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SUPPORTING ADHERENCE TO PHYSICAL ACTIVITY IN PEOPLE WITH MULTIPLE SCLEROSIS

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SUPPORTING ADHERENCE TO PHYSICAL ACTIVITY IN PEOPLE WITH MULTIPLE SCLEROSIS

by

Rachel Louise Dennett

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DOCTOR OF PHILOSOPHY

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Acknowledgements

Where do I start when it comes to acknowledging the positive influence that others have had on my research journey so far? I have many people to thank for their role in presenting this research portfolio.

Firstly, I am grateful to Professor Jenny Freeman for her example, encouragement and guidance throughout the last five years. Her wealth of research and clinical experience has been invaluable as has her constant support throughout my time at the University of Plymouth. I would also like to thank Dr Hilary Gunn my second supervisor, for her guidance during the compilation of this research portfolio, for the many 'in-car' discussions and her enthusiasm and support establishing the exercise groups at the South West MS Therapy Centre.

I would like to thank each of my co-authors for their collaboration and contributions. I am grateful to have had the opportunity to have been part of such experienced and encouraging teams. I am additionally grateful to the people affected by MS that I have worked with over recent years who have been central to this work, offering unique perspectives and a willingness to contribute. Also, my thanks go to those in the South West MS Therapy Centre exercise groups who have allowed me to discuss, implement and reflect on our findings in an informal setting.

I am very grateful to my friends and family for all the support I have received over what I am sure has felt more like 10 years. For the houses I have borrowed to get writing completed, for the coffees shared and for showing interest in what I have been up to even when you have probably been wondering why it has taken me so long! Paul, thank you for your constant belief in me being able to complete this; for your wisdom, support and ability to listen to and encourage my pondering!

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Thank you everyone

Author's Declaration

At no time during the registration for the degree of Doctor of Philosophy has the author been registered for any other University award without prior agreement of the Doctoral College Quality Sub-Committee.

Work submitted for this research degree at the University of Plymouth has not formed part of any other degree either at the University of Plymouth or at another establishment.

The work submitted has been undertaken from 2016-2021. Throughout this time the author has been working as a researcher in the School of Health Professions at the University of Plymouth. In addition, the author has continued to work clinically, one day a week, as a physiotherapist at the South West MS Therapy Centre.

Each of the outputs included in this portfolio have been co-authored. This author's role in each is described in section 1.1 and the details of contributions are summarised in chapter 3.

Word count of Integrative Summary (Chapter 1): 15537

Signed: Rachel Dennett

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Abstract

Supporting Adherence to Physical Activity in People with Multiple Sclerosis

Rachel Louise Dennett

Background

The benefits of exercise and physical activity for people with multiple sclerosis are well recognised, as are the challenges faced by many in adhering to these activities over the long term. Adherence is considered by some to be the single most important modifiable factor affecting outcome. With years lived with disability increasing and healthcare resources limited, the need to develop and implement effective and acceptable interventions and support people with adherence to physical activity is pressing.

Aim

This integrative summary presents work from three related areas regarding exercise and physical activity in people with multiple sclerosis. The body of work represents a systematic and rigorous approach to the topic and comprises outputs from three streams of work:

1) Web-based intervention studies; a systematic review and a qualitative study exploring the participant’s experience.
2) Evaluation of a home-based standing frame programme; a randomised controlled trial evaluating the clinical and cost-effectiveness, a qualitative study exploring experiences of using the standing frame, and production of a series of four short films to present these experiences using both images and the voices of the people involved.

3) A systematic review of adherence to exercise interventions in people with multiple sclerosis that presents recommendations regarding trial design in this area.

The Behaviour Change Wheel is used as a “reflection framework” to facilitate integration of my current work and consider areas for future study. The reflection process has helped highlight important ‘threads’ that bring my work together and has informed the development of two concepts that provide a fresh perspective in this field.

Conclusion

This summary draws together work from a variety of studies encompassing original research and systematic reviews, which demonstrate the creation and interpretation of new knowledge in the field of physical activity in people with multiple sclerosis.

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Paper 2 83

Dennett R, Coulter E, Paul L, Freeman J. A qualitative exploration of the participants' experience of a web-based physiotherapy program for people with multiple sclerosis: Does it impact on the ability to increase and sustain engagement in physical activity? Disability and Rehabilitation. 2020a:42(21) 3007-3014 https://doi.org/10.1080/09638288.2019.1582717

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Freeman J, Hendrie W, Jarrett L, Hawton A, Barton A, Dennett R, Jones B, Zajicek J, Creanor S. Assessment of a home-based standing frame programme in people with progressive multiple sclerosis (SUMS): a pragmatic, multi-centre, randomised, controlled trial and cost-effectiveness analysis. The Lancet Neurology. 2019:18(8):736-747.

https://doi.org/10.1016/S1474-4422(19)30190-5

Paper 4 105

Dennett R, Hendrie W, Jarrett L, Creanor S, Barton A, Hawton, A, Freeman J. "I'm in a very good frame of mind": A qualitative exploration of the experience of standing frame use in people with progressive multiple sclerosis. British Medical Journal Open 2020b:10:e037680 http://doi.org/10.1136/bmjopen-2020-037680

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Dennett R, Hendrie W, Jarrett L, Creanor S, Barton A, Hawton A, Freeman J. “I’m in a very good frame of mind”: A qualitative exploration of the experience of standing frame use in people with progressive multiple sclerosis. Four Short Films. 2019 on study website: https://www.plymouth.ac.uk/research/sums

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Dennett R, Madsen LT, Connolly L, Hosking J, Dalgas U, Freeman J. Adherence and drop-out in randomized controlled trials of exercise interventions in people with multiple sclerosis: A systematic review and meta-analyses. Multiple Sclerosis and Related Disorders. 2020c: 43(8) 1-16 https://doi.org/10.1016/j.msard.2020.102169

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Integrative Summary

Section 1: Introduction to the topic

Setting the scene

As a clinical physiotherapist with twenty years' experience of working with people with long-term neurological conditions, I am acutely aware of the importance of supporting individuals to become and remain as physically active as possible throughout their lives. All too often, people come to see a physiotherapist, set and achieve goals in a range of aspects of life and then, despite best efforts end up referred back six months later once the initial improvements have ebbed away. I was part of a "good" clinical team… neurology specialists… informed, knowledgeable, motivated. We considered ourselves listeners, example setters, researchers, inspirers. But still, the frustration remained that no matter how effective interventions were at the point of delivery, benefits were not maintained if people weren't (for whatever reason) able to sustain the changes long-term. For whatever reason…?

Then came an exciting opportunity… a secondment from clinical practice into a research post at the University of Plymouth. A study hoping to address one aspect of the challenge to support people to be active. Web-based physiotherapy for people with multiple sclerosis (pwMS). Could this make a difference? I had been keen to be more involved in the world of research and here was an opportunity to step into something new for a couple of years. I was fortunate enough to be working with Professor Freeman. Jenny. An inspiring, encouraging, supportive, person-focused, well-respected researcher and clinical physiotherapist. It has been her example, guidance, provision of opportunity and belief in me that has enabled this body of work to come together.

My work has been completed over the five years I have worked at the University of Plymouth where I have been a key member of the research team on studies involving pwMS. I have played an integral role within each of the studies presented in this portfolio. I was the trial co-ordinator for the standing programme study and led the qualitative analysis, both the thematic analysis and production of the films. In addition, I led the web-based qualitative sub-study from conception and design through implementation to completion. Finally, I led both systematic reviews from conception and design through implementation to completion, including leading a team of researchers from the United Kingdom (UK) and Denmark for the adherence review. The studies have afforded me the opportunity to undertake original research that has added to knowledge regarding supporting pwMS adhere to a more physically active lifestyle. In addition, the work has enhanced our understanding of the person's experience of engaging in such interventions and has enabled me to compose a body of work that contributes new knowledge and understanding in the field.

1.1 Background

The challenge of supporting adherence to increased levels of physical activity (PA) is an international one that has required a global action plan (World Health Organisation, 2018). The issues involved are wide ranging, affecting not only the individual but other people with whom they are in contact, their communities and the wider social and political environments. It is known that levels of PA are lower in those living with a chronic health condition than the general population, highlighting the need for research in this area. One such population is pwMS (Kinnett–Hopkins et al., 2017). Multiple sclerosis (MS) is a progressive neurological condition, affecting 2.5 million people worldwide, which can result in a range of physical, cognitive and emotional symptoms. It commonly presents in early adulthood and progresses over time, frequently leading to increasing disability and a significant increase in societal economic costs (Kobelt et al., 2017, Ness et al., 2020).

The terms PA and exercise are often, but not always used interchangeably within the literature. Exercise is defined as a form of PA that is planned, structured and repetitive, and is undertaken with the objective of improving or maintaining at least one aspect of physical fitness; that is strength, flexibility or aerobic endurance (Caspersen et al., 1985). PA is defined as any bodily movement produced by skeletal muscles that requires energy expenditure (Caspersen et al., 1985). Within this summary I will use the term PA unless there is clear definition that the intervention(s) are exercise.

Additional definitions used in this work include 'short-term', defined as less than or equal to three months post intervention, and 'long-term', more than three months, in accordance with Khan et al (Khan et al., 2015).

