UHASSELT

KNOWLEDGE IN ACTION

Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

Early development of fine and gross motor skills in boys with Duchenne Muscular Dystrophy

Manon Simons
Valerie Snellings

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

PROMOTOR :

Prof. dr. Katrijn KLINGELS

BEGELEIDER :

Mevrouw Jasmine HOSKENS

2021
2022

UHASSELT
KNOWLEDGE IN ACTION

www.uhasselt.be
Universiteit Hasselt
Campus Hasselt:
Martelarenlaan 42 | 3500 Hasselt
Campus Diepenbeek:
Agoralaan Gebouw D | 3590 Diepenbeek

UHASSELT

KNOWLEDGE IN ACTION

Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

Early development of fine and gross motor skills in boys with Duchenne Muscular Dystrophy

Manon Simons
Valerie Snellings

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

PROMOTOR :

Prof. dr. Katrijn KLINGELS

BEGELEIDER :

Mevrouw Jasmine HOSKENS

2nd Master in Rehabilitation Science and Physiotherapy
Academic year: 2021-2022

Early development of fine and gross motor skills in boys with Duchenne Muscular Dystrophy

"Are there differences in both fine and gross motor skills between preschool boys with Duchenne Muscular Dystrophy and aged matched typically developing children in the first six years of life?"

Manon Simons (1745652)
Valerie Snellings (1747428)
Promotor: Prof. Dr. Klingels K.
Mentor: Dra. Hoskens J.

Acknowledgement

In this preface, we would like to thank a number of people who have played an important role in the realization of this master's thesis.

First of all, we would like to thank our mentor Dra. Hoskens J. for coaching us and helping us whenever we were in trouble. We are also grateful to her for being able to participate in her PhD study and to use some of her data.

Next, we would like to acknowledge our promotor Prof. Dr. Klingels K. for rereading our master's thesis and for the good feedback we received.

We would also like to thank KULeuven and UHasselt for lending us the standardized material to perform the tests.

Furthermore, we would like to gratitude the children and their parents who participated in the tests to collect our data. We are very grateful to them for volunteering and making time for our research.

We would also like to thank the SPSS program. It was a very accessible program which allowed us to easily calculate our statistical analysis.

We would also like to acknowledge our family and friends who have supported us unconditionally during our studies. They have always believed in us.

Finally, we would like to thank each other for the excellent collaboration. Together, we were able to bring this master's thesis to a successful ending.

Veldstraat 18 3500 Hasselt, 6/06/2022 M.S.

Hasseltsestraat 77 3740 Bilzen, 6/06/2022 V.S.

Research context

This master's thesis can be situated within the research domain of pediatric rehabilitation, more specifically within the field of development of boys with Duchenne Muscular Dystrophy (DMD). The relevance of this research contributes to the better understanding of early fine and gross motor deficits in young DMD boys compared to typically developing (TD) boys and thereby early initiation of appropriate treatment methods.

This master's thesis is part of an ongoing research project by Dra. Hoskens J. in collaboration with KU Leuven and UZ Leuven called "Evaluation of early developmental domains in infants and young children with Duchenne Muscular Dystrophy", under the supervision of Prof. Dr. Klingels K.

A quantitative, cross-sectional study was conducted for this duo-master's thesis. Both students contributed equally to the completion of this thesis.

As the research design had already been elaborated within an ongoing research project, it was only partially determined by both students. Participant recruitment and data acquisition was mostly conducted within the research project of Dra. Hoskens J., both students recruited a number of TD children and acquired the data from these children. Data processing was performed completely independently by collaboration of both students with feedback and guidance from Dra. Hoskens J. Further, the two students contributed equally to the academic writing process and the completion of the thesis.

Part 2: Academic research

Table of content

1. Abstract

Background: Duchenne Muscular Dystrophy (DMD) is an X-linked recessive disease that affects 1/5000 boys. The disease is caused by a mutation in the dystrophin gene that causes progressive muscle weakness with a proximodistal course. The mean age of diagnosis is around 5 years, but deficits in fine and gross motor skills can already be seen at a very young age. Early detection and diagnosis of DMD is important for the initiation of early treatment.

Objectives : This cross-sectional study was aimed to describe and evaluate early fine and gross motor development of preschool boys with DMD between the ages of 0 and 6 years, compared to age matched typically developing (TD) children.

Participants: A total of 18 DMD boys (mean age: 3 year 9 months ± 1 year 8 months) and 18 age matched TD children (mean age: 3y 9m ± 1y 7m) were assessed in this study.

Measurements: The Bayley Scales of Infant and Toddler Development (Bayley-III-NL) and Peabody Developmental Motor Scale (PDMS-II) were used to evaluate both fine and gross motor skills. In addition, the North Star Ambulatory Assessment (NSAA), Timed Function tests (TFTs) and the Motor Function Measure for neuromuscular diseases (MFM-20) were conducted.

Results: The results of the Bayley-III-NL and the PDMS-II demonstrated that both fine and gross motor skills are affected significantly in DMD boys compared to TD children, with gross motor skills being more severely impaired at this young age. Likewise, for the NSAA, TFTs and MFM-20 boys with DMD scored significantly lower than TD children.

Conclusion: The overall conclusion of this study is that there are significant differences in both fine and gross motor skills between preschool boys with DMD and aged matched TD children in the first six years of life. In addition, it is of great importance that therapy does not only focus on gross motor skills but also on fine motor skills and that it is tailored to the child's individual needs.

Keywords: Duchenne Muscular Dystrophy, typically developing children, infant, preschool child, fine motor development, gross motor development

2. Introduction

Duchenne Muscular Dystrophy (DMD) is an X-linked recessive disease that affects 1/5000 boys, making it the most common form of muscular dystrophy (Yiu & Kornberg, 2015). The disease is caused by a mutation in the dystrophin gene that is located on the X chromosome. This mutation results in the absence or disruption of the protein dystrophin, which is found in various tissues, particularly skeletal muscle and neurons in certain parts of the CNS (Anderson et al., 2002). This causes progressive muscle weakness manifesting from proximal to distal (Sussman, 2002). The proximal weakness manifests itself in the typical Gower's maneuver in young children with DMD. Progression of muscle weakness results in loss of ambulation between the age of 12-13 years old (Bushby et al., 2010). At a later stage, cardiovascular and respiratory complications are a major cause of morbidity and mortality (Birnkrant et al., 2018).

Differences in fine motor (FM) and gross motor (GM) skills have already been observed in young DMD boys compared to typically developing (TD) children (e.g. the typical Gower's maneuver, delays in the achievement of fine and gross motor milestones, lower scores on outcome measures) (van Dommelen et al. 2020; Connolly et al., 2013; Arora et al., 2018). In this young population of DMD boys, fine motor skills are less affected than gross motor skills (Connolly et al., 2013). Several longitudinal studies reported that motor skills may still improve until an age of approximately 6-7 years old due to normal growth and development, but the gap between DMD and TD does increase (Alfano et al., 2017; Mazzone et al., 2011; Mazzone et al., 2013; Pane et al., 2014b; Connolly et al., 2013; Connolly et al., 2014).

The mean age of diagnosis is around 5 years, but first signs or symptoms can already be seen at a very young age (Ciafaloni et al., 2009). Often, there is a delay of 2.5 years between the onset of symptoms and the diagnosis (Verma et al. 2010). This delay has a detrimental effect on the treatment because it has been widely suggested that any intervention that potentially modifies the natural history of the condition may be of greater benefit in less damaged muscles; in other words, in younger children. Early detection and diagnosis of DMD therefore provides a better quality of life and clinical outcome for the boys. (van Ruiten et al., 2014)

Despite the fact that many studies have already been conducted around DMD, more information is still needed on the early motor development of DMD boys under the age of 6, especially on fine motor skills. Many of these studies were also retrospective, did not compare to TD children or examined only fine or only gross motor skills (Sarrazin et al., 2014; van Dommelen et al., 2020; Ricotti et al., 2019; Hyde et al., 2001; Nair et al., 2001; Alfano et al., 2017; Arora et al., 2018; De Sanctis et al., 2015; Doglio et al., 2011; Fowler et al., 2018; Henricson et al., 2012; Janssen et al., 2014; Mazzone et al., 2011; Mazzone et al., 2013; McDonald et al., 2010; Pereira et al., 2020).

