compared to 10 years ago, mean pegs/sec also improved by 0.07 pegs/sec. This can be attributed to the VAS score which was 7 at baseline testing and 1 during the current tests but can't be said for certain. ARAT score did not change, but there might be a ceiling effect as her score was 55 out of 57 at both moments of testing. MAM-36 score decreased by 25 points, current difficult tasks include: carrying groceries, buttoning a shirt, opening medicines with child proof closures, and opening jars. These activities received a score of 0-1 where they scored 4 at baseline.

GRS overall arm-hand function: her test scores increased. This can be due to a VAS score of 1 (at baseline she scored 7). Her objective test scores do not match with her GRS.

GRS general health: EDSS went from 4 to 6. She now requires a walking aid. MAM scores decreased. ADL tasks such as carrying groceries, opening bottles and jars etc is more difficult. Her interpretation of her overall general health compared to 10 years ago feels much worse, but her objective measures did not as drastically decline as she pointed out.

Patient 2. The oldest patient of the included sample at 71 years old. This patient had a longer disease duration than any of the other patients, having lived with the disease for 40 years since her diagnosis. In the 10 years since the baseline data, her EDSS score remained at 3. Where she was ambidextrous at baseline, she now favors her right hand. The outcome measures where she lost the most are the hand grip strength test, losing around 10 kgs of force in her dominant hand and the CIQ where she now scores a 10 compared to her previous score of 19.5. Her score for the NHPT with her dominant hand was 0.43 pegs/sec which is around the normative data for healthy females of 70-74 years of age, who score 0.44 pegs/sec[23]. Her ARAT score with the dominant hand is 56 now, compared to 57 10 years later.

She scores a 7 on the Depression HADS and an 8 on the anxiety part, this suggests a possible depressive or anxiety disorder using the cut-off value of 7.

GRS overall arm-hand function: In line with objective scores. Grip strength decreased lightly as well as NHPT and ARAT for her dominant hand

GRS general health: Objective measures are in line with her GRS. EDSS score remained stable.

Patient 3. Patient 3 is a female patient of 65 years old, with 6.5 she has the second highest EDSS score of the sample. She is also one of the 6 participants who currently have the secondary progressive form of MS. During baseline testing she had a VAS score of 0, but during the current testing she scored an 8 on this scale. Regardless, scores on outcome measures remained relatively unchanged after 10 years. She did score an 8 on the anxiety part of the HADS, 1 point above the cut-off of 7 for possible anxiety disorders.

GRS overall arm-hand function: outcome measures remained relatively unchanged, this is in line with the GRS.

GRS general health: EDSS score did not change compared to 10 years ago

Patient 4. At 48 years old, she is the second youngest participant apart from patient 5. She has a disease duration of 26 years, meaning she was diagnosed at just 22 years old. With the average diagnosis being given between 20-40 years, she is at the younger end of this range[1]. Her EDSS score is the highest of the sample at 8/10. She is confined to a wheelchair which she requires to stay mobile, this also shows in her Ambulation index where she scores a 9. She has the lowest scores of all patients on the Hand grip strength test, CIQ, NHPT, ARAT and MAM-36. The last of these 3 are outcome measures on the activity level of the ICF. Her HADS scores are also the highest of the sample, with 10 on the depression part and 15 on the anxiety part.

GRS overall arm-hand function: According to her, arm-hand function feels very much worse compared to 10 years ago. While she was unable to complete certain tasks with her hands, objective outcome measures did not drastically change.

GRS general health: EDSS did not change but is already high (8/10). She found her general health to have minimally worsened.

Patient 5. One of the only 2 male patients and coincidentally the youngest participant of the current study at 43 years old. From baseline his form of MS changed from relapsing-remitting to secondary progressive. Currently he has the best scores on hand grip strength and the Roylan Monofilaments test of the group. While he scores the maximum of 57 on the ARAT with both hands, his NHPT score is significantly less than the average for healthy males of his age[23], his score being 0.40 pegs/sec and the average being 0.50 pegs/sec. On the Depression part of the HADS he scores a 7, this is right on the cut-off value.

GRS overall arm-hand function: No self-perceived change in arm-hand function, objective measures remained relatively stable

GRS general health: No self-perceived change, EDSS score did not change over the course of 10 years.

Patient 6. The other male patient of the group, he is 67 years of age and his MS type also changed from relapsing-remitting to secondary progressive in the last 10 years. His EDSS score increased from 3 to 6.5. While his right hand remained his dominant hand, his dominant hand grip strength decreased with 16.6 kgs and his non-dominant hand grip strength decreased with 12.49 kgs. He is the only patient who scored the maximum of 100 on the Manual Ability Measure, indicating that he has no difficulties in ADL activities. However, his score of only 10 on the community integration questionnaire suggests difficulties on the participation level. He scored an 8 on the social integration subscale of the CIQ, but scored a 1 on both the home integration and the integration in productive activities subscales.

GRS overall arm-hand function: No difficulties with ADL activities according to the MAM-36.

GRS general health: EDSS score went from a 3 to a 6,5, objectively this also means that general health has worsened.

Patient 7. Patient 7 is a female patient of 52 years old. Noteworthy is that her EDSS score is the only one that decreased. Rather than increase or remain stable it dropped from 3 to 2.5. After 10 years, she is the only remaining patient in the included sample with the relapsing-remitting form of MS. His VAS score during testing increased from 0 at baseline to 6 during the tests 10 years later. His NHPT score with the dominant hand 0.48 pegs/sec was the best of the entire sample, this is relative as it does not take the different ages of the participants

into account. On the anxiety part of the HADS, he scored a 10 and he also had the lowest score on the MSSM-r of the sample.

GRS overall arm-hand function: This patient did not perceive any change in arm-hand function, this can also be seen in the objective measures, which did not drastically change.

GRS general health: EDSS score decreased compared to 10 years ago, this is not in line with the self-perceived change.

5. Discussion

5.1 Research questions and results

The objective of this study was to investigate long-term effects of MS on the upper limb on the different levels of the ICF. On group level, significant results were found for the GNDS-mob and the CIQ meaning that scores changed significantly after 10 years when compared to baseline. In 10 years, 4 out of 7 patients (pt. 1,2,3,6) passed the age of 65 (the age of retirement in Belgium), this could partially explain the drop in CIQ score as going to work is a big part of the participation level of the ICF. Regarding influencing factors, a significant correlation between scores on the MSSM-r and the CIQ was found. This suggests that the self-management of one's disease might have an influence on the participation level of the ICF. This outcome measure was not included at baseline so changes in self-management score could not be investigated. No other significant changes were found on group level. On the body structures and functions level most mean scores had visibly decreased after 10 years but no significant changes were found. On the activity level, the mean NHPT and mean ARAT scores even remained relatively unchanged. Due to the small sample size of the current study, individual case analyses were made for every patient. Individual results indicate that an increase of EDSS score has a negative influence on most outcome measures. The biggest effect is seen in the ambulation index, this can be explained by the fact that EDSS score is based partially on the mobility of a person. But the person with the highest score on the EDSS of the sample (pt. 4) also had the lowest scores on several outcome measures of the upper limb, including NHPT, ARAT and the MAM-36. This patient also had the highest score on both subscales of the HADS. Only one patient (pt.7) with relapsing-remitting MS was included in the sample, the others had a secondary progressive form. This patient did not only have the lowest EDSS score of the sample but also did not have any outcome measures that significantly decreased compared to 10 years ago. None of the patients changed their dominant hand after 10 years, with only one person going from ambidextrous to favoring their right hand (pt. 2). However, several patients scored worse on some outcome measures with their dominant hand than with their non-dominant hand. Two participants (pt. 1, 4) had mild spasticity in their dominant hand and no spasticity in their non-dominant hand. Also two participants (pt. 1, 2)

scored better on the NHPT with their non-dominant hand. For the RMT sensibility test again two patients (pt. 1, 2) had a better score with their non-dominant hand.
Results were meant to be used to help predict the extent of upper limb disability for the development of physical rehabilitation strategies. While the study provides interesting results, the sample size is too small to draw a general conclusion that can be adapted to the entire population.

5.2 Research context

The original concept for this study was to conduct a follow-up study to the study of Lamers et al. (2015) which was executed 10 years ago[6]. The original study had a cross-sectional design with 50 participants from Belgian origin. After recruitment for the current study only 7 of those 50 patients remained. Due to the drastic decrease in participants, the design of a case series was chosen to adapt to the new sample size. The size of the current sample did not make it possible to divide patients into different groups (according to EDSS-score) to determine if another kind of evolution would be observed in patients in a more severe stage of MS. The individualized approach of a case series makes it difficult to come to any generalized conclusions as the group is too heterogeneous for this and the sample does not closely relate to the general population of PwMS. Newsome et al. (2019), who conducted a similar longitudinal study assessing decrease of hand function in PwMS, reported that half of their sample (n=84) had a 20% decrease in hand grip strength and 27/85 patients had a 20% decrease in NHPT score at follow-up (up to 5 years)[8]. On a group level, this study did not find such significant changes for these specific outcome measures.

