Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

Content and effectiveness of mHealth tools for self-assessment and rehabilitation intervention on functioning according to ICF in adult persons with multiple sclerosis: a systematic review

Charlotte Deschryvere
Maite Noels
Eerste deel van het scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en

de kinesitherapie

PROMOTOR :

Prof. dr. Bart VAN WIJMEERSCH

COPROMOTOR :

Prof. dr. Peter FEYS

BEGELEIDER :

Msc. Aki RINTALA

2020
2021

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CONTENT AND EFFECTIVENESS OF MHEALTH TOOLS FOR SELF-ASSESSMENT AND REHABILITATION INTERVENTION ON FUNCTIONING ACCORDING TO ICF IN ADULT PERSONS WITH MULTIPLE SCLEROSIS: A SYSTEMATIC REVIEW

"What types of mHealth tools exist for self-assessment and rehabilitation intervention of functioning according to ICF in adult persons with multiple sclerosis?"

AND

"What is the effectiveness of mHealth tools for self-assessment and rehabilitation intervention in adult persons with multiple sclerosis?"

- Six mHealth tools exist for self-assessment and six for rehabilitation of fatigue, cognition, pain, physical activity and quality of life in persons with multiple sclerosis, each leading to different outcomes.
- This study found that mHealth tools can help to significantly improve fatigue, cognition, pain, physical activity and quality of life.
- Further research on this topic is recommended for mHealth tools used in rehabilitation intervention for possible long-term effects.

Students:

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Promotor: Prof. Dr. Bart Van Wijmeersch

Co-promotor: Prof. Dr. Peter Feys

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▶▶ UHASSELT

Context

This master thesis is situated in the neurological rehabilitation research domain of physiotherapy. This research project will be performed at the Faculty of Rehabilitation Sciences at Hasselt University. The focus is on mobile health (mHealth) tools for tracking functioning by self-assessment and rehabilitation intervention of functioning in persons with multiple sclerosis (pwMS).

Research is needed in the rehabilitation of pwMS concerning mHealth for self-assessment of functioning and measuring functioning in a rehabilitation intervention. MHealth is an interesting and promising possibility for monitoring of functioning according to International Classification of Functioning, Disability and Health (ICF). Usually, pwMS are monitored annually and subtle changes or minor relapses may be missed. Therapists and neurologists do not always know the current functioning at home. MHealth may be an opportunity to collect information during months preceding a consultation or to control current functioning.

Subsequently, mHealth tools are an interesting tool for rehabilitation and personalizing multiple sclerosis (MS) treatment. There is not always a possibility to have the pwMS in a multidisciplinary perspective. Therefore, mHealth can be a tool for patients to perform rehabilitation themselves or under remote supervision.

This master's thesis is an individual research project without a prior project request. No funding source is involved and the authors have no competing interests. This first part of the master's thesis consists of a systematic review (SR) and a research protocol using the central format and written by two master students, Charlotte Deschryvere (CD) and Maite Noels (MN), under supervision of Prof. Dr. Bart Van Wijmeersch (promotor), Prof. Dr. Peter Feys (co-promotor) and MSc. Aki Rintala. The SR is also discussed with Mrs. Marianne Roesner and Mr. Bruno Bonnechere.

The research topic was provided by promotor Prof. Dr. Bart Van Wijmeersch. The purpose and research questions of the SR were formulated by CD and MN in consultation with Prof. Dr. Peter Feys. The goal was to investigate the following two research questions: "What types of mHealth tools exist for self-assessment and rehabilitation intervention of functioning according to ICF in adult persons with multiple sclerosis?" and "What is the effectiveness of mHealth tools for self-assessment and rehabilitation intervention in adult persons with multiple sclerosis?"

It is a duo master's thesis with an equal contribution between two master students. Both authors independently executed the search strategy, quality assessment and data extraction to increase reliability and quality. Afterwards, a consensus was reached and the SR and research protocol was written together, taking into account the different internship periods of the master students.

The second part of the master's thesis consists of a new evidence-based research protocol prepared by the two master students. The study protocol will investigate the following research question: "What is the short- and long-term effectiveness of WalkWithMe app on physical activity in daily life of adult persons with multiple sclerosis with walking disability?" The research project will be performed at the MS centrum 'Noorderhart' in Pelt under supervision of Prof. Dr. Bart Van Wijmeersch, Prof. Dr. Peter Feys and Dr. Ilse Lamers. This protocol will run from July 2021 until May 2022. Both students will be involved in the recruitment of participants, measurement and data extraction of the study.

Part 1: Literature review

Table of contents

1 Abstract

Background: MHealth is a promising tool for tracking functioning and personalizing rehabilitation with follow-up care of pwMS.

Method: PubMed and Web of Science were searched and 13 articles were included. Sample size, participants' characteristics, design, purpose, mHealth tool, functioning according to ICF, outcomes, intervention and results were extracted. For each article, the Downs & Black checklist was applied.

Results: Twelve studies encompassing 1 493 pwMS diagnosis were included. The mean subjects were female, an average of 46 years with Relapsing-Remitting MS (RRMS) and a range of Expanded Disability Status Scale (EDSS) from null to five point five. Six mHealth tools for self-assessment and six mHealth tools for rehabilitation were found with varying efficiency of study quality. The use of some mHealth tools showed significant improvement on pain, cognition, fatigue, physical activity and quality of life.

Discussion and conclusion: This SR found a variety in the methodologies. However, different results were still found on functioning with an overview of the available mHealth tools per specific topic of functioning.

Purpose of the research: To investigate the effectiveness of WalkWithMe app on physical activity in daily life in pwMS with walking disability.

Operationalization research question: "What is the short- and long-term effectiveness of WalkWithMe app on physical activity in daily life of adult persons with multiple sclerosis with walking disability?" The study will be performed at 'Noorderhart' in Pelt under supervision of Prof. Dr. Bart Van Wijmeersch, Prof. Dr. Peter Feys and Dr. Ilse Lamers.

Important keywords: mHealth, self-assessment, rehabilitation, functioning, MS, adult

2   Introduction

Multiple sclerosis (MS) is a chronic, inflammatory and demyelinating disease of the central nervous system in adults (Compston & Coles, 2008; Walton et al., 2020). The disease affects an estimated 2.8 million people worldwide with increasing prevalence since 2013 and a female majority (ratio 3:1) (Walton et al., 2020). The variety of symptoms consists of loss of strength, visual and sensation disorders, coordination and balance problems, fatigue, walking disability and memory problems (Barin et al., 2018; Beer, Khan, & Kesselring, 2012).

The disease burden is associated with a progressive limitation of functioning in daily living, mental health and quality of life (Barin et al., 2018). It has a multidimensional impact on person's activity, participation and environment (Khan, McPhail, Brand, Turner-Stokes, & Kilpatrick, 2006). The International Classification of Functioning, Disability and Health (ICF) is a model for clinicians to categorize human functioning and health complaints (WHO, 2001). The prognosis and presentation of MS depend on age, the type of MS and characterised number of exacerbations and relapses, the nature of symptoms and interval time between onset and relapse (Hammond, McLeod, Macaskill, & English, 2000).

Due to the heterogeneous and unpredictable course, the management of MS will be complex and individually different (Smith, Hale, Olson, Baxter, & Schneiders, 2013). Organising proper and personalized guidance adapted to the specific situation of pwMS is challenging for care providers. Typical monitoring of pwMS is on a yearly basis and subtle changes or minor relapses may be missed (Cohen, 2018). Therapists and neurologists do not always know how pwMS function is at home and if it is progressing or not (Kalincik et al., 2017). It would help therapists to receive information about functioning during the months preceding a consultation, that is collected by pwMS at home (Isaksson, 2005). The same goes for rehabilitation. There is not always a possibility of going regularly to physiotherapists. Alternative strategies can allow pwMS doing rehabilitation at home. This problem could be partly solved by means of digital healthcare (Cohen, 2018).

E-health is relevant in the management of pwMS. There are digital and electronic tools to provide the healthcare sector with symptom monitoring about pwMS at various places and times. It could also enhance rehabilitation (Lavorgna et al., 2018). This is useful for

personalizing MS treatment. Some examples of eHealth are mobile phone apps, patient platforms, wearable devices and assistive technology.

Chow, Ariyarathna, Islam, Thiagalingam, and Redfern (2016) defined mHealth as "medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices and other wireless devices." MHealth creates alternative opportunities for healthcare, symptom and treatment monitoring, educational apps and social platforms to discuss conditions. The field of mHealth tools is growing, but the wide heterogeneity regarding the quality, reliability, relevance and cost is worrying at the moment. Lacking regulation of the medical data can cause problems such as privacy, safety and inaccurate app content. Europe will label medical apps as "mHealth Quality" if the app meets the required quality process (Cohen, 2018).

Mhealth can evaluate the visual (Black et al., 2013; Cohen, 2018) and cognitive function (Cohen, 2018; Rentz et al., 2016) more accurately than EDSS-scores or classic tests in a clinic setting. The lack of assessing the content of apps or quality of the research study is an important concern, because they may not be appropriate for clinical practice (Cohen, 2018). On the other hand, apps can positively influence adherence and can offer support to personalize rehabilitation (Becker et al., 2013).

Interventions using mHealth are able to educate, promote self-monitoring of symptoms and biometrics, and support rehabilitation goals (Giunti, Guisado Fernández, Dorronzoro Zubiete, & Rivera Romero, 2018). MHealth rehabilitation is an innovative way of rehabilitation care using mobile technology-enabled intervention. Currently, most rehabilitation literature is feasibility and pilot studies and describes mobile health interventions within cardiac rehabilitation or rehabilitation of mental disorders and brain injuries (Ramey, Osborne, Kasitinon, & Juengst, 2019). Literature is largely limited to evaluating mobile apps on self-assessment and rehabilitation and to performing quality assessment, applied to pwMS.

This literature review will examine mHealth tools for monitoring symptoms in pwMS and will look at possibilities for rehabilitation. The objective of this study is to investigate current literature regarding mHealth tools for rehabilitation intervention and assessment of functioning according to ICF in pwMS. The impact on functioning will also be investigated.

3   Method

3.1   Research question

This SR consists of two research questions. One research question investigated which mHealth tools exist for self-assessment of functioning according to ICF in pwMS. The side question was to look if mHealth tools for self-assessment can track changes or deterioration of patient functioning according to ICF.

The other research question investigated which mHealth tools exist for rehabilitation intervention of functioning according to ICF in pwMS. The side question was to look at the effectiveness of longitudinal intervention results on functioning according to ICF observed in rehabilitation intervention in pwMS using mHealth tools.

The PICO of the research question is drawn up in Table 1.

Table 1
PICO

Population	pwMS, aged 18-65 years
Intervention	mHealth tools or web-based platforms for self-assessment and intervention rehabilitation
Comparison	/
Outcome	functioning according to ICF, existing mHealth tools

3.2   Literature search

A literature search was performed of studies published in two online scientific databases (PubMed and WoS) in 11 March 2021. An updated search was conducted from the same databases in 16 May 2021. The used keywords, Medical Subject Heading (MeSH) terms and the various combinations with Boolean operators are described in Tables 2 and 3. No time limit was used for literature search of published articles.

The final search strategy most related to the research questions for PubMed was: '((multiple sclerosis) OR (ms) OR (multiple sclerosis[MeSH Terms])) AND ((ehealth[MeSH Terms]) OR (ehealth) OR (mhealth) OR (mobile apps) OR (smartphone applications) OR (apps)) AND ((self-monitoring) OR (self-assessment) OR (functioning) OR (intervention) OR (rehabilitation))'.

The search strategy for WoS was: 'ALL=(multiple sclerosis OR ms) AND ALL=(ehealth OR mhealth OR mobile apps OR smartphone applications OR apps) AND ALL=(self-monitoring OR self-assessment OR functioning OR intervention OR rehabilitation)'.

All duplicates were removed and the remaining articles were screened for title and abstract. Full texts were studied in a second screening. All articles were assessed for eligibility with the pre-defined inclusion and exclusion criteria, described in paragraph 3.3.

Table 2

Search strategy for PubMed

MeSH terms and keywords		Hits March 2021	Hits May 2021
#1 population	(multiple sclerosis) OR (ms) OR (multiple sclerosis[MeSH Terms])	509 464	510 099
#2 mHealth tool	(ehealth[MeSH Terms]) OR (ehealth) OR (mhealth) OR (mobile apps) OR (smartphone applications) OR (apps)	68 569	68 807
#3 disease management	(self-monitoring) OR (self-assessment) OR (functioning) OR (intervention) OR (rehabilitation)	19 478 664	19 493 401
#1 AND #2 AND #3	((multiple sclerosis) OR (ms) OR (multiple sclerosis[MeSH Terms])) AND ((ehealth[MeSH Terms]) OR (ehealth) OR (mhealth) OR (mobile apps) OR (smartphone applications) OR (apps)) AND ((self-monitoring) OR (self-assessment) OR (functioning) OR (intervention) OR (rehabilitation))	1 057	1 063

Table 3

Search strategy for Web of Science

Keywords		Hits March 2021	Hits May 2021
#1 population	ALL=(multiple sclerosis OR ms)	1 781 012	1 783 588
#2 mHealth tool	ALL=(ehealth OR mhealth OR mobile apps OR smartphone applications OR apps)	48 133	48 314
#3 disease management	ALL=(self-monitoring OR self-assessment OR functioning OR intervention OR rehabilitation)	6 582 265	6 592 146
#1 AND #2 AND #3	ALL=(multiple sclerosis OR ms) AND ALL=(ehealth OR mhealth OR mobile apps OR smartphone applications OR apps) AND ALL=(self-monitoring OR self-assessment OR functioning OR intervention OR rehabilitation)	379	380

3.3 Selection criteria

The inclusion criteria consisted of individual studies from randomized controlled trials (RCT), experimental trials or observational studies which assessed or used an mHealth tool during rehabilitation in adult persons diagnosed with MS. The included studies had to be reporting a longitudinal or intervention study for at least one week and had to examine functioning as defined by the ICF.

The exclusion criteria consisted of qualitative studies, case reports, study protocols and reviews of an mHealth tool without separate experimental data analysis of pwMS. Studies including mHealth without the independent use of the digital tool by the pwMS were also excluded from this SR.

3.4   Quality assessment

After screening the literature, a quality assessment was performed on the included articles. The critical appraisal of the methodological quality was based on the Downs and Black checklist (Downs & Black, 1998), because the included articles had different study designs. The conclusion of Deeks et al. (2003) was that the Downs and Black checklist was one of the best appropriated assessments for evaluating the quality for both RCT and non-RCT.

The Downs and Black checklist is a scale-based tool for assessment of methodological quality consisting out of 27 questions to refer the power of the study (Table 4). The different subitems will visualize the strengths and limitations of the studies.

Items from the articles that did not answer the questions received zero points and items that did answer the questions were given one point. Except for question five, an article received two points if it was clearly described and (only) one point if it was partially described.

In this SR a modified version of the checklist was used (Trac et al., 2016). Question 27 rated if the study performed a power calculation whereas in the original checklist it was a rating according to a range of study powers. The maximum score of question 27 was not five anymore but one. Consequently, the total score that could be obtained was 28 instead of 32. The score ranges of the checklist corresponded to a quality level of the article, reported by (Hooper, Jutai, Strong, & Russell-Minda, 2008): excellent (26-28), good (20-25), fair (15-19) and poor (≤ 14).

Table 5 gave a summary of the strengths and weaknesses of the included articles. The topics were: level of evidence, sample size, results, percentage of drop-out, population, quality assessment according to Downs and Black checklist and risk of bias.

3.5 Data extraction

All relevant data of the included articles that answer the research question were extracted in paragraph 4.3. Table 6 lists the characteristics of the participants of all included articles, namely sample size, sex, age, type of MS and level of disability. The other data extraction of the included articles were split into two groups. Table 7 consists of data from articles of self-assessment and Table 8 of rehabilitation interventions. The topics were the study design, kind of mHealth tool, purpose, outcome measures, intervention and significant results. It was the best way to give a clear vision to answer the two research questions.