The aim of this cross-sectional study is to describe and evaluate early fine and gross motor development of boys with DMD between the ages of 0 and 6 years, compared to TD children. The relevance and added value of this study is therefore to obtain more information about the early symptoms in children with DMD, not only in terms of gross motor skills but also in terms of fine motor skills. This is formulated as the following research question: “Are there differences in both fine and gross motor skills between preschool boys with Duchenne Muscular Dystrophy and aged matched typically developing children in the first six years of life?”

3. Methods

3.1. Participants

Infants and young boys between the ages of 0 and 6 years, diagnosed with Duchenne Muscular Dystrophy, were recruited from the Neuromuscular Reference Center of the University Hospital (UZ) of Leuven. For each Duchenne boy, one age matched TD boy between 0 and 6 years was recruited from kindergartens and day-care centers. Information and consent forms were handed out here. From the group of children whose parents gave permission, children were selected based on their date of birth.

DMD boys participating in the study must meet the following criteria:

- Genetic diagnosis of DMD.
- Aged between 0 and 6 years old.
- Able to complete assessment scales.

TD boys participating in the study must meet the following criteria:

- No musculoskeletal, neurological, or cardiorespiratory conditions.
- Aged between 0 and 6 years old.
- Able to complete assessment scales.

Children were excluded from the study if they did not meet the predefined inclusion criteria.

3.2. Medical ethics

This study was evaluated by the medical ethics committee at UZ Leuven, which gave a positive opinion (S59068).

3.3. Procedure

Most of the scales and questionnaires will be implemented in the standard evaluations that take place during consultations at UZ Leuven. If necessary an extra evaluation will be planned at home, at the day-care center or at school. The evaluations of TD children will be planned in consultation with the parents at an appropriate location. The boys were evaluated by three evaluators. All the DMD boys were assessed by Dra. Hoskens J. and the TD boys were also evaluated by Dra. Hoskens J. or by the two master students. At the beginning of the evaluation, the Bayley Scales of Infant and Toddler Development - third edition - Nederlandse versie (Bayley-III-NL) and/or the Peabody Developmental Motor Scale - second edition

(PDMS-II) were applied. Then North Star Ambulatory Assessment (NSAA), Timed Function Tests (TFTs) and the Motor Function Measure for neuromuscular diseases (MFM-20) were performed. Five-minute rest periods were inserted between the tests to prevent fatigue. Different motor evaluation scales were used according to the age of the child (Figure 1).

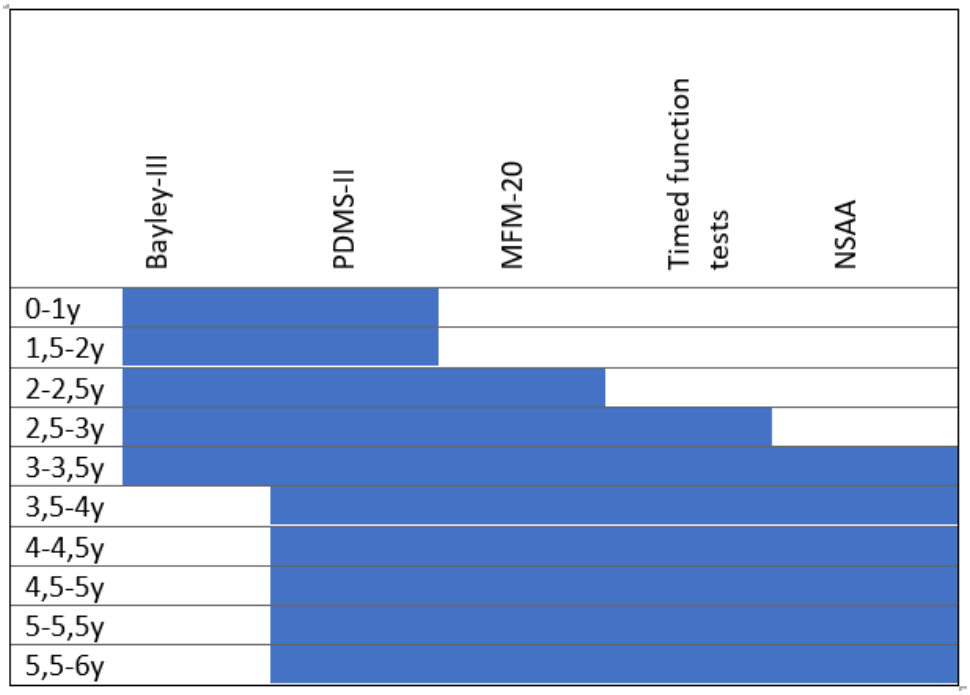


Figure 1. Overview assessment tools by age

3.3.1. Primary outcomes

Bayley Scales of Infant and Toddler Development - third edition - Nederlandse versie (Bayley-III-NL)

This scale measures the development of babies and children from 16 days to 42 months and consists of five different scales that can be administered separately. The 5 domains that are evaluated are: cognition (91 items); language, subdivided into receptive communication (49 items) and expressive communication (46 items); motor skills, subdivided into fine (66 items) and gross motor skills (72 items); social emotional development (35 items) and adaptive behavior (241 items). The last two domains are evaluated via parent interviews. A raw score is calculated per subscale, which can be used to determine scale scores, index scores, percentile scores, growth scores and a developmental age equivalent (Bayley, 2006; Pearson, 2015). For this study, only scale scores of FM and GM skills and total motor index score were included. The scale has been shown to be reliable and valid (Deroma et al., 2013).

Peabody Developmental Motor Scale - second edition (PDMS-II)

The PDMS-II evaluates fine and gross motor skills in infants and young children aged 0 to 6 years. This scale consists of six domains. Reflexes (8 items), stationary (30 items), locomotion (89 items) and object manipulation (24 items), for assessing gross motor skills. Reflexes are usually integrated by the time a child is 12 months old, therefore the subscale "reflexes" is only given to children from birth to 11 months. The subscale "object manipulation" is only given to children 12 months and older because these skills only become evident when a child reaches the age of 11 months. For assessing fine motor skills, grasping (26 items) and visual-motor integration (72 items) are evaluated. Raw scores, percentiles, age equivalents and standard scores can be recorded for each subscale and for overall gross and fine motor skills. This study included standard scores and quotient scores. The scale has been shown to be reliable and valid. (Folio & Fewell, 2000)

(Revised) North Star Ambulatory Assessment (NSAA)

The NSAA is a functional scale for gross motor skills specifically developed to measure ambulatory status in DMD boys older than 4 years. The test consists of 17 items with an ordinal scale scoring system of zero to two. The total score on 34 points was included in this study. A modified version exists for children aged 3 to 5 years old called the revised NSAA (Mercuri et al. 2016). The scale has been shown to be valid and reliable from the age of 3 years and 6 months (Eagle et al., 2007; Mazzone et al., 2009; De Sanctis et al., 2015).

Timed Function Tests (TFTs)

The Timed Function Tests consist of four tasks that are performed separately: time to rise from floor (TRF), walking/running 10 meters (10m walk/run), climbing 4 stairs, and descending 4 stairs. These tasks need to be performed as quickly as possible. The speed and quality of execution of the tasks are assessed (Mazzone et al., 2010). TFTs have been shown to be feasible, inexpensive and safe measures of submaximal endurance and function, especially in young children. Normative data and percentile curves were used from TD boys between 2.5 and 6 years of age. (Hoskens et al., 2019)

Motor Function Measure for neuromuscular diseases (<7 years) (MFM-20)

The MFM-20 is a shortened version of the MFM-32 for children from 2 to 6 years old with neuromuscular diseases and evaluates the severity and progression of motor function. The MFM-20 consists of 20 items subdivided in three domains, namely: standing position and transfers (8 items), axial and proximal motor function (8 items) and distal motor function (4 items). Scoring is on a 4-point Likert scale. The total score and subscores are expressed as a percentage of the maximum possible score obtained by healthy children. The total percentage score was recorded for this test. High inter-rater and intra-rater reliability and good discriminant validity were found for the MFM-20 (de Lattre et al., 2013).