PA, including exercise as a subset (Caspersen et al., 1985) has been demonstrated to result in a wide range of health benefits in pwMS (Dalgas et al., 2019, Edwards and Pilutti, 2017, Freeman et al., 2019, Heine et al., 2015, Jorgensen et al., 2017, Pearson et al., 2015). In addition, disease specific guidelines have been developed to aid the promotion and prescription of PA in people with different levels of disability (Kalb et al., 2020, Latimer Cheung et al., 2013). Recent work (Canning and Hicks, 2020, Coote et al., 2017, Learmonth et al., 2017) has evaluated the effectiveness of adhering to the guidelines for pwMS with mild-moderate disability (Latimer Cheung et al., 2013) where a range of benefits including a moderate increase in self-reported PA and improvements in fitness, mobility, fatigue and quality of life in those that adhered were demonstrated.

For people to benefit from the positive effects of PA throughout their lives, it is imperative that they are supported to continue long-term. The multi-dimensional construct (Heeson et al, 2015) 'adherence' is commonly used in both research and clinical practice to describe this sustained behaviour. Adherence is defined by the World Health Organisation (WHO) as the extent to which a person's behaviour corresponds with agreed recommendations from a healthcare provider (WHO, 2003, p. 3). In line with other researchers working in the field (Bollen et al., 2014, Essery et al., 2017, Frost et al., 2017), it is this definition that I have used throughout this integrative summary.

Given the low levels of reported PA in pwMS, developing an understanding of the factors associated with adherence is key to guide the development of supportive interventions. A number of reviews have explored a wide range of potential correlates of PA. Casey and colleagues conducted a systematic review and meta-analyses of modifiable psychosocial constructs associated with PA participation. Of the 26 included studies, 12 were included in meta-analyses which demonstrated significant, moderate, positive correlations between PA (both self-reported and objectively measured) and exercise self-efficacy, and self-reported PA and exercise goal setting (Casey et al., 2017). These findings are supported by several other researchers including Streber and colleagues who, additionally, report positive correlations of PA with education level and employment status and an inverse correlation with disability level, particularly walking limitations (Streber et al., 2016).

Another area of focus with respect to PA adherence has been on understanding the many barriers and facilitators that both pwMS and clinicians have reported in recent qualitative studies and surveys. Firstly, a range of disease-related factors including fluctuating symptoms and fatigue (Learmonth and Motl, 2016) are reported. Secondly, personal factors including lack of confidence (Crank et al., 2017), self-efficacy and intrinsic motivation (Fasczewski et al., 2020, Riemann-Lorenz et al., 2020b) are suggested. Finally, other barriers reported include the physical environment such as transport and accessibility of venues (Adamson et al., 2020, Barnard et al., 2020, Learmonth et al., 2015, Streber et al., 2016) and social environment, such as lack of expectation and health professional support (Adamson et al., 2020, Hale et al., 2012, Learmonth et al., 2015, Riemann-Lorenz et al., 2020a, Streber et al., 2016,). In addition, specific facilitators of PA reported include positive, constructive, social and professional support, positive outcome expectation (Christensen et al., 2015) and ability to have choice and control over PA opportunities (Hale et al., 2012). It is noted that in reality, optimum adherence is frequently impacted by more than one of these factors (WHO., 2003) and in this regard recent pilot and feasibility studies have emphasised the importance of targeting a range of factors within programme design and delivery (Baird et al., 2020, Hayes et al., 2017, Latchem-Hastings et al., 2021, Learmonth et al., 2017).

As our understanding of the benefits and correlates of PA, and the related barriers and facilitators have expanded, so has the drive to develop specific interventions to support adherence. This complex issue of adherence to PA has inspired extensive research involving pwMS (with a range of disability levels), carers and health care professionals over recent years, using a range of research methodologies (Jeong et al., 2019, McAuley et al., 2007, Riemann-Lorenz et al., 2020b).

A key area of work has been the development of behavioural interventions. Behavioural interventions, defined as interventions, based upon behavioural science theory involving specific techniques, aim to change the health behaviours of individuals, communities or whole populations (Michie et al., 2011, NICE, 2014a). The effectiveness of such interventions (used either alone or in combination with exercise or PA) has been investigated on self-reported and objectively measured PA in pwMS in recent feasibility and pilot interventional studies (Baird et al., 2020, Coote et al., 2017, Hayes et al., 2017) and is currently being evaluated in a phase III RCT (Silveira et al., 2019) and single-arm feasibility trial (Latchem-Hastings et al., 2021). Results from the pilot work (Coote et al., 2017, Hayes et al., 2017) suggest a positive effect on self-reported PA and objectively measured walking endurance (6-minute walk test), but not objectively measured PA (SenseWear Arm band). Behavioural intervention effectiveness has also been considered by authors of several systematic reviews (Coulter et al., 2020, Kim et al., 2020, Sangelaji et al., 2016). Sangelaji reports a statistically significant improvement in PA (using combined subjective and objective measures) immediately post intervention and at three-month follow-up (Sangelaji et al., 2016). Similarly, Coulter and colleagues report that 25 of their 30 included studies investigated total PA or leisure time PA with the majority (n=20) reporting significant improvements. They highlight however, that of the included studies, only six included objective measurement of PA, and of these only one reported a significant improvement in PA. Kim and colleagues (Kim et al., 2020) also report moderate effectiveness of behavioural interventions in terms of increasing PA immediately post intervention and at short-term (three month) follow-up. In addition, their moderator analysis identified a trend for larger increases in PA as determined by self-report compared to objectively measured PA, and for purely educational behavioural interventions compared to those delivered in combination with exercise, or exercise alone. This latter finding is particularly interesting given it might have been assumed that a combination of education and exercise would have afforded greater changes in PA. It is possible that if interventions had been PA focused rather than specifically exercise, there may have been enhanced improvements in PA. Further work could explore these relationships, paying close attention to whether the exercise or PA elements of combined behavioural interventions are being delivered at effective doses.

It was whilst reading about behavioural interventions that I became aware of the Behaviour Change Wheel Framework (Michie et al., 2011). Whilst initially developed to facilitate the design and evaluation of interventions in areas such as smoking cessation and weight loss, the framework has also been used to structure systematic reviews, explore challenges surrounding intervention implementation and retrospectively analyse gaps in the process of facilitating behaviour change. It has been widely used across a range of disciplines and topics regarding behaviour change, and by a variety of agencies including Public Health England (McManus et al., 2018, West et al., 2019), the National Institute for Health and Care Excellence (NICE, 2014a) and the WHO (Dodson et al., 2018). Within the field of MS research, it has been used to develop a questionnaire exploring possible determinants of adherence to PA (Riemann-Lorenz et al., 2020b), conduct a review of interventions promoting behaviour change (Plow and Finlayson, 2019) and develop an internet-based intervention to change PA behaviour (Casey et al., 2019). In addition, the framework is recognised to provide a valuable structure for reflection and analysis, enabling researchers to “retro fit” interventions to identify any components that may be missing (Michie et al., 2011). I had initially planned to use the WHO “five dimensions of adherence” (WHO, 2003) framework to contextualise my research given its focus on adherence, however, when reflecting on the extensive, contemporary use of the Behaviour Change Wheel Framework within the area I decided it was a preferable option.

1.2 Structure of this research portfolio

This research portfolio is comprised of three streams of work. The first was designed when I was employed as a research physiotherapist on a feasibility Randomised Controlled Trial (RCT) of a web-based physiotherapy intervention (WebPaMS). I wanted to know what the evidence was for such interventions increasing PA in this population and was particularly interested in the participant's experience at a depth greater than would be achieved through the study process evaluation exit interviews. These questions gave rise to the web-based stream of work; a systematic review and a qualitative study exploring the participant's experience.

A second area requiring investigation was the need for effective supported self-management options for people with progressive disease and higher levels of disability. Much of the current literature regarding PA interventions had been conducted in people with mild to moderate relapsing remitting disease. Working as the trial co-ordinator and research assessor for the Standing Up in MS (SUMS) study gave me the opportunity to be a key member of a team conducting a RCT evaluating the clinical and cost-effectiveness of a home-based standing frame programme with an embedded qualitative study to explore the participant and carer experience.

The final area that this research portfolio sought to address was regarding adherence to exercise interventions. Given it is imperative that research findings can be implemented into clinical practice, I wanted to know what is reported about adherence to and drop-out from exercise intervention trials that may guide clinicians seeking to implement evidence-based practice.

My work is presented in these streams to highlight the new knowledge that each has added to the evidence base in this field. I have then used the Behaviour Change Wheel Framework to reflect on, bring together and analyse my work, and consider areas for future research.

Although I refer to the work presented in this portfolio as ‘my’ work, it is important to acknowledge that each output is co-authored work as detailed in Chapter 3.

Section 2: Contribution of published works to knowledge

2.1 Introduction to published works

My (our) work has contributed to the knowledge surrounding supporting adherence to PA in pwMS in a number of ways. I have chosen to discuss these in terms of the three work streams which occurred sequentially. Several of the areas of new knowledge are interlinked as I will demonstrate. The outputs comprise five peer-reviewed papers and the production of four short films as detailed in table 1. They have been colour coded to highlight the work streams (blue-web-based, green- standing programme, grey-adherence) and numbered to enable the content from papers to be more easily incorporated within the following critical discussion.