An mHealth tool could be web-based or an app. Both had to be able to be used on a smartphone to have met the criteria. Under description in the table, functioning of the mHealth tool was explained. Screenshots of the tools can be found in appendix 2.

Table 9 summarized mHealth tools per topic of functioning. Fatigue, pain, cognition, physical activity and quality of life were overarching topics that were not literally described in the ICF. The topics of outcome measures regarding to functioning according to ICF were fatigue (b130 energy and drive functions), physical activity (b789 movement functions, other specified and unspecified), cognition (b144 memory functions), pain (b280 pain sensation) and quality of life (b122 global psychosocial functions) (WHO, 2001). For example, the study investigated walking measured by six-minute walking test (6MWT) and it is summarized in the topic of physical activity.

4   Results

4.1   Study selection

On 11March 2021, the final search strategy resulted in 1 057 articles in PubMed and 379 in WoS. That is a total of 1 436 articles. No articles by hand search were attached. One hundred and ten duplicates were removed via Endnote.

At 16 May 2021, the search strategy was repeated to re-search the databases for any new potential articles that could answer the research questions of this SR. There were six new articles in PubMed and one in WoS. No duplicates were present. All new articles were excluded based on population, intervention and design.

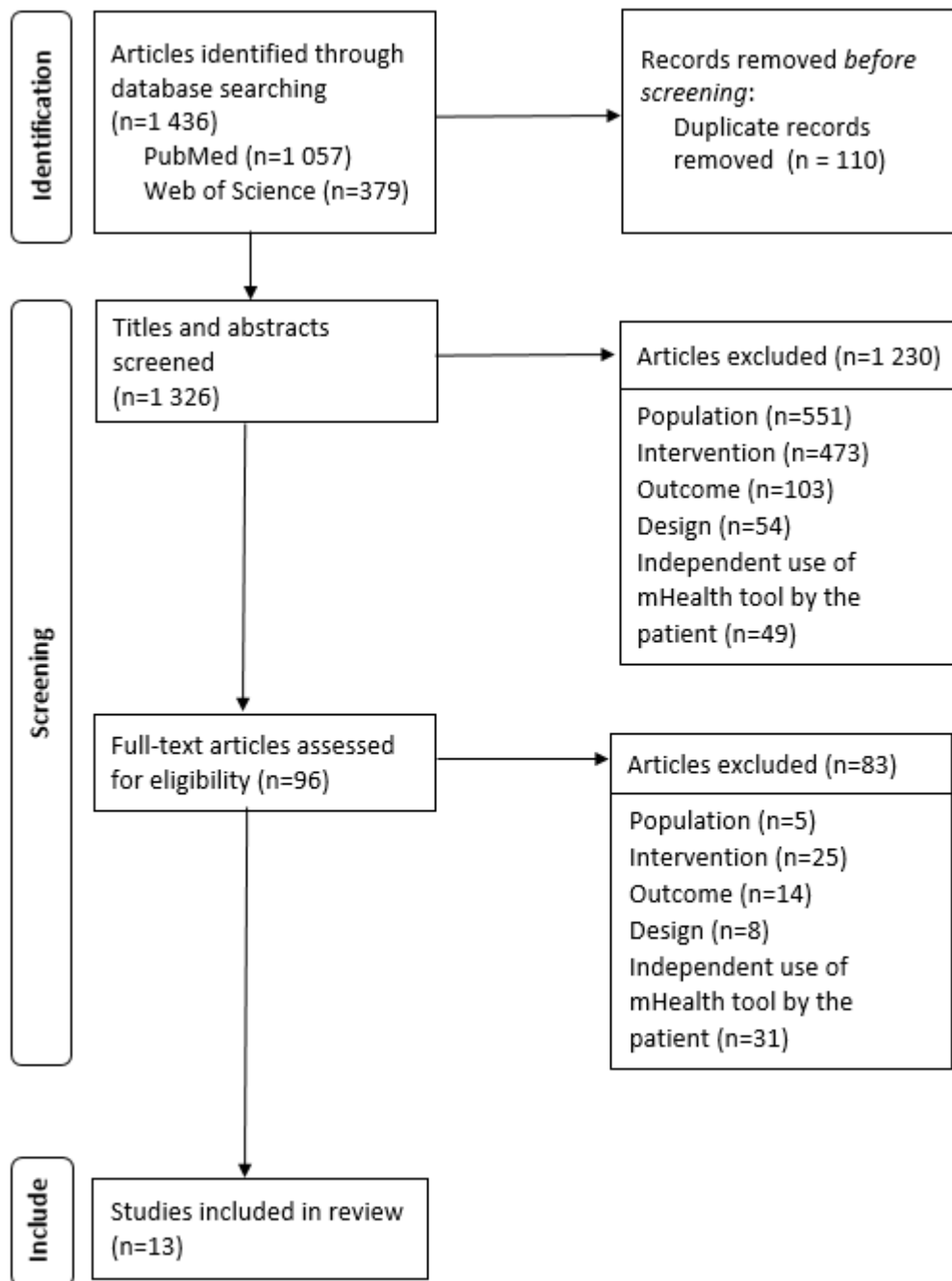The flow diagram, based on the Prisma template, showed the selection process in Fig. 1.

Figure 1. Flow diagram of the selection process of the included articles

4.1.1 Excluded articles

The first screening checked the titles and abstracts of 1 326 articles for exclusion criteria. On title/abstract level, 1 230 articles were excluded through one or more exclusion criteria. The reasons for ineligibility on title/abstract were shown in the flow diagram (Fig. 1), the figures were: population (551), intervention (473), outcome (103), design (54) and independent use of mHealth tool by the pwMS (49). When the information in the title or abstract was too unclear, this article was evaluated in the second screening.

The second screening analysed the full texts of the potential 96 studies to answer the research questions. Eighty-three articles were excluded and shown in Appendix 1. The reasons for ineligibility on title/ abstract were: population (5), intervention (25), outcome (14), design (8) and independent use of mHealth tool by the pwMS (31).

4.1.2 Included articles

Thirteen included articles were studied for the existence and effectiveness of mHealth tools for self-assessment and rehabilitation intervention on functioning according to ICF in adult pwMS. Six articles (D'hooghe et al., 2018; Greiner, Sawka, & Imison, 2015; Midaglia et al., 2019; Miller et al., 2011; Newland, Oliver, Newland, & Thomas, 2019; Pratap et al., 2020) described mHealth tools for self-assessment and seven articles (Bove et al., 2020; Charvet et al., 2017; Conroy, Zhan, Culpepper, Royal, & Wallin, 2017; Fuchs et al., 2019; Geurts, Van Geel, Feys, & Coninx, 2019; Minen, Schaubhut, & Morio, 2020; Van Geel, Geurts, Abasıyanık, Coninx, & Feys, 2020) described using mHealth tools during rehabilitation. The topics of outcome measures regarding to functioning according to ICF were fatigue, physical activity, cognition, pain and quality of life.

It is remarkable that two included articles (Greiner et al., 2015; Miller et al., 2011) were older than five years. This was important because this SR investigated a niche topic in physiotherapy, namely mHealth and telerehabilitation.

4.2 Quality assessment

4.2.1 Downs and Black checklist

Different types of study designs were present in the included articles (see Table 7 and Table 8). Five articles were RCTs (Bove et al., 2020; Charvet et al., 2017; Conroy et al., 2017; Miller et al., 2011; Minen et al., 2020). Four articles were cohort studies (D'hooghe et al., 2018; Geurts et al., 2019; Newland et al., 2019; Van Geel et al., 2020). Three articles had an observational design (Greiner et al., 2015; Midaglia et al., 2019; Pratap et al., 2020). One article had an experimental study design (Fuchs et al., 2019).

Table 4 showed the results of the methodological quality assessment of all included articles by means of the Downs and Black checklist. Each question was rated by two independent researchers and reached a consensus. Some questions were not possible to answer by each study design or it was not mentioned, in which case this is indicated with 'unable to determine' (UTD).

To allow easier interpretation, the focus was rather on the type of score category than the final score. Not every question had the same preponderance within each type of article. Considering score categories, described in paragraph 3.4, two articles (Bove et al., 2020; Charvet et al., 2017) had excellent quality, eight articles (Conroy et al., 2017; D'hooghe et al., 2018; Fuchs et al., 2019; Midaglia et al., 2019; Miller et al., 2011; Minen et al., 2020; Pratap et al., 2020; Van Geel et al., 2020) had good quality and two articles (Greiner et al., 2015; Newland et al., 2019) had fair quality. These assessed articles were included for data extraction. Only one article (Geurts et al., 2019) had poor quality. After screening the strengths and weaknesses of the articles in Table 5, it would be an option to exclude this article from data extraction on account of the quality assessment.

Important common results for all included articles were that the subjects to the population at a similar time period were representative. Also, the purpose, main outcomes and findings, patient characteristics, interventions, adverse events, data dredging and appropriate statistical tests were clearly reported. There were no representative facilities to treatment (more specifically using mHealth).

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Almost all articles scored high on each question of reporting and on most of the questions regarding internal validity (bias), exception to blinding of study subjects and research staff. The scores of internal validity (confounding) and sufficient power were very diverse across the articles. It was remarkable that blinding research staff, who measure outcomes, (D'hooghe et al., 2018; Fuchs et al., 2019; Geurts et al., 2019; Midaglia et al., 2019; Newland et al., 2019; Van Geel et al., 2020) and the recruitment of the participants over the same period of time (Conroy et al., 2017; D'hooghe et al., 2018; Geurts et al., 2019; Miller et al., 2011; Minen et al., 2020; Newland et al., 2019) were not mentioned in the articles.

The articles with a score in the excellent quality category (Bove et al., 2020; Charvet et al., 2017) scored maximum on reporting and internal validity (bias and confounding). The articles of the good quality category (Conroy et al., 2017; D'hooghe et al., 2018; Fuchs et al., 2019; Midaglia et al., 2019; Miller et al., 2011; Minen et al., 2020; Pratap et al., 2020; Van Geel et al., 2020), the fair quality category (Greiner et al., 2015; Newland et al., 2019) and the article of the poor quality category (Geurts et al., 2019) scored low on adequate adjustment for confounding.

Table 4

Downs and Black checklist

Author, Year of publication	Bove et al. (2021)	Charvet et al. (2017)	Conroy et al. (2017)	D'hooghe et al. (2018)	Fuchs et al. (2019)	Geurts et al. (2019)	Greiner et al. (2015)	Midaglia et al. (2019)	Miller et al. (2011)	Minen et al. (2020)	Newland et al. (2019)	Pratap et al. (2020)	Van Geel et al. (2020)
REPORTING													
Hypothesis/aim/objective clearly described	1	1	1	1	1	1	1	1	1	1	1	1	1
Main outcomes clearly described in Introduction or Methods	1	1	1	1	1	1	1	1	1	1	1	1	1
Patient characteristics clearly described	1	1	1	1	1	1	1	1	1	1	1	1	1
Interventions clearly described	1	1	1	1	1	1	1	1	1	1	1	1	1
Principal confounders clearly described	2	2	2	2	2	1	2	2	2	2	2	2	2
Main findings clearly described	1	1	1	1	1	1	1	1	1	1	1	1	1
Estimates of the random variability provided for main outcomes	1	1	1	1	1	0	1	1	1	1	1	1	1
Adverse events reported	1	1	1	1	1	1	1	1	1	1	1	1	1
Patient characteristics lost to follow-up described	1	1	1	1	1	0	1	1	1	1	1	1	1
Probability values reported for main outcomes	1	1	1	1	1	0	0	1	1	1	0	1	1
EXTERNAL VALIDITY													
Subjects asked to participate representative of population	1	1	1	1	1	1	1	1	1	1	1	1	1
Subjects prepared to participate representative of population	1	1	1	1	1	1	1	1	1	1	1	1	1

Staff, places, and facilities representative to treatment	0	0	0	0	0	0	0	0	0	0	0	0	0
INTERNAL VALIDITY – BIAS													
Blind study subjects	1	1	0	0	0	0	0	0	1	1	0	0	0
Blind those measuring outcomes	1	1	1	UTD	UTD	UTD	0	UTD	0	1	UTD	0	UTD
Data dredging clearly described	1	1	1	1	1	1	1	1	1	1	1	1	1
Time period similar	1	1	1	1	1	1	1	1	1	1	1	1	1
Appropriate statistical tests performed	1	1	1	1	1	1	1	1	1	1	1	1	1
Reliable compliance of intervention	1	1	0	1	1	0	1	1	1	1	1	1	1
Outcome measures used accurate	1	1	1	1	1	1	1	1	1	1	1	1	1
INTERNAL VALIDITY – CONFOUNDING (SELECTION BIAS)													
All participants recruited from the same population	1	1	1	0	0	0	0	0	1	1	0	0	0
All participants recruited over the same period of time	1	1	UTD	UTD	1	UTD	1	1	UTD	UTD	UTD	1	1
Study subjects randomized to intervention	1	1	1	0	0	0	0	0	1	1	0	0	0
Randomized assignment concealed until complete recruitment	1	1	1	0	0	0	0	0	1	UTD	0	0	0
Adequate adjustment for confounding	1	1	1	1	1	0	0	0	1	1	0	0	0
Account losses of patients to follow-up	1	1	1	1	1	1	UTD	1	1	UTD	1	1	1
POWER													
Sufficient power	0	0	0	1	1	UTD	0	0	0	0	0	1	1
Total score (28)	**26**	**26**	**23**	**21**	**22**	**14**	**18**	**20**	**24**	**23**	**18**	**21**	**21**

Scoring: 1=yes, 0=no, UTD=unable to determine

4.2.2 Strengths and weaknesses

4.2.2.1   Strengths. Five individual studies (Bove et al., 2020; Charvet et al., 2017; Conroy et al., 2017; Miller et al., 2011; Minen et al., 2020) were RCTs and categorized as level of evidence 1b. Ten out of 13 articles (Bove et al., 2020; Charvet et al., 2017; Conroy et al., 2017; D'hooghe et al., 2018; Fuchs et al., 2019; Midaglia et al., 2019; Miller et al., 2011; Minen et al., 2020; Pratap et al., 2020; Van Geel et al., 2020) described complete and exact values of the results. Two articles (Bove et al., 2020; Charvet et al., 2017) had an excellent quality assessment and eight articles (Conroy et al., 2017; D'hooghe et al., 2018; Fuchs et al., 2019; Midaglia et al., 2019; Miller et al., 2011; Minen et al., 2020; Pratap et al., 2020; Van Geel et al., 2020) had a good quality assessment.

4.2.2.2   Weaknesses. One article (Geurts et al., 2019) had a small sample size. Four articles (Conroy et al., 2017; D'hooghe et al., 2018; Geurts et al., 2019; Van Geel et al., 2020) had a high drop-out rate above 20%. Six articles (Geurts et al., 2019; Greiner et al., 2015; Miller et al., 2011; Minen et al., 2020; Pratap et al., 2020; Van Geel et al., 2020) did not describe all details about the population. Two articles (Greiner et al., 2015; Newland et al., 2019) had a fair quality assessment and only one article (Geurts et al., 2019) had a poor quality assessment.

There were different types of biases found. Seven articles (D'hooghe et al., 2018; Fuchs et al., 2019; Geurts et al., 2019; Greiner et al., 2015; Midaglia et al., 2019; Newland et al., 2019; Pratap et al., 2020) had a risk of selection bias, because a selective sampling resulted in an imperfect representation of the population. Two articles (Conroy et al., 2017; Miller et al., 2011) had a risk of performance bias, because differences in intervention groups could affect the results of the subjects. Allocation bias and detection bias were found in one article (Fuchs et al., 2019). Allocation bias arose because there was a lack of correct randomization of the subjects. Also detection bias arose because blinding of the research staff lacked. Information bias was found in one article (Newland et al., 2019), because the results of a qualitative research could have been influenced by the interviewer.