3.4. Data-analysis

The characteristics of the two groups were described via descriptive statistics. Mean and standard deviation (SD) or median and interquartile range (IQR) were used depending on data distribution, as well as the 95% Confidence Interval and the applied p-value. To check the normality of the data, the Shapiro-Wilk test and visual inspection of distribution plots were used. The significance level of 0.05 was applied. Parametric two-samples t-test was used to analyze differences in the Bayley-III-NL between DMD boys and TD boys. Equal variances were assumed for the Bayley-III-NL, based on the Levene's test for equality of variances. For the PDMS-II, NSAA, TFTs and MFM-20, non-parametric tests were carried out using the Mann-Whitney U-test for comparison between DMD boys and TD boys. For tests with multiple outcome measures (Bayley-III-NL, PDMS-II, TFTs), the significance level was adjusted with the Bonferroni correction.

Statistical analysis was performed by Statistical Package for the Social Sciences software (SPSS version 28.0).

4. Results

Eighteen DMD boys between 0 and 6 years old met the inclusion criteria and participated in this study. Baseline age and anthropometric characteristics are presented in Table 1. Individual anthropometric characteristics and mutations of these DMD boys can be found in Table 5 in the appendix. Subsequently, 18 randomly selected TD boys were matched with the DMD boys based on age. No significant differences were observed in age, height and body weight between the two groups at baseline.

Table 1
Participant characteristics

Characteristics	DMD (n=18)	TD (n=18)	Two-sided p-value
	X ± SD	X ± SD	
Age (years months)	3y 9m ± 1y 8m	3y 9m ± 1y 7m	0.963
Height (cm)	99.22 ± 11.70	103.39 ± 15.24	0.363
Body weight (kg)	16.17 ± 4.54	16.12 ± 4.50	0.973

DMD: Duchenne Muscular Dystrophy; TD: Typically developing; X: Mean; SD: Standard deviation; cm: centimeters; kg: kilogram.

Eight boys with DMD (mean age: 2y 3m) and 8 TD boys (mean age: 2y 2m) completed the Bayley-III-NL. The results showed significant differences in gross motor (p= <0.001), fine motor (p= <0.001) and total motor (p= <0.001) subscales, in favor of the TD boys. The DMD boys had a mean (SD) FM scale score of 4.75 (± 2.82) while the TD boys had a mean (SD) FM scale score of 10.13 (± 2.59). The mean (SD) GM scale score for the boys with DMD was even lower than the FM scale score, namely 3.75 (± 1.67). Whereas in TD boys this was 10.38 (± 2.72). Detailed results can be found in Table 2 and Figure 2a, 2b, 2c.

Table 2
Results Bayley-III-NL

Bayley-III-NL	DMD (n=8; mean age: 2y 3m)	TD (n=8; mean age: 2y 2m)	95% Confidence Interval		One-sided p-value
	X ± SD	X ± SD	Lower	Upper	
FM scale score	4.75 ± 2.82	10.13 ± 2.59	-8.28	-2.48	<0.001*
GM scale score	3.75 ± 1.67	10.38 ± 2.72	-9.05	-4.20	<0.001*
TM index score	65.50 ± 11.45	101.88 ± 13.25	-49.65	-23.10	<0.001*

DMD: Duchenne Muscular Dystrophy; TD: Typically developing; y: Years old; m: Months; X: Mean; SD: Standard deviation; FM: Fine Motor; GM: Gross Motor; TM: Total Motor.
*Significant at the p<0.0125 level.

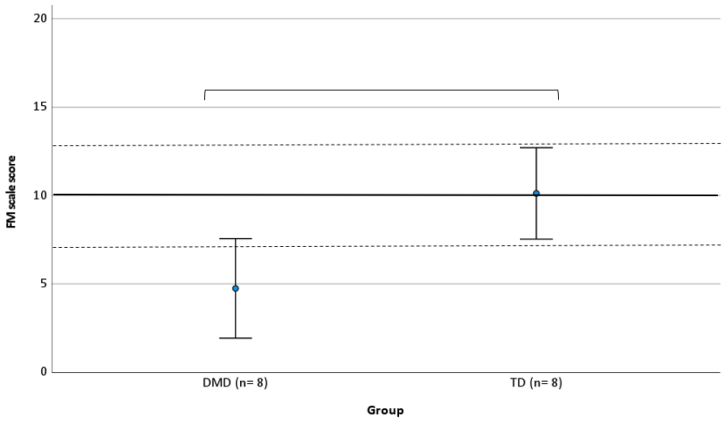


Figure 2a. Mean and SD
Bayley-III-NL Fine Motor scale scores
(average scale score: 10, SD: 3)

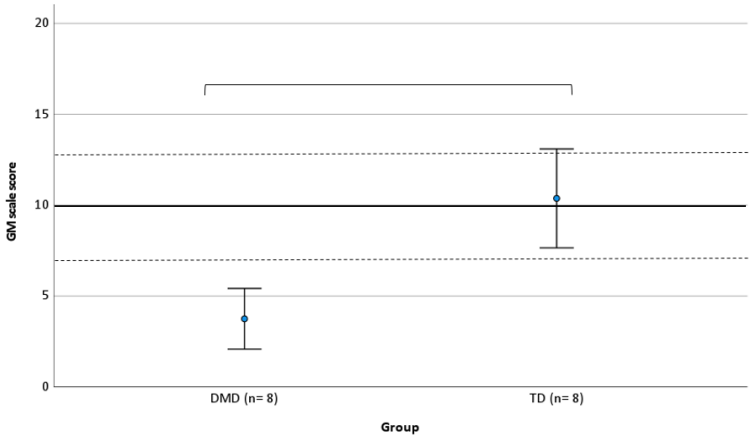


Figure 2b. Mean and SD
Bayley-III-NL Gross motor scale scores
(average scale score: 10, SD: 3)

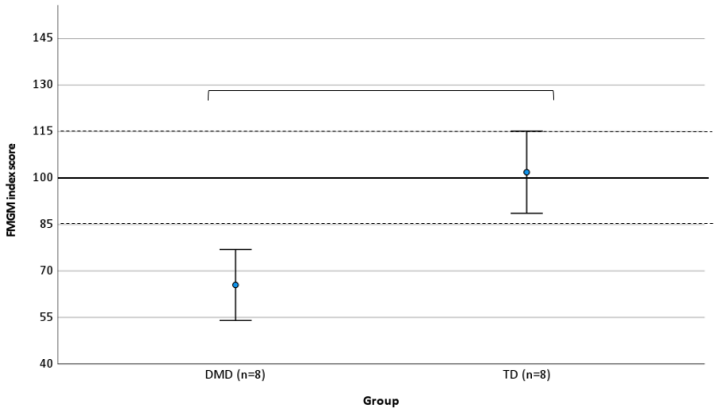


Figure 2c. Mean and SD
Bayley-III-NL Total motor index scores
(average index score: 100, SD: 15)

(the brackets indicate significant differences)

In 17 DMD boys (mean age: 3y 7m) and 17 TD boys (mean age: 3y 7m), the PDMS-II was administered. Significant differences were also found between DMD boys and TD children in all subscales within gross motor skills (p= <0.001) with the DMD children having lower scores. For the fine motor subscales, a significant difference was seen for visuomotor integration (p= <0.001) and total fine motor scores (p= <0.001). No significant difference was observed between the two groups for subscale grasping (p= 0.045). Total motor subscales also showed a significant difference (p= <0.001) between the two groups. For DMD boys the median (IQR) GM quotient score was 70.00 (67.00-75.00), while for the TD children this was 102.00 (98.00-104.00). Median (IQR) FM quotient score was again higher than GM quotient score, being 85.00 (82.00-91.00) for DMD boys and 97.00 (89.50-103.00) for TD boys. Table 3 and Figure 3a, 3b, 3c present the details on these findings.

Table 3
Results PDMS-II

PDMS-II	DMD (n=17; mean age: 3y 7m)	TD (n=17; mean age: 3y 7m)	Mann-Whitney U test p-value
	M (IQR)	M (IQR)	
Stationary standard score	7.00 (5.50-7.00)	11.00 (11.00-12.00)	<0.001*
Locomotion standard score	4.00 (4.00-5.00)	10.00 (9.00-11.00)	<0.001*
Object Manipulation standard score	6.00 (5.00-6.75)	9.00 (8.00-11.00)	<0.001*
Grasping standard score	8.00 (5.50-9.50)	10.00 (7.50-10.50)	0.045
Visual-Motor Integration standard score	8.00 (6.00-9.00)	10.00 (9.00-12.50)	<0.001*
GM quotient	70.00 (67.00-75.00)	102.00 (98.00-104.00)	<0.001*
FM quotient	85.00 (82.00-91.00)	97.00 (89.50-103.00)	<0.001*
TM quotient	75.00 (73.00-80.75)	101.00 (95.50-106.50)	<0.001*

DMD: Duchenne Muscular Dystrophy; TD: Typically developing; y: Years old; m: Months; M: Median; IQR: Interquartile range; GM: Gross Motor; FM: Fine Motor; TM: Total Motor.
*Significant at the p<0.003 level.