Table 1: Published works by work stream

Dennett R, Gunn H and Freeman J. Effectiveness of and user experience with web-based interventions in increasing physical activity levels in people with multiple sclerosis: A systematic review. Physical Therapy. 2018:98 (8) 679-690. https://doi.org/10.1093/ptj/pzy060	Paper 1
Dennett R, Coulter E, Paul L, Freeman J. A qualitative exploration of the participants' experience of a web-based physiotherapy program for people with multiple sclerosis: Does it impact on the ability to increase and sustain engagement in physical activity? Disability and Rehabilitation. 2020a:42(21) 3007-3014 https://doi.org/10.1080/09638288.2019.1582717	Paper 2
Freeman J, Hendrie W, Jarrett L, Hawton A, Barton A, Dennett R, Jones B, Zajicek J, Creanor S. Assessment of a home-based standing frame programme in people with progressive multiple sclerosis (SUMS): A pragmatic, multi-centre, randomised, controlled trial and cost-effectiveness analysis. The Lancet Neurology. 2019:18(8) 736-747 https://doi.org/10.1016/S1474-4422(19)30190-5	Paper 3
Dennett R, Hendrie W, Jarrett L, Creanor S, Barton A, Hawton, A, Freeman J. "I'm in a very good frame of mind": A qualitative exploration of the experience of standing frame use in people with progressive multiple sclerosis. British Medical Journal Open 2020b:10:e037680 http://doi.org/10.1136/bmjopen-2020-037680	Paper 4
Dennett R, Hendrie W, Jarrett L, Creanor S, Barton A, Hawton A, Freeman J. "I'm in a very good frame of mind": A qualitative exploration of the experience of standing frame use in people with progressive multiple sclerosis. Four Short Films. 2019 on study website: https://www.plymouth.ac.uk/research/sums	Short films
Dennett R, Madsen LT, Connolly L, Hosking J, Dalgas U, Freeman J. Adherence and drop-out in randomized controlled trials of exercise interventions in people with multiple sclerosis: A systematic review and meta-analyses. Multiple Sclerosis and Related Disorders. 2020c: 43(8) 1-16 https://doi.org/10.1016/j.msard.2020.102169	Paper 5

2.2 : Web-based stream

The use of web-based interventions to increase PA is an intervention delivery model with potential to help people adhere to PA. Paper 1 reports the first systematic review of this specific model of delivery in pwMS. Although previous reviews had considered a variety of telerehabilltation interventions (including gaming and using pedometers), this was the first to focus solely on interventions delivered over the internet. Our meta-analysis of self-reported PA data demonstrated a moderate positive effect on PA in the short-term in participants with mild disability. There were, however, insufficient data to conduct an analysis of objectively measured PA at any time point or analyses of self-report at any longer-term follow-up points. An additional aim of our review had been to examine whether the use of web-based interventions enable pwMS to achieve recommended levels of PA (Latimer-Cheung 2013) whilst engaging in the intervention, and further if people were able to maintain these levels after the intervention had ceased. However, coupled with limited short-term follow-up data and an absence of long-term follow-up assessments, we also found that none of the included papers reported PA in line with recommendations, so we were unable to address this aim. Paper 1 therefore presented the headline results and highlighted the need for the research community to consider effectiveness at both short and long-term follow-up, in people with higher levels of disability, using objective measurement of PA and against disease specific PA recommendations in future work. It is encouraging that these issues are now being incorporated in recent studies as discussed below and in section 1.2. Another noteworthy finding of the review was that although nine papers were included, they only reported on (the development of) two different interventions. This was a good reminder for researchers to ensure transparency of reporting, and clinicians to not assume that multiple papers regarding web-based interventions indicate the area has been thoroughly researched.

The key findings from this study in relation to my research portfolio were that the web-based interventions had a short-term positive effect on self-reported PA in ambulant pwMS. As such, they may be a useful approach for some people wanting to become more active. These interventions might, for example, be an option to discuss with people who are pre diagnosis or recently diagnosed, and those experiencing lower levels of disability, adding a potential ‘view’ to Riemenschneider’s “window of opportunity” (Riemenschneider et al, 2018). The relevance of web-based interventions within the context of the current Coronavirus pandemic is undeniable. Given the rapidly changing landscape in the use of telerehabilitation, it will be particularly important to gain contemporaneous insights into the effectiveness of this mode of intervention delivery and its use within a hybrid model of healthcare provision.

In order to consider whether such interventions help adherence to PA we looked at the specific adherence data which was presented by six of the nine included studies. In these six papers, intervention adherence was reported in terms of the percentage of participants that logged in to the web-based programme each week (n=3), average number of weeks participants were logged in for (n=4), average number of video coaching sessions attended (n=2), percentage of participants who participated in specific components of the intervention (including coaching) (n=1) and percentage of participants who documented completion of at least 80% of their prescribed training programme (n=1). This use of a range of definitions, and the question of which specific aspects of adherence are being measured may lead to a lack of clarity surrounding measurement and reporting of adherence and are issues discussed more fully in the adherence stream section below. In these studies, although adherence was reported to be high (range 73-96%) in the short-term, half of them reported that adherence dropped to around 50% or lower by eight-twelve weeks (Dlugonski et al., 2011, Motl et al., 2011, Tallner et al., 2016). Jeong and colleagues, recognising the need to address such challenges with adherence to telerehabilitation, conducted a study to identify predictors of adherence. They reported that personalising training and providing feedback and support were particularly important for people with low levels of adherence. Further, they suggested that early identification of such people could enable their requirements to be prioritised by clinicians and potentially result in increased likelihood of life-long adherence (Jeong et al., 2019). My own clinical experience resonates with this, where it is apparent that providing personalised support at an early stage (of starting a new PA) appears crucial. Some of the work I will present in papers 3 and 4 suggests that facilitating pwMS to gain the knowledge, skills and confidence to self-manage PA was instrumental in supporting adherence. Further, I postulate that positive early PA experiences encourage longer-term adherence where people are more likely to experience physical and psychological improvements that may then act as motivators to continue, as we were able to report in papers 2 and 4. In addition, it is suggested that there may be an association between previous positive exercise experience and adherence to PA (Essery et al., 2017, Kayes et al 2011), potentially an area for further research.

The issue of personalised support resonates throughout much of my work and is one of the key threads throughout this portfolio. One option for provision of support within telerehabilitation is that of remotely delivered coaching sessions. The addition of such sessions was demonstrated to be instrumental in increasing adherence to a behavioural intervention during its development process, as reported in two of the included studies in paper 1 (Dlugonski et al., 2012, Pilutti et al., 2014). Further research is required to explore which aspects of a coaching session (e.g. mode of delivery, quality of the coaching relationship, level of support) may be key to facilitating increased adherence to better understand *how* and *why* coaching may lead to enhanced adherence. A recently published protocol suggests that these factors may be addressed through an embedded process evaluation (Latchem-Hastings et al., 2021), results of which may help both fill gaps in knowledge and direct future work. With respect to longer term impact of web-based interventions, due to the absence of long-term follow-up assessments in the included studies, it is not possible to comment on whether they can support an increase in PA in the long-term. Current research in the field, however, incorporates longer-term follow-up (Silveira et al., 2019) and may therefore start to answer this question.

Finally, an original aim of the systematic review had been to include both qualitative and quantitative data, however no qualitative studies were identified by the searches. This was acknowledged, and researchers were encouraged to consider qualitative work especially given the current exponential rise of effectiveness studies in this area.

My next piece of work, reported in paper 2, was an opportunity to address this absence of qualitative data. The study explored the participant experience of a web-based physiotherapy intervention (webbasedphysio.com) on perceived levels of PA. Analysis of this first qualitative study of web-based interventions in pwMS led to the development of three themes, all of which are related to supporting adherence to PA. The first theme was especially pertinent to the question of *how* the web-based intervention might support people to become more active. “It’s all in one place” encompassed the benefits that the accessibility, flexibility and portability of the intervention brought the individual. In addition, factors such as feeling safer and more confident to exercise at a challenging level at home, choosing when to exercise and not having to travel were also raised as important. These findings are supported by others including Christensen and colleagues in their meta-synthesis of qualitative work exploring the intention to exercise and execution of exercise in pwMS (Christensen et al., 2015).

With respect to *who* may find such an intervention helpful, the second theme “keeping an eye” pointed to those who not only value flexibility and are technology literate but to those who prefer to exercise independently and already have the confidence and skills to do so. In our study, half the participants felt the level of support provided was sufficient to help them continue to be active whilst the other half suggested that increased support would have been valued. This issue is discussed further in the standing programme section below. The lack of interaction with other people was a specific issue raised by some of those who wanted more support, with one lady suggesting “There’s nothing negative about it apart from the fact that it’s just not social is it…? It’s the [lack of] contact isn’t it, it’s the interaction I suppose [that wasn’t enough]”. The value of interaction is a factor highlighted by a team in Ireland seeking to design a web-based resource to encourage pwMS adopt increased PA (Casey et al., 2016). Participants suggested that interactive components could help develop a sense of community and provide peer support which they recognised as being important for such a resource (Casey et al., 2016). Busse and colleagues also acknowledge and address this issue in their intervention development work (Busse et al., 2021, Latchem-Hastings et al., 2021). It is possible that addition of a more interactive element to the webbasedphysio.com intervention during its on-going development may help to address the reported lack of social contact.