5.3 Limitations

There was an already existing selection bias for the sample, as patients for the original study were only recruited in specific rehabilitation centers. All participants were invited for a testing moment of 1.5 hours, all testing's were done by the same researcher. This is not the same researcher that tested all patients 10 years ago, which might have led to differences in the way patient performance was assessed. To minimize differences between the assessing of patients compared to 10 years ago, the first patient was assessed together with a researcher

of the original study. The same score forms from baseline were used 10 years later, standardized instructions were also used to have corresponding testing moments with baseline. As seen in the outcome measures and results, VAS scores which describe the pain level of a patient at the moment of testing, varied greatly for most participants when compared with their significant scores 10 years prior. This variance in pain levels could have influenced test performance negatively when VAS scores were higher than 10 years ago, or positively when this score is much lower than the previous time[24,25]. The same can be said about depression, the HADS was included to measure possible depressive symptoms as research has proven that these can negatively influence functional performance[26]. In contrast to the VAS scores, HADS scores cannot be compared to 10 years ago as this scale was not included in the previous study's outcome measures. Another scale added to measure the possible influencing factors on functional outcomes is the MSSM-r, this scale assesses self-management concerning MS. Regarding influencing factors, one factor that was not taken into account is possible changes in medication. Information about medication was only known about a few patients and was for this reason not included in the patient characteristics. Despite not being included in the results, a change in medication compared to 10 years ago could have had an effect on various outcome measures.

5.4 Suggestions for future research

Suggestions for future follow-up research would be to include more outcome measures describing influencing factors of disease evolution and trying to create a more homogeneous sample size. Setting up a study only including patients with a mild EDSS score could lead to conclusions more easily applicable to the general population. The possible effect of changes in medication could be taken into account in further longitudinal research to determine if there is an effect on outcome measures for the upper limb. The influence of depression, anxiety and self-management on individual case results suggests that a multidisciplinary approach of upper limb rehabilitation is necessary. This means that the inclusion of psychologists and occupational therapists in individual therapy programs could have a beneficial effect on at least the outcome measures on the participation level, as supported by the correlation between the MSSM-r and the CIQ scales.

6. Conclusion

For the general population, results suggest that the self-management of MS has a significant effect on the participation of an individual. Over the course of 10 years, the mobility score and the community integration decreases significantly. On an individual basis, depressive and anxiety symptoms seem to have an influence on multiple outcome measures. Also the type of MS seems to matter, as the only patient with relapsing-remitting MS had the most unchanged outcome measures after 10 years. Influencing factors appear to have a significant effect on the evolution of the disease and should be investigated further.