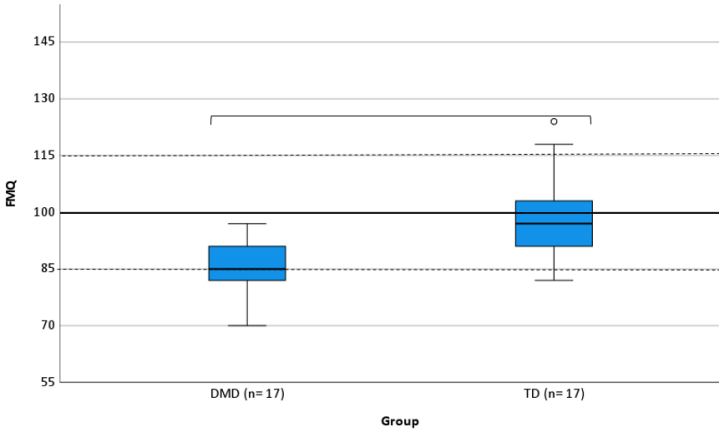


Figure 3a. Boxplots with Median and IQR PDMS-II Fine Motor Quotient scores (average quotient score: 100, SD: 15)

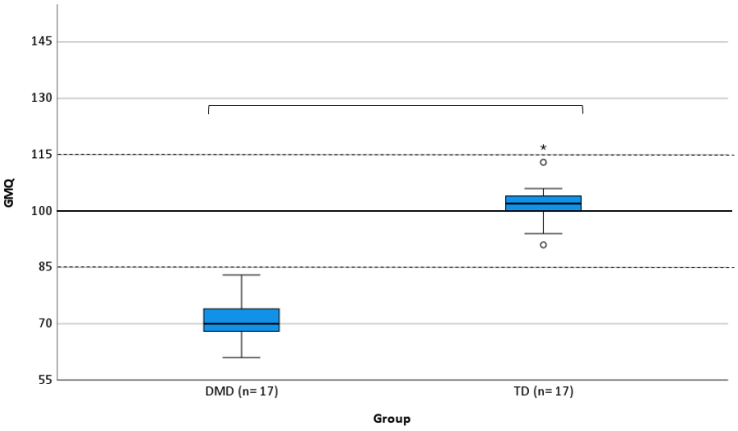


Figure 3b. Median and IQR PDMS-II Gross Motor Quotient scores (average quotient score: 100, SD: 15)

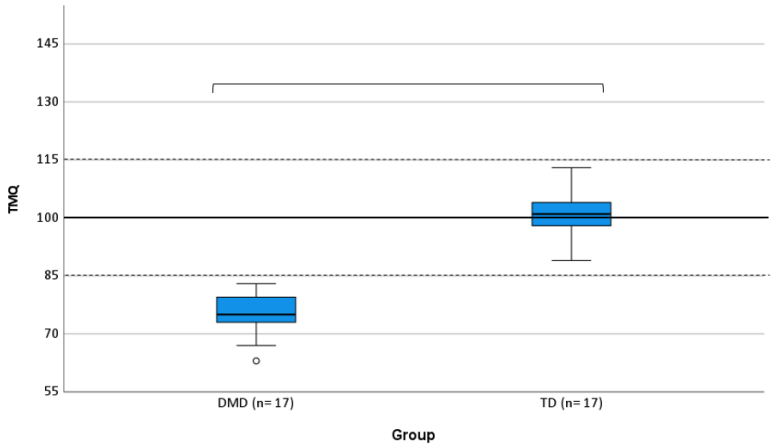


Figure 3c. Median and IQR
PDMS-II Total Motor Quotient scores
(average quotient score: 100, SD: 15)

°: outlier; *: extreme outlier; (the brackets indicate significant differences)

Ambulatory status was assessed by the NSAA in 12 DMD boys (mean age: 4y 8m) and 12 TD children (mean age: 4y 8m). The results showed that DMD boys scored significantly lower than TD children (p=<0.001). The median value (IQR) for TD children on the NSAA was 34 (33-34). For DMD boys, the median value (IQR) was 23 (18-27.25). Details can be seen in Figure 4.

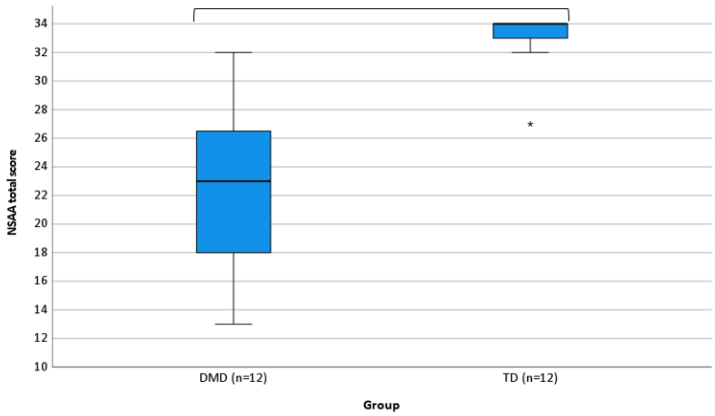


Figure 4. Median and IQR
NSAA total scores

*: extreme outlier; (the brackets indicate significant differences)

Eleven boys with DMD (mean age: 4y 10m) and 11 TD boys (mean age: 4y 10m) performed the TRF and the 10m walk/run test and 10 of them also performed the climbing and descending 4 stairs test. One TD boy was excluded for the TRF test and the 10m walk/run. For the climbing and descending 4 stairs tests, two TD boys were excluded. This was done to equalize the groups, as the outcome data of the aged matched DMD boys were not reliable for these tests. The results of the TFTs showed significant differences for the TRF (p= <0.001), the 10m walk/run test (p=0.004), climbing 4 stairs (p=0.036) and descending 4 stairs (p=0.05). In which boys with DMD require approximately 1.5x more time than TD children to complete these timed functions tests and thus they performed significantly longer. Detailed results can be found in Table 4 and Figure 5a, 5b, 5c, 5d.

Table 4
Results TFTs

TFTs	DMD (n=10/11; mean age: 4y 10m)	TD (n=10/11; mean age: 4y 10m)	Mann-Whitney U test p-value
	M (IQR)	M (IQR)	
TRF (sec)	3.65 (2.47-5.94)	2.10 (1.00-2.30)	<0.001*
10m walk/run (sec)	5.43 (4.55-6.50)	3.60 (3.20-4.00)	0.002*
Climbing 4 stairs (sec)	2.56 (2.07-5.00)	1.54 (1.28-2.02)	0.009*
Descending 4 stairs (sec)	3.32 (2.25-4.87)	1.83 (1.34-2.38)	0.009*

DMD: Duchenne Muscular Dystrophy; TD: Typically developing; M: Median; IQR: Interquartile range; sec: Seconds.
*Significant at the p<0.0125 level.