The final theme developed was ‘hopes and expectations’ where the importance of having open and honest conversations with people, especially those with progressive disease is discussed. This aligns with one of the consistent findings reported by Kulnik and colleagues (Kulnik et al., 2018) in their exploration of experiences of self-management support for people with progressive neurological long-term conditions, where key concerns included anxiety and fear about further deterioration. This sense of uncertainty in respect to what changes an individual might expect to experience or how their condition may change was echoed by some of our participants. Specifically, one participant noted “If I’m being brutally honest with myself, I think I’ve gone down even though I’ve been working quite hard and that has been quite hard [emotionally] I think”. Another participant added, “I thought that by doing the exercises I’d build up some stamina and I wouldn’t have noticed it [fatigue] quite so much… but it was the fatigue… that was the annoying bit if you like, you know, I had hoped that I’d go through a barrier and come out the other side. I think it’s the nature of the beast, perhaps it was my expectations that needed to be managed…” Clearly these are examples of where communication regarding expectations could have been improved.

A closely related challenge (Kulnik et al., 2018) is that of the use of terminology, particularly within the context of supporting goal setting with people who are being active alongside a background of a deteriorating (progressive) disease. In these situations, it is especially important to clarify the meanings of commonly used rehabilitation terms such as “progress” and “improvements”. For example, as clinicians and researchers we often use the term “progression” to describe an increase in the prescribed dose of PA, however it is important to ensure that a person with MS recognises (and would want to use) such a term where their understanding of progression may be more related to an increase in disability. Similarly, use of the word “improvement” requires careful thought. Here, it is important to differentiate between improvement in terms of increased PA, strength or function (for example) and improvement in confidence to self-manage, where a realistic goal may be to maintain, rather than improve PA, strength or function over a period of time. Although both situations demonstrate a positive outcome (an improvement), the expectation of how that improvement presents for an individual needs consideration and discussion. For example, it is likely that a more thorough discussion of the individual's hopes of the web-based physiotherapy intervention with careful use of terminology may have avoided the person's experience that their expectations needed to have been better managed (quote above).

The importance of effective communication within healthcare is widely recognised and has been reported specifically within the field of MS and PA (Crank et al., 2017, Davies et al., 2015, Ploughman et al., 2012). My work has demonstrated that open and honest conversations are important to facilitate provision of the 'right' type of intervention and the 'right' support. This notion that there is no "one size that fits all" resonates with my clinical experience and is supported by others acknowledging that individuals often employ a range of different strategies to facilitate self-management (Busse et al., 2021, Christensen et al., 2015, Ploughman et al., 2012, Riemann-Lorenz et al., 2020a) and that it is important for clinicians to attempt to understand the person's own perceptions of living with MS, the challenges they face and how this impacts their PA intentions and actions, when seeking to support PA provision (Christensen et al., 2015).

An additional finding of the web-based study (Paper 2) was in relation to two participants who reported that their PA had declined over the study timeline. Their interviews described the way in which the web-based intervention benefitted them, in making it possible to seek timely advice from a physiotherapist when their mobility deteriorated. This appeared to enable them to maximise their PA when without support they may have had to stop being active completely. This significant role, described further in the paper's "hopes and expectations" theme is interesting, suggesting that the purpose of web-based PA interventions in people with higher levels of disability may be different from those who are ambulant. The first study (to my knowledge) of web-based physiotherapy specifically in pwMS and higher levels of disability (moderate to severe) is a pilot RCT conducted in Canada (Donkers et al., 2020). Donkers et al used the same intervention (webbasedphysio.com) as our participants in paper 2. Interestingly however, neither study demonstrated a significant difference in adherence to exercise between the web-based and active comparator groups suggesting the web-based intervention did not support increased adherence to exercise in either population. The Canadian study (Donkers et al., 2020) did not report a qualitative component and hence it is not possible to compare our qualitative findings. The use of web-based PA interventions in people with higher levels of disability is an area requiring further exploration, where incorporating a different focus (such as satisfaction with access to healthcare support- the importance of which I will discuss further later) may be informative.

Additional reflections from this study include that several participants did not engage with the web-based element of the programme other than at the very beginning. Some felt that they had "learned" their exercises so no longer needed to access the website, and others reported that just seeing the intervention website address on their computer acted as a prompt to be more active. These factors are important to consider in respect to how well people adhered to the intervention where numbers of 'log-ins' were used to measure adherence. It highlights an important issue in study design where using logins as a proxy for completing an exercise programme may not accurately capture adherence to an exercise programme. This could, for example, lead to underestimation in cases where participants exercised but did not log in to the website, or overestimation where people logged in to the site but did not complete the exercises as prescribed. Similar issues are raised with respect to completion of paper diaries or activity logs which are commonly used to measure adherence in exercise and PA studies. This key aspect of study design, specifically with respect to adherence is considered in more detail in the adherence stream discussion (paper 5).

A further notable finding was that some people reported that it was commitment to the study that gave them motivation to continue to exercise. This issue is supported by other authors, including this statement from a participant of Crank and colleagues (Crank et al., 2017) "…I am the kind of person that will stick to an arrangement I've made. I will stick to a commitment". It raises the question as to whether it was the intervention itself or other study-related factors (such as this commitment to the research process) that helped participants continue to be active. Unfortunately, because control group participants were not interviewed in our study it is not possible to comment further on this. Research from the field of psychology however has explored the sense of commitment within the context of joint actions, where doing something such as signing a contract (perhaps comparable to a consent form) may provide the motivation for an individual to feel and act committed to a process or plan (Michael et al., 2016). Although not specifically within the context of health research the potential for this "externalising" of commitment remains a consideration in the interpretation of adherence data within the context of a research study.

Finally, it is important to acknowledge that the participant perceptions of increased PA levels we report in paper 2 were not supported by the objective (accelerometer) data from the main study (Paul et al., 2019). This discrepancy in PA levels when data is collected via self-report outcome measures compared to being objectively measured is well established (Coulter et al., 2020, Prince et al., 2008) and is likely to also exist when people share their perceptions of PA via interview.

2.3 Standing programme stream

The second stream of work I present was developed to evaluate the clinical and cost-effectiveness of a standing programme in people with progressive MS (Standing Up in MS (SUMS) study), and explore the experiences of a subgroup of people allocated to the standing programme and their standing assistants. This pragmatic RCT is the largest physical rehabilitation trial in people with progressive MS to date. Paper 3 describes the standing intervention provided to this under-researched population as one method of supporting people with severe disability to undertake PA and reports the effectiveness results. In summary, the main findings were that the standing intervention (plus usual care) resulted in a significant increase in motor function compared to usual care alone. In addition, longer standing times were associated with greater improvements in motor function. Of note, at the end of the trial 66% of participants were continuing to stand at least once a week and conclusions from the study were that the programme was implementable in clinical practice in the UK. In respect to the focus of this research portfolio, the results support the implementation of a standing programme in this population to enable people to be more physically active, and further, that those who were adherent to the standing programme for longer total duration over the nine months demonstrated greater benefits. The issue as to who and why some people adhered to the programme and others did not is likely to be multifactorial. Several potential issues are discussed in greater depth in the qualitative component of the study (paper 4) described below.

An additional factor may have been the incorporation of a number of behaviour change techniques based on the Social Cognitive Theory (SCT) (Bandura, 1986), the most widely used theory in the field. These “active ingredients” included goal setting and problem solving, both of which were incorporated in the two face-to-face home-based physiotherapy session and six follow-up phone calls. Educational resources (web-based, paper-based and DVD) designed to enhance self-efficacy, were also integral to the intervention package. These, primarily focused on intrapersonal factors (such as disease-related factors, knowledge and motivation). In addition, interpersonal factors, such as supporting the role of the standing assistant, and environmental factors; providing a home-based intervention to facilitate accessibility, were addressed. Although this study incorporated behaviour change techniques in line with SCT some researchers recommend using the social ecological theory (McLeroy et al., 1988) in future research, where more "multi-level" (i.e. intrapersonal and interpersonal but in addition community, organisational and policy levels) interventions are explored (Riemann-Lorenz et al., 2020a). These considerations are also supported by findings of reviews of adherence to behaviour change in other populations (DiMatteo, 2004, Middleton et al., 2013) where social support, including peer support and relapse management are associated with increased adherence. Other authors suggest that future studies are designed, evaluated and implemented in a way that behaviour change theory drives the process (Michie et al., 2011). Improved description of the theoretical underpinning of an intervention, linking chosen behaviour change technique to the theory, incorporating constructs of the theory within outcome assessments and considering the relationship between results and theory in any discussion are suggested (Motl et al., 2018). In light of this, critical examination of the SUMS study indicates that it incorporated a range of behaviour change techniques effectively within the trial design, implementation and dissemination components. This may have been enhanced by measuring one of the SCT constructs, such as self-efficacy as an outcome. Enhanced detail regarding the underpinning theory within the publication (paper 3) would have provided more information regarding the efficacy of the behavioural intervention components of the standing programme. However, at a pragmatic level, explaining other key methodological factors (such as the selection of outcome measures and the sample size justification) were prioritised within the limitation of the journal word count. It may have been, that building a formal process evaluation into the study, and reporting it in a separate article, would have enabled us to explore and report this further. Busse and colleagues provide a good example of such reporting of both the development of a theory informed model on which an intervention is based (Busse et al., 2021) and the protocol for its subsequent feasibility trial (Latchem-Hastings et al., 2021). A further consideration with respect to enhancing the impact of the selected behaviour change techniques could have been the incorporation of longer-term planned opportunities to review and modify goals across the study timeline. This, among other issues are highlighted as components of goal setting that are currently under-implemented in practice (Kang et al., 2021).