Overall, Geurts et al. (2019) had the most weaknesses next to a poor quality assessment. Geurts et al., 2019 was excluded from this SR for data extraction.

Table 5

Strengths and weaknesses

Article	Strength	Weakness
Bove et al. (2020)	• LoE: 1b • Complete and exact values of results described • Excellent quality assessment (26/28)	
Charvet et al. (2017)	• LoE: 1b • Complete and exact values of results described • Excellent quality assessment (26/28)	
Conroy et al. (2017)	• LoE: 1b • Complete and exact values of results described • Good quality assessment (23/28)	• High drop-out: 52,9% • Risk of performance bias
D'hooghe et al. (2018)	• Complete and exact values of results described • Good quality assessment (21/28)	• High drop-out: 24% • Risk of selection bias
Fuchs et al. (2019)	• Complete and exact values of results described • Good quality assessment (22/28)	• Risk of selection bias, allocation bias and detection bias
Geurts et al. (2019)		• Small sample size (n<30) • Population: no description of level of disability • High drop-out: 38,5% • Poor quality assessment (14/28) • Risk of selection bias
Greiner et al. (2015)		• Fair quality assessment (18/28) • Population: no description of type of MS and level of disability • Risk of selection bias
Midaglia et al. (2019)	• Complete and exact values of results described • Good quality assessment (20/28)	• Risk of selection bias
Miller et al. (2011)	• LoE: 1b • Complete and exact values of results described • Good quality assessment (24/28)	• Population: no description of type of MS and level of disability • Risk of performance bias

Minen et al. (2020)	• LoE: 1b • Complete and exact values of results described • Good quality assessment (23/28)	• Population: no description of level of disability
Newland et al. (2019)		• Fair quality assessment (18/28) • Risk of selection bias and information bias
Pratap et al. (2020)	• Complete and exact values of results described • Good quality assessment (21/28)	• Population: no description of level of disability • Risk of selection bias
Van Geel et al. (2020)	• Complete and exact values of results described • Good quality assessment (21/28)	• Population: no description of level of disability • High drop-out: 36,8% of pwMS • Risk of selection bias

Abbreviations: LoE: Level of Evidence, pwMS: patients of Multiple Sclerosis

4.3   Data extraction

4.3.1   Population

Twelve articles encompassing 1 493 pwMS met criteria for inclusion. In each article, there were at least 30 participants. According to Portney and Watkins (2013), this is an important critical point. However, this should be viewed with caution before applying the statistics. As could be expected, the percentage of female participants was more than 50% in every article, except the self-referred pwMS and controls in Pratap et al. (2020). Only Van Geel et al. (2020) had a 100% female population. Age ranges of pwMS were from 21 years (Minen et al., 2020) to 73 years (Minen et al., 2020). The mean age was not described in all articles, but it is estimated from the obtained data. Across all articles the estimated age of pwMS was 46 years.

It was disadvantageous that two articles (Greiner et al., 2015; Miller et al., 2011) did not specify a type of MS and that five articles (Greiner et al., 2015; Miller et al., 2011; Minen et al., 2020; Pratap et al., 2020; Van Geel et al., 2020) did not describe a level of disability. Minen et al. (2020) did not give a specific number of participants of each type of MS.

Overall, RRMS was the most common type of MS in eight articles which described specific numbers (Bove et al., 2020; Charvet et al., 2017; D'hooghe et al., 2018; Fuchs et al., 2019; Midaglia et al., 2019; Newland et al., 2019; Pratap et al., 2020; Van Geel et al., 2020). EDSS ranges of all articles, which described a specific number, were from 0 to 5,5.

Table 6

Characteristics pwMS

Study ID Author (year)	Population Sample size	Type of MS	Level of disability (EDSS)	Female, %	Age (mean, range, SD)
Bove et al. (2020)	N=44	RRMS: 33, SPMS: 7, PPMS: 2, CIS: 1, Undetermined: 1	Median: 3,5 IQR: [2,5; 4,5]	79,50%	Mean: 51 y ± 13 y
Charvet et al. (2017)	N=135	RRMS: 89, SPMS: 35, PPMS: 7	Median: 3,5 IQR: ± 4,0	77,04%	Mean: 50 y ± 12 y
Conroy et al. (2017)	N=51	RRMS: 14, SPMS: 35, PPMS: 2	PDSS Mean: 4,4	58,82%	Mean: 51 y
D'hooghe et al. (2018)	N=75	RRMS: 75	Mean: 2,0	66,70%	Mean: 39 y ± 10 y
Fuchs et al. (2019)	N=51	RRMS: 68,60%, SPMS: 23,50%, PPMS: 7,80%	Median: 4,0 IQR: [2,0;6,0]	70,60%	Mean: 56 y
Greiner et al. (2015)	N=76	Not mentioned	Not mentioned	68,42%	18-40 y: 30; 41-50 y: 33; >50 y: 13
Midaglia et al. (2019)	N=101 (n=76 pwMS)	RRMS: 69, SPMS: 4, PPMS: 3	Mean: 2,4 ± 1,4	MS: 70,00% HCs: 28,00%	Mean MS: 40 y Mean HCs: 35 y
Miller et al. (2011)	N=206	Not mentioned	Not mentioned	MCCO-original: 85,00% MCCO-enhanced: 72,00%	Mean MCCO-original: 48 y ± 10 y Mean MCCO-enhanced: 48 y ± 10 y

Minen et al. (2020)	N=62	All types of MS included	Not mentioned	89,00%	Mean: 40 y Range: 21-73 y
Newland et al. (2019)	N=32	RRMS: 30, SPMS: 2	Mean: 3,0 IQR: [2;4,8]	81,30%	Mean: 49 y ± 11 y
Pratap et al. (2020)	N=629 (n=495 pwMS)	MS (self-referred): RRMS: 300, SPMS: 25, PPMS: 34 MS (clinic-referred): RRMS: 123, SPMS: 5, PPMS: 6, not sure: 2	Not mentioned	Controls: 20,15% MS (self-referred): 42,90% MS (clinic-referred): 57,35%	Mean controls: 40 y ± 11 y Mean MS (self-referred): 45 y ± 12 y Mean MS (clinic-referred): 49 y ± 11y
Van Geel et al. (2020)	N=31 (n=19 pwMS)	RRMS: 18, SPMS: 1	Not mentioned	100,00%	Median: 43 y Range: 35-66 y

Abbreviations: ACR: Adaptive Cognitive Remediation, CIS: Clinically Isolated Syndrome, EDSS: Expended Disability Status Scale, HCs: Healthy controls, IQR: Interquartile range, MCCO: Mellen Center Care Online, MS: Multiple Sclerosis, PDDS: Patient Determined Disease Steps, PPMS: Primary Progressive Multiple Sclerosis, RRMS: Relapsing-Remitting Multiple Sclerosis, SD: Standard Deviation, SPMS: Secondary Progressive Multiple Sclerosis, Y: years

4.3.2 MHealth for self-assessment

4.3.2.1   Researched mHealth tools. Keep in mind that each article conducted an individual study of different mHealth examples. Some were an application (app) and others were web-based, but it was mentioned in Table 7.

D'hooghe et al. (2018) assessed the feasibility and telemonitored fatigue and physical activity of the web-based mHealth tool MS TeleCoach. Greiner et al. (2015) explored the usability and collected data on pain, fatigue and cognition via MSdialog. There was a web-based and app version. Midaglia et al. (2019) used the Floodlight app for self-assessing cognition and physical activity. Miller et al. (2011) assessed differences between the web-based original Mellen Center Care Online (MCCO)-platform and the expanded and enhanced MCCO-system to monitor MS-related symptoms on quality of life. Newland et al. (2019) collected data of fatigue by means of the FatigueApp. Pratap et al. (2020) assessed quality of life and MS-related health information by means of the app ElevateMS.

4.3.2.2   Impact of MS on functioning. D'hooghe et al. (2018) described that MS TeleCoach had significant decreased fatigue over 12 weeks by the Fatigue Scale for Motor and Cognitive Functions (FSMC) total score -3,76 (p= 0,009) and -1,73 motor (p = 0,007) and cognitive subscores -2,02 (p = 0,02). It was remarkable that one-third with severe fatigue changed to lower FSMC category for total and subscores Modified Fatigue Impact Scale (MFIS) -3,96 (p= 0,03) between baseline and study end.

Greiner et al. (2015) was a six-week study and showed that MSdialog was important to monitor patient reported outcomes (PROs), especially fatigue (99%), physical health (96%), cognitive deficits (93%), pain (91%) and sleep quality (91%). These percentages were the results of the number of participants that scored the MS quality-of-life questionnaire between five and seven, 1= "not important at all" to 7= "extremely important".

Midaglia et al. (2019) showed that Floodlight had an acceptable impact on daily activities after 24 weeks including cognition and physical activity for 80% of people with MS by means of active monitoring and passive monitoring intervention.

Miller et al. (2011) described that there was a group difference between the MCCO-original and MCCO-enhanced group. MCCO-original had a higher European Quality of Life(E-Qol) (p= 0,04) after 12 months of self-monitoring their quality of life. It was evaluated by the outcome measure MSFC.

Newland et al. (2019) reported that the FatigueApp had the ability to collect self-reported symptoms with Patient-Reported Outcomes Measurement Information System (PROMIS). After five weeks, the mean value of PROMIS were fatigue (55,2), EDSS (8,2), visual analogue scale (VAS) (2,1) and cognitive (42,7).

Pratap et al. (2020) described that ElevateMS collected these most common symptoms over a period of 12 weeks: fatigue (62,60%), memory issues (42,20%), difficulty walking (41,40%). There was a significant increase in functional performance (finger-tapping: p<0,001; Digit Symbol Substitution Test (DSST): p=0,005; gait: p=0,001; finger-to-nose: p=0,01). Furthermore, the quality of life was significantly improved with functional tests of physical activity (finger-tapping: p<0,001; walk and balance: p=0,02; DSST: p=0,03).

Table 7

Data extraction, tools for self-assessment (part 1)

Study ID Author (year)	Study design	mHealth tool (web-based or app)	Functioning according to ICF	Description	Purpose of study
D'hooghe et al. (2018)	Cohort study	MS TeleCoach (Web-based)	Fatigue	Combination of monitoring, self-management and motivational messages, focusing on energy management of physical activity with the goal of improving fatigue levels Two components: telemonitoring (physical activity through accelerometers and self-reported fatigue impact levels) and telecoaching (motivational messages and advices)	Assess feasibility and telemonitoring of fatigue and telecoaching of physical activity and energy management
Greiner et al. (2015)	Pilot study	MSdialog (Web-based and app)	Pain, cognition, fatigue	Weekly health reports via one questionnaire or five short questionnaires	Exploring usability and collecting and storing real-time data about clinical outcomes and PROs by patients via personal computer or smartphone from RebiSmart and health
Midaglia et al. (2019)	Observational study	Floodlight (App)	Cognition, physical activity	Combining continuous sensor data capture and standard clinical outcome measures. Performing a set of daily active tests and contribute sensor data via passive monitoring.	Adherence to smartphone- and smartwatch-based assessments and feedback on schedule of assessments and impact on daily activities Association between Floodlight and clinical outcomes, can Floodlight differentiate between participants?

Miller et al. (2011)	RCT	MCCO-enhanced (Web-based)	Quality of life	Electronical messaging between clinician and patient. Expanded functionality with a self-monitoring and self-management system to assess MS-symptoms and to receive graphical feedback. Evaluating symptom changes and making decision about responding to changes. Additional component to conduct appointment preparation.	Assess differences between the original and the expanded system, which monitor MS-related symptoms, make decisions about seeking help for symptoms and notify clinicians of issues to discuss at upcoming appointments
Newland et al. (2019)	Pilot study	FatigueApp.com (App)	Fatigue	Collecting data to correlate fatigue measures with other symptoms and quality. Self-reporting symptoms. Completing fatigue questionnaires every morning for 6 more days and then again 4 weeks later.	Test the use of FatigueApp.com as a PRO data collection tool
Pratap et al. (2020)	Observational pilot study	ElevateMS (App)	Physical activity, Quality of life	Collecting real-world data: self-reported measures of symptoms and health via "check-in"-surveys Independent assessments of motor function via sensor-based active functional tests Encouraging to complete surveys daily and notifications to perform more comprehensive functional tests once a week.	Feasibility and utility of gathering MS-related health information using a dedicated smartphone app

Abbreviations: App: Application, ICF: International Classification of Functioning, Disability and Health, MCCO: Mellen Center Care Online, mHealth: Mobile Health, MS: Multiple Sclerosis, PROs: Patient Reported Outcomes, RCT: Randomized Controlled Trial

Table 7

Data extraction, tools for self-assessment (part 2)

Study ID	Outcome		Intervention	Results
Author (year)	Primary	Secondary		
D'hooghe et al. (2018)	Total score FSMC	FSMC cognitive and motor subscales, MFIS SF-36	2-week run-in period: assess baseline activity level per patient 12-week period: target number of activity counts gradually increased through telecoaching	FSMC total score -3,76 between baseline and study end (p = 0,009); motor and cognitive subscores (-1,73 p = 0,007 and -2,02 p = 0,02) significant decreased; 1/3 with severe fatigue changed to lower FSMC category for total and subscores MFIS -3,96 (p=0,03) between baseline and study end; MFIS physical -2 (p<0,05)
Greiner et al. (2015)	1 MS QoL questionnaire or 5 questionnaires on pain, cognition, fatigue, mental health and social support		6-week study, following stages: 5-min online survey, training teleconference, weekly health reports, 5-min usability Survey at week 3 and 6, follow-up call interview with selected patients	Important to monitor PROs: fatigue (99%), physical health (96%), cognitive deficits (93%), pain (91%) and sleep quality (91%) - Percentage: scores between 5 and 7 (1="not important at all", 7="extremely important")
Midaglia et al. (2019)	SDMT, T25FW, BBS, FSMC, PHQ-9 PwMS only: MSIS-29		<u>Active monitoring for 24 weeks</u> DMQ daily, ST: fortnightly & ad hoc, MSIS-29: fortnightly, SDMT: weekly, pinching test: daily, Draw a Shape Test: daily, SBT: daily, 5UTT: daily, 2MWT: daily <u>Passive monitoring:</u> gait behavior: continuous, mobility pattern: continuous	Acceptable impact on daily activities in 80% of people with MS

Miller et al. (2011)	SIP, MSFC, Control subscale of MSSE, SGSPQC, E-QoL	Self-reported healthcare utilization	12 months: self-monitoring functioning at any moment, comparing MCCO-original with MCCO-enhanced	Between group difference: MCCO-original higher Euro-QoL (p=0,04)
Newland et al. (2019)	VAS, PROMIS		FatigueApp.com: collect data for 5 weeks on PROMIS	Ability to collect data on self-reported symptoms with PROMIS (mean values): PROMIS fatigue (55,2); ESDS (8,2); VAS (2,1); PROMIS cognitive (42,7)
Pratap et al. (2020)	PRO: physical ability		12 weeks	Most common symptoms: fatigue (62,60%), memory issues (42,20%), difficulty walking (41,40%)
	Survey: MS symptoms Survey: health, mobility, Neuro-QoL domains		Completed baseline assessments, including self-reported physical ability and longitudinal assessments of quality of life and daily health	Baseline PDDS significant functional performance (finger-tapping: p<0,001; DSST: p=0,005; gait: p=0,001; finger-to-nose: p=0,01)
	Active functional test: finger-tapping, walk and balance, DSST, Finger-to-nose		Completed functional tests as an independent assessment of MS-related motor activity	Neuro-QoL significant with functional tests (finger-tapping: p<0,001; walk and balance: p=0,02; DSST: p=0,03)

Abbreviations: 2MWT: 2 Minute Walk Test, 5 UTT: 5 U-Turn Test, 9HPT: 9-Hole Peg Test, BBS: Berg Balance Scale, DMQ: Daily Mood Question, DSST: Digit Symbol Substitution Test, EDSS: Expanded Disability Status Scale, EuroQol: European Quality of Life, FSMC: Fatigue Scale for Motor and Cognitive Functions, MCCO: Mellen Care Center Online, MFIS SF-36: Modified Fatigue Impact Scale Short Form-36, MS: Multiple Sclerosis, MSFC: Multiple Sclerosis Functional Composite, MSIS-29: Multiple Sclerosis Impact Scale–29, MSSE: Mini Mental State Examination, Neuro-QoL: neurological-Quality of Life, P: p-value, PDDS: Patient Determined Disease Steps, PHQ-9: Patient Health Questionnaire–9, PROMIS: Patient-Reported Outcomes Measurement Information System, PROs: Patient Reported Outcomes, SBT: Static Balance Test, SDMT: Symbol Digit Modalities Test, SGSQC: Senior' General Satisfaction an Physician Quality of Care, SIP: Sickness, Impact Profile, ST: Symptom Tracker, T25FW: Timed 25-Foot Walk test, VAS: visual analogue scale, WHO: World Health Organization

4.3.3 MHealth in rehabilitation

4.3.3.1 Researched mHealth tools. Bove et al. (2020) assessed cognition and fatigue in a videogame-like treatment to a control group by means of the web-based AKL-T03. Charvet et al. (2017) tested the efficacy of the web-based adaptive Cognitive Remediation (ACR) program to assess cognition against an active control comparison. Conroy et al. (2017) assessed physical activity and quality of life during exercises by means of the web-based multiple sclerosis home-automated tele-management (MS HAT) system. Fuchs et al. (2019) investigated cognition to predict the response to a previously validated approach to the web-based platform BrainHQ. Minen et al. (2020) was a study of the RELAXaHEAD app to assess physical activity and pain. Van Geel et al. (2020) evaluated feasibility of prolonged use of the WalkWithMe app and tested the impact on physical activity, quality of life, fatigue and cognition.