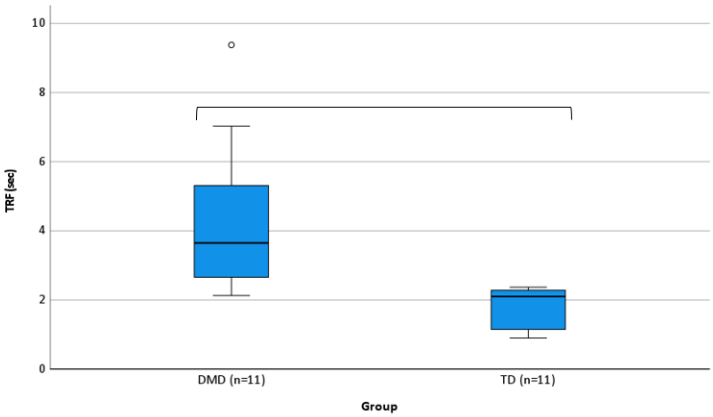


Figure 5a. Median and IQR TRF in seconds

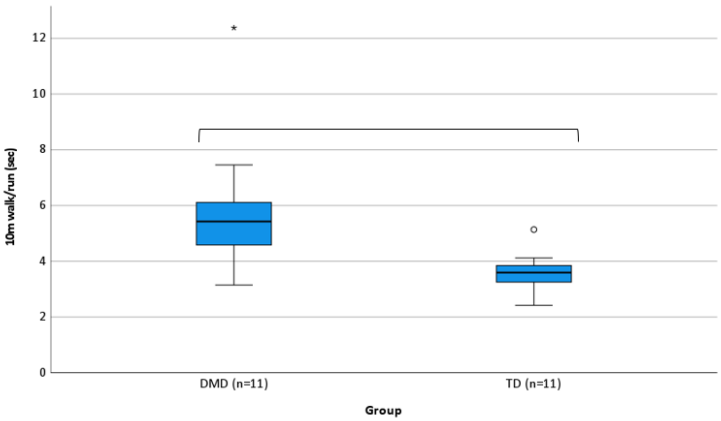


Figure 5b. Median and IQR 10m walk/run in seconds

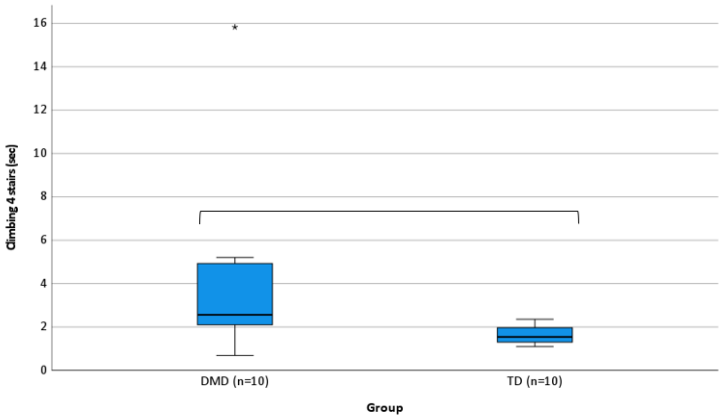


Figure 5c. Median and IQR
Climbing 4 stairs in seconds

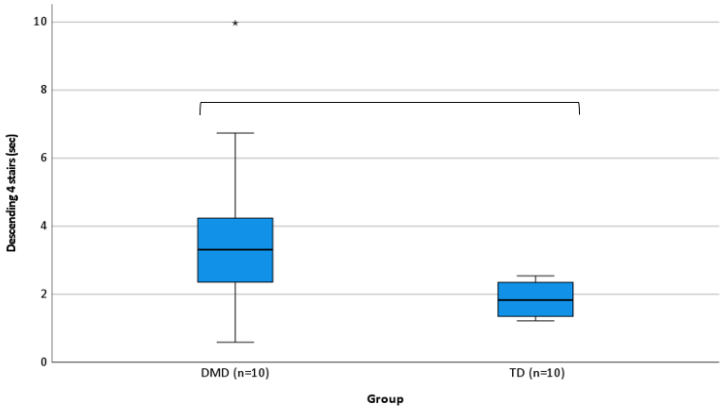


Figure 5d. Median and IQR
Descending 4 stairs in seconds

°: outlier; *: extreme outlier; (the brackets indicate significant differences)

Lastly, 16 DMD boys (mean age: 4y 1m) and 16 TD boys (mean age: 4y 0m) completed the MFM-20. TD boys had a median (IQR) of 100% (95.75%-100%) of the expected total score. For DMD boys, the median value (IQR) was 86% (80.50%-92%). Significant results, in disadvantage of the boys with DMD, were also observed for this test with a p-value of <0.001. Figure 6 illustrates these results.

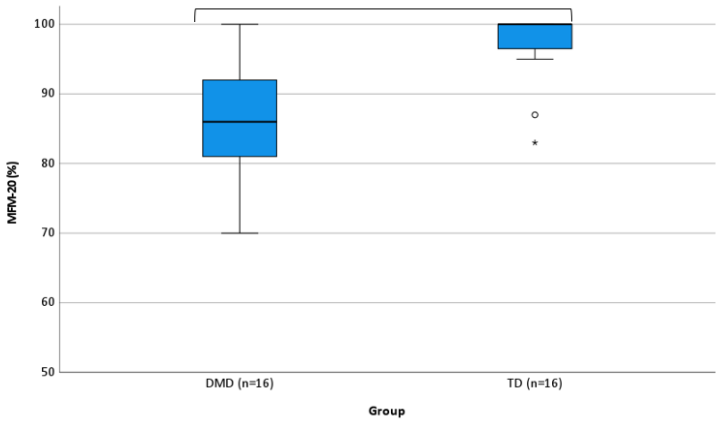


Figure 6. Median and IQR
MFM-20 percentages

°: outlier; *: extreme outlier; (the brackets indicate significant differences)

5. Discussion

The aim of this cross-sectional study was to evaluate early fine and gross motor development of boys with DMD between the ages of 0 and 6 years, compared to TD boys, using a comprehensive protocol of standardized and reliable tests (Bayley-III-NL, PDMS-II, NSAA, TFTs and MFM-20). This study showed that boys with DMD are already lagging behind at a young age in both gross and fine motor skills compared to TD boys.

Previous research has also concluded that gross motor skills are already affected before the age of 6 in boys with DMD. Different studies showed significantly lower scores on motor outcome measures (e.g. Bayley-III, NSAA, TFTs), delays in achievement of motor milestones and the presence of the typical Gower's sign (Connolly et al., 2013; Connolly et al., 2014; De Sanctis et al., 2015; Arora et al., 2018; Beenakker et al., 2005; Doglio et al., 2011).

The Bayley-III is the most widely used standardized test in clinical research for developmentally delayed children (Connolly et al., 2013). The results of our study are consistent with other studies using Bayley-III (Connolly et al., 2013; Connolly et al., 2014). DMD boys scored on average 1 standard deviation below the mean for fine motor skills and 2 standard deviations below the mean for gross motor skills, which also proves that gross motor skills are more affected than fine motor skills at this young age. These results are consistent with other studies about FM skills being less affected than GM skills in this young population due to proximodistal involvement (Connolly et al., 2013; Pane et al., 2014a). So proximal muscle weakness of the lower extremities and trunk is more prevalent in early childhood, followed later by involvement of the upper extremities and distal muscles (Yiu & Kornberg, 2015; Sussman, 2002).

For the PDMS-II, significant differences between the two groups were seen on all subtests except for the subtest grasping. This could be explained by the fact that fine motor skills are less severely affected than gross motor skills at this young age as mentioned above. This is confirmed by the quotient scores in Figure 3a and Figure 3b, where gross motor skills appear to be more severely impaired in DMD boys with a mean score of two standard deviations below the mean. It should certainly also be considered that the order of the test items can have a determining influence on the total scores, this especially for the subtest locomotion

(mean score 2 standard deviations below the mean). If the children achieve a score of zero on three consecutive test items, the subtest is terminated. The sequence of the test items is arranged according to motor milestones. As DMD boys have difficulty with specific tasks requiring a lot of proximal muscle strength (e.g. jumping), there is a high probability that they will fail on these items. Whereas further on in the test, for example, the item tiptoe walking is assessed, on which they have less difficulty. Higher test scores could therefore be achieved if the order of the test items was different. This was effectively observed for the majority of DMD boys.

A possible explanation for the early impairment of fine motor skills is the influence of cognition. Connolly et al. (2013) found that the mean cognition, receptive language and expressive language were already lower in early childhood compared to normal children. This cognitive impairment can be linked to the absence of dystrophin in the central nervous system affecting the brain (Anderson et al., 2002). They also reported that although a consistent profile of cognitive impairment in DMD boys can be seen, variation is possible due to different dystrophin gene mutations. Cognition may be more affected in DMD children with deletions affecting expression of the Dp140 or Dp71 isoforms of dystrophin. (Felisari et al., 2000; Daoud et al., 2009). Eleven of the 18 included DMD boys have mutations between exons 45 and 62 which cause a disruption of Dp140 (Ricotti et al., 2015). Van der Fels et al. (2014) found a correlation between fine motor skills and cognition, namely that when cognition is poor, fine motor skills may be affected because these skills have a high cognitive demand.
Another possible explanation could be that in DMD boys, at a young age, they mainly focus on gaining gross motor skills because these are already strongly affected and neglect fine motor skills.