An interesting component of the dissemination work of the SUMS study has been talking with clinicians about their current use of standing frames. My clinical experience and that of most clinicians I have spoken to is that standing frames are not commonly incorporated into rehabilitation management plans. When included, they are typically used with people who are entirely dependent on a wheelchair for their mobility. This study has provided robust evidence that the frames are clinically and cost-effective for people who can mobilise up to 20 metres with bilateral assistance. This novel finding has potential therefore to change the practice of therapists. Also of note regarding development of clinical practice, is the importance of clinicians having a good understanding of behaviour change techniques which may be invaluable when supporting an individual implementing a new activity such as supported standing. Of note, this is an area that is specifically being addressed in a current feasibility trial of a blended physiotherapy intervention for people with progressive multiple sclerosis (Latchem-Hastings et al., 2021). One way in which we have tried to address this is through provision of information for clinicians on our study website as will be discussed later.

Recommended in the design of RCT's is the recording of adverse events (Ioannidis et al., 2004, Schulz et al., 2010). Unfortunately, systematic reviews highlight that this is not commonly undertaken (Hodkinson et al., 2013). It is therefore of note that participants in the SUMS study were asked to systematically record in a daily diary any adverse or serious adverse events (defined in paper 3). This facilitated comprehensive consideration of the difficulties participants faced in terms of new and existing symptoms and the impact of infections (urinary tract (UTI) and chest (CI)) on ability to sustain standing over the nine-month study timeline. On a practical level there were some challenges with the accurate recording of this data, for example how people defined a "new symptom". Nevertheless, the comprehensive nature of the adverse events data collected has provided useful, and novel insights into the issues faced by those involved. This has enhanced the clinical relevance of our dissemination work, by providing a detailed understanding of the potential short-term aches and pains that may be experienced when re-engaging with standing. Such information has not been previously reported in the literature. This finding links well with the "hopes and expectations" theme from paper 2, in that, if a person is part of an open and honest conversation about short-term aches and pains when first standing or has a plan of how to manage standing (or not) with a UTI (for example) they are more likely not to be put off by these issues but to 'journey' with them. By continuing to engage with supported standing, benefits are more likely to be experienced and it is postulated that this may lead to increased motivation to continue to stand.

One serendipitous discovery whilst analysing the adverse event data with respect to commonly reported problems such as UTIs, was that standing times for some people decreased for several days before the person recorded having a UTI or CI. It may be that reduced ability to stand, even in this supported position may be a "warning light" for some people who experience such infections. Recognition of this "warning" may potentially improve detection and treatment of infections and so limit the impact they can have on function. This, I suggest, is another potential area for future research.

Paper 4 presents the findings of the qualitative component of the SUMS study. The new knowledge from this output was developed into four themes. The first, "feeling like the old me" describes how standing helped people feel reconnected to their 'old selves', which was frequently combined with the sense of enjoyment. The importance of this 'sense of enjoyment' is also reported in other qualitative studies (Fasczewski et al., 2020, Hendrie et. al., 2015), RCTs of exercise or PA interventions (Mayo et al., 2020, McAuley et al., 2007) and systematic reviews (Casey et al., 2017, Moss Morris et al., 2021). New understanding reported in the "noticing a difference" theme included the wide range of physical and psychological differences that people reported such as a reduction in spasms, resultant need for less medication and being able to be more involved in family life. Also noted was that even in the absence of improved motor function, people reported other physical and psychological benefits that led them to choose to continue to stand. These qualitative findings demonstrate the value of incorporating a qualitative component within interventional research, as is increasingly being recognised in the evaluation of complex interventions guidance (Craig et al., 2013, Mohler et al., 2015). Although measurement of secondary outcomes such as spasm frequency and quality of life (for example) was part of the main RCT, the trial was not powered for these outcomes and as a result, without the qualitative results, the significance of such important benefits from the user perspective may not have been conveyed.

Participants in the SUMS study described differences in the level of support that they would have liked in similar ways to participants in the web-based study (paper 2) where some felt they had enough, but others would have liked more. With respect to provision of support in the context of living with a progressive disease others have reported similar issues (Davies et al., 2015). For example, there is a striking resemblance between a participant quote from Davies et al “you are just left to get on with it” and one we use in paper 4 “you do feel left alone a little bit…” These quotes draw us back to the notion that individuals need provision of the ‘right’ intervention and the ‘right’ support. This issue of personalising support is being addressed in a current feasibility trial of a physiotherapy intervention for people with progressive multiple sclerosis (Latchem-Hastings et al., 2021) where participants are provided with an initial physiotherapy coaching session either face-to-face or online and are then given the choice of accessing up to a further five coaching sessions during the three-month intervention period.

The longitudinal nature of the multi-window methodology used in paper 4 highlighted that additional support was mostly needed when people first started supported standing and when there were any changes to individual’s health or environmental situation. Similarly, Davies et al (Davies et al., 2015) also note the importance of providing support at key points in the life of a pwMS, in their study, when transitioning to secondary progressive MS. This reinforces the importance of asking people about what support they feel they need in open and honest conversations: again, the ‘right’ intervention, with the ‘right’ support at the ‘right time’.

The skills of goal setting and problem solving, built into the face-to-face and telephone sessions of the main trial appeared to help many participants to “get it right” in terms of when, where and how to use the frame. This is in line with Christensen and colleagues (Christensen et al., 2015) where positive support through provision of helpful tips, helping to identify PA limits, treating people as individuals and regular monitoring were seen as important in facilitating the “execution” of exercise. Interestingly, it may have been that had more of this “teaching” been built into the web-based physiotherapy intervention (paper 2) a higher proportion of participants may have felt they received enough support and adherence may have improved. Further, it is possible that the provision of additional coached standing sessions across the SUMS study timeline (in line with the findings from the web-based SR (paper 1)) may have enhanced standing effectiveness, participant adherence and experience. This intervention however was specifically designed to be feasible to deliver within the resource-limited National Health Service (NHS) where community provision of rehabilitation is limited (Thames Valley Strategic Clinical Network, 2016, The Neurological Alliance, 2018).

The final theme “you have a good day, you have a bad day” incorporated the challenges people faced when implementing this self-managed standing programme in the face of a progressive and fluctuating condition. This again resonated with work from paper 2 “hopes and expectations”; the importance of planning for good and bad days, talking openly and honestly about expectations and acknowledging the complexity of individual situations. Davies and colleagues (Davies et al., 2015) describes such conversations as “anticipatory preparation” where clinicians share knowledge of what to expect and helpful strategies to support pwMS manage future change (Davies et al., 2015). Similarly, our SUMS study participants reported that it was many of the small changes they made to their standing routines following the initial physiotherapy sessions (the “helpful tips” (Christensen et al., 2015)) that were instrumental in supporting their long-term adherence.

Our findings are encouraging given those of another recent investigation of experiences of a tailored exercise programme as part of a RCT (Crank et al., 2017), where participants reported that despite their positive experiences of exercise in a supervised environment, maintaining the self-directed exercise sessions at home was much more challenging. Some participants suggested the difficulty was due to a lack of structure and many of the participants reported that attending the supervised sessions were important for sustaining their motivation to exercise. This challenge of self-managing a home-based exercise programme has also been reported by Christenson and colleagues (Christensen et al., 2015). Our research however, has demonstrated that a standing frame programme, built into a daily routine, was both effective and acceptable to pwMS and standing assistants and could be used to support adherence to PA, at least for the nine months of the study timeline. Our study participants gained knowledge and experienced enjoyment but perhaps even more importantly, they developed the skills to problem solve, establish routines and gain confidence in their ability to self-manage this aspect of their lives.

To my knowledge this was the first study in pwMS to use an audio diary methodology to collect contemporaneous data to gain insight into participant experience throughout their standing journey. The methodology was chosen as it had the potential to reveal people’s ongoing, everyday experiences as they undertook a new activity (supported standing) over a period of time. In addition, it helped to address the potential issues of recall bias, known to be a problem particularly for people with memory impairment, and poor dexterity which may impact writing in exercise diaries. As well as providing day-to-day detail of participant experience, the method also provided a “bigger picture” of how participant’s experiences changed over time longitudinally at multi-occasional windows. These experiences, not ones that would be easily picked up using a more traditional interview method are supported by others using similar methods of data collection (Rayment et al., 2019, Rieger et al., 2018). Another learning experience in respect to the use of this methodology was that, despite providing verbal and written instructions, some audio diaries were returned with minimal data recorded. One practical issue reported by a couple of people was that they struggled to use the audio recorders because the buttons were too small for them to operate independently. In future, selecting recorders with larger buttons and simpler design, piloting their use, and having a formalised approach to check for any problems, such as through scheduled phone calls may address these issues.