4.3.3.2 Effectiveness of rehabilitation intervention. Bove et al. (2020) described that the web-based AKL-T03 increased cognition and decreased fatigue over a period of six weeks. The intervention group used the in-home, videogame-like digital treatment with AKL-T03 and the control group used an active tablet-based placebo control with AKL-T09. Symbol Digit Modalities Test (SDMT) increased at the second visit to +6,10 for AKL-T03 (p < 0,001) and +3,55 for AKL-T09 (p=0,024). After the third visit, 70% of the AKL-T03 had a clinically 4+ point increase SDMT above baseline, compared with 37% for AKL-T09 (p = 0,038). The MFIS became a mean change decrease of -4,79 (p= 0,004).

Charvet et al. (2017) showed that the ACR platform had significantly greater improvement of cognitive functioning (composite 0,25 vs. 0,09; p = 0,03), despite the greater training time in the active control condition (56,9 vs. 37,7 hours played; p = 0,006) over 12 weeks. The intervention group performed 15 exercises of the ACR platform and the control group used a software gaming suite.

Conroy et al. (2017) tested the web-based MS HAT system and there was no statistically significant difference on physical activity in timed 25-foot walk test (T25FW) at six months (p= 0,44). The 6MWT showed a negative change for MS HAT relative to control group (p= 0,04) at six months.

Fuchs et al. (2019) showed that BrainHQ had a significant improvement of cognition after training (p<0,001) and a SDMT improvement correlated positively with treatment (p = 0,007) after a 12-week training period. No control group was mentioned.

Minen et al. (2020) described that RELAXaHEAD had no significant change in migraine disability or MS pain scores from baseline to endpoint (41 and 29) and between groups (p=0,0519). For ninety days, the intervention group filled in a daily headache diary and two progressive muscle relaxation (PMR) sessions a day. The control group used the app without PMR sessions, but completed the daily headache diary.

Van Geel et al. (2020) described that the WalkWithMe app had a significant improvement on quality of life (International Physical Activity Questionnaire (IPAQ) walking and leisure, p = 0,04 and p = 0,02; 36-Item Short Form Health Survey (SF-36) functioning, p = 0,02), cognition (p = 0,01), cognitive fatigability (Paced Autitory Serial Addition Test (PASAT), p = 0,05), lower limb strength (five-repetition sit-to-stand test (5-STS), p = 0,05) and dominant hand function (nine hole peg test (9HPT), p = 0,002). No control group was mentioned.

Table 8

Data extraction, tools for rehabilitation (part 1)

Study ID Author (year)	Study design	mHealth tool (web-based or mobile)	Functioning according to ICF	Description	Purpose of study
Bove et al. (2020)	RCT	AKL-T03 (Web-based)	Cognition, fatigue	Engaging patient in simultaneous sensory and motor tasks and designed to engage frontal neural network Enabling real-time monitoring of progress and continuously challenges patient so that the test is never too easy or difficult Encouraging patients to improve performance	Assessing whether a videogame-like treatment is superior to a control in improving processing speed
Charvet et al. (2017)	RCT	Adaptive Cognitive Remediation (ACR) (Web-based)	Cognition	Online ACR program: central management and a set of 15 exercises targeting speed, attention, working memory and executive function through visual and auditory domains Initial low level of challenge with adjustments on individual basis as learning and abilities improve over time Each exercise: multiple stimulus sets to span relevant dimensions of real-world stimuli	Testing the efficacy of ACR program in MS against an active control comparison of ordinary computer games

Conroy et al. (2017)	RCT	MS HAT system (Web-based)	Physical activity	Supporting patient-centered care, self-management and patient-provider communication. Three interfaces: patient unit, server and clinical unit. Patient unit had interactive options for data collection, educational content, exercise information and therapist-patient communication Access to exercises, respond to exercise specific assessments and document exercise data from home Exercise adherence feedback via diary entries, calendars and graphs	Hypothesis: HAT system customized for MS exercise with elements of self-efficacy for self-monitoring, and asynchronous therapist communication would improve ambulation speed, balance, exercise compliance
Fuchs et al. (2019)	Experimental study	BrainHQ (Web-based)	Cognition	Selected exercises: improve cognitive processing speed. 1 training session/day (45-60 min), for 5 days each week. Difficulty increased as users improve by adapting parameters such as speed of processing and distractor stimuli	Investigating clinical characteristics to predict response to a previously validated approach to home-based restorative cognitive training
Minen et al. (2020)	RCT	RELAXaHEAD (App)	Pain	Containing headache diary, which includes features for tracking headache characteristics, headache medications and sleep, and tracking medication side effects and menstrual cycles	A study of RELAXaHEAD app in MS-migraine patients to assess change in migraine and MS pain-related disability

| Van Geel et al. (2020) | Cohort study | WalkWithMe (App) | Cognition, fatigue, physical activity, quality of life | Tracking walking activities and follow up on progress. The app detects walking speed and gives feedback during walking with verbal feedback by the virtual coach | Evaluating feasibility of prolonged use of WalkWithMe and testing its effect on physical activity, walking, fatigue and cognition in persons with MS |

Abbreviations: ACR: adaptive Cognitive Remediation, ICF: International Classification of Functioning, Disability and Health, mHealth: mobile Health, MS: Multiple Sclerosis, RCT: Randomized Controlled Trail

Table 8

Data extraction, tools for rehabilitation (part 2)

Study ID	Outcome		Intervention		Results
Author (year)	Primary	Secondary	Intervention group	Control group	
Bove et al. (2020)	SDMT	PROs: CESD, STAI, MFIS	6 weeks, 25 minutes daily, 5 days weekly In-home, videogame-like digital treatment (AKL-T03)	Using an active tablet-based placebo control (AKL-T09)	SDMT increased at visit 2 to AKL-T03 +6,10 (*p* < 0,001) and AKL- T09 +3,55 (p=0,024) Visit 3, 70% AKL-T03: clinically 4+ point increase SDMT above baseline, compared with 37% for AKL-T09 (*p* = 0,038) MFIS mean change -4,79 (p=0,004)
Charvet et al. (2017)	PASAT, WAIS-IV, SRT, BVMT-R, DKEFS		12 weeks, 1 hour per day, 5 days per week ACR program, research version of BrainHQ 15 exercises: cognition and executive function through visual and auditory domains	12 weeks, 1 hour per day, 5 days per week Software gaming suite: active placebo control to account for nonspecific treatment effects	ACR: significantly greater improvement of cognitive functioning (composite 0,25 vs 0,09; p = 0,03), despite greater training time in the active control condition (56,9 vs 37,7 hours played; p = 0,006)
Conroy et al. (2017)	T25FW, 6MWT, BBS	MSWS-12	6 months, daily functional exercises MS HAT group: written exercises and access to messaging for exercise updates via HAT platform	Individualized functional exercise in hand-out form with instruction for repetitions and sets. No contact with the therapist outside the on-site evaluation visits	No statistically significant difference in T25FW at six months (p= 0,44) 6MWT: negative change for MS HAT relative to control group (p=0,04) after 6 months

Fuchs et al. (2019)	BICAMS, SDMT, BVMTR, CVLT-II, DKEFS , FSS		12 weeks, 1 training session/day (45-60 min), for 5 days each week	Not mentioned	Significant improvement after training (p<0,001), SDMT improvement correlated positively with treatment (p = 0,007)
Minen et al. (2020)	Not related	MIDAS, PES	RELAXaHEAD app with PMR: daily headache diary and 15-minute and a 5-minute PMR session a day for 90 days	App without PMR: complete the daily headache diary	No significant change in migraine disability or MS Pain scores from baseline to endpoint (41 and 29) and between groups (p=0,0519)
Van Geel et al. (2020)	IPAQ 6MWT	T25FW, 5-STS, 9HPT PASAT, SDMT SF-36	10 weeks, minimum target goal of 30 min in 1 session Weekly schedule: target goal minus 45 min and exceeding 45 min Start: walking at least two times a week, each week a maximum of five minutes added	Not mentioned	Significant improvement: quality of life (IPAQ walking and leisure, p = 0,04 and p = 0,02; SF-36 functioning, p = 0,02), cognition (SDMT, p = 0,01), cognitive fatigability (PASAT, p = 0,05), lower limb strength (5-STS, p = 0,05), dominant hand function (9HPT, p = 0,002)

Abbreviations: 5-STS: 5-repetition Sit-to-Stand, 6MWT: 6 Minute Walking Test, 9HPT: 9 Hole Peg Test, ACR: adaptive Cognitive Remediation, BBS: Berg Balance Scale, BICAMS: Brief International Cognitive Assessment for Multiple Sclerosis, BVMT-R: Brief Visuospatial Memory Test Revised, CESD: Center for Epidemiologic Studies Depression Scale, CVLT-II: California Verbal Learning Test II, DKEFS: Delis-Kaplan Executive Function System, FSS: Fatigue Severity Scale, IPAQ: International Physical Activity Questionnaire, LCLA: Low-contrast letter acuity test, MET: Metabolic Equivalent of Task, MFIS: Modified Fatigue Impact Scale, MIDAS: Migraine Disability Assessment Scale, MS: Multiple Sclerosis, MSFC4: Multiple Sclerosis Functional Composite 4, MSIS-29: Multiple Sclerosis Impact Scale-29, MSNQ-P: Patient-Report Multiple Sclerosis Neuropsychological Screening Questionnaire, MSWS-12: Multiple Sclerosis Walking Scale-12, PASAT: Paced Auditory Serial Addition Test, PES: Pain Effect Scale, PMR: progressive muscle relaxation, PROs: Patient Reported Outcomes, SDMT: Symbol Digit Modalities Test, SF-36: 36-item Short-Form Health Survey, SRT: Selective Reminding Test, STAI: State-Trait Anxiety Inventory, T25FW: Timed 25-foot walk, WAIS-IV: Wechsler Adult Intelligence Scale

4.3.4   Summary per topic of functioning

For the assessment of pain, there was an app and a web-based version of MSdialog for self-assessment (Greiner et al., 2015) and a rehabilitation app RELAXaHEAD (Minen et al., 2020). Greiner et al. (2015) described that 91% of the participants of MSdialog thought it is important to monitor pain, measured by MS quality of life (QoL) questionnaire. Minen et al. (2020) showed that RELAXaHEAD found no significant change in MS-related disability or the migraine pain score, measured by Pain Effect Scale (PES).

For the assessment of cognition, there were two apps, MSdialog (Greiner et al., 2015) and Floodlight (Midaglia et al., 2019) for self-assessment. There were also one app, WalkWithMe (Van Geel et al., 2020) and three web-based programs, ACR program (Charvet et al., 2017), BrainHQ (Fuchs et al., 2019) and AKL-T03 (Bove et al., 2020), for rehabilitation. Greiner et al. (2015) described that 93% of the participants of MSdialog thought it was important to monitor cognition, measured by MS QoL (quality of life) questionnaire. Midaglia et al. (2019) showed that Floodlight had an acceptable impact on daily activities including cognition, measured by SDMT. Charvet et al. (2017) found that ACR program had a significantly greater improvement of cognitive functioning, despite greater training time in the active control group, measured by a composite score. Fuchs et al. (2019) described that BrainHQ had an improvement and a positive correlation with treatment, measured by SDMT. Van Geel et al. (2020) found that WalkWithMe showed a significant improvement of cognition and cognitive fatigability, measured by SF-36. Bove et al. (2020) described that AKL-T03 had a clinically improvement on processing speed of the cognitive function, measured by SDMT.

For the assessment of fatigue, there were two apps, MSdialog (Greiner et al., 2015) and FatigueApp (Newland et al., 2019) and two web-based programs, MSdialog (Greiner et al., 2015) and MS TeleCoach (D' hooghe et al., 2018), for self-assessment. There was also one app WalkWithMe (Van Geel et al., 2020) and one web-based program, AKL-T03 (Bove et al., 2020), for rehabilitation. Greiner et al. (2015) described that 99% of the participants of MSdialog thought it was important to monitor fatigue, measured by MS QoL questionnaire. Van Geel et al. (2020) found that WalkWithMe showed a significant improvement of fatigue, measured by PASAT. D' hooghe et al. (2018) showed that MS TeleCoach decreased fatigue and one third of pwMS with severe fatigue changed to a lower fatigue category, measured by FSMC and MFIS. Newland et al. (2019) found that the FatigueApp had the ability to collect date of self-reported fatigue, measured by PROMIS and VAS. Bove et al. (2020) described that AKL-T03 had a decreased mean change of -4,79, measured by MFIS.

For the assessment of physical activity, there were two apps, Floodlight (Midaglia et al., 2019) and ElevateMS (Pratap et al., 2020), for self-assessment. There was also one app, WalkWithMe (Van Geel et al., 2020), and one web-based, MS HAT system (Conroy et al., 2017), for rehabilitation. Midaglia et al. (2019) showed that Floodlight had an acceptable impact on daily activities including physical activity, measured by T25FW, Berg Balance Sale (BBS) and FSMC. Pratap et al. (2020) showed that ElevateMS found 41,4% of the participants had a walking difficulty and also a significant functional performance was found, measured by active functional tests like finger-tapping, walk and balance exercises, DSST and finger-to-nose. Van Geel et al. (2020) found that WalkWithMe showed a significant improvement on lower limb strength and dominant hand function, measured by 5-STS and 9HPT. Conroy et al. (2017) showed that the MS HAT system had no significant difference on physical activity at six months, measured by T25FW and 6MWT.

For the assessment of quality of life, there was one app, ElevateMS (Pratap et al., 2020), and one web-based program, MCCO-enhanced (Miller et al., 2011) for self-assessment. There was also one app, WalkWithMe (Van Geel et al., 2020), for rehabilitation. Van Geel et al. (2020) found that WalkWithMe showed a significant improvement of quality of life, measured by IPAQ. Miller et al. (2011) showed that MCCO-enhanced had no difference in the results of quality of life, measured by E-QoL. Pratap et al. (2020) described that ElevateMS had a significant impact on the improvement of quality life, measured by Neuro-QoL and functional tests.