6. References

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7. Appendix

Figure 1.1

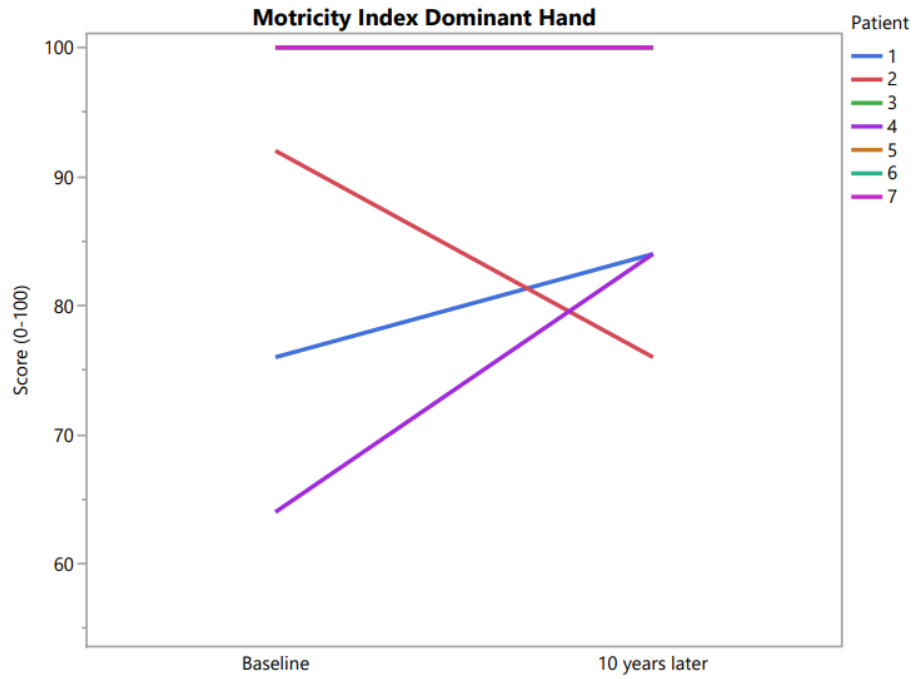


Figure 1.2

Figure 2.1

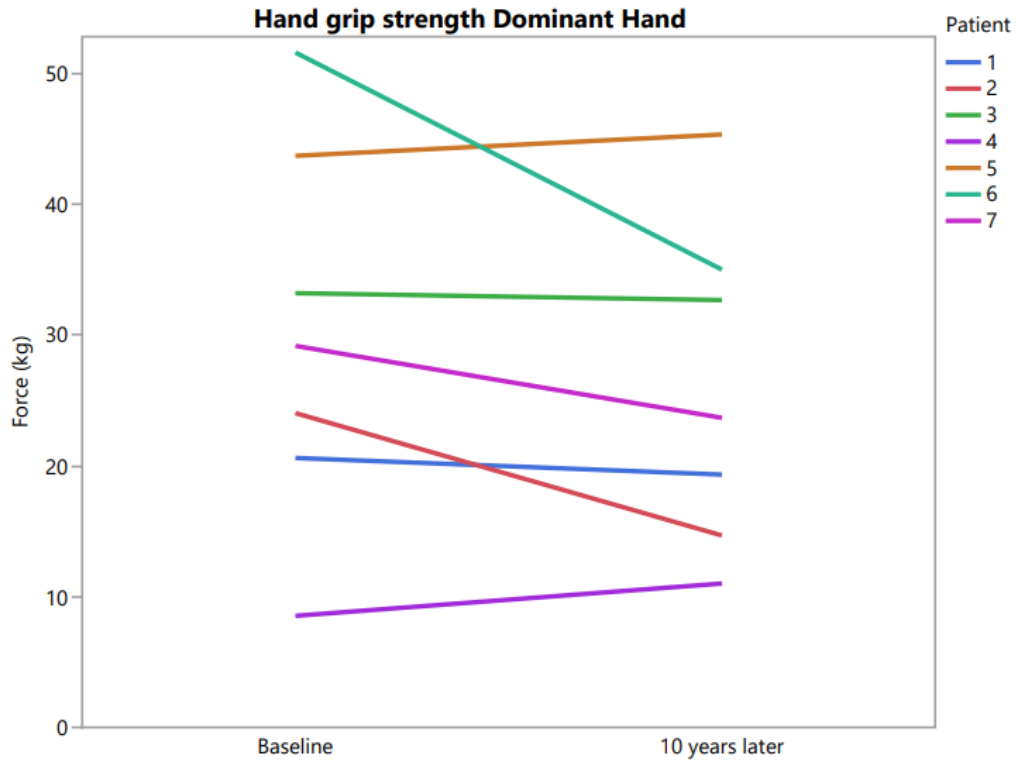


Figure 2.2

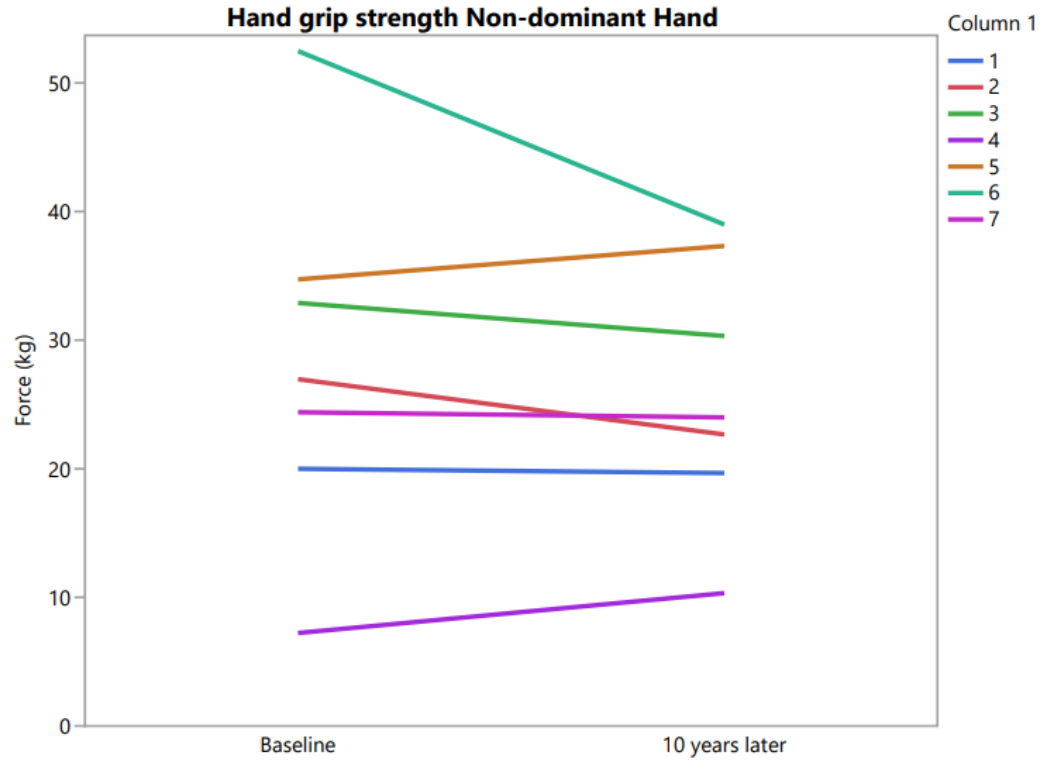


Figure 3.1

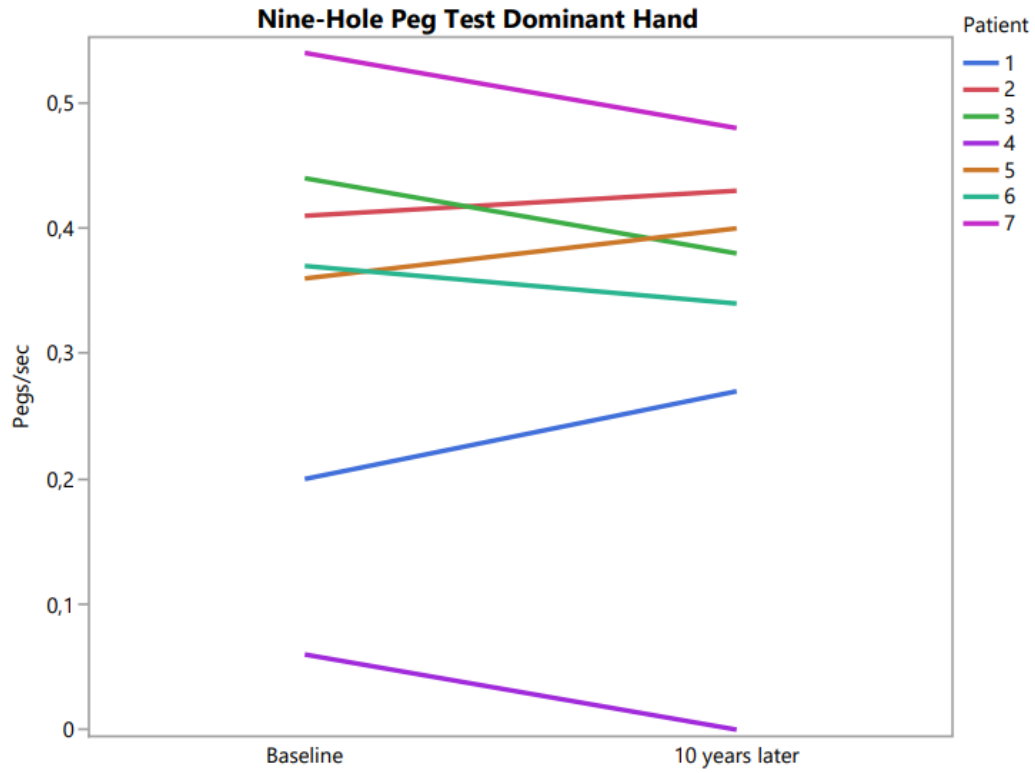


Figure 3.2

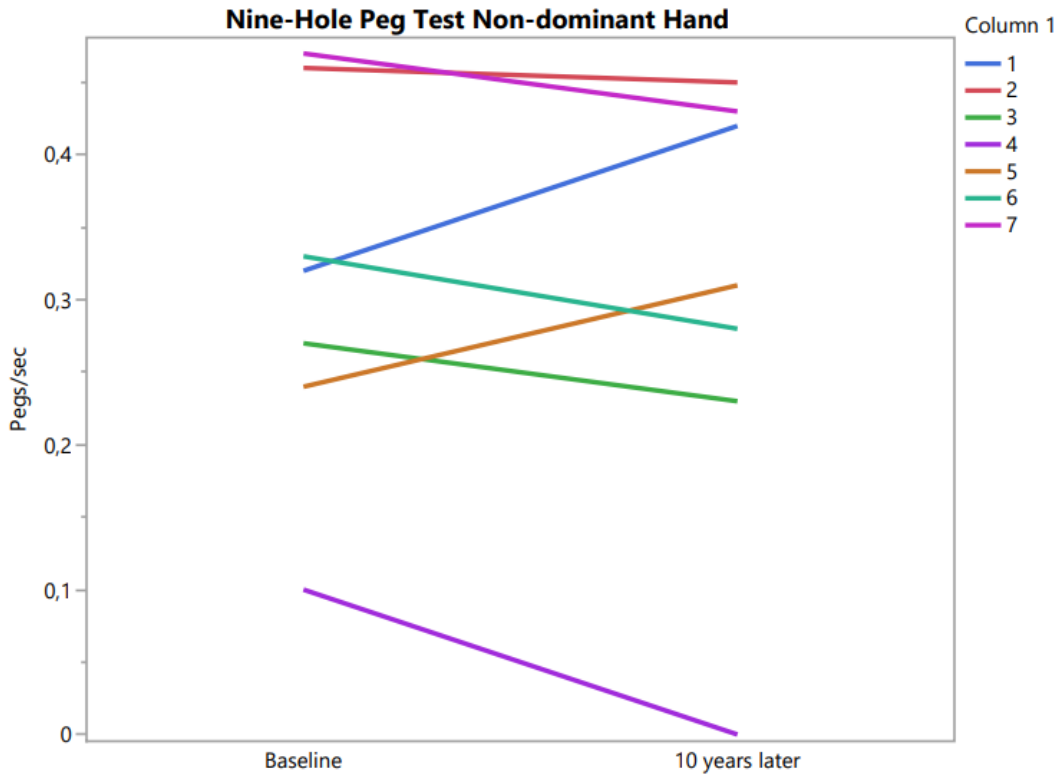


Figure 4.1

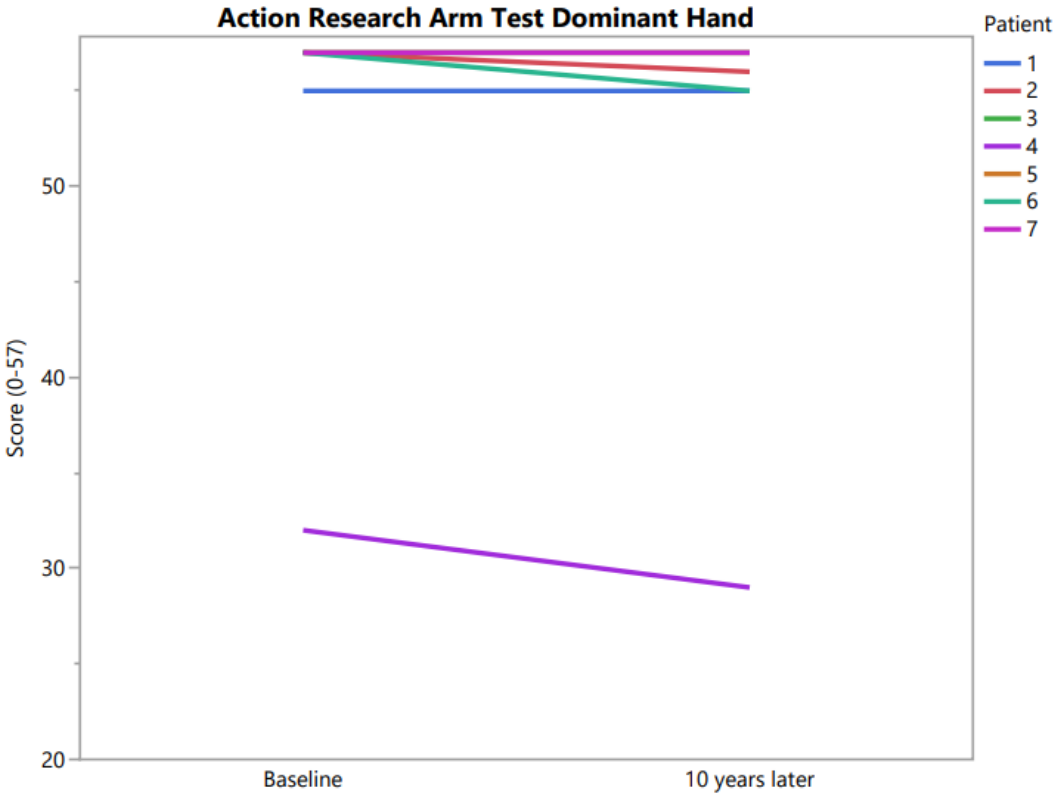


Figure 4.2

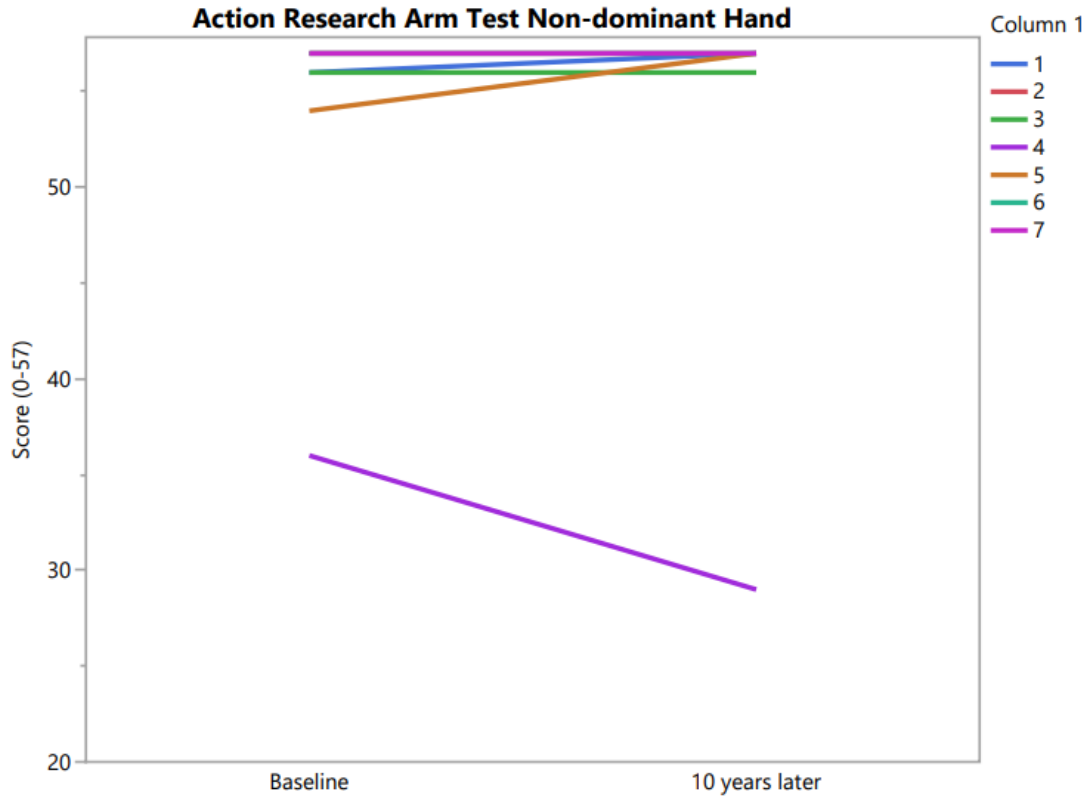


Figure 5

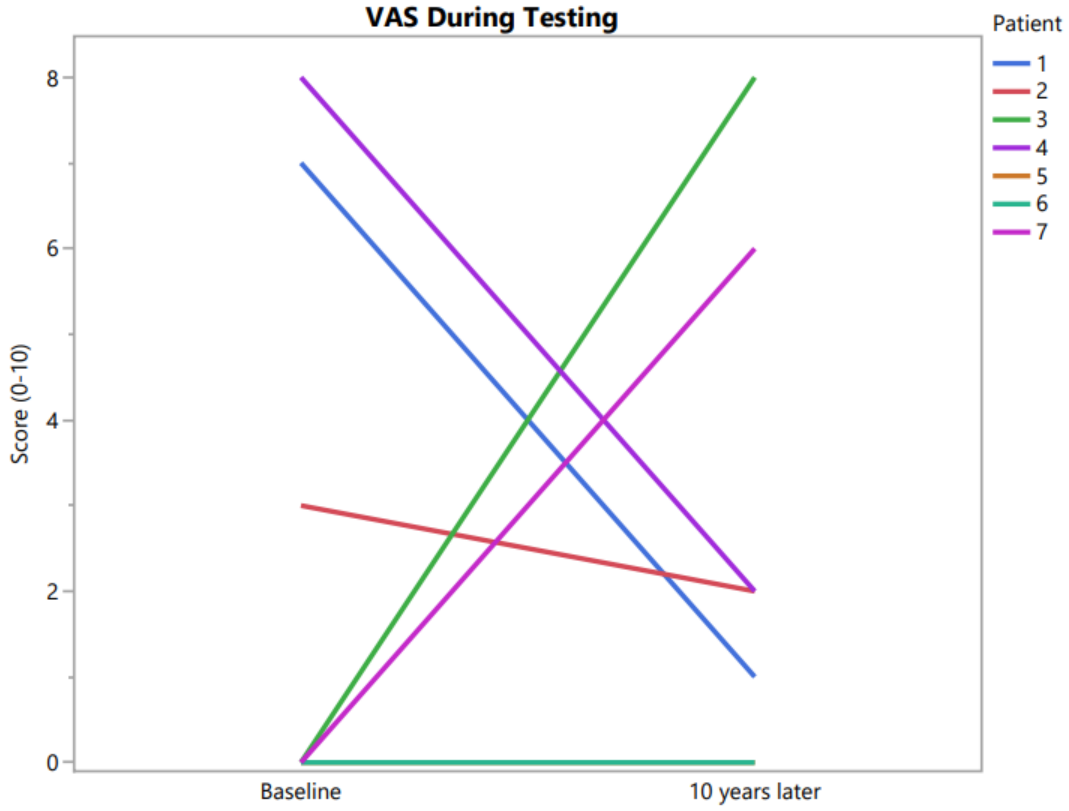


Figure 6

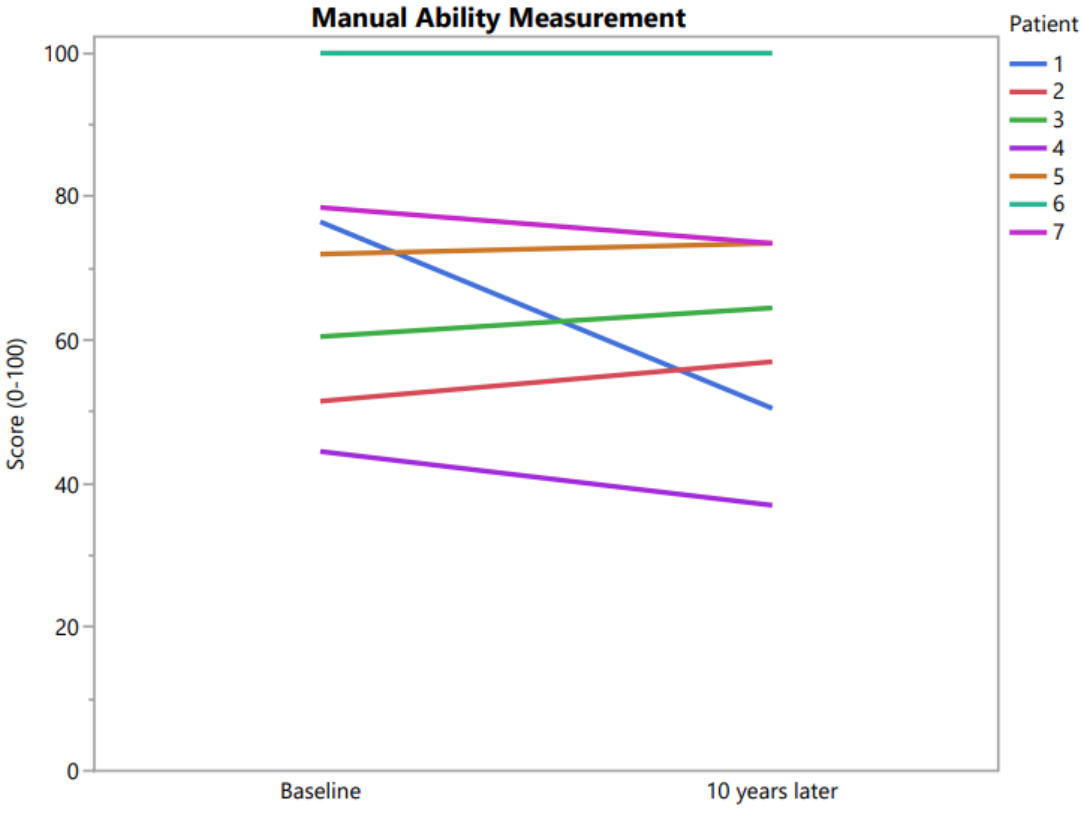
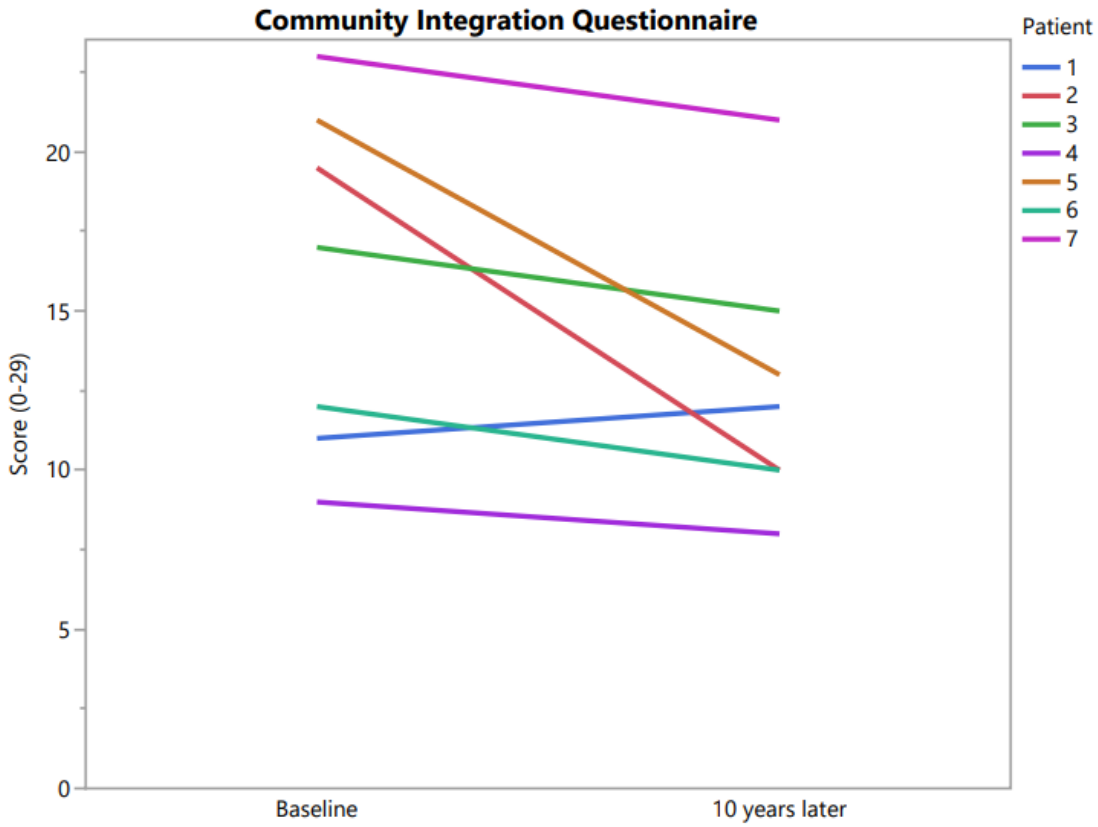


Figure 7


Community Integration Questionnaire
Patient
1
2
3
4
5
6
7
Score (0-29)
0
5
10
15
20
Baseline
10 years later

Verklaring op Eer

Ondergetekende, student aan de Universiteit Hasselt (UHasselt), faculteit RWS aanvaardt de volgende voorwaarden en bepalingen van deze verklaring:

1. Ik ben ingeschreven als student aan de UHasselt in de opleiding Revalidatiewetenschappen en Kinesitherapie, waarbij ik de kans krijg om in het kader van mijn opleiding mee te werken aan onderzoek van de faculteit RWS aan de UHasselt. Dit onderzoek wordt beleid door Prof. Dr. Peter Feys en kadert binnen het opleidingsonderdeel "Wetenschappelijke stage/masterproef deel 2". Ik zal in het kader van dit onderzoek creaties, schetsen, ontwerpen, prototypes en/of onderzoeksresultaten tot stand brengen in het domein van Neurologische Revalidatie (hierna: "De Onderzoeksresultaten").