To complement the written analysis of the SUMS qualitative study my next output was the production of four “filmlets”, which I led. Each of the films were based on one of the four themes developed in the study. They were produced in collaboration with a local media company (http://www.fotonow.org) through an iterative process, over a period of months following the data analysis. The project involved a process of combining narratives from the audio diaries with photographic images from some of the participants to create the final products. The films have played a significant role in the study dissemination at local, national and international conferences. Consistent with our approach to dissemination, other authors also encourage the use of participant collaboration and the incorporation of a “remix” of traditional research outputs with innovative options such as audio-visual summaries, art installations or dance performances to maximise the reach of the dissemination (Mirkovski et al., 2019, Ross-Hellauer et al., 2020). In addition, by nature of being freely accessible via the study website there is anecdotal evidence that these films have been helpful for pwMS and clinicians from the UK and internationally in supporting informed decision making. In this way the films (along with the other study documentation) are providing a degree of peer support, a facilitator of adherence to PA in pwMS (Riemann-Lorenz et al., 2020a) and a key factor to consider in driving service delivery (Kulnik et al., 2018).

The process of producing these films was personally one of the most rewarding parts of this research portfolio. It came with its own challenges, a key one being how to influence the creative process to ensure the images captured accurately reflected the stories being shared. It was an experience that demonstrated to me the value of being fully involved in both the research and the creative process: selecting audio extracts; planning photo shoots; capturing images; and compiling the films. It was my depth of understanding from having been immersed in the data that enabled me to bring to life the spoken word with images used in the appropriate context and portraying the emotion with which the narrative was delivered. I love personal stories! In my clinical role it is often the personal story of change that gives purpose to what I do. This opportunity therefore has enabled me draw together two of my passions- scientifically robust, comprehensible research and personal stories that, when combined effectively are accessible to many and have the potential to transform the experience of others. My hope is that these films will continue to have a positive influence on people affected by MS, clinicians and other researchers considering ways to disseminate study findings. Sharing new knowledge in this way has for us proven to be a powerful tool to support adherence to PA.

A final comment with respect to the SUMS study is the collaborative approach that was incorporated throughout the study process. People with MS were involved from design to dissemination in keeping with the National Institute of Health Research (NIHR) guidance (NIHR, 2021) and NHS clinicians delivered the intervention. In addition, members of the research team are clinical NHS neurological physiotherapists and as such provided clinician engagement throughout the study process, a factor that has been reported to improve benefits to patients, staff and organisations (Boaz et al., 2015, Harding et al., 2016). On-going work from the SUMS study is focusing on the implementation of the RCT evidence including exploring barriers to and solutions for implementing a home-based standing frame programme in UK healthcare. It is hoped that this continuing work will help embed our “real world” research in practice and minimise the knowledge-practice gap that is widely reported (Lynch et al., 2018, Morris et al., 2020), a vital component of the mission to support adherence to PA in this population.

2.4 Adherence stream

My final stream of work focused specifically on the topic of adherence. Reflecting back on my recent journey in research this final piece of work took me back to where the questions all began… no matter how effective the intervention was at the point of delivery, benefits were not maintained if people were not (for whatever reason) able to adhere to the changes long-term. By now I had gained knowledge and experience regarding strategies and interventions to help people adhere to PA but I wanted to explore what, as a research community we measure and report about participant adherence to interventions. The clinician in me wanted to know whether, even the highly motivated and mildly disabled pwMS, typical of many rehabilitation research participants, adhere to study interventions (and for how long). Further, given that this potentially biased sample was not reflective of my clinical caseload, even if participants did adhere, could I expect generalisability of the results into my clinical “real world”? The issue of participant selection leading to biased samples is raised and discussed, along with other methodological considerations, in a recent paper in MS rehabilitation research (Das Nair et al., 2019). The authors suggest that criticisms of biased samples can be addressed by specifying whether a trial is an efficacy trial (where a homogenous sample is needed) or an effectiveness trial (where generalisability of results, and a more heterogeneous sample, like my patients, is important). The design of the SUMS study (paper 3) addressed these factors where the broad eligibility criteria ensured that participant recruitment enabled generalisability of results.

In our review we sought to summarise the reported adherence and drop-out data from RCTs of exercise interventions in pwMS and identify moderators of adherence. We chose exercise rather than PA interventions due to the large numbers of studies involved and the different nature of targeted exercise and more general PA interventions. The results of this systematic review, the first in the area, were revealing. Only just over half of all the 93 included RCTs conducted over the last 25 years reported adherence and drop-out. Definitions of adherence were not consistent and rarely described any aspect of adherence to, or deviation from, an exercise protocol. When drop-outs were reported, in the vast majority of cases, the level of detail did not allow the reader to establish if dropping out had been due to the intervention or not. These omissions therefore made it impossible to draw conclusions about whether participants were able to complete the exercise intervention per protocol and, indeed, whether the intervention results could translate into practice. A further finding was that only 4% of studies included adherence data at any follow-up point, clearly an issue if looking to implement an intervention to support someone with a long-term condition such as MS over time.

The issue of researchers using a range of definitions of adherence is in keeping with previous reviews of adherence in other populations (Bollen et al., 2014, Hawley-Hague et al., 2016, Levy et al., 2019). We have additionally highlighted the importance of acknowledging the many facets of adherence and being clear on what aspect is being measured. For example, it may be sufficient to use session attendance as a measurement of adherence to a community exercise class as part of a feasibility trial, but this would not be an appropriate measure for a proof of concept exercise intervention study where adherence to a specific protocol, including aspects such as duration and intensity would be required. It is my opinion that the sole use of session attendance is not a sufficient measure even for a pragmatic feasibility trial. I suggest that whilst such a measure may allow confidence that a programme would be sufficiently well attended to justify its set-up (for example), it does not enable consideration of whether participants are able to complete the intervention as intended, a key consideration for any future interventional trial.

We used the terms “content adherence” and “session adherence” in our review to describe attending sessions (session adherence) and adherence to the specific exercise protocol (content adherence). Others, (Visek et al., 2011) have suggested use of four separate measures of adherence: completion (of the whole intervention), attendance (session adherence), duration adherence and intensity adherence. They suggest that doing so would enable calculation of session and content adherence and would also give a “total” intervention dose. Further exploration in this manner may provide additional insight into how an intervention is delivered and adhered to over time. For example, if an individual can adhere to 100% of the sessions but only 50% of the content, might the ‘right’ delivery of the intervention for them be an increased number of shorter sessions? Or could this lead to an insufficient dose or a reduction in session adherence? These are complex considerations, but they resonate with the way in which many SUMS study participants adjusted their standing programme (such as by doing more frequent shorter stands) to enable them to still achieve recommended standing times over a week. Teaching such problem-solving skills is a clear example of how the NHS clinicians involved in the study were able to work with the individual to offer the ‘right’ support at the ‘right’ time to facilitate adherence.

The wide range of methods of measuring PA adherence that we noted in our systematic review (most commonly activity diaries, logs, accelerometer, pedometer) are also reported by other review authors (Bollen et al., 2014, Frost et al., 2017, Hawley-Hague et al., 2016, Levy et al., 2019). In addition, limitations such as over-inflation in self-reporting, limited adherence to wearing an accelerometer for objective activity measurement, and the motivating effect of such devices are also acknowledged (Bollen et al., 2014). In addition to the measures listed above there are several other self-report questionnaires, designed to measure adherence, that have been reported (Bollen et al., 2014, Frost et al., 2017). These authors conclude however that almost all the identified questionnaires lacked any validation (Bollen et al., 2014), also a finding of another more recent systematic review (Levy et al., 2019). There are a couple of self-report questionnaires that do report some level of validation; the Problematic Experiences of Therapy Scale (Kirby et al., 2014) and the Exercise Adherence Rating Scale (Newman-Beinart et al., 2017). These measures allow an individual to report reasons for poor/non-adherence (within the bounds of the available questions) and could be used to facilitate discussion about what aspects of adherence may be most challenging and may help ensure provision of the ‘right’ support. None of these measures to my knowledge however have been validated in pwMS or were used in any of the included studies of paper 5.

With respect to moderators, in view of the current literature it was surprising that incorporation of a behavioural intervention component was not identified as a moderator of adherence in our review (paper 5). This may have been because only one third of the included studies contained any such element and in those that did, the content was limited. A final issue highlighted during the review process was the importance of more clear and transparent reporting of studies in terms of adherence and dropout. This issue of poor reporting quality has also been highlighted in a recent scoping review of methodological issues in rehabilitation research (Arienti et al., 2021). Paper 5 therefore concludes by challenging fellow researchers to closely follow published guidelines some of which already make recommendations with respect to measuring and reporting adherence (Page et al., 2017; Slade et al., 2016; Mohler et al., 2015).

It is important to acknowledge that recent trials involving pwMS are starting to incorporate both longer follow-up periods (Hayes et al., 2017, Silveira et al., 2019) and to measure and report adherence, drop-out and adverse events (Canning and Hicks, 2020, Coote et al., 2017, Hayes et al., 2017, Heine et al., 2017, Latchem-Hastings et al., 2021, Learmonth et al., 2017) which is encouraging for the interpretation and implementation of future research.