Table 9

Overview mHealth tools

Functioning according to ICF	mHealth tool	Self-assessment or rehabilitation	Relevant outcomes
Pain	MS dialog	Self-assessment	MS QoL questionnaire
	RELAXaHEAD	Rehabilitation	PES
Cognition	MS dialog	Self-assessment	MS QoL questionnaire
	Floodlight	Self-assessment	SDMT
	AKL-T03	Rehabilitation	SDMT
	ACR	Rehabilitation	Composite score
	BrainHQ	Rehabilitation	SDMT
	WalkWithMe	Rehabilitation	SF-36
Fatigue	MS Telecoach	Self-assessment	FSMC, MFIS
	MS dialog	Self-assessment	MS QoL questionnaire
	FatigueApp	Self-assessment	PROMIS, VAS
	AKL-T03	Rehabilitation	MFIS
	WalkWithMe	Rehabilitation	PASAT
Physical activity	Floodlight	Self-assessment	T25FW, BBS, FSMC
	ElevateMS	Self-assessment	Neuro-QoL, functional tests
	MS HAT system	Rehabilitation	T25FW, 6MWT
	RELAXaHEAD	Rehabilitation	MIDAS
	WalkWithMe	Rehabilitation	5-STS, 9HPT
Quality of life	MCCO-enhanced	Self-assessment	E-QoL
	ElevateMS	Self-assessment	Neuro-QoL, functional tests
	WalkWithMe	Rehabilitation	IPAQ

Abbreviations: 5-STS: 5-repetition Sit-to-Stand, 6MWT: 6 Minute Walking Test, 9HPT: 9 Hole Peg Test, ACR: adaptive Cognitive Remediation, BBS: Berg Balance Scale, FSMC: Fatigue Scale for Motor and Cognitive Functions, ICF: International Classification of Functioning, Disability and Health, IPAQ: International Physical Activity Questionnaire, MCCO: Mellen Care Center Online, MFIS: Modified Fatigue Impact Scale, mHealth: mobile Health, MIDAS: Migraine Disability Assessment Scale, MS: Multiple Sclerosis, MS QoL questionnaire: Multiple Sclerosis Quality of Liefe questionnaire, Neuro-QoL: neurological-Quality of Life, PASAT: Paced Auditory Serial Addition Test, PES: Pain Effect Scale, PROMIS: Patient-Reported Outcomes Measurement Information System, SDMT: Symbol Digit Modalities Test, SF-36: 36-item Short-Form Health Survey, T25FW: Timed 25-foot walk, VAS: Visual Analogue Scale

5   Discussion

5.1   Quality studies

Because mHealth is a standard tool that has not yet been used in the treatment of pwMS, all articles had a small generalizability because of a lack of external validity. A second reason for a small external validity is the specific population. An adequate adjustment of confounding is only applied in seven articles of 13 articles (Bove et al., 2020; Charvet et al., 2017; Conroy et al., 2017; D'hooghe et al., 2018; Fuchs et al., 2019; Miller et al., 2011; Minen et al., 2020). This reduced the risk of confounding bias and was important for interpreting the results.

The published date of the article is important. Eleven articles (Bove et al., 2020; Charvet et al., 2017; Conroy et al., 2017; D'hooghe et al., 2018; Fuchs et al., 2019; Geurts et al., 2019; Midaglia et al., 2019; Minen et al., 2020; Newland et al., 2019; Pratap et al., 2020; Van Geel et al., 2020) were quite recently, but two articles (Greiner et al., 2015; Miller et al., 2011) were older than five years. It should be addressed when considering the results that the developed devices were maybe too old for a current niche topic in physiotherapy as mHealth. Underdeveloped tools could give biased results.

Five individual studies (Bove et al., 2020; Charvet et al., 2017; Conroy et al., 2017; Miller et al., 2011; Minen et al., 2020) were an RCT and categorized as level of evidence 1b. An RCT is the most reliable individual studies, but only three articles (Bove et al., 2020; Charvet et al., 2017; Minen et al., 2020) had an adequate double blinding for participants and research staff. This reduces the risk of bias. Miller et al. (2011) has less preponderance to answer the research questions because the article is older than five years. It was a web-based version of mHealth and so it should be taken into account that web-based platforms have existed longer than apps. Also, the preponderance of Conroy et al. (2017) is doubtful, because the study has a high drop-out rate of 52,9% of 51 participants.

This SR was a reflection of the results of all included articles according to article age, percentage of drop-out, quality assessment by means of the Downs and Black checklist and their strengths and weaknesses. Three of 13 articles (Bove et al., 2020; Charvet et al., 2017; Minen et al., 2020) are assessed as the most preponderance. Six of 13 articles had a good preponderance assessment (D' hooghe et al., 2018; Fuchs et al., 2019; Midaglia et al., 2019; Miller et al., 2011; Pratap et al., 2020; Van Geel et al., 2020). Three articles (Conroy et al., 2017; Greiner et al., 2015; Newland et al., 2019) had a small preponderance, because the article age, big limitations or quality assessment was not good. According to the results of quality assessment, Geurts et al. (2019) was excluded from data extraction, because the quality was too poor. Van Geel et al. (2020) also used the WalkWithMe app and is an expansion of Geurts et al. (2019).

5.2   Findings in function of research questions

The impact of mHealth tools for self-assessment and rehabilitation was examined by different types and examples of mHealth on different items of functioning according to ICF. The purpose of this literature review was to discuss and compare the rehabilitation results of mHealth tools on functioning.

It was not possible to draw a solid conclusion on mHealth assessing pain, because there was only one option for self-assessment (Greiner et al., 2015) and one for rehabilitation (Minen et al., 2020). Regarding the quality assessment of the articles, RELAXaHEAD (Minen et al., 2020) seems to be the best option for monitoring pain, but no significant change in migraine disability and MS-related pain was found. There was also no description of the level of evidence at baseline. It would be a good idea to retest RELAXaHEAD in a new study setting of an RCT to reduce the risk of bias and increase reliability.

Two mHealth tools (Greiner et al., 2015; Midaglia et al., 2019) assessed cognition by self-monitoring, but with other measure outcomes. Floodlight (Midaglia et al., 2019) had an acceptable impact on daily activities including cognition, but the participants had a large range of disability that possibly influenced the results. The impact on cognition for rehabilitation was investigated in four mHealth tools (Bove et al., 2020; Charvet et al., 2017; Fuchs et al., 2019; Van Geel et al., 2020). Bove et al. (2020) and Fuchs et al. (2019) used both SDMT as measure outcome. The improvement results of rehabilitation with BrainHQ (Fuchs et al., 2019) were possibly doubtful because there was no comparison with an active control group. Both Charvet et al. (2017) and Van Geel et al. (2020) found a significant improvement of the cognitive function, but Van Geel et al. (2020) had no active control group and a high drop-out of 36,8%. Participants of a medical setting will also tend to have more adherence to rehabilitation intervention. Therefore, the AKL-T03 (Bove et al., 2020) and ACR program (Charvet et al., 2017) were the best options of a web-based mHealth tool for rehabilitation of the cognitive function.

Three mHealth tools for self-assessment (D'hooghe et al., 2018; Greiner et al., 2015; Newland et al., 2019) assessed fatigue. Considering the quality assessment and weaknesses of the articles, it seems that MS TeleCoach (D'hooghe et al., 2018) is the best mHealth tool to monitor fatigue. The results were remarkable because MS TeleCoach decreased fatigue and one-third of pwMS with severe fatigue changed to a lower fatigue category, but there was also a drop-out of 24%. So being careful in interpreting the results is advised. Two articles (Bove et al., 2020; Van Geel et al., 2020) assessed fatigue in a rehabilitation intervention by means of mHealth tools. Van Geel et al. (2020) found that WalkWithMe showed a significant improvement on fatigue, but there was no active control group, no description of the level of disability, high drop-out of 36,8% and a risk of selection bias. Therefore, the web-based mHealth tool, AKL-T03 (Bove et al., 2020), would be the best option for assessing fatigue in rehabilitation.

Two studies (Midaglia et al., 2019; Pratap et al., 2020) investigated physical activity by self-assessment mHealth. They used different measure outcomes, but ElevateMS (Pratap et al., 2020) alone showed a significant improvement of functional physical activity. The level of disability was not mentioned, which possibly affected the results. Three mHealth tools (Conroy et al., 2017; Van Geel et al., 2020) for rehabilitation also assessed physical activity by other measure outcomes. Conroy et al. (2017) showed that MS HAT system had no significant difference on physical activity by six months. The disadvantages of the article were a drop-out rate of 52,9% and risk of performance bias. Therefore, it is possible that the results are influenced. Van Geel et al. (2020) found that WalkWithMe showed a significant improvement on a part of the physical capabilities, especially lower limb strength and dominant hand function, but there was no active control group, no description of the level of disability, high drop-out rate of 36,8% and a risk of selection bias. So, both mHealth tools had big disadvantages. It is difficult to choose the best mHealth tool considering the study designs of the articles.

Two articles (Miller et al., 2011; Pratap et al., 2020) assessed the quality of life by means of mHealth tools for self-assessment. Miller et al. (2011) showed that MCCO-enhanced had no difference in the results of quality of life. It was a year-long study, but type of MS and level of disability were not mentioned. Based on the results, ElevateMS would be a better self-assessment app for rehabilitation of quality of life, because this mHealth tool did register a significant improvement within 12 weeks. There was only one article (Van Geel et al., 2020) that assessed quality of life in a rehabilitation intervention. WalkWithMe showed a significant improvement in quality of life, but there were no active control group, no description of the level of disability, high drop-out rate of 36,8% and a risk of selection bias. A double-blinded, randomized and controlled setting of the study would have been a better option to test this app in an MS population.

Except for Pratap et al. (2020), all included articles had a female majority of participants which can be explained by the fact that more women suffer from MS (Walton et al., 2020). This increased the generalization of the data to MS population. Also, the relapsed-Remitting type of MS (RRMS) was the most included type of MS in eight of 12 articles (Bove et al., 2020; Charvet et al., 2017; D' hooghe et al., 2018; Fuchs et al., 2019; Midaglia et al., 2019; Newland et al., 2019; Pratap et al., 2020; Van Geel et al., 2020), if it was mentioned. But actually, RRMS is the most common type of MS (Ohlmeier et al., 2020). The complaints proceed in a wave motion. There are periods of exacerbations followed by periods of recovery, which is why describing the level of disability and the type of MS is important to know if they affect the results. Five articles (Greiner et al., 2015; Miller et al., 2011; Minen et al., 2020; Pratap et al., 2020; Van Geel et al., 2020) described the level of disability of the participants. It is useful because it can make an estimate of the results of physical activity at baseline and the realistic progression. The results of (Van Geel et al., 2020) should be interpreted with caution due to an unknown cause for the improvement of physical activity. It is not clear whether the intervention or the extra attention for physical activity by means of mHealth caused the improvement.

5.3   Strengths and limitations of the literature study

This SR has three strengths. Firstly, the method is extensively described in detail with all key words, clear research questions and selection criteria which reduced the risk of sampling bias and increased the reproducibility. Secondly, all parts of this review (the selection process, quality assessment, data extraction and discussion) have been double-checked by two independent researchers. Thirdly, this literature review has multiple and broad research questions which included multiple topics of functioning. For mHealth, the broad sense of the word has also been used to include articles, especially any digital tool available on smartphone or tablet. In this way, the risk of confirmation bias was limited.

This SR has four major limitations. Firstly, the literature search was only via PubMed and WoS, but the majority of the articles retrieved via WoS were appeared not fitting the topic. For example, the Physiotherapy Evidence Database (PEDro) and Scopus database, might also have been good databases to look up relevant medicine studies. Secondly, all included articles investigated several mHealth tools. It makes it less uniform, because the results could not be compared per mHealth tool and there was a lot of information in the data extraction. Thirdly, different types of individual studies have been included, but only including RCTs would reduce the risk of bias and improve the reliability of this SR. Fourthly, the psychometric properties of the apps were not investigated. Participants could respond to questionnaires differently due to environmental factors. This could influence the interpretation of the results and decrease the reliability of this review.

5.4   Recommendations for future studies

It is useful to investigate if mHealth tools give significant results in future rehabilitation interventions. An individual study with an RCT study design is the best option for future research because the risk of different biases is reduced. It would be interesting to investigate the WalkWithMe app on physical activity and fatigue in a two-armed, single-blinded RCT study, with an intervention group and an active placebo control group. This is a proposal for the study protocol of future research.

6 Conclusion

This systematic review showed that there are several mHealth tools already available for self-assessment and rehabilitation interventions of different items on functioning according to ICF in adult pwMS. The mHealth tools showed significant improvement in fatigue, cognition, physical activity and quality of life. Further research on the effectiveness of mHealth tools in rehabilitation intervention in MS is recommended to find out more about the reliability of these results and generalisation of the MS population.

7   List of abbreviations

5-STS: five-repetition sit-to-stand test
6MWT: six-minute walking test
9HPT: nine hole peg test
ACR: adaptive Cognitive Remediation
App: application
BBS: berg balance scale
CD: Charlotte Deschryvere
DSST: Digit Symbol Substitution Test
EDSS: Expanded Disability Status Scale
E-Qol: European Quality of Life
FSMC: Fatigue Scale for Motor and Cognitive Functions
ICF: International Classification of Functioning, Disability and Health
IPAQ: International Physical Activity Questionnaire
MN: Maite Noels
MCCO: Mellen Care Center Online
MeSH: Medical Subject Heading
MFIS: Modified Fatigue Impact Scale
MHealth: mobile health
MS: multiple sclerosis
MS HAT: multiple sclerosis home-automated tele-management
PASAT: Paced Autitory Serial Addition Test
PEDro: Physiotherapy Evidence Database
PES: Pain Effect Scale
PMR: progressive muscle relaxation
PRO: patient reported outcome
PROMIS: Patient-Reported Outcomes Measurement Information System
pwMS: persons with multiple sclerosis
QoL questionnaire: quality of life questionnaire
RCT: randomised controlled trial
RRMS: relapsing remitting multiple sclerosis
SDMT: symbol Digit Modalities Test
SF-36: 36-Item Short Form Health Survey
SR: systematic review
T25FW: Timed 25-Foot Walk
VAS: visual analoge scale
WoS: Web of Science

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9   Annexes literature study

Appendix 1

Reason for excluded articles after full text analysis (n=83)

Reason for exclusion	Number of articles	Reference of the articles
Population	5	Klein et al. (2015); Price et al. (2019); Recio-Rodriguez et al. (2014); Rogante et al. (2006); Silva Almodovar et al. (2018)
Intervention	25	Alschuler et al. (2016); Armstrong et al. (2020); Austin et al. (2014); Babbage et al. (2019); Balto et al. (2016); Bove et al. (2019); Bove et al. (2015); Casey et al. (2019); Giunti et al. (2018); Jakobsen et al. (2019); Jeong et al. (2020); Jeong et al. (2020); Karnoe et al. (2017); Korb et al. (2016); Kratz et al. (2020); Li et al. (2020); Mäurer et al. (2016); Parks et al. (2020); Preziosa et al. (2020); Ranjan et al. (2019); Romeo et al. (2020); Tonheim et al. (2018); Tonheim et al. (2018); Van Kessel et al. (2021); Winberg et al. (2019);
Outcome	14	Apolinàrio-Hagen et al. (2018); Bauer et al. (2018); Block et al. (2017); Eguiluz-Perez et al. (2014); Engelhard et al. (2017); Finkelstein et al. (2009); Giunti et al. (2020); Lavorgna et al. (2017); Manor et al. (2018); Rimmer et al. (2018); Schleimer et al. (2020); Tacchino et al. (2015); Thirumalai et al. (2018); Zissman et al. (2012)
Design	8	Boeschoten et al. (2012); Galea et al. (2019); Giunti et al. (2016); Motl et al. (2018); Plow et al. (2020); Sesel et al. (2019); Silveira et al. (2019); Simpson et al. (2015)
Independent use of mHealth tool by the patient	31	Bombardier et al. (2013); Böttrich et al. (2020); Boukhvalova et al. (2019); Boukhvalova et al. (2018); Bove et al. (2019); Broussard et al. (2019); Capra et al. (2020); Carignan et al. (2015); Ehde et al. (2018); Gutiérrez et al. (2013); Haase et al. (2018); Healey et al. (2019); Hermens et al. (2008); Hsu et al. (2021); Huijgen et al. (2008); Jongen et al. (2020); Kahraman et al. (2020); Kayser et al. (2018); Lang et al. (2019); Maillart et al. (2020); Mercier et al. (2015); Moss-Morris et al. (2012); Motl et al. (2019); Ortiz-Gutiérrez et al. (2013); Paul et al. (2014); Paul et al. (2019); Plow et al. (2019); Plow et al. (2012); Shaw et al. (2021); Tacchino et al. (2020); Thomas et al. (2019)

Appendix 2

Available screenshots mHealth tools

MS TeleCoach

(D'hooghe et al., 2018)

Fig. 1. Home screen of the MS TeleCoach.