2. Bij de creatie van De Onderzoeksresultaten doe ik beroep op de achtergrondkennis, vertrouwelijke informatie[1], universitaire middelen en faciliteiten van UHasselt (hierna: de "Expertise").

3. Ik zal de Expertise, met inbegrip van vertrouwelijke informatie, uitsluitend aanwenden voor het uitvoeren van hogergenoemd onderzoek binnen UHasselt. Ik zal hierbij steeds de toepasselijke regelgeving, in het bijzonder de Algemene Verordening Gegevensbescherming (EU 2016-679), in acht nemen.

4. Ik zal de Expertise (i) voor geen enkele andere doelstelling gebruiken, en (ii) niet zonder voorafgaande schriftelijke toestemming van UHasselt op directe of indirecte wijze publiek maken.

5. Aangezien ik in het kader van mijn onderzoek beroep doe op de Expertise van de UHasselt, draag ik hierbij alle bestaande en toekomstige intellectuele eigendomsrechten op De Onderzoeksresultaten over aan de UHasselt. Deze overdracht omvat alle vormen van intellectuele eigendomsrechten, zoals onder meer – zonder daartoe beperkt te zijn – het auteursrecht, octrooirecht, merkenrecht, modellenrecht en knowhow. De overdracht geschiedt in de meest volledige omvang, voor de gehele wereld en voor de gehele beschermingsduur van de betrokken rechten.

6. In zoverre De Onderzoeksresultaten auteursrechtelijk beschermd zijn, omvat bovenstaande overdracht onder meer de volgende exploitatiewijzen, en dit steeds voor de hele beschermingsduur, voor de gehele wereld en zonder vergoeding:

   - het recht om De Onderzoeksresultaten vast te (laten) leggen door alle technieken en op alle dragers;
   - het recht om De Onderzoeksresultaten geheel of gedeeltelijk te (laten) reproduceren, openbaar te (laten) maken, uit te (laten) geven, te (laten) exploiteren en te (laten) verspreiden in eender welke vorm, in een onbeperkt aantal exemplaren;

[1] Vertrouwelijke informatie betekent alle informatie en data door de UHasselt meegedeeld aan de student voor de uitvoering van deze overeenkomst, inclusief alle persoonsgegevens in de zin van de Algemene Verordening Gegevensbescherming (EU 2016/679), met uitzondering van de informatie die (a) reeds algemeen bekend is; (b) reeds in het bezit was van de student voor de mededeling ervan door de UHasselt; (c) de student verkregen heeft van een derde zonder enige geheimhoudingsplicht; (d) de student onafhankelijk heeft ontwikkeld zonder gebruik te maken van de vertrouwelijke informatie van de UHasselt; (e) wettelijk of als gevolg van een rechterlijke beslissing moet worden bekendgemaakt, op voorwaarde dat de student de UHasselt hiervan schriftelijk en zo snel mogelijk op de hoogte brengt.

- het recht om De Onderzoeksresultaten te (laten) verspreiden en mee te (laten) delen aan het publiek door alle technieken met inbegrip van de kabel, de satelliet, het internet en alle vormen van computernetwerken;
- het recht De Onderzoeksresultaten geheel of gedeeltelijk te (laten) bewerken of te (laten) vertalen en het (laten) reproduceren van die bewerkingen of vertalingen;
- het recht De Onderzoeksresultaten te (laten) bewerken of (laten) wijzigen, onder meer door het reproduceren van bepaalde elementen door alle technieken en/of door het wijzigen van bepaalde parameters (zoals de kleuren en de afmetingen).

De overdracht van rechten voor deze exploitatiewijzen heeft ook betrekking op toekomstige onderzoeksresultaten tot stand gekomen tijdens het onderzoek aan UHasselt, eveneens voor de hele beschermingsduur, voor de gehele wereld en zonder vergoeding.

Ik behoud daarbij steeds het recht op naamvermelding als (mede)auteur van de betreffende Onderzoeksresultaten.

7. Ik zal alle onderzoeksdata, ideeën en uitvoeringen neerschrijven in een "laboratory notebook" en deze gegevens niet vrijgeven, tenzij met uitdrukkelijke toestemming van mijn UHasseltbegeleider Prof. Dr. Peter Feys

8. Na de eindevaluatie van mijn onderzoek aan de UHasselt zal ik alle verkregen vertrouwelijke informatie, materialen, en kopieën daarvan, die nog in mijn bezit zouden zijn, aan UHasselt terugbezorgen.

Gelezen voor akkoord en goedgekeurd,

Naam: HAMAEKERS MATS

Adres: AARDBERGSTRAAT 15, 3511 TUILT

Geboortedatum en -plaats : 15/08/1999, LEUVEN

Datum: 06/06/2022

Handtekening:

Verklaring op Eer

Ondergetekende, student aan de Universiteit Hasselt (UHasselt), faculteit RWS aanvaardt de volgende voorwaarden en bepalingen van deze verklaring:

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Gelezen voor akkoord en goedgekeurd,

Naam: Gilson Helena

Adres: Heksenheide 19, 3511 Hasselt

Geboortedatum en –plaats : 28 juni 1999 te Hasselt

Datum: 6 juni 2022

Handtekening: Gilson Helena

www.uhasselt.be
Campus Hasselt | Martelarenlaan 42 | BE-3500 Hasselt
Campus Diepenbeek | Agoralaan gebouw D | BE-3590 Diepenbeek
T + 32(0)11 26 81 11 | E-mail: info@uhasselt.be

UHASSELT
KNOWLEDGE IN ACTION

INVENTARISATIEFORMULIER WETENSCHAPPELIJKE STAGE DEEL 2

DATUM	INHOUD OVERLEG	HANDTEKENINGEN
13/07/2021	OPZET MP 2	Promotor: Copromotor/Begeleider: Student(e): [signature] Student(e):
19/10/2021	ETHISCHE COMMISSIE OPSTART	Promotor: Copromotor/Begeleider: Student(e): [signature] Student(e):
11/01/2022	CME VERGADERING	Promotor: Copromotor/Begeleider: Student(e): [signature] Student(e):
08/02/2022	OVERLEG DATA VERZAMELING	Promotor: Copromotor/Begeleider: Student(e): [signature] Student(e):
22/04/2022	STATISTIEK, RESULTATEN	Promotor: Copromotor/Begeleider: Student(e): [signature] Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):

In te vullen door de promotor(en) en eventuele copromotor aan het einde van MP2:

Naam Student(e): ..... **Datum:**.....

Titel Masterproef: .....

1) Geef aan in hoeverre de student(e) onderstaande competenties zelfstandig uitvoerde:
   - NVT: De student(e) leverde hierin geen bijdrage, aangezien hij/zij in een reeds lopende studie meewerkte.
   - 1: De student(e) was niet zelfstandig en sterk afhankelijk van medestudent(e) of promotor en teamleden bij de uitwerking en uitvoering.
   - 2: De student(e) had veel hulp en ondersteuning nodig bij de uitwerking en uitvoering.
   - 3: De student(e) was redelijk zelfstandig bij de uitwerking en uitvoering
   - 4: De student(e) had weinig tot geringe hulp nodig bij de uitwerking en uitvoering.
   - 5: De student(e) werkte zeer zelfstandig en had slechts zeer sporadisch hulp en bijsturing nodig van de promotor of zijn team bij de uitwerking en uitvoering.

Competenties	NVT	1	2	3	4	5
Opstelling onderzoeksvraag	O	O	O	O	O	O
Methodologische uitwerking	O	O	O	O	O	O
Data acquisitie	O	O	O	O	O	O
Data management	O	O	O	O	O	O
Dataverwerking/Statistiek	O	O	O	O	O	O
Rapportage	O	O	O	O	O	O

2) Niet-bindend advies: Student(e) krijgt toelating/geen toelating (schrappen wat niet past) om bovenvermelde Wetenschappelijke stage/masterproef deel 2 te verdedigen in bovenvermelde periode. Deze eventuele toelating houdt geen garantie in dat de student geslaagd is voor dit opleidingsonderdeel.

3) Deze wetenschappelijke stage/masterproef deel 2 mag wel/niet (schrappen wat niet past) openbaar verdedigd worden.

4) Deze wetenschappelijke stage/masterproef deel 2 mag wel/niet (schrappen wat niet past) opgenomen worden in de bibliotheek en docserver van de UHasselt.