As well as this work being published, I have had the opportunity to share these new findings with colleagues working in the field as a member of the MoXFo (Moving exercise research in multiple sclerosis forward (Dalgas et al., 2020)) international study design group where I hope the findings may impact study design at an international level. If as a research community we can improve the way we define, measure and report factors such as adherence and drop-out and pay greater attention to the impact of protocol deviations on study results and how they are shared, we are likely to have a significant influence on how implementable future interventions are. Here lies (I believe) an ethical challenge too. All well designed studies have the potential to advance knowledge in the field, which is important, however it is imperative the knowledge gained, particularly from interventional research reaches those it intends to support. Researchers therefore have the responsibility to consider the design of their studies to ensure that (often charity) funded research is reported, disseminated and (if effective) implemented effectively (NIHR, 2019). With respect to adherence, it is encouraging to recognise that as a research community we can support adherence to PA, indirectly, in several ways. These include working collaboratively to reach consensus on adherence definitions, developing a battery of valid and reliable outcome measures, suitable for both clinical trials and practice that capture relevant aspects of adherence, and by ensuring that our studies are clearly and transparently reported.

In summary, these three streams of my work have each added new knowledge within the area of supporting pwMS adhere to PA. The work outputs have enabled an in-depth critical discussion from different perspectives, using different interventions and study designs. I now seek to provide a synthesis of my work and propose some areas for further research from a newly formed perspective.

Section 3: Synthesis of my work

In section 2 the range of ways the individual streams of work have contributed to knowledge regarding supporting pwMS to engage with and adhere to PA were discussed. In this section the Behaviour Change Wheel Framework (Michie et al., 2011) will be used to reflect on and synthesise the work within this research portfolio.

Before doing so it is important to address the complexity of the term ‘adherence’. Historically, the term was introduced by the WHO in an attempt to move away from the term ‘compliance’ that was deemed to carry a paternalistic air (Bissell et al., 2004). It was hoped that ‘adherence’ implied that the individual agreed with, rather than just obeyed recommendations. The debate regarding paternalistic connotations of this ‘new’ term ‘adherence’ however, continues (Bissonnette, 2008). Previously, adherence was a term mainly used in relation to following prescribed medication advice in line with the WHO definition: the extent to which a person’s behaviour corresponds with agreed recommendations from a healthcare provider (WHO, 2003, p. 3). Within the field of MS research, the first international meeting of the Adherence in MS group (then part of the European Rehabilitation in MS network (RIMS)) was held in 2013 and in line with this original perspective, focused primarily on adherence to medication. A second meeting in 2014 expanded the focus to summarise current knowledge of adherence to a range of behavioural interventions in MS. At this meeting the group defined adherence as “active agreement, consent and involvement of patients in their medical treatment” (Heeson et al., 2015).

In addition to these two definitions, paper 5 highlights other terms (such as concordance, compliance, participation or partnership) that are used by authors in this, and other fields as described in section 2.4. It also reports the variety of definitions of adherence used in exercise studies such as: the number or proportion of participants attending a particular number of sessions; the number or proportion of participants attending all sessions; the total number of prescribed exercise sessions attended; mean number of sessions attended by participants. Other terms widely used with respect to PA are engagement and sustaining. Initially within this portfolio of work these terms were used: engage, to refer to people making a choice to start an activity (such as by using a standing frame or a web-based exercise programme) and sustain, to describe an on-going engagement of PA over time (such as continuing with the prescribed standing or web-based programmes). However, given both terms could be described as being different components of the same construct the decision was made to use ‘adherence’ on each occasion for consistency.

Paper 5 also suggests a need for a greater depth of understanding of the meaning of the term adherence and how it is measured in relation to that definition. An example of providing greater depth in paper 5 was choosing to report adherence not only in terms of “session adherence” but additionally “content adherence” with the aim of providing extra information regarding intensity and duration; important components of any exercise intervention session. Bissonnette (Bissonnette, 2008) in her content analysis of adherence within nursing, psychology, pharmacy and general medicine also points to the need for further exploration of adherence in terms of clinician’s perception and understanding of adherence. One way in which Bissonnette and colleageues have taken forward their work is through conceptualising the term ‘adherence’ in terms of “adherence to choice” and “adherence to treatment” in a review of decision making tools designed to enhance adherence to medication (Trenamen et al., 2016). The adherence framework developed facilitated differentiation between tools that supported initial medication choice and those that captured whether a medication had been continued at follow-up, so enhancing clarity about what aspects of adherence were being measured. With respect to this body of work it could be that these terms represent “choosing to engage in PA” and “sustaining PA over a period of time”. Furthermore it may be that such decision making tools could facilitate a dialogue regarding PA between pwMS and their clinicians. Additionally, reflections based on work from this portfolio suggest the importance of exploring researcher and patient opinions to move understanding forward and facilitate the development of a greater mutual appreciation of its complexities. On-going discussion regarding a range of issues related to adherence, some of which have been discussed in this portfolio continues through the work of the MoXFo adherence sub-group.

3.1 The Behaviour Change Wheel Framework

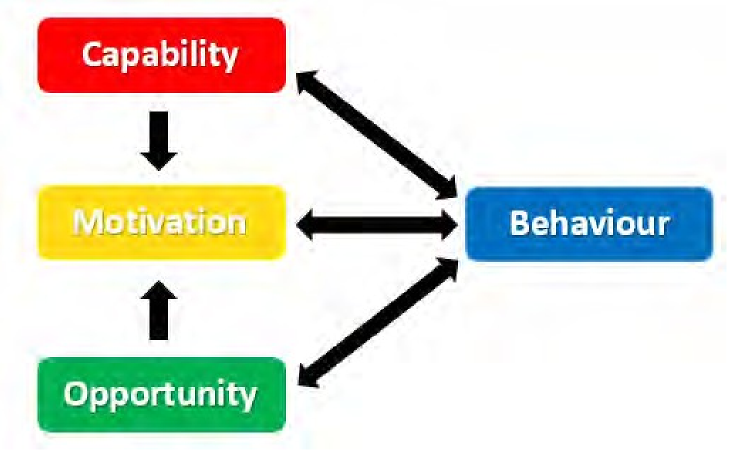
As introduced in section 1.2, the Behaviour Change Wheel Framework (Michie 2011) was developed to synthesise existing behaviour change models into a single framework that would facilitate comprehensive design and evaluation of behavioural interventions. The framework comprises the *COM-B, intervention functions* and *policy categories*.

3.1.1 Mapping my work to the framework

3.1.1.1 COM-B

The *COM-B* is at the heart or “hub” of the Behaviour Change Wheel Framework. It comprises the interacting components considered necessary for a given behavioural change to take place (in this context, adhering to PA) as illustrated in figure 1.

Figure 1: COM-B



Modified from Michie et al., 2011

Capability, the individual's capacity to engage in the activity concerned includes a person having the appropriate knowledge and skills to make a behaviour change. Distinction is made between having the physical capability (such as strength to stand or finances to pay to attend a gym or access the internet) and psychological capability (knowledge of the exercise guidelines, ability to plan, trouble shoot and adapt a situation). Opportunity, described as physical and social opportunity, is defined as factors external to the individual that support or inhibit a behaviour (such as having a PA intervention they are physically able to use and timely access to support). Motivation is defined as the brain processes that direct behaviour, with distinction made between automatic motivation; an individual's natural disposition, confidence and emotions, and reflective motivation; being able to set goals, reflect and evaluate behaviour (Michie et al., 2011).

The arrows in the *COM-B* represent the potential influence that the individual components can have on each other. For example, improving a person's opportunity to be active (such as by providing them with a standing frame or individualised web-based programme) can increase their motivation to be active. This increased motivation may then have a direct influence on their activity behaviour (they are more active), which in turn may influence motivation to continue (Michie et al., 2011, West et al., 2019).

The initial stage of synthesising this work involved reflecting on each of the individual works according to the *COM-B*. This enabled note to be made of ways that the work demonstrated it had influenced each of its components as summarised in figure 2. Colours were used to link the capability, opportunity and motivation components from the COM-B to the relevant works.

Figure 2: Summary of published works categorised using the COM-B

Physical capability (Physical capacity to engage in PA)

- Paper 2: Most participants perceived that using the web-based intervention helped increase PA
- Paper 3: Objective evidence of standing programme effectiveness on improved motor function
- Paper 4/ films: Participants reported positive changes in activities such as sitting balance, improved continence, strength, walking and transfers

Psychological capability (cognitive capacity e.g. ability to plan/ problem solve/ memory)

- Paper 2: Web-based programme aided memory of exercise programme, facilitated planning and organisation of when/ where to exercise "it's all in one place" theme
- Paper 3: Provision of multimedia information, problem solving advice and goal-setting in face-to-face and telephone sessions were key components
- Paper 4/ films: Participants reported that they learned to modify the standing programme to suit their needs and manage difficulties that arose

Physical opportunity (provided by the environment e.g. equipment, space, cost)

- Paper 1: Web-based interventions have a short-term positive effect on self-reported PA
- Paper 2: Web-based programme was reported to be "flexible, accessible and convenient"
- Paper 3/4: Films: Home-based provision of standing frame programme; reducing need for transport. Able to stand when convenient re assistance/ symptoms

Social opportunity (Factors from social and cultural environments that influence the behaviour)

- Paper 1: Video coaching sessions were demonstrated to increase participation
- Paper 2: Accessibility/ flexibility/ convenience of web-based interventions
- Paper 3/ films: Involvement from standing assistant, building standing into everyday routine
- Paper 3: Freely available website advice for clinicians/ carers/ people with multiple sclerosis
- Paper 3: Evidence of cost-effectiveness within NICE threshold for being provided by the NHS
- Paper 5: Can researchers incorporate improved adherence measuring/ reporting?