Floodlight

(Midaglia et al., 2019)

Figure 2. FLOODLIGHT active tests and their schedule frequency. DMQ: Daily Mood Question; MSIS-29: Multiple Sclerosis Impact Scale–29; SBT: Static Balance Test; SDMT: Symbol Digit Modalities Test; ST: Symptom Tracker; 2MWT: Two-Minute Walk Test; 5UTT: 5 U-Turn Test.

ElevateMS

(Pratap et al., 2020)

Figure 1. Example screenshots from the elevateMS study app.
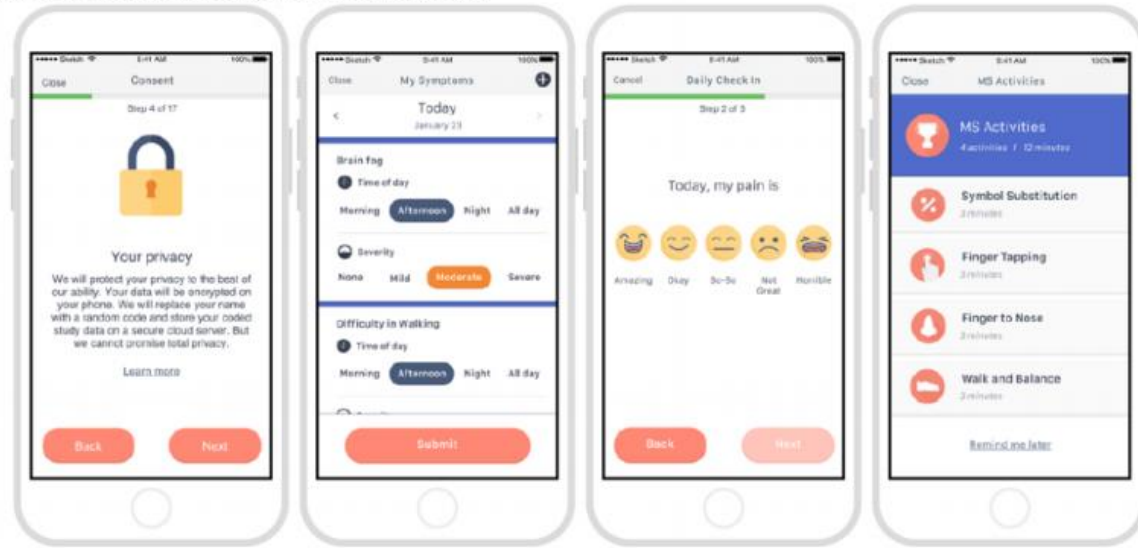
MS HAT system

(Conroy et al., 2017)
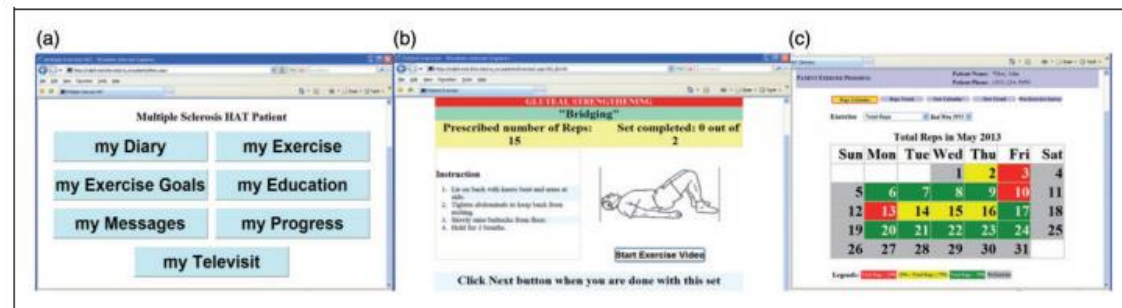
Figure 1. Multiple sclerosis (MS) home automated tele-management system webpage: (a) menu options; (b) exercise prescription, instruction and exercise video link and (c) exercise adherence feedback in calendar format.

RELAXaHEAD

(Minen et al., 2020)

Fig. 1. RELAXaHEAD application.

WalkWithMe

(Van Geel et al., 2020)

a) Home screen   b) Personal scheme   c) Walking activity   d) 6 minute walk test

e) Activity overview   f) Weekly overview   g) Community
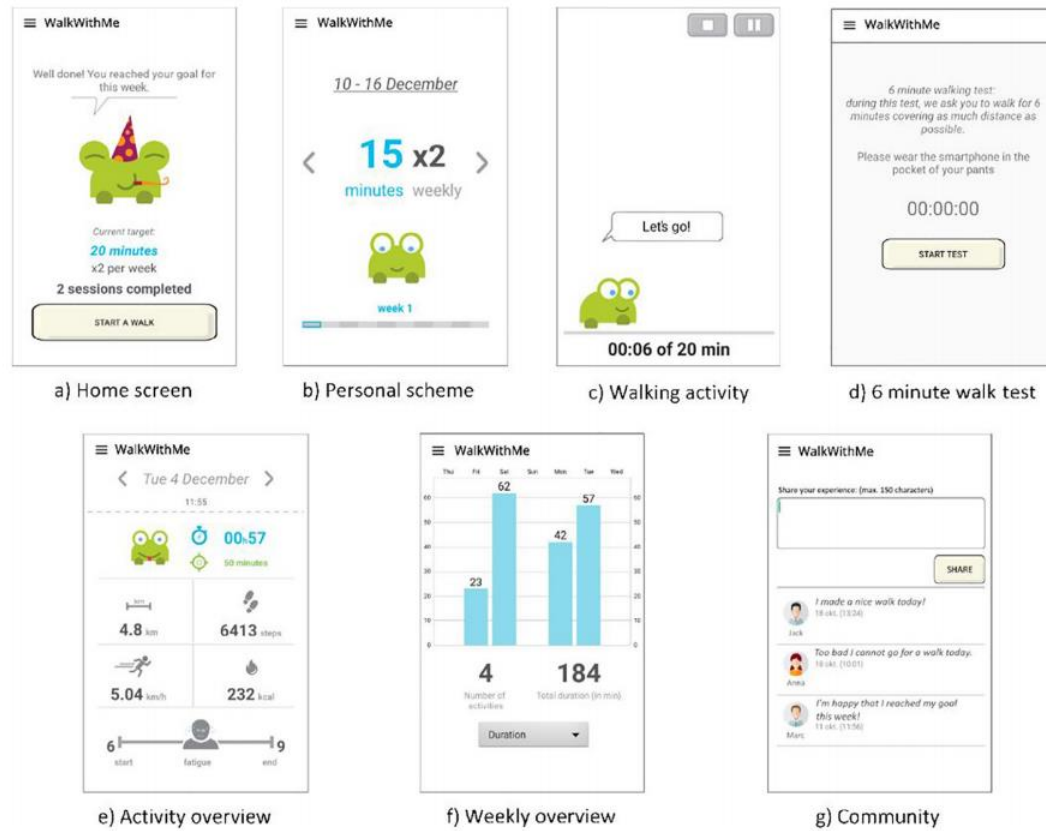
Fig. 1. Overview of the WalkWithMe application options and screens (a. Home Screen; b. Personal scheme; c. Walking activity; d. 6 minute walk test; e. Activity overview; f. Weekly overview; g. Community).

Part 2 Study protocol

Table of content

1   Introduction

Multiple sclerosis (MS) is a progressive, inflammatory disease of the central nervous system in young adults (Compston & Coles, 2008; Walton et al., 2020). The significant variety of symptoms consists of loss of strength, visual and sensation disorders, coordination and balance problems, fatigue, walking disability and memory problems (Barin et al., 2018; Beer et al., 2012). The disease burden is associated with a progressive limitation of functioning in daily living, mental health and quality of life (Barin et al., 2018). The prognosis and presentation of MS depends on age, the type of MS and characterised number of exacerbations and relapses, the nature of symptoms and interval time between onset and relapse (Hammond et al., 2000).

Physical activity, especially walking disability and balance disorders, is the most frequently impaired bodily function of persons with MS (pwMS) (Flegel, Knox, & Nickel, 2012). This increases the risk of falling (Catteneo et al., 2002) and reduces the quality of life (Barin et al., 2018). Walking consists of several components, including speed, cadence, walking pattern and endurance. Rehabilitation of walking endurance increased the maximal walking distance by 650 +/- 474m, but had no improvement on fatigue, depression and quality of life in pwMS complaining motor fatigue (Dettmers, Sulzmann, Ruchay-Plössl, Gütler, & Vieten, 2009). Over a six-month program, brisk walking showed a more significant improvement of walking endurance rehabilitation in physically deconditioned older women (Blain et al., 2017). Research into the effectiveness of brisk walking on walking endurance is still lacking in the MS population.

Mobile applications (apps) used in health care are an easily accessible way that possibly can create and motivate pwMS to improve health behaviour (Lavorgna et al., 2018). Physical functioning by means of mobile health (mHealth) can improve the personalized management of recovery to increase physical activity (Van Geel et al., (2020). Further research is needed on the effectiveness of technology-based rehabilitation to show an improvement on physical activity, especially on walking, in distance physical rehabilitation compared to treatment interventions in pwMS (Rintala et al., 2017).

Van Geel et al. (2020) investigated the WalkWithMe app and showed some non-clinically meaningful improvements in physical activity, cognition and lower and upper limb strength. The results of (Van Geel et al., 2020) should be interpreted with caution due to an unknown cause for the improvement of physical activity. It is not clear whether the intervention or the extra attention for physical activity by means of mHealth caused the improvement. This study protocol will use the WalkWithMe app executed in a randomized clinical trial (RCT) about physical rehabilitation that will be carried out during the second master's thesis year.

The objective is to examine whether the WalkWithMe app can provide improvement of person-specific rehabilitation in daily life of ambulatory pwMS with walking disability in the short- (ten weeks) and long- (two months after intervention) term in a randomised controlled trial setting.

2   Purpose of the research

2.1   Research question

The study will investigate the following research question: "What is the short- and long-term effectiveness of WalkWithMe app on physical activity in daily life of adult persons with multiple sclerosis with walking disability?"

This study protocol will be performed as an RCT and executed at the MS centrum 'Noorderhart' in Pelt under supervision of Prof. Dr. Bart Van Wijmeersch, Prof. Dr. Peter Feys and Prof. Ilse Lamers.

2.2   Hypotheses

The main null hypothesis of this study is that there is no difference of improvement in physical activity between the intervention group and the control group in pwMS with walking disability for pre-and postintervention.

The sub-null hypothesis is that there is no correlation between the secondary outcomes and physical activity in pwMS with walking disability in the two study groups.

These described expectations of the WalkWithMe app are partly based on the results of the uncontrolled study of Van Geel et al. (2020). They evaluated the feasibility of prolonged use of the WalkWithMe app for ten weeks and tested the impact on physical activity, quality of life, fatigue and cognition. The population was more heterogeneous because the Expanded Disability Status Scale (EDSS) score was not described.

3   Method

3.1   Research design

The study will be a two-armed, single-blinded RCT of 10 weeks with a follow-up period of two months. Data collection will begin November 2021 through April 2022. The intervention group will get conventional therapy whereby adding the mHealth tool 'WalkWithMe app' which sends notifications as a reminder to increase walking in daily life. The control group will get conventional therapy whereby adding a paper of self-guided instructions with tips to increase walking in everyday life. Both conventional therapies will be executed at the MS center 'Noorderhart' in Pelt by professional physiotherapists.

At the screening visit, the participants will be informed with general information about the study. When it is determined which participants are allowed to participate based on the selection criteria, an administrator not involved in the trial will receive a list of the participants and randomly assign the ambulatory participants to one of the two study groups. To avoid selection bias, the external administrator will use a computerized randomisation stratification approach with a randomisation scheme in blocks of four. The allocation list is only accessible to the administrator and research coordinator. At the baseline assessment, the research coordinator will inform the participants independently to which study group they belong. Both study groups will receive detailed information (study protocol, risks, benefits) on reality about the intervention they belong to organized by the research staff.

The outcome measure assessors will be blinded to group allocation and randomisation list. Unblinding of these researchers is inadmissible. The participants and two physiotherapists involved in the trial cannot be blinded to the intervention groups. Two blinded researchers will perform all assessments (T0 – T3) of all participants. The research coordinator will check the accuracy of the outcome measures and record all outcome data in a spreadsheet on a personal password-protected computer. Once randomisation is complete, exchanging between groups is not permissible. The participants can only interrupt the intervention group in case of an unforeseen medical condition.

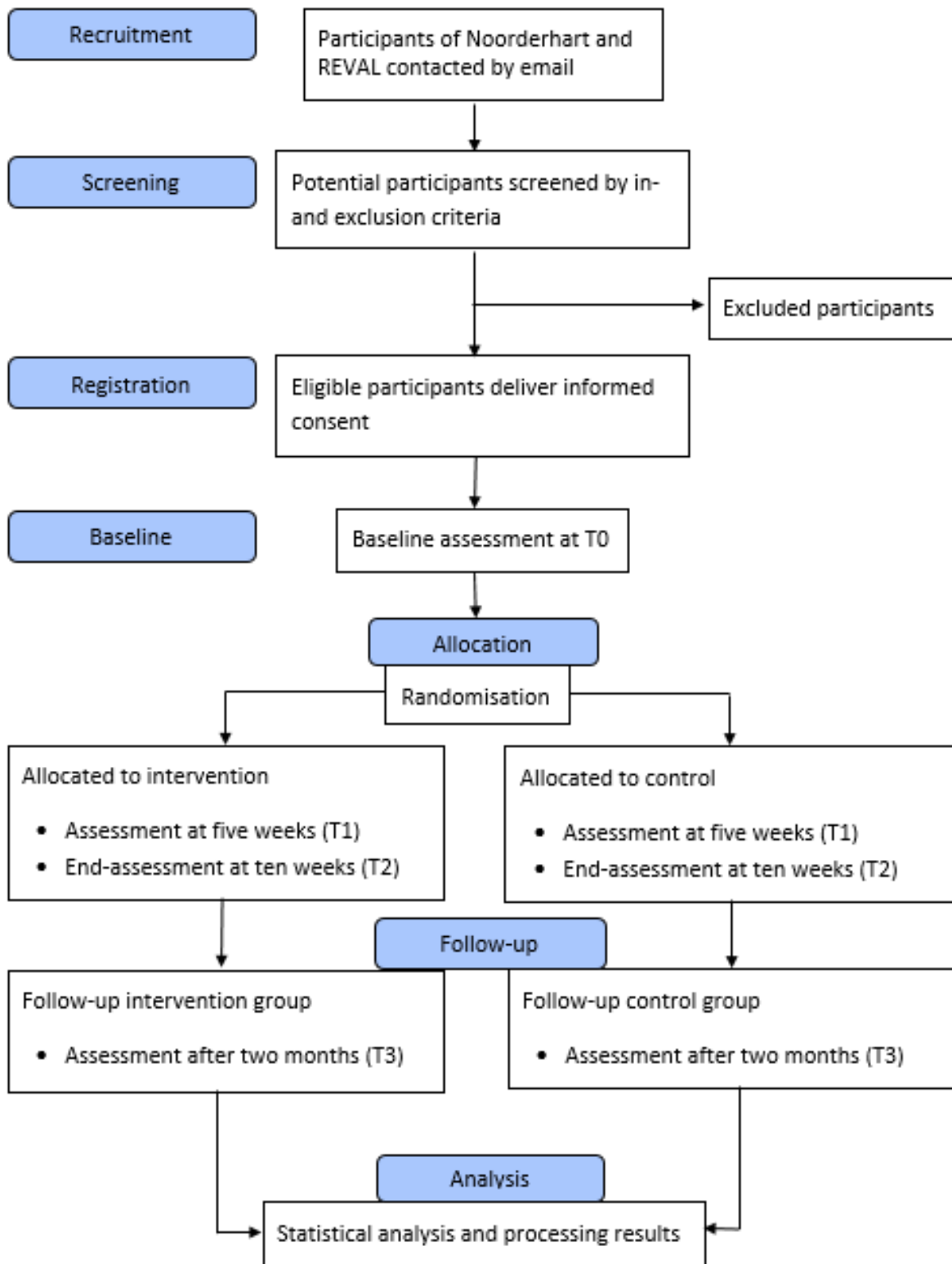Figure 1 showed a flow diagram, based on the Consort template, of the study protocol.