Datum en handtekening Student(e)	Datum en handtekening promotor(en)	Datum en handtekening Co-promotor(en)
06/06/2022		

www.uhasselt.be
Campus Hasselt | Martelarenlaan 42 | BE-3500 Hasselt
Campus Diepenbeek | Agoralaan gebouw D | BE-3590 Diepenbeek
T + 32(0)11 26 81 11 | E-mail: info@uhasselt.be

UHASSELT
KNOWLEDGE IN ACTION

INVENTARISATIEFORMULIER WETENSCHAPPELIJKE STAGE DEEL 2

DATUM	INHOUD OVERLEG	HANDTEKENINGEN
13/07/2021	OPZET MP 2	Promotor: Copromotor/Begeleider: Student(e): Student(e):
19/10/2021	ETHISCHE COMMISSIE OPSTART	Promotor: Copromotor/Begeleider: Student(e): Student(e):
11/01/2022	CME VERGADERING	Promotor: Copromotor/Begeleider: Student(e): Student(e):
08/02/2022	OVERLEG DATA VERZAMELEN	Promotor: Copromotor/Begeleider: Student(e): Student(e):
22/04/2022	STATISTIEK, RESULTATEN	Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):

In te vullen door de promotor(en) en eventuele copromotor aan het einde van MP2:

Naam Student(e): ..... **Datum:**.....

Titel Masterproef: .....

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Opstelling onderzoeksvraag	O	O	O	O	O	O
Methodologische uitwerking	O	O	O	O	O	O
Data acquisitie	O	O	O	O	O	O
Data management	O	O	O	O	O	O
Dataverwerking/Statistiek	O	O	O	O	O	O
Rapportage	O	O	O	O	O	O

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Datum en handtekening Student(e)	Datum en handtekening promotor(en)	Datum en handtekening Co-promotor(en)
06/06/2022		

Eindwerk - toelating tot indiening

Inbox ×

Peter FEYS
aan mij, Helena, Ilse

ma 30 mei 15:08 (7 dagen geleden)

Dag Mats en Helena

We geven jullie toelating tot indiening.
Blijf echter goed en zorgvuldig werken om probleemloos de MP succesvol te verdedigen.

Mvg
Peter feys

--

Peter Feys

Decaan - Hoogleraar
Faculteit 'Revalidatiewetenschappen'

Dean - Professor
Faculty of Rehabilitation Sciences

REVAL Rehabilitation Research center

T +32(0)11 26 21 23 - GSM +32(0)486 74 44 09
Twitter: 'peterfeys_'

www.uhasselt.be
Universiteit Hasselt - Campus Diepenbeek
Agoralaan Gebouw A - B-3590 Diepenbeek
Kantoor BMO-A08

Inschrijvingsformulier verdediging masterproef academiejaar 2021-2022,
Registration form jury Master's thesis academic year 2021-2022,

GEGEVENS STUDENT - *INFORMATION STUDENT*

Faculteit/School: **Faculteit Revalidatiewetenschappen**
Faculty/School: ***Rehabilitation Sciences***

Stamnummer + naam: **1746858 Hamaekers Mats**
Student number + name

Opleiding/*Programme*: **2 ma revalid. & kine neuro**

INSTRUCTIES - *INSTRUCTIONS*

Neem onderstaande informatie grondig door.

Print dit document en vul het aan met DRUKLETTERS.

In tijden van van online onderwijs door COVID-19 verstuur je het document (scan of leesbare foto) ingevuld via mail naar je promotor. Je promotor bezorgt het aan de juiste dienst voor verdere afhandeling.

Vul luik A aan. Bezorg het formulier aan je promotoren voor de aanvullingen in luik B. Zorg dat het formulier ondertekend en gedateerd wordt door jezelf en je promotoren in luik D en dien het in bij de juiste dienst volgens de afspraken in jouw opleiding.
Zonder dit inschrijvingsformulier krijg je geen toegang tot upload/verdediging van je masterproef.

Please read the information below carefully.

Print this document and complete it by hand writing, using CAPITAL LETTERS.

In times of COVID-19 and during the online courses you send the document (scan or readable photo) by email to your supervisor. Your supervisor delivers the document to the appropriate department.

Fill out part A. Send the form to your supervisors for the additions in part B. Make sure that the form is signed and dated by yourself and your supervisors in part D and submit it to the appropriate department in accordance with the agreements in your study programme.
Without this registration form, you will not have access to the upload/defense of your master's thesis.

LUIK A - VERPLICHT - IN TE VULLEN DOOR DE STUDENT
PART A - MANDATORY - TO BE FILLED OUT BY THE STUDENT

Titel van Masterproef/*Title of Master's thesis:*

O behouden - *keep*

● wijzigen - *change to*:
UPPER LIMB DYSFUNCTION IN MULTIPLE SCLEROSIS: A FOLLOW-UP STUDY

/:

O behouden - *keep*

O wijzigen - *change to*:

In geval van samenwerking tussen studenten, naam van de medestudent(en)/*In case of group work, name of fellow student(s)*:

● behouden - *keep* HELENA GILSON

O wijzigen - *change to:*

LUIK B - VERPLICHT - IN TE VULLEN DOOR DE PROMOTOR(EN)
PART B - MANDATORY - TO BE FILLED OUT BY THE SUPERVISOR(S)

Wijziging gegevens masterproef in luik A/*Change information Master's thesis in part A:*

O goedgekeurd - *approved*

O goedgekeurd mits wijziging van - *approved if modification of:*

Scriptie/*Thesis:*

O openbaar (beschikbaar in de document server van de universiteit)- *public (available in document server of university)*

O vertrouwelijk (niet beschikbaar in de document server van de universiteit) - *confidential (not available in document server of university)*

Juryverdediging/*Jury Defense:*

De promotor(en) geeft (geven) de student(en) het niet-bindend advies om de bovenvermelde masterproef in de bovenvermelde periode/*The supervisor(s) give(s) the student(s) the non-binding advice:*

O te verdedigen/*to defend the aforementioned Master's thesis within the aforementioned period of time*

O de verdediging is openbaar/*in public*

O de verdediging is niet openbaar/*not in public*

O niet te verdedigen/*not to defend the aforementioned Master's thesis within the aforementioned period of time*

LUIK C - OPTIONEEL - IN TE VULLEN DOOR STUDENT, alleen als hij luik B wil overrulen
PART C - OPTIONAL - TO BE FILLED OUT BY THE STUDENT, only if he wants to overrule part B

In tegenstelling tot het niet-bindend advies van de promotor(en) wenst de student de bovenvermelde masterproef in de bovenvermelde periode/*In contrast to the non-binding advice put forward by the supervisor(s), the student wishes:*

O niet te verdedigen/*not to defend the aforementioned Master's thesis within the aforementioned period of time*

O te verdedigen/*to defend the aforementioned Master's thesis within the aforementioned period of time*

LUIK D - VERPLICHT - IN TE VULLEN DOOR DE STUDENT EN DE PROMOTOR(EN)
PART D - MANDATORY - TO BE FILLED OUT BY THE STUDENT AND THE SUPERVISOR(S)

Datum en handtekening student(en)
Date and signature student(s)

28/05/2022

Datum en handtekening promotor(en)
Date and signature supervisor(s)

Peter Feys 30/05/2022

UHASSELT
KNOWLEDGE IN ACTION

Inschrijvingsformulier verdediging masterproef academiejaar 2021-2022,
Registration form jury Master's thesis academic year 2021-2022,

GEGEVENS STUDENT - *INFORMATION STUDENT*

Faculteit/School: **Faculteit Revalidatiewetenschappen**
Faculty/School: ***Rehabilitation Sciences***

Stamnummer + naam: **1746608 Gilson Helena**
Student number + name

Opleiding/*Programme*: **2 ma revalid. & kine musc.**

INSTRUCTIES - *INSTRUCTIONS*

Neem onderstaande informatie grondig door.

Print dit document en vul het aan met DRUKLETTERS.

In tijden van van online onderwijs door COVID-19 verstuur je het document (scan of leesbare foto) ingevuld via mail naar je promotor. Je promotor bezorgt het aan de juiste dienst voor verdere afhandeling.

Vul luik A aan. Bezorg het formulier aan je promotoren voor de aanvullingen in luik B. Zorg dat het formulier ondertekend en gedateerd wordt door jezelf en je promotoren in luik D en dien het in bij de juiste dienst volgens de afspraken in jouw opleiding.
Zonder dit inschrijvingsformulier krijg je geen toegang tot upload/verdediging van je masterproef.

Please read the information below carefully.

Print this document and complete it by hand writing, using CAPITAL LETTERS.

In times of COVID-19 and during the online courses you send the document (scan or readable photo) by email to your supervisor. Your supervisor delivers the document to the appropriate department.

Fill out part A. Send the form to your supervisors for the additions in part B. Make sure that the form is signed and dated by yourself and your supervisors in part D and submit it to the appropriate department in accordance with the agreements in your study programme.
Without this registration form, you will not have access to the upload/defense of your master's thesis.