The NSAA, a disease specific gross motor test, also found significant differences between DMD boys and TD boys. All TD boys achieved a score between 32-34 out of 34, with the exception of one boy, with an age of 2y 8m (27/34). He is the only TD boy under the age of 3 years and 6 months who completed the NSAA. So the fact that the test is not yet reliable and valid below this age must be taken into account (Eagle et al., 2007; Mazzone et al., 2009). This finding is in agreement with the study of De Sanctis et al. (2015), they found that before the age of 4 years more than 15% of the TD boys did not achieve full scores on all the items. In the DMD

group a clear trend is visible, namely that young DMD boys achieved lower scores and older DMD boys obtained higher scores. This explains the high variability across scores for this test. However, no DMD boy reached the maximum score of 34 which proves again that gross motor skills are already strongly affected. The fact that older DMD children score better than younger DMD boys is consistent with the finding that motor skills can still improve up to the age of about 6-7 years as a result of normal growth and development (Alfano et al, 2017; Mazzone et al, 2011; Mazzone et al, 2013; Pane et al, 2014b; Connolly et al, 2013; Connolly et al., 2014). However, both total and individual item scores in DMD boys were still far from those of TD children of the same age (De Sanctis et al., 2015).

Several studies reported that DMD boys needed significantly more time to perform the TRF test and 10m walk/run test (Arora et al., 2018; Beenakker et al., 2005; Doglio et al., 2011; Mazzone et al., 2013; Pereira et al., 2020). These findings are confirmed in this study (Figure 5a, Figure 5b). Likewise for climbing 4 stairs, the results of this study are consistent with previous research. Namely that DMD children need significantly more time than TD children to perform this test (Arora et al., 2018). Our results showed that younger DMD boys take more time to complete the TRF test and 10m walk/run test and as they get older the time decreases. These findings are consistent with those of Hoskens et al. (2019). The outlier that can be seen in the boxplots of the TRF test, climbing and descending 4 stairs (Figure 5a, Figure 5c, Figure 5d) is the same DMD boy aged 3y 10m (Table 5). This child achieves poor scores on all TFTs administered. This can be attributed to the difficulties he had with explosive items, which required high muscle power. Another outlier can be seen in the boxplot of the 10m walk/run test, the reliability of this outcome may be questionable, considering the climbing and descending 4 stairs tests were excluded for this boy because he could not perform these tests.

Regarding the MFM-20, a wide range can be seen in the results of the DMD boys (Figure 6). This large range may be explained by the fact that younger DMD boys (≤ three years) achieve lower scores because certain test items may still be difficult for them, whereas older DMD boys (> three years) tend more toward the maximum scores. Although two older DMD boys, aged 4y 10m and 3y 11m, achieved a score of 80/100 and thus scored weaker than expected at this age. It is remarkable that DMD boys score worse especially in domain 1, namely

standing and transfers, which could be due to the fact that trunk and lower limbs are more required in performing these tasks and are earlier and more severely affected in DMD boys (Yiu & Kornberg, 2015). In TD children, overall higher scores are observed, this may be attributed to the MFM-20 being developed for the assessment of children with neuromuscular disorders (Figure 6).

The results of the different tests also showed that there is a lot of variation between the DMD boys (see boxplots). Cognitive and behavioral factors, such as understanding the test procedure and attention can cause possible variation in scores, especially in very young children (Hoskens et al., 2019). Some variability might also be explained by the differences in the site of the mutation (Flanigan et al., 2009; Pane et al., 2014c).

This study also has some limitations. A first limitation of our study is that it has a small sample size ($n<30$). Another limitation is that not all tests had the full age range (0-6 years) which made the sample size per test even smaller. The assessments of the boys were done by three assessors, 1 PhD student and 2 physiotherapy students, this can also be a weakness. Due to the difference in encouragement and enthusiasm, there may be slight differences in the instructions which may affect the boys' performance. However, to limit inter-rater variability, a standardized protocol was followed. Further, another limitation of our study is the fact that TD children were excluded for equal distribution of the groups. Lastly, a healthy user bias may also be present in the recruitment of TD children, because parents of tested children may have given permission only if they knew their child will perform well.

Our study contributes to academic research and the clinical field to better understand the early development of FM and GM skills in order to enable earlier initiation of treatment and more targeted interventions. Further research on fine motor skills in young DMD boys is recommended. Longitudinal studies could also be valuable to evaluate the different changes over time. More research is also suggested on the site of mutation in DMD boys as well as its effect on both fine and gross motor skills.

6. Conclusion

In this study, a comprehensive protocol was used in which several standardized motor assessment scales were administered that have been proven to be valid and reliable. The overall conclusion of this study is that there are significant differences in both fine and gross motor skills between preschool boys with DMD and aged matched TD children in the first six years of life. The natural proximodistal course of the disease mainly results in the impairment of gross motor skills at this young age, although fine motor skills are also affected but to a lesser extent. Fine motor skills may be affected by the possible influence of cognition/site of mutation or by diminished focus on these skills in daily life. Further research is recommended to allow early intervention to be even more tailored to the needs of the child including FM and GM skills.

7. Appendices

Table 5
Details DMD boys

Code name	Age (years months)	Height (cm)	Body weight (kg)	Mutation in dystrophin gene
DMD01	*5y 11m*	*110.50*	*18.00*	*deletion of exons 45 to 52*
DMD02	*2y 2m*	*92.30*	*14.10*	*deletion of exon 51*
DMD03	*2y 8m*	*86.80*	*11.70*	*duplication of exon 2*
DMD04	*3y 2m*	*92.60*	*14.60*	*deletion of exon 45*
DMD05	*4y 9m*	*105.30*	*20.10*	*deletion of exons 46 to 52*
DMD06	*5y 11m*	*116.00*	*25.30*	*deletion of exons 3 to 7*
DMD07	*4y 10m*	*104.50*	*16.80*	*frameshift mutation in exon 24*
DMD08	*3y 10m*	*105.70*	*19.00*	*deletion of exon 45*
DMD09	3*y 10m*	108.80	21.60	deletion of exons 45 to 50, exon 51 skip
DMD10	4y 0m	97.00	17.30	deletion of exons 45 to 50, out-of-frame deletion
DMD11	2y 3m	97.00	11.50	deletion of exons 49 to 52
DMD12	2y 0m	86.00	11.00	duplication of exons 8 to 13
DMD13	2y 2m	97.00	11.50	deletion of exons 46 to 51, out-of-frame deletion
DMD14	4y 10m	106.00	17.70	frameshift mutation of exon 8
DMD15	0y 11m	72.00	8.77	deletion of exon 45
DMD16	6y 5m	115.40	22.60	duplication of exons 8 and 9
DMD17	2y 2m	86.00	12.50	deletion of exons 48 to 50
DMD18	5y 6m	107.00	17.00	deletion of exons 8 to 41

8. Reference list

Alfano, L. N., Miller, N. F., Berry, K. M., Yin, H., Rolf, K. E., Flanigan, K. M., et al. (2017). The 100-meter timed test: Normative data in healthy males and comparative pilot outcome data for use in Duchenne muscular dystrophy clinical trials. *Neuromuscul Disord*, 27(5), 452-457. https://doi.org/10.1016/j.nmd.2017.02.007

Anderson, J. L., Head, S. I., Rae, C., & Morley, J. W. (2002). Brain function in Duchenne muscular dystrophy. *Brain*, 125(1), 4–13. https://doi.org/10.1093/brain/awf012

Arora, H., Willcocks, R. J., Lott, D. J., Harrington, A. T., Senesac, C. R., Zilke, K. L., et al. (2018). Longitudinal timed function tests in Duchenne muscular dystrophy: ImagingDMD cohort natural history. *Muscle Nerve*, 58(5), 631-638. https://doi.org/10.1002/mus.26161

Bayley (2006). Bayley-III: Bayley Scales of infant and toddler development. Third edition *Pearson*.