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Figure 1. Flow diagram of study protocol

3.2 Participants

3.2.1 Inclusion criteria

Persons with a diagnosis of MS by McDonald criteria (Polman et al., 2011) will be included if they meet the following inclusion criteria: (1) age 18-65 years, (2) Dutch fluency, (3) in the possession of a smartphone and (4) able to use a smartphone application, (5) walking disability defined by a level of EDSS (Kurtzke, 1983) ranging from four to five point five. The included participants will have the ability to walk for at least 100m without walking assistance or rest. This will obtain resembling groups regarding the baseline physical capacity (Meyer-Moock et al., 2014).

Upon recruitment and written consent, the potential participants will undergo a baseline physical and cognitive evaluation during a first visit before participating the study. These inclusion criteria will be (6) an evaluation for walking ability defined by the Timed Up and Go (TUG) (Christopher et al., 2019) score < 20 seconds and (7) a cognitive assessment identified by the Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005) score ≥ 26/30.

3.2.2 Exclusion criteria

The exclusion criteria are defined as: (1) a confounding factor (for example a MS exacerbation, changes in drug therapy or botulinum toxin injections) during three months preceding the start of the study, (2) neurological or medical conditions in addition to MS because this may affect the motor function that would hinder completing the study protocol, (3) muscle spasticity defined by a Modified Ashworth Scale (MAS) (Bohannon & Smith, 1987) score >3, (4) no possibility to arrange independent transport to the MS centrum 'Noorderhart' in Pelt for all appointments during the trial.

3.2.3 Recruitment

In September 2021, ambulatory individuals affected by all types of MS will be contacted by email via the MS centrum 'Noorderhart' in Pelt and REVAL of the University of Hasselt (UHasselt) with information about this trial. The interested pwMS who wish to participate in the study will verify the compliance of the selection criteria. Completing all steps of the selection process, the pwMS will agree to take part in the study. An adequate study power will be above 30 subjects per study group.

3.3 Medical ethics

The performed procedure of this study will be registered by the Medical Ethics Committee (CME) of UHasselt and the local Medical Ethics Review Committee (METC) of Noorderhart. All participants meeting the selection criteria will provide an informed written consent prior to the study procedure. The application form established by CME will be send to CME@uhasselt.be. This study will be executed by two master students, Charlotte Deschryvere (CD) and Maite Noels (MN), under supervision of Prof. Dr. Bart Van Wijmeersch, Prof. Dr. Peter Feys and Prof. Ilse Lamers.

3.4   Intervention

The treatment period will last ten weeks with three performed assessments to investigate the short-term effects. The first one will be a baseline assessment (T0) at the first day of treatment. The intermediate assessment (T1) will be executed at five weeks. At the end of the treatment period, the third assessment will be performed (T2). Afterwards, there will also be a follow-up assessment after two months to investigate the long-term effects (T3). This last assessment will be executed 18 weeks after the start of treatment.

The baseline assessment will also assess following demographic information: age (years), type of MS (Relapsing remitting MS, Primary Progressive MS or Secondary Progressive MS), disease duration (years), gender (male or female) and level of disability (level of EDSS). Participants who miss the baseline assessment (T0) or the end-assessment at 10 weeks (T2) or more than three training sessions will drop out from the study. The reason of absence will be requested by phone. If participants will miss the intermediate-assessment (T1) and/or the follow-up assessment (T3), this will be described and calculated in the statistical analysis.

3.4.1 WalkWithMe group

This intervention group will receive group-based conventional therapy of one-hour sessions over ten weeks. Each group will exist of five participants in a two sessions/week pattern. The conventional therapy will consist of walking therapy combined with functional strength and coordination exercises guided by professional physiotherapists in the MS centrum 'Noorderhart'. The physiotherapist will adjust the intensity of the treatment to the capabilities and goals of the participant. Taking a rest will be based on a BORG (Shariat et al., 2018) score higher than 7/10. The structure of each session will start with a warming-up of ten minutes by functional exercises. The duration of the following walking treatment will be 25 minutes of alternating upper and lower limb strength exercises. The cooling-down will be ten minutes by stretching and relaxing exercises.

The physiotherapist will establish realistic baseline possibilities together with the participant for treatment sessions and set them in the app to personalize the training scheme. The target goals will be established following the exercise guideline (Kim et al., 2019) for adult pwMS recommending two or three days per week aerobic training (ten to 45 minutes of moderate intensity) of brisk walking alternating with usual speed and two or three days per week functional resistance training (one to three sets between eight and 15 repetitions maximum) guided by videos on the app. After ten weeks, the minimum extra activity with the app will be 30 minutes without interruptions depending on the physical level of the participant.

The mHealth tool 'WalkWithMe app' will send notifications as a reminder to use the app three times a week. The minimum duration of walking at the end of the study will be determined by the physiotherapist and participant. The participants will register their goal setting in the WalkWithMe app. The app will create a schedule with an increasing duration over ten weeks. At that point, the participants can accomplish their extra physical activity sessions at any place they want. Every evening the app will track the level of fatigue by giving a score from one to ten for 18 weeks. The application will track the participants progression in walking speed, distance and number of steps during the extra activity sessions, fatigue and adherence to give feedback to the physiotherapist and the research staff.

3.4.2 Conventional therapy group

This active control group will receive the same conventional therapy as the intervention group. Additionally, the control group will get a paper of self-guided instructions with tips to increase walking and physical activity in daily life. The instructions will be that the participants go for walks of ten to 40 minutes three times a week depending on their physical capacity with a minimum of interruptions. Strength exercises will also be added. They are asked to record their extra physical activity and level of fatigue by giving a score from one to ten for 18 weeks in a diary.

3.5 Outcome measures

3.5.1 Baseline outcome measures

Participants will perform a cognitive and physical assessment to see if they can participate in this study. The included walking ability will be defined by the TUG (Christopher et al., 2019) score < 20 seconds. The TUG test is a continuous measurement of gait speed, balance, coordination and lower-limb strength. The participant's task will involve standing up from a chair, walking three meters, turning 360° around his/her own axis, walking back and sitting down. Time will be recorded in seconds with a stopwatch. The best of three trials will be used for the analysis. This test is considered a reliable and valid clinical gait performance measure in MS (Bennett, Bromley, Fisher, Tomita, & Niewczyk, 2017).

The cognitive assessment will be identified by a MoCA score ≥ 26/30. The multidimensional structure of the MoCA assesses a wide range of cognitive functions, such as short-term memory, executive functions, visuospatial abilities, language, attention, concentration, working memory, temporal and spatial orientation (Nasreddine et al., 2005). This questionnaire has an ordinal ranging score from null to 30. The results of Freitas et al. (2016) showed that the MoCA is a valid screening tool for identifying mild cognitive impairment (MCI) in MS. The power of MoCA is the high sensitivity and specificity for detecting MCI in patients with a normal score on the Mini-Mental State Examination (MMSE) (Nasreddine et al., 2005).

3.5.2 Primary outcome measures

Physical activity is the primary outcome measure to answer the research question. This will be measured by the International Physical Activity Questionnaire (IPAQ) (Hagströmer, Oja, & Sjöström, 2006). This questionnaire measures four domains of physical activity: work-related, transportation, housework/gardening and leisure-time activity. There is an ordinal scoring at three levels: low, moderate and high category based on the IPAQ scoring protocol guidelines (IPAQ scoring protocol). Hagströmer et al. (2006) showed an acceptable validity in healthy adults.

3.5.3 Secondary outcome measures

Walking endurance is a secondary outcome measured by the Six-Minute Walking Test (6MWT) (Langeskov-Christensen et al., 2017). This test measures the walking distance traveled in six minutes in function of continuous results. This long walking test will show the strongest correlation with EDSS score (Langeskov-Christensen et al., 2017). It is also considered a reliable and valid clinical gait performance measure in MS (Bennett et al., 2017).

The 21-item Modified Fatigue Impact Scale (MFIS) (Kos et al., 2003) is an ordinal questionnaire that measures the perceived impact of fatigue on physical, cognitive and psychosocial functioning. The participant is asked to read 21 problems and indicate how often he suffered from fatigue in the past four weeks. Each item will rate the level of presence of fatigue from one to four. Learmonth et al. (2013) proved MFIS had an acceptable reliability during six months and is an important outcome in clinical research of rehabilitation for managing fatigue.

The 36-item Short-Form Health Survey (SF-36) will be performed to assess health-related quality of life (Hobart et al., 2001). This is an ordinal self-assessment instrument containing eight subscales for physical functioning, physical role limitations, mental health, general health, vitality, social function, emotional role limitations and pain. The score range is from null to 100 and a higher score corresponds to a better state of health. The several subjects of the subscales can confound the results of the primary outcomes. So, it will be crucial taking these into account. The SF-36 was tested in many clinical studies, which showed that SF-36 gave a more differentiated picture of the patients' symptoms of MS and was a valuable complement to the EDSS (Isaksson, 2005).

3.5.4 Confounders

It is expected that this study group will need more intrinsic motivation to achieve the instructed goals, because they do not receive automatic reminders via smartphone. The diary is a subjective approach and the WalkWithMe app is an objective approach. Therefore, if there is a large difference in physical activity between groups, adherence can be looked at.

3.6   Data-analysis

The software for the statistical analysis will be JMP PRO 15.2. The average, standard deviation and median of all measures will be described. The p-value will be considered statistically significant when <0,05 in all statistics. The statistical parameters were set at a power rate of 80% with 0,05 type I/II error rate.
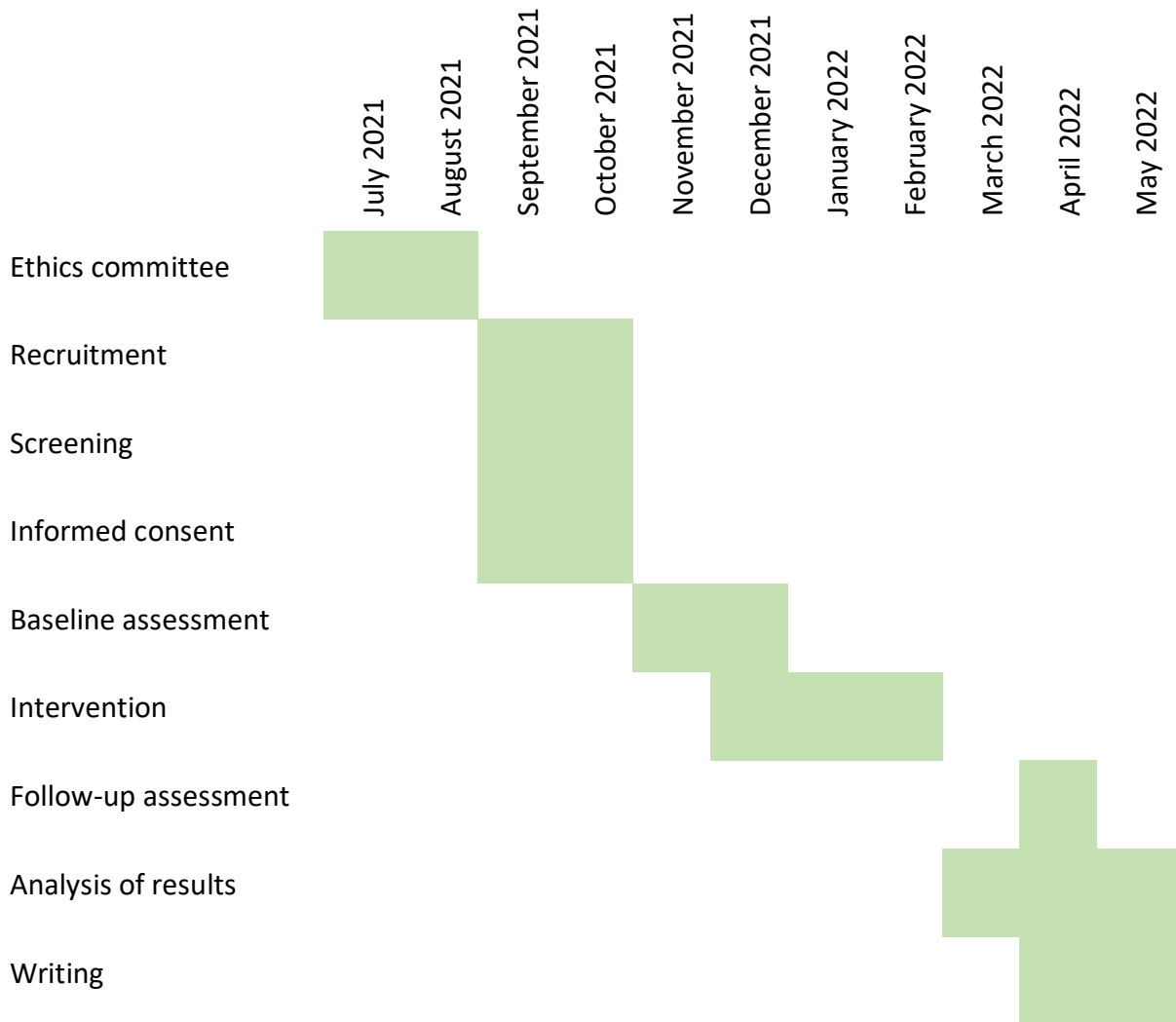
After collecting the data of the assessments, normal distribution will be checked using the Shapiro-Wilk W Test, equal variance will be checked with the Brown-Forsythe test and independence will comply with the conditions. To test the main hypothesis, the dependent variable physical activity will be calculated with a mixed model. The independent covariate of this statistical analysis will be the group (intervention and control group) and the pre- and postintervention measures. Post hoc test with Bonferroni correction are applied when appropriate.

The sub-null hypothesis will test the correlation between fatigue, walking endurance and quality of life as covariates and physical activity as dependent variable in the intervention group and control group. After collecting data, the linearity and constant variance will be checked using a Residuals Plot and normality will be checked using the Shapiro-Wilk W Test. Independence will still comply. This hypothesis will be tested using a general linear model.

To know if there is a significant difference between pre-and postintervention measures of the secondary outcome measures, a mixed model will be used. The same conditions as described for the main hypothesis must be met.

4   Time planning

This study protocol will run from July 2021 until May 2022.