LUIK A - VERPLICHT - IN TE VULLEN DOOR DE STUDENT
PART A - MANDATORY - TO BE FILLED OUT BY THE STUDENT

Titel van Masterproef/*Title of Master's thesis:*

O behouden - *keep*

X wijzigen - *change to:*

UPPER LIMB DYSFUNCTION IN MULTIPLE SCLEROSIS : A FOLLOW-UP STUDY

/:

O behouden - *keep*

O wijzigen - *change to:*

In geval van samenwerking tussen studenten, naam van de medestudent(en)/*In case of group work, name of fellow student(s):*

X behouden - *keep* MATS HANAEKERS

O wijzigen - *change to:*

LUIK B - VERPLICHT - IN TE VULLEN DOOR DE PROMOTOR(EN)
PART B - MANDATORY - TO BE FILLED OUT BY THE SUPERVISOR(S)

Wijziging gegevens masterproef in luik A/*Change information Master's thesis in part A:*

O goedgekeurd - *approved*

O goedgekeurd mits wijziging van - *approved if modification of:*

Scriptie/*Thesis:*

O openbaar (beschikbaar in de document server van de universiteit)- *public (available in document server of university)*

O vertrouwelijk (niet beschikbaar in de document server van de universiteit) - *confidential (not available in document server of university)*

Juryverdediging/*Jury Defense:*

De promotor(en) geeft (geven) de student(en) het niet-bindend advies om de bovenvermelde masterproef in de bovenvermelde periode/*The supervisor(s) give(s) the student(s) the non-binding advice:*

O te verdedigen/*to defend the aforementioned Master's thesis within the aforementioned period of time*

O de verdediging is openbaar/*in public*

O de verdediging is niet openbaar/*not in public*

O niet te verdedigen/*not to defend the aforementioned Master's thesis within the aforementioned period of time*

LUIK C - OPTIONEEL - IN TE VULLEN DOOR STUDENT, alleen als hij luik B wil overrulen
PART C - OPTIONAL - TO BE FILLED OUT BY THE STUDENT, only if he wants to overrule part B

In tegenstelling tot het niet-bindend advies van de promotor(en) wenst de student de bovenvermelde masterproef in de bovenvermelde periode/*In contrast to the non-binding advice put forward by the supervisor(s), the student wishes:*

O niet te verdedigen/*not to defend the aforementioned Master's thesis within the aforementioned period of time*

O te verdedigen/*to defend the aforementioned Master's thesis within the aforementioned period of time*

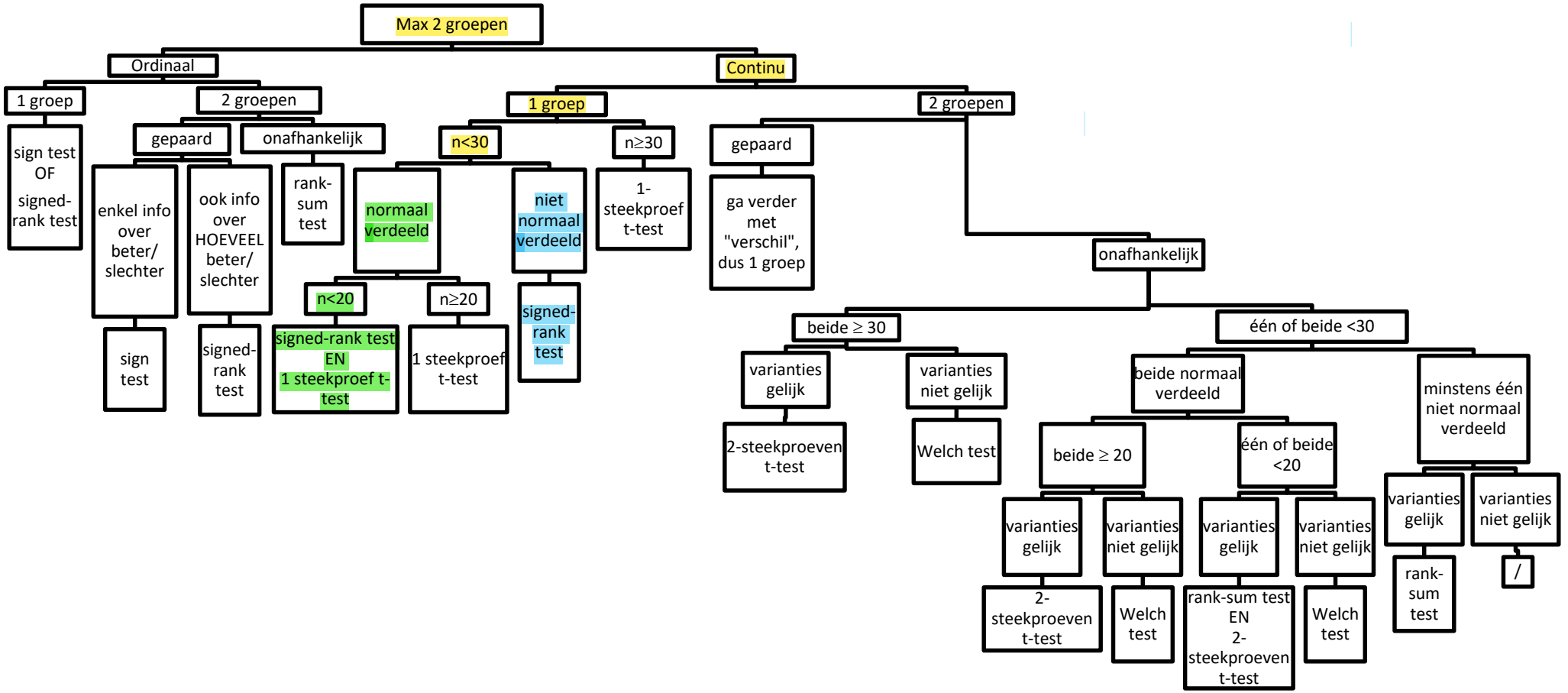
LUIK D - VERPLICHT - IN TE VULLEN DOOR DE STUDENT EN DE PROMOTOR(EN)
PART D - MANDATORY - TO BE FILLED OUT BY THE STUDENT AND THE SUPERVISOR(S)

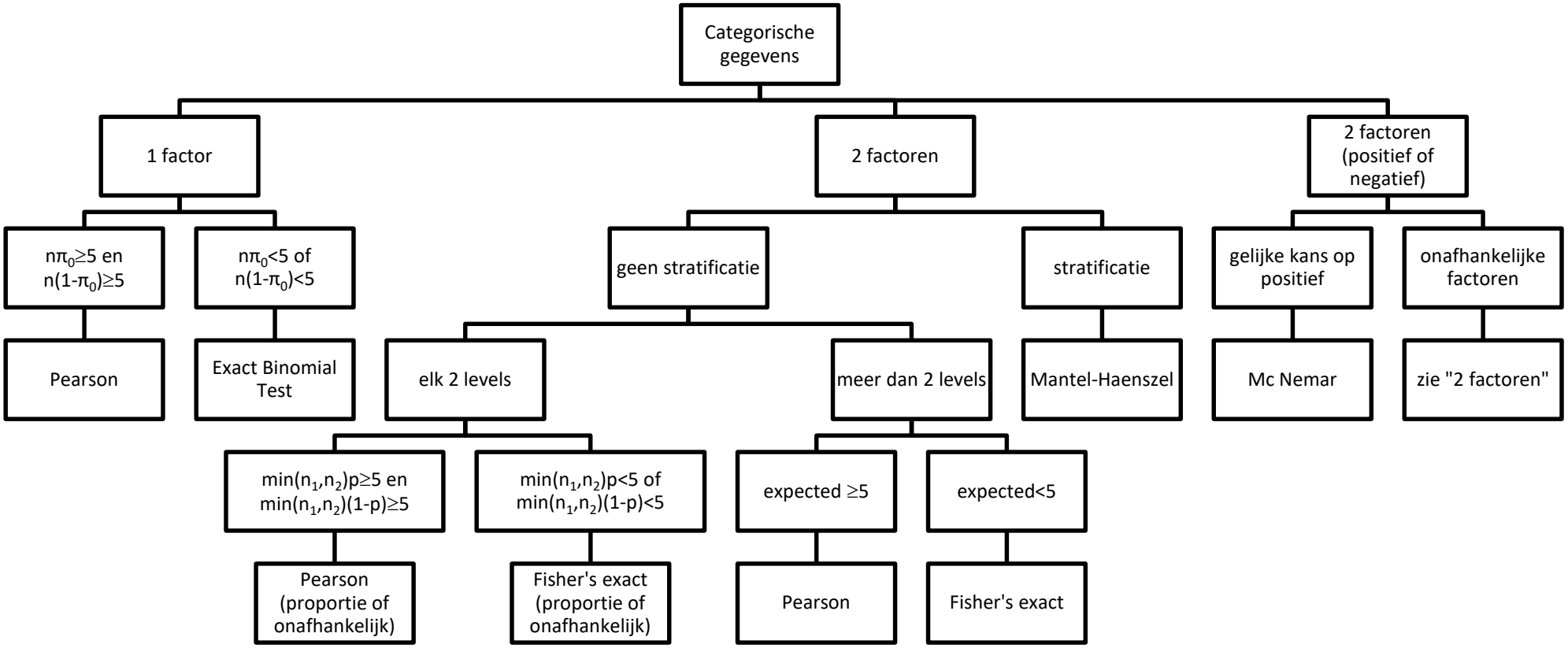
Datum en handtekening student(en)
Date and signature student(s)