Beenakker, E. A., Maurits, N. M., Fock, J. M., Brouwer, O. F., & van der Hoeven, J. H. (2005). Functional ability and muscle force in healthy children and ambulant Duchenne muscular dystrophy patients. *Eur J Paediatr Neurol*, 9(6), 387-393. https://doi.org/10.1016/j.ejpn.2005.06.004

Birnkrant, D. J., Bushby, K., Bann, C. M., Alman, B. A., Apkon, S. D., Blackwell, A., et al. (2018). Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management. *The Lancet Neurology*, 17(4), 347-361. https://doi.org/10.1016/S1474-4422(18)30025-5

Bushby, K., Finkel, R., Birnkrant, D. J., Case, L. E., Clemens, P. R., Cripe, L., et al. (2010). Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. *The Lancet Neurology*, 9(1), 77-93. https://doi.org/10.1016/S1474-4422(09)70271-6

Ciafaloni, E., Fox, D. J., Pandya, S., Westfield, C. P., Puzhankara, S., Romitti, P. A., et al. (2009). Delayed diagnosis in duchenne muscular dystrophy: data from the Muscular Dystrophy Surveillance, Tracking, and Research Network (MD STARnet). *The Journal of pediatrics*, 155(3), 380-385. https://doi.org/10.1016/j.jpeds.2009.02.007

Connolly, A. M., Florence, J. M., Cradock, M. M., Malkus, E. C., Schierbecker, J. R., Siener, C. A., et al. (2013). Motor and cognitive assessment of infants and young boys with Duchenne Muscular Dystrophy: results from the Muscular Dystrophy Association DMD Clinical Research Network. *Neuromuscul Disord*, 23(7), 529-539. https://doi.org/10.1016/j.nmd.2013.04.005

Connolly, A. M., Florence, J. M., Cradock, M. M., Eagle, M., Flanigan, K. M., McDonald, C. M., et al. (2014). One year outcome of boys with Duchenne muscular dystrophy using the Bayley-III scales of infant and toddler development. *Pediatr Neurol*, 50(6), 557-563. https://doi.org/10.1016/j.pediatrneurol.2014.02.006

Daoud, F., Angeard, N., Demerre, B., Martie, I., Benyaou, R., Leturcq, F., Cossee, M., Deburgrave, N., Saillour, Y., Tuffery, S., Urtizberea, A., Toutain, A., Echenne, B., Frischman, M., Mayer, M., Desguerre, I., Estournet, B., Reveillere, C., Penisson-Besnier, . . . Chelly, J. (2009). Analysis of Dp71 contribution in the severity of mental retardation through comparison of Duchenne and Becker patients differing by mutation consequences on Dp71 expression. *Human Molecular Genetics*, 18(20), 3779–3794. https://doi.org/10.1093/hmg/ddp320

De Lattre, C., Payan, C., Vuillerot, C., Rippert, P., de Castro, D., Bérard, C., et al. (2013). Motor function measure: validation of a short form for young children with neuromuscular diseases. *Archives of physical medicine and rehabilitation*, 94(11), 2218-2226. https://doi.org/10.1016/j.apmr.2013.04.001

De Sanctis R., Pane M., Sivo S., Ricotti V., Baranello G., Frosini S., et al. (2015). Suitability of north star ambulatory assessment in young boys with Duchenne muscular dystrophy. *Neuromuscul Disord*, 25(1), 14-18. https://doi.org/10.1016/j.nmd.2014.09.015

Deroma, L., Bin, M., Tognin, V., Rosolen, V., Valent, F., Barbone, F., et al. (2013). Interrater reliability of the Bayley III test in the Italian Northern-Adriatic Cohort II. *Epidemiologia e prevenzione*, 37(4-5), 297-302.

Doglio, L., Pavan, E., Pernigotti, I., Petralia, P., Frigo, C., & Minetti, C. (2011). Early signs of gait deviation in Duchenne muscular dystrophy. *Eur J Phys Rehabil Med*, 47(4), 587-594.

Eagle, M., Scott, E., Main, M., Sheehan, J., Michelle, M., & Guglieri, M. (2007). Steroids in Duchenne muscular dystrophy (DMD): natural history and clinical evaluation using the North Star Ambulatory Assessment (NSAA). *Neuromuscul Disord*, 17, 774. https://doi.org/10.1016/j.nmd.2007.06.048

Felisari, G., Boneschi, F. M., Bardoni, A., Sironi, M., Comi, G. P., Robotti, M., Turconi, A. C., Lai, M., Corrao, G., & Bresolin, N. (2000). Loss of Dp140 dystrophin isoform and intellectual impairment in Duchenne dystrophy. *Neurology*, 55(4), 559–564. https://doi.org/10.1212/wnl.55.4.559

Flanigan, K. M., Dunn, D. M., von Niederhausern, A., Soltanzadeh, P., Gappmaier, E., Howard, M. T., et al. (2009). Mutational spectrum of DMD mutations in dystrophinopathy patients: application of modern diagnostic techniques to a large cohort. *Hum Mutat*, 30(12), 1657-1666. https://doi.org/10.1002/humu.21114

Folio M, Fewell R. Peabody Developmental Motor Scales Examiner's Manual (2nd ed.) 2000. *Pro-Ed*, Austin, TX.

Fowler, E. G., Staudt, L. A., Heberer, K. R., Sienko, S. E., Buckon, C. E., Bagley, A. M., et al. (2018). Longitudinal community walking activity in Duchenne muscular dystrophy. *Muscle Nerve*, 57(3), 401-406. https://doi.org/10.1002/mus.25743

Henricson, E., Abresch, R., Han, J. J., Nicorici, A., Goude Keller, E., Elfring, G., et al. (2012). Percent-predicted 6-minute walk distance in duchenne muscular dystrophy to account for maturational influences. *PLoS Curr*, 4, Rrn1297. https://doi.org/10.1371/currents.RRN1297

Hoskens, J., Goemans, N., Feys, H., De Waele, L., Van den Hauwe, M., & Klingels, K. (2019). Normative data and percentile curves for the three-minute walk test and timed function tests in healthy Caucasian boys from 2.5 up to 6 years old. *Neuromuscular Disorders*, 29(8), 585-600. https://doi.org/10.1016/j.nmd.2019.06.597

Hyde, S. A., Steffensen, B. F., Fløytrup, I., Glent, S., Kroksmark, A. K., Salling, B., Werlauff, U., & Erlandsen, M. (2001). Longitudinal data analysis: an application to construction of a natural history profile of Duchenne muscular dystrophy. *Neuromuscular Disorders*, 11(2), 165–170. https://doi.org/10.1016/s0960-8966(00)00175-9

Janssen, M. M., Bergsma, A., Geurts, A. C., & de Groot, I. J. (2014). Patterns of decline in upper limb function of boys and men with DMD: an international survey. *J Neurol*, 261(7), 1269-1288. https://doi.org/10.1007/s00415-014-7316-9

Mazzone, E., Messina, S., & Vasco, G. (2009). Reliability of the North Star Ambulatory Assessment in a multicentric setting. *Neuromuscul Disord*, 19(7), 458-461. https://doi.org/10.1016/j.nmd.2009.06.368

Mazzone, E., Martinelli, D., Berardinelli, A., Messina, S., D'Amico, A., Vasco, G., et al. (2010). North Star Ambulatory Assessment, 6-minute walk test and timed items in ambulant boys with Duchenne muscular dystrophy. *Neuromuscul Disord*, 20(11), 712-716. https://doi.org/10.1016/j.nmd.2010.06.014

Mazzone, E., Vasco, G., Sormani, M. P., Torrente, Y., Berardinelli, A., Messina, S., et al. (2011). Functional changes in Duchenne muscular dystrophy: a 12-month longitudinal cohort study. *Neurology*, 77(3), 250-256. https://doi.org/10.1212/WNL.0b013e318225ab2e

Mazzone, E. S., Pane, M., Sormani, M. P., Scalise, R., Berardinelli, A., Messina, S., et al. (2013). 24 month longitudinal data in ambulant boys with Duchenne muscular dystrophy. *PLoS One*, 8(1), e52512. https://doi.org/10.1371/journal.pone.0052512

McDonald, C. M., Henricson, E. K., Han, J. J., Abresch, R. T., Nicorici, A., Elfring, G. L., et al. (2010). The 6-minute walk test as a new outcome measure in Duchenne muscular dystrophy. *Muscle Nerve*, 41(4), 500-510. https://doi.org/10.1002/mus.21544

Mercuri, E., Coratti, G., Messina, S., Ricotti, V., Baranello, G., D'Amico, A., et al. (2016). Revised North Star Ambulatory Assessment for young boys with Duchenne muscular dystrophy. *PLoS One*, 11(8). https://doi.org/10.1371/journal.pone.0160195

Nair, K. S., Vasanth, A., Gourie-Devi, M., Taly, A. B., Rao, S., Gayathri, N., & Murali, T. (2001). Disabilities in children with Duchenne muscular dystrophy: a profile. *Journal of rehabilitation medicine*, 33(4), 147-149. https://doi.org/10.1080/16501970120927

Pane, M., Mazzone, E. S., Fanelli, L., De Sanctis, R., Bianco, F., Sivo, S., et al. (2014a). Reliability of the Performance of Upper Limb assessment in Duchenne muscular dystrophy. *Neuromuscul Disord*, 24(3), 201-206. https://doi.org/10.1016/j.nmd.2013.11.014

Pane, M., Mazzone, E. S., Sivo, S., Sormani, M. P., Messina, S., D'Amico, A., et al. (2014b). Long term natural history data in ambulant boys with Duchenne muscular dystrophy: 36-month changes. *PLoS One*, 9(10), e108205. https://doi.org/10.1371/journal.pone.0108205

Pane, M., Mazzone, E. S., Sormani, M. P., Messina, S., Vita, G. L., Fanelli, L., et al. (2014c). 6 Minute walk test in Duchenne MD patients with different mutations: 12 month changes. *PLoS One*, 9(1), e83400. https://doi.org/10.1371/journal.pone.0083400

Pearson (2015). Bayley Scales of infant and toddler development. Third edition. Dutch version: *Technische handleiding*.