	July 2021	August 2021	September 2021	October 2021	November 2021	December 2021	January 2022	February 2022	March 2022	April 2022	May 2022
Ethics committee	■	■									
Recruitment			■	■							
Screening			■	■							
Informed consent			■	■							
Baseline assessment					■	■					
Intervention						■	■	■			
Follow-up assessment									■	■	
Analysis of results									■	■	
Writing										■	■

5   List of abbreviations

6MWT: Six-Minute Walking Test

Apps: applications

CD: Charlotte Deschryvere

CME: Medical Ethics Committee

EDSS: Expanded Disability Status Scale

IPAQ: International Physical Activity Questionnaire

MAS: Modified Ashworth Scale

MCI: mild cognitive impairment

METC: Medical Ethics Review Committee

MFIS: Modified Fatigue Impact Scale

MHealth: mobile health

MMSE: Mini-Mental State Examination

MN: Maite Noels

MoCA: Montreal Cognitive Assessment

MS: Multiple sclerosis

PwMS: persons with MS

RCT: randomized clinical trial

SF-36: 36-item Short-Form Health Survey

TUG: Timed Up and Go

UHasselt: university of Hasselt

6   Reference list

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7 Annexes study protocol

Appendix 1: Contract of scientific internship part 1

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

CONTRACT WETENSCHAPPELIJKE STAGE DEEL 1

Datum: 6/11/2020

Student(e) 1: Maite Noels
Student(e) 2: Charlotte Deschryvere
Promotor: Prof. Bart Van Wijmeersch
Copromotor: Prof. Peter Feys

Situering masterproef:
☐ Vormt onderdeel van lopend onderzoeksproject, nl. ....
☐ Vormt onderdeel van opstartend onderzoeksproject, nl. ....
☒ Individuele studie
☐ Andere, nl. ....

Nederlandstalige werktitel masterproef:
Smartphone gebaseerd monitoren van het functioneren van personen met MS.

Engelstalige werktitel masterproef (indien van toepassing)
Smartphone based monitoring of functioning in persons with MS.

Voorlopige onderzoeksvraag literatuurstudie (indien gekend)
/

Formatkeuze van format MP1
☒ Centrale format (conform met masterproefrichtlijnen)
☐ Alternatieve format (zie richtlijnen alternatieve format), nl.
....
....
....
....
....
....

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

Uitsluitend van toepassing indien CENTRAL FORMATKEUZE

	Doelstelling	Akkoord	Niet akkoord	NVT
1.	De student(e) formuleert (in samenspraak met de promotor) een duidelijke vraag in functie van de literatuurstudie. Duid NVT aan indien de vraagstelling voor de literatuurstudie volledig door de promotor wordt aangereikt en formuleer een doelstelling voor de student(e):	☒	☐	☐
2.	De student(e) voert een literatuurstudie uit conform de richtlijnen MP deel 1.	☒	☐	
3.	De student(e) schrijft de literatuurstudie uit in academische taal conform met de richtlijnen MP deel 1.	☒	☐	
4.	De student(e) formuleert, op grond van de gerealiseerde literatuurstudie een onderzoeksvraag voor het eigenlijke wetenschappelijke onderzoek (MP 2). Duid NVT aan indien de student(e) deelneemt aan een lopend onderzoeksproject en de onderzoeksvraag al geformuleerd is en formuleer een doelstelling voor de student(e):	☒	☐	☐
5.	De student(e) kiest een onderzoeksdesign en maakt een kritische keuze van de te hanteren methodologie en materialen. Duid NVT aan indien de student(e) gebruik maakt van een uitgewerkt onderzoeksdesign (lopend onderzoeksproject) en formuleer een doelstelling voor de student(e)	☒	☐	☐
6.	De student(e) schrijft de methodologiesectie van zijn/haar onderzoek uit conform de richtlijnen MP deel 1. Duid NVT aan indien de student(e) gebruik maakt van een uitgewerkt onderzoeksprotocol (lopend onderzoeksproject) en formuleer een doelstelling voor de student(e)	☒	☐	☐
7.	De student(e) schrijft het onderzoeksprotocol uit in academische taal conform met de richtlijnen MP1.	☒	☐	
8.	De student(e) voert reeds in deze fase (een deel van) de data acquisitie uit. Duid NVT aan indien de data-acquisitie voltooid wordt/werd zonder inbreng van de student(e) en formuleer een doelstelling voor de student(e)...	☐	☒	☐
9.	De student(e) voert reeds in deze fase (een deel van) de data verwerking uit. Duid NVT aan indien de dataverwerking voltooid wordt/werd zonder inbreng van de student(e) en formuleer een doelstelling voor de student(e)...	☐	☒	☐
10.	Bijkomende afspraken: ✓ ✓	☐	☐	☒

Datum & handtekening student(e)

6/11/2020 *[handtekening]*

[handtekening]

Datum & handtekening promotor

Peter Frey[handtekening]   08112020

Maak een kopie van het ondertekende contract voor de student(e), de promotor en het studentensecretariaat.

De kopie voor het studentesecretariaat wordt ter attentie van mevrouw Vicky Vanhille (gebouw D) ingediend.

Appendix 2: Declaration on honour

Charlotte Deschryvere

- 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. Bart Van Wijmeersch en prof. 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: Charlotte Deschryvere

Adres: Lindeveldweg 1,1750 Lennik

Geboortedatum en –plaats : 09/04/1998 te Asse

Datum: 06/11/2020

Handtekening:

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▶▶ UHASSELT

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 prof. Bart Van Wijmeersch en prof. Peter Feys en kadert binnen het opleidingsonderdeel wetenschappelijke stage/masterproef deel 1. 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. Bart Van Wijmeersch en prof. 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: Maite Noels

Adres: Stotert 43, 2491 Olmen

Geboortedatum en –plaats : 21/04/1998 te Mol

Datum:06/11/2020

Handtekening:

Appendix 3: Progress form scientific internship part 1

VOORTGANGSFORMULIER WETENSCHAPPELIJKE STAGE DEEL 1

DATUM	INHOUD OVERLEG	HANDTEKENINGEN
woe 04/11/2020 18u30-19u15	Kennismakingsafspraak: - bespreking onderzoekstopic (o.a. eerder geschreven wetenschappelijke artikels) - het opstellen van onderzoeksstrategie bespreken	Promotor: Prof. Dr. Bart Van Wijmeersch (niet aanwezig) Copromotor/begeleider: prof. Dr. Peter Feys Student(e): Maite Noels Student(e): Charlotte Deschryvere
di 17/11/2020 19u - 20u	- Voorleggen van een globale onderzoeksstrategie + bespreken - Specifiëren van onderzoeksstrategie - Besluit gemaakt om ons toe te spitsen op assessment rond functioneren bij MS patiënten	Promotor: prof. Bart Van Wijmeersch (niet aanwezig) Copromotor/begeleider: Prof. Dr. Peter Feys Student(e): Maite Noels Student(e): Charlotte Deschryvere

woe 25/11/2020 18u-19u	- voorleggen gespecificeerde onderzoeksstrategie
	  - besluit gemaakt om toch meer globaal te zoeken
	  - volgende keer voorstellen criteria
		Promotor: Prof. Dr. Bart Van Wijmeersch (niet aanwezig)
		Copromotor/begeleider: Prof. Dr. Peter Feys, Msc. Aki Rintala
		Student(e): Maite Noels
		Student(e): Charlotte Deschryvere

ma 07/12/2020 18u-19u	- voorleggen gespecificeerde zoekstrategie + artikels - bespreken criteria - overlopen wat er tegen de volgende afspraak moet gebeuren: criteria, zoekstrategie + artikels, checklist	Promotor: Prof. Dr. Bart Van Wijmeersch (niet aanwezig) Copromotor/begeleider: Prof. Dr. Peter Feys, Msc. Aki Rintala Student(e): Maite Noels Student(e): Charlotte Deschryvere
woe 24/02/2021 18u30-19u15	- voorleggen definitieve zoekstrategie + selectiecriteria - voorleggen gevonden artikels adhv samenvatting - bespreken of interventie bij de zoekstrategie wordt toegevoegd - bespreken onderzoeksvraag	Promotor: prof. Bart Van Wijmeersch (niet aanwezig) Copromotor/begeleider: Prof. Dr. Peter Feys, Msc. Aki Rintala Student(e): Maite Noels Student(e): Charlotte Deschryvere
woe 28/04/2021 15u-16u	- Bespreken geïncludeerde artikels - Verbeteren eerste versie inleiding en methode - Bespreken van onderzoeksvraag - Checklist kwaliteitsbeoordeling voorleggen ter goedkeuring - Verder verloop bespreken	Promotor: Prof. Dr. Bart Van Wijmeersch (niet aanwezig) Copromotor/begeleider: Prof. Dr. Peter Feys, Mrs. Marianne Roesner en Mr. Bruno Bonnechere Student(e): Maite Noels Student(e): Charlotte Deschryvere

Masterproefcoördinatie Revalidatiewetenschappen en Kinesitherapie   Prof. R. Meesen Agoralaan Gebouw A Room 0.05 Campus Diepenbeek raf.meesen@uhasselt.be

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do 20/05/2021 18u30-19u30	- Feedback SR - Brainstorm protocol	Promotor: Prof. Dr. Bart Van Wijmeersch (niet aanwezig) Copromotor/begeleider: Prof. Dr. Peter Feys, Msc. Aki Rintala, Mrs. Marianne Roesner en Mr. Bruno Bonnechere Student(e): Maite Noels Student(e): Charlotte Deschryvere
do 03/06/2021 17u30-18u30	- Feedback SR - Feedback protocol - Goedkeuring voor verdediging vragen	Promotor: Prof. Dr. Bart Van Wijmeersch (niet aanwezig) Copromotor/begeleider: Prof. Dr. Peter Feys Student(e): Maite Noels Student(e): Charlotte Deschryvere
	Niet-bindend advies: De promotor verleent hierbij het advies om de masterproef WEL te verdedigen.	Promotor: Prof. Dr. Bart Van Wijmeersch Copromotor/begeleider: Prof. Dr. Peter Feys, Msc. Aki Rintala, Mrs. Marianne Roesner en Mr. Bruno Bonnechere Student(e): Maite Noels Student(e): Charlotte Deschryvere

Masterproefcoördinatie Revalidatiewetenschappen en Kinesitherapie   Prof. R. Meesen Agoralaan Gebouw A Room 0.05 Campus Diepenbeek raf.meesen@uhasselt.be

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Appendix 4: Registration from jury Master's thesis

Charlotte Deschryvere

UHASSELT
KNOWLEDGE IN ACTION

Inschrijvingsformulier verdediging masterproef academiejaar 2020-2021,
Registration form jury Master's thesis academic year 2020-2021,

GEGEVENS STUDENT - *INFORMATION STUDENT*

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

Stamnummer + naam: **1745659 Deschryvere Charlotte**
Student number + name

Opleiding/*Programme*: **1 ma revalid. wet. & kine**

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*: CONTENT AND EFFECTIVENESS OF MHEALTH TOOLS FOR SELF-ASSESSMENT AND REHABILITATION INTERVENTION ON FUNCTIONING ACCORDING TO ICF IN ADULT PERSONS WITH MULTIPLE SCLEROSIS: A SYSTEMATIC REVIEW

● behouden - *keep*

O 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)*: MAITE NOELS

● behouden - *keep*

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*

99

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)

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

05/06/2021

Peter Feys

05/06/2021

07/06/2021

Maite Noels

<table>
<tr><td>Inschrijvingsformulier verdediging masterproef academiejaar 2020-2021,
Registration form jury Master's thesis academic year 2020-2021,</td></tr>
</table>

GEGEVENS STUDENT - *INFORMATION STUDENT*

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

Stamnummer + naam: **1747598 Noels Maite**
Student number + name

Opleiding/*Programme*: **1 ma revalid. wet. & kine**

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:* CONTENT AND EFFECTIVENESS OF MHEALTH TOOLS FOR SELF-ASSESSMENT AND REHABILITATION INTERVENTION ON FUNCTIONING ACCORDING TO ICF IN ADULT PERSONS WITH MULTIPLE SCLEROSIS: A SYSTEMATIC REVIEW

<table>
<tr><td>● behouden - keep</td></tr>
</table>

<table>
<tr><td>O wijzigen - change to:</td></tr>
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UHvoorlev5   1/06/2021

101

/:

| 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)*: CHARLOTTE DESCHRYVERE

| ● behouden - *keep* |
| 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)

05/06/2021

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

Peter Feys

05/06/2021

07/06/2021

Appendix 5: Advice of co-promotor

Peter FEYS
aan Bart, Aki, Marianne, mij, Maite, Bruno ▾

X͞A Taal herkennen ▾ 〉 Nederlands ▾ Bericht vertalen

Uitschakelen voor: Engels ✕

Dear Maite and Charlotte
cc Bart
cc Aki, Bruno, Marianne

Thank you for your email. You may add Aki Rintala as 'begeleider' for your master thesis given the feedback given during the full year.
He may also sign the 'voortgang formulier' attached. It is not needed that Bruno and Marianne sign this.
I have no memory of Ilse Lamers joining us.

I have signed the permission to submit the master thesis.
Bart, you can sign these as well.

Good luck with the finalization of the thesis
Peter Feys

Appendix 6: Self-evaluation report

LITERATUURSTUDIE	Gestelde deadline	Behaald op	Reflectie
De belangrijkste concepten en conceptuele kaders van het onderzoeksdomein uitdiepen en verwerken	03/11/2020	03/11/2020	Goed
De belangrijkste informatie opzoeken als inleiding op de onderzoeksvraag van de literatuurstudie	03/11/2020	03/11/2020	Goed
De opzoekbare onderzoeksvraag identificeren en helder formuleren in functie van de literatuurstudie	24/02/2021	24/02/2021	Goed
De zoekstrategie op systematische wijze uitvoeren in relevante databanken	24/02/2021	24/02/2021	Goed
De kwaliteitsbeoordeling van de artikelen diepgaand uitvoeren	20/05/2021	20/05/2021	Goed
De data-extractie grondig uitvoeren	20/05/2021	20/05/2021	Goed
De bevindingen integreren tot een synthese	20/05/2021	20/05/2021	Goed

ONDERZOEKSPROTOCOL	Gestelde deadline	Behaald op	Reflectie
De onderzoeksvraag in functie van het onderzoeksprotocol identificeren	20/05/2021	20/05/2021	Goed
Het onderzoeksdesign bepalen en/of kritisch reflecteren over bestaande onderzoeksdesign	20/05/2021	20/05/2021	Goed
De methodesectie (participanten, interventie, uitkomstmaten, data-analyse) uitwerken	03/06/2021	03/06/2021	Goed

ACADEMISCHE SCHRIJVEN	Gestelde deadline	Behaald op	Reflectie
Het abstract to the point schrijven	20/05/2021	20/05/2021	Goed
De inleiding van de literatuurstudie logisch opbouwen	20/05/2021	20/05/2021	Goed
De methodesectie van de literatuurstudie transparant weergegeven	20/05/2021	20/05/2021	Goed
De resultatensectie afstemmen op de onderzoeksvragen	20/05/2021	20/05/2021	Goed
In de discussiesectie de bekomen resultaten in een wetenschappelijke tekst integreren en synthetiseren	20/05/2021	20/05/2021	Goed
Het onderzoeksprotocol deskundig technisch uitschrijven	03/06/2021	03/06/2021	Goed
Referenties correct en volledig weergeven	03/06/2021	03/06/2021	Goed

ZELFSTUREND EN WETENSCHAPPELIJK DENKEN EN HANDELEN	Aanvangsfase	Tussentijdse fase	Eindfase
Een realistische planning opmaken, deadlines stellen en opvolgen	Goed	Goed	Goed
Initiatief en verantwoordelijkheid opnemen ten aanzien van de realisatie van de wetenschappelijke stage	Goed	Goed	Goed
Kritisch wetenschappelijk denken	Goed	Goed	Goed
De contacten met de promotor voorbereiden en efficiënt benutten	Goed	Goed	Goed
De richtlijnen van de wetenschappelijke stage autonoom opvolgen en toepassen	Goed	Goed	Goed
De communicatie met de medestudent helder en transparant voeren	Goed	Goed	Goed
De communicatie met de promotor/copromotor helder en transparant voeren	Goed	Goed	Goed