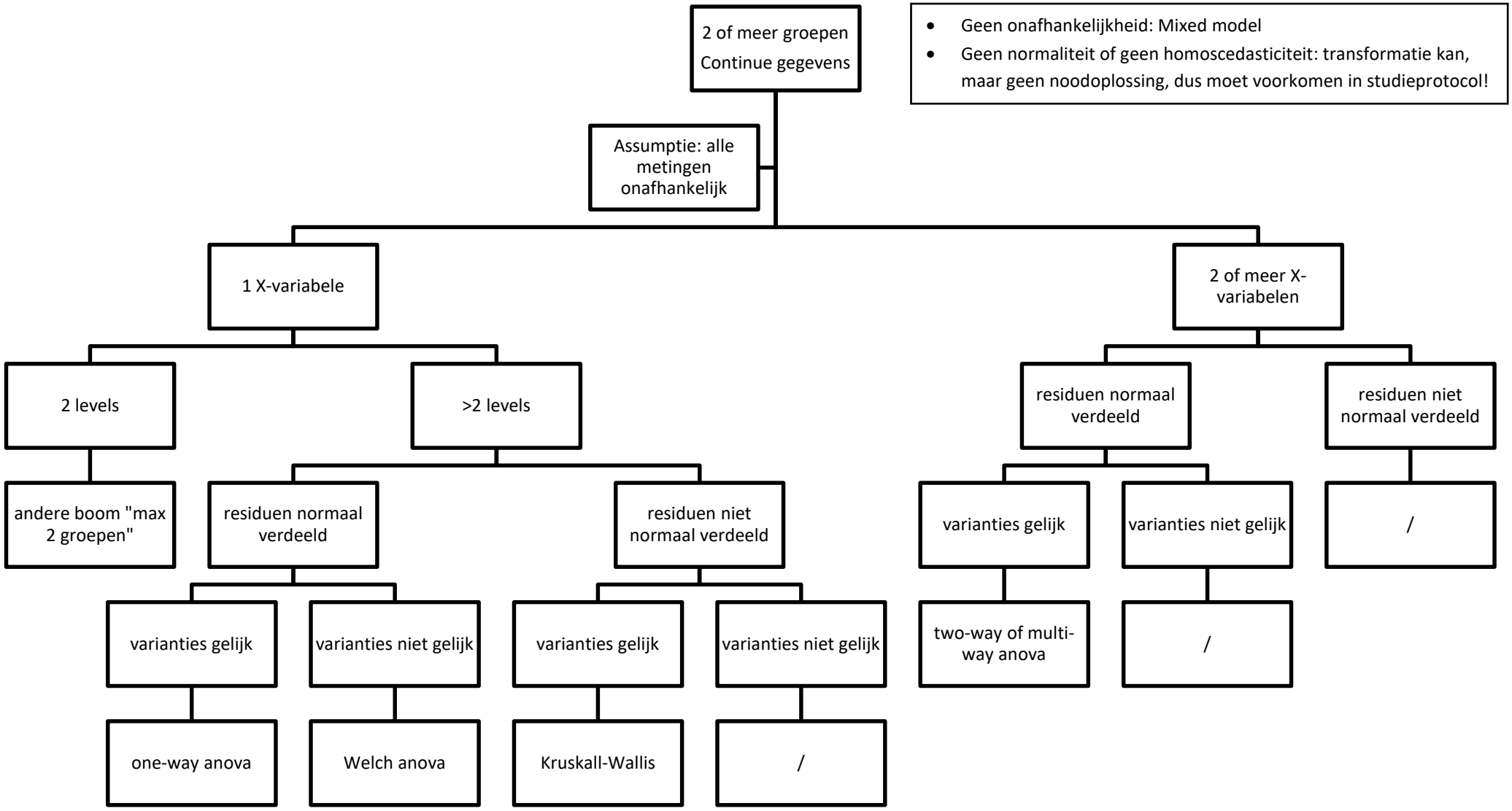
28/05/2022

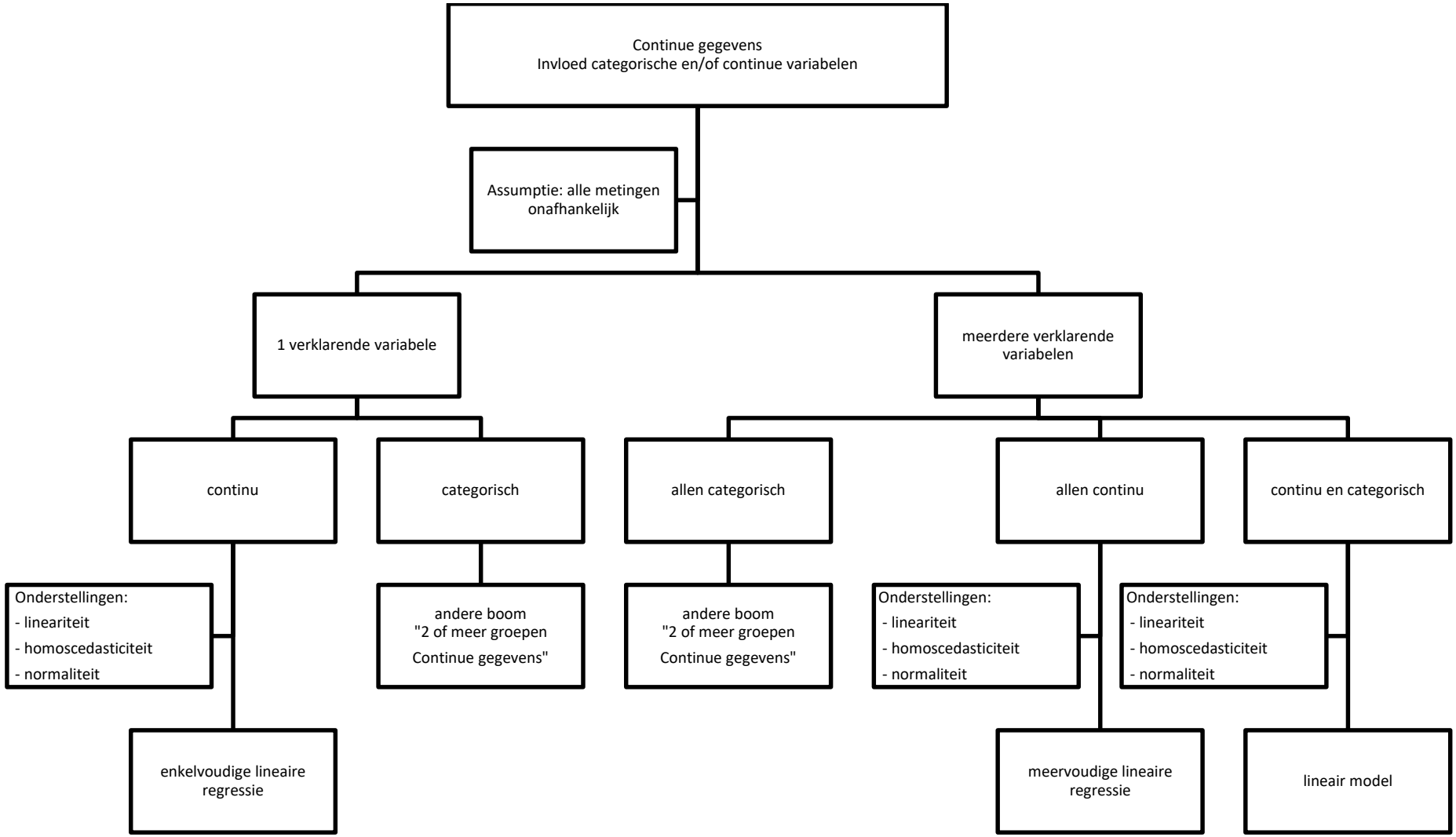
Datum en handtekening promotor(en)
Date and signature supervisor(s)

Peter Feys 30/05/2022


Max 2 groepen
Ordinaal
1 groep
sign test OF signed-rank test
2 groepen
gepaard
enkel info over beter/ slechter
sign test
ook info over HOEVEEL beter/ slechter
signed-rank test
onafhankelijk
rank-sum test
Continu
1 groep
n<30
normaal verdeeld
n<20
signed-rank test EN 1 steekproef t-test
n≥20
1 steekproef t-test
niet normaal verdeeld
signed-rank test
n≥30
1-steekproef t-test
2 groepen
gepaard
ga verder met "verschil", dus 1 groep
onafhankelijk
beide ≥ 30
varianties gelijk
2-steekproeven t-test
varianties niet gelijk
Welch test
één of beide <30
beide normaal verdeeld
beide ≥ 20
varianties gelijk
2-steekproeven t-test
varianties niet gelijk
Welch test
één of beide <20
varianties gelijk
rank-sum test EN 2-steekproeven t-test
varianties niet gelijk
Welch test
minstens één niet normaal verdeeld
varianties gelijk
rank-sum test
varianties niet gelijk
/


Categorische gegevens
1 factor
2 factoren
2 factoren (positief of negatief)
$n\pi_0 \geq 5$ en $n(1-\pi_0) \geq 5$
$n\pi_0 < 5$ of $n(1-\pi_0) < 5$
geen stratificatie
stratificatie
gelijke kans op positief
onafhankelijke factoren
Pearson
Exact Binomial Test
elk 2 levels
meer dan 2 levels
Mantel-Haenszel
Mc Nemar
zie "2 factoren"
$\min(n_1,n_2)p \geq 5$ en $\min(n_1,n_2)(1-p) \geq 5$
$\min(n_1,n_2)p < 5$ of $\min(n_1,n_2)(1-p) < 5$
expected ≥5
expected<5
Pearson (proportie of onafhankelijk)
Fisher's exact (proportie of onafhankelijk)
Pearson
Fisher's exact


2 of meer groepen
Continue gegevens
Assumptie: alle metingen onafhankelijk
1 X-variabele
2 of meer X-variabelen
2 levels
>2 levels
residuen normaal verdeeld
residuen niet normaal verdeeld
andere boom "max 2 groepen"
residuen normaal verdeeld
residuen niet normaal verdeeld
varianties gelijk
varianties niet gelijk
varianties gelijk
varianties niet gelijk
varianties gelijk
varianties niet gelijk
/
two-way of multi-way anova
/
one-way anova
Welch anova
Kruskall-Wallis
/
Geen onafhankelijkheid: Mixed model
Geen normaliteit of geen homoscedasticiteit: transformatie kan, maar geen noodoplossing, dus moet voorkomen in studieprotocol!


Continue gegevens
Invloed categorische en/of continue variabelen
Assumptie: alle metingen onafhankelijk
1 verklarende variabele
meerdere verklarende variabelen
continu
categorisch
allen categorisch
allen continu
continu en categorisch
Onderstellingen:
- lineariteit
- homoscedasticiteit
- normaliteit
andere boom
"2 of meer groepen
Continue gegevens"
andere boom
"2 of meer groepen
Continue gegevens"
Onderstellingen:
- lineariteit
- homoscedasticiteit
- normaliteit
Onderstellingen:
- lineariteit
- homoscedasticiteit
- normaliteit
enkelvoudige lineaire regressie
meervoudige lineaire regressie
lineair model