Pereira, A. C., Araújo, A., & Ribeiro, M. G. (2020). Can simple and low-cost motor function assessments help in the diagnostic suspicion of Duchenne muscular dystrophy? *J Pediatr (Rio J)*, 96(4), 503-510. https://doi.org/10.1016/j.jped.2019.02.003

Ricotti, V., Mandy, W. P. L., Scoto, M., Pane, M., Deconinck, N., Messina, S., Mercuri, E., Skuse, D. H., & Muntoni, F. (2015). Neurodevelopmental, emotional, and behavioural problems in Duchenne muscular dystrophy in relation to underlying dystrophin gene mutations. *Developmental Medicine & Child Neurology*, 58(1), 77–84. https://doi.org/10.1111/dmcn.12922

Ricotti, V., Selby, V., Ridout, D., Domingos, J., Decostre, V., Mayhew, A., ... & Muntoni, F. (2019). Respiratory and upper limb function as outcome measures in ambulant and non-ambulant subjects with Duchenne muscular dystrophy: a prospective multicentre study. *Neuromuscular Disorders*, 29(4), 261-268. https://doi.org/10.1016/j.nmd.2019.02.002

Sarrazin, E., von der Hagen, M., Schara, U., von Au, K., & Kaindl, A. M. (2014). Growth and psychomotor development of patients with Duchenne muscular dystrophy. *Eur J Paediatr Neurol*, 18(1), 38-44. https://doi.org/10.1016/j.ejpn.2013.08.008

Sussman, M. (2002). Duchenne muscular dystrophy. *J Am Acad Orthop Surg*, 10(2), 138-151. https://doi.org/10.5435/00124635-200203000-00009

Van der Fels, I. M., Te Wierike, S. C., Hartman, E., Elferink-Gemser, M. T., Smith, J., & Visscher, C. (2015). The relationship between motor skills and cognitive skills in 4–16 year old typically developing children: A systematic review. *Journal of Science and Medicine in Sport*, 18(6), 697–703. https://doi.org/10.1016/j.jsams.2014.09.007

van Dommelen, P., van Dijk, O., de Wilde, J. A., & Verkerk, P. H. (2020). Early developmental milestones in Duchenne muscular dystrophy. *Dev Med Child Neurol*, 62(10), 1198-1204. https://doi.org/10.1111/dmcn.14623

Van Ruiten, H. J. A., Straub, V., Bushby, K., & Guglieri, M. (2014). Improving recognition of Duchenne muscular dystrophy: a retrospective case note review. *Archives of Disease in Childhood*, 99(12), 1074–1077. https://doi.org/10.1136/archdischild-2014-306366

Verma, S., Anziska, Y., Cracco, J. (2010). Review of Duchenne muscular dystrophy (DMD) for the pediatricians in the community. *Clinical Pediatrics*, 49(11), 1011–1017. https://doi.org/10.1177/0009922810378738

Yiu, E. M., & Kornberg, A. J. (2015). Duchenne muscular dystrophy. *Journal of paediatrics and child health*, 51(8), 759-764. https://doi.org/10.1111/jpc.12868

Verklaring op Eer

Ondergetekende, student aan de Universiteit Hasselt (UHasselt), faculteit [revalidatiewetenschappen] 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 [revalidatiewetenschappen] aan de UHasselt. Dit onderzoek wordt beleid door [Katrijn Klingels en Jasmine Hoskens] en kadert binnen [wetenschappelijke stage / masterproef deel I] Ik zal in het kader van dit onderzoek creaties, schetsen, ontwerpen, prototypes en/of onderzoeksresultaten tot stand brengen in het domein van [pediatrische 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 [Katrijn Klingels en Jasmine Hoskens].

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:

- Manon Simons
- Valerie Snellings

Adres:

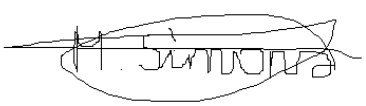
- Veldstraat 18, 3500 Hasselt
- Hasseltsestraat 77, 3740 Bilzen

Geboortedatum en –plaats:

- Geboren op 21/09/1999 te Hasselt
- Geboren op 05/07/1999 te Tongeren

Datum: 06/11/2020

Handtekening:



Manon Simons <manon.simons@student.uhasselt.be>

Masterproef deel 2

Katrijn KLINGELS <katrijn.klingels@uhasselt.be> 25 mei 2022 om 11:15
Aan: Valerie Snellings <valerie.snellings@student.uhasselt.be>
Cc: Manon Simons <manon.simons@student.uhasselt.be>, Jasmine HOSKENS <jasmine.hoskens@uhasselt.be>

Beste Valerie en Manon,
Via deze mail geef ik jullie goedkeuring om je MP in te dienen. Ik mail maandag de formulieren door.
Met vriendelijke groeten,
Katrijn Klingels

Prof.dr. Katrijn Klingels

Associate professor

Pediatrische Revalidatie - Faculteit Revalidatiewetenschappen

Onderzoeksgroep REVAL

T +32(0)11 26 93 94

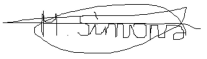
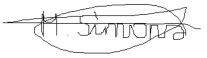
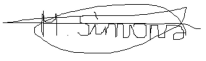
www.uhasselt.be
Universiteit Hasselt - Campus Diepenbeek
Agoralaan Gebouw A - B-3590 Diepenbeek
Kantoor BMO-A027

Op ma 23 mei 2022 om 21:11 schreef Valerie Snellings <valerie.snellings@student.uhasselt.be>:
[Tekst uit oorspronkelijke bericht is verborgen]

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
11/10/2021	Algemene bespreking masterproef deel II	Promotor: Copromotor/Begeleider: ONLINE Student(e):  Student(e): 
17/02/2022	Bespreking data acquisitie	Promotor: Copromotor/Begeleider: ONLINE Student(e):  Student(e): 
24/03/2022	Bespreking data acquisitie en data analyse	Promotor: Copromotor/Begeleider: ONLINE Student(e):  Student(e): 
14/04/2022	Bespreking data analyse	Promotor: Copromotor/Begeleider: ONLINE Student(e):  Student(e): 
19/04/2022	Bespreking schrijven resultaten	Promotor: ONLINE Copromotor/Begeleider: ONLINE Student(e):  Student(e): 

02/05/2022	Bespreking schrijven discussie	Promotor: Copromotor/Begeleider: ONLINE Student(e):  Student(e): 
23/05/2022	Bespreking finale product masterproef, laatste vragen	Promotor: Copromotor/Begeleider: ONLINE 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)

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: **1745652 Simons Manon**
Student number + name

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

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:*

☒ behouden - *keep* EARLY DEVELOPMENT OF FINE AND GROSS MOTOR SKILLS IN BOYS WITH DUCHENNE MUSCULAR DYSTROPHY

☐ wijzigen - *change to*:

/:

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* VALERIE SNELLINGS

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)

29/05/2022

M. Simons

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

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: **1747428 Snellings Valerie**
Student number + name

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

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:*

● behouden - *keep* EARLY DEVELOPMENT OF FINE AND GROSS

○ wijzigen - *change to*: MOTOR SKILLS IN BOYS WITH DUCHENNE MUSCULAR DYSTROPHY

/:

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* MANON SIMONS

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)

29/05/2022

Bnelling

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