Reflective motivation (processes to direct behaviour e.g. goal setting, self-reflection, habits)

- Paper 2: Importance of discussing "hopes and expectations"
- Paper 3: Setting goals/ plans/ progression
- Paper 4/ films: "Feeling like the old me"- reflecting on previous roles/ experience/enjoyment
- Paper 5: Methodological challenges of improved measuring/ reporting of adherence

Automatic motivation (Automatic processes e.g. emotions and innate dispositions)

- Paper 2: Importance of discussing hopes and expectations of an intervention
- Paper 3: Use of established Behaviour Change Techniques to optimise adherence
- Paper 4/ films: sense of enjoyment acted as a motivator to continue

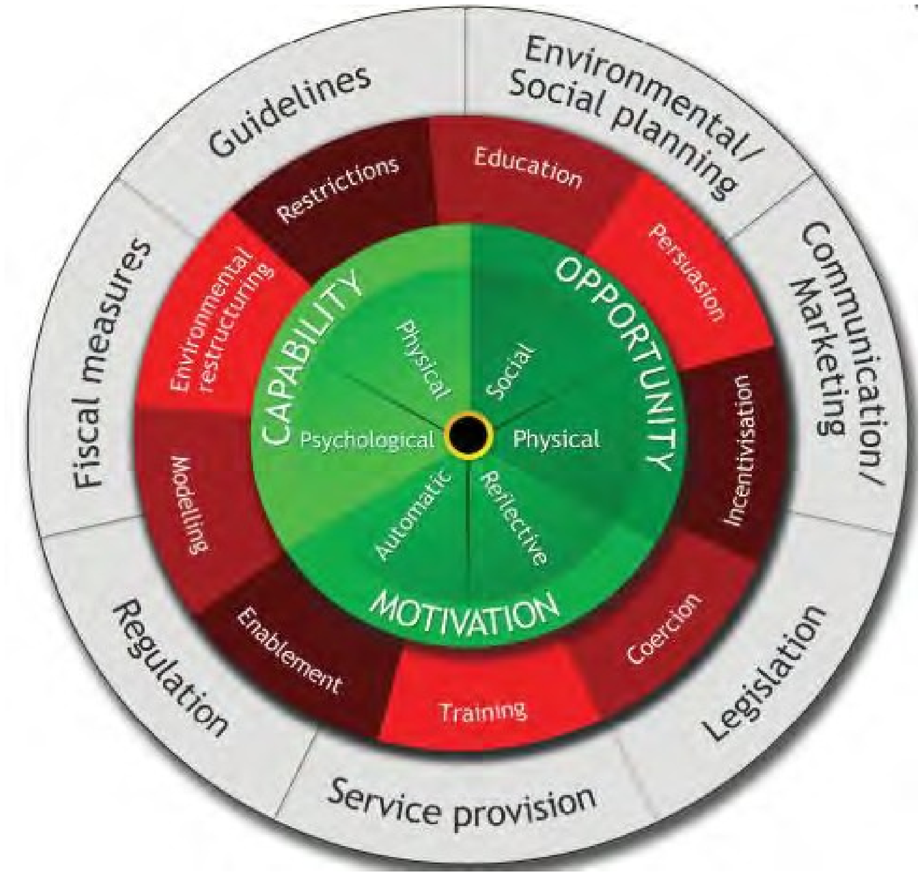
Legend: Abbreviations: PA: Physical activity, NICE: National Institute of Health and Care Excellence, NHS: National Health Service.

The next stage of reflection involved considering the work in the context of the framework's *intervention function* and *policy categories.*

3.1.1.2 Intervention Functions and Policy Categories

Michie (Michie et al., 2011) describe two layers that surround the COM-B hub. The inner layer includes nine *intervention functions*; broad categories of behaviour change intervention, each associated with a range of Behaviour Change Techniques. The outer layer consists of seven *policy categories*; factors suggested to be important to consider when developing an intervention's implementation strategy. These layers, combined with the COM-B hub comprise the Behaviour Change Wheel Framework as illustrated in figure 3.

Figure 3: The Behaviour Change Wheel



Michie et al., 2011, Intervention Science with permission

The main *intervention function* components this work demonstrates are education (increasing knowledge or understanding) training and enablement (increasing means/ reducing barriers to increase capability or opportunity). These functions were core to the standing stream work (Papers 3 and 4), from study design and intervention delivery to dissemination. For example, the freely accessible SUMS study website (www.plymouth.ac.uk/research/SUMS) which includes a range of multi-media educational resources, provides tangible evidence of the importance placed on education of all parties involved; pwMS, standing assistants and clinicians. This widely accessed website, with 150-200 visits each month (analytics from 2018-July 2021), has facilitated two-way communication with people affected by MS, clinicians and researchers at a local, national and international level. Emails received by the study team include feedback from pwMS able to remain active by using a standing frame at home throughout the Covid-19 pandemic, and from clinicians reporting changes in clinical practice such as increased ordering of standing frames and initiation of standing groups in rehabilitation settings. A further example of how this work has provided education is through the dissemination of each output. In addition to presenting each of the works at international, national and local conferences, the SUMS study team held feedback events in village halls across the South West of England and East Anglia for participants and their family members. Some clear examples of how this work has demonstrated enablement is through the provision of a standing frame (Papers 3 and 4) and a web-based exercise programme (Paper 2) to intervention group participants in the respective studies (Paper 3 and Paper 2, Paul et al., 2019).

With respect to the *policy categories*, communication, guidelines and service provision are represented by this work. The outputs from the standing programme stream of work (papers 3 and 4) along with the study website, twitter account and engagement with the media have demonstrated a thorough approach to communication. They have included lay people, generalist and specialist clinicians and the research community, and in doing so have been identified by the NIHR as an example of good practice. Specifically, paper 4 was selected for inclusion as an NIHR Alert; a short accessible summary of the findings that the NIHR reviewers believe should inform practice. The 'alert' was posted on the NIHR website https://evidence.nihr.ac.uk/, included in their monthly newsletter and communicated through NIHR social media. On-going work from the study dissemination plan seeks to increase the depth and breadth of impact with the aim of influencing the development of policy (local and national) within this area. The work has also been submitted for consideration of inclusion in the NICE guideline, Multiple sclerosis in adults: management (NICE, 2014b) which is currently being updated.

3.1.1.3 Synthesis of works in relation to concept of adherence

In this section, the contribution of each paper to the conceptual understanding of interventions that impact (or not) on adherence is considered through the interpretative lens of the Behaviour Change Wheel. Findings from paper 1 suggest that provision of web-based interventions (physical opportunity) had a short-term positive effect on self-reported PA but that adherence to the interventions dropped to around 50% or lower by 8-12 weeks. Provision of support (social opportunity) through additional coaching sessions appeared to enhance adherence up to three months post intervention. There was no data available post three months and as such it is not known how web-based interventions impact adherence long-term.

Paper 2 highlighted that participants perceived that the webbasedphysio intervention helped them engage in increased PA during the study timeline; that is to say, they were able to adhere to increased levels of PA. Themed reasons for this were the accessibility, flexibility and portability of the intervention (physical and social opportunity, psychological and physical capacity). For further debate in this study was whether the intervention provided sufficient support (social opportunity) to enhance adherence where only half of the participants felt it did.

Results from paper 3 demonstrated that provision of the standing frame (physical opportunity) with support from a physiotherapist (social opportunity) enabled participants to increase their motor function (physical capacity) and that those with increased adherence to the intervention (based on the CACE analysis) made greater gains. The qualitative findings from paper 4 and the films supported these findings and additionally reported improved problem solving skills (psychological capability) and ability to reflect on previous roles, experience and enjoyment (reflective motivation) which individuals reported helped them continue to stand. At present however, the audio diary data has not been explored in light of the individual's actual level of adherence to the intervention and as such it is not possible to comment on any potential association between the factors reported in paper 4 and adherence. Papers 3, 4 and the films additionally demonstrate education, training and enablement functions, particularly through the study website, that have the potential to impact adherence to PA in people not involved in the SUMS study.

Finally, paper 5 highlighted the complexity of the definition, measurement and reporting of adherence, prompting researchers to work together with people with MS and clinicians to continue to consider the concept of adherence in this population.

The findings from this portfolio, in keeping with an aim of the Behaviour Change Wheel Framework, suggest that interventions that incorporate a range of factors to target each component of the COM-B hub (capability, opportunity and motivation) have considerable potential to positively impact adherence Additionally, enablement, education and training, communication, guidelines and service provision also appear to be important in enhancing adherence. It is noted that only a limited number of BCW ‘intervention function’ and ‘policy categories’ were investigated in this work and the relative importance of these components compared to those that were not addressed would need further exploration. In addition this work is limited to a standing programme and web-based interventions and as such, caution is required in drawing overall conclusions regarding interventions that enhance adherence to PA.

3.2 Reflection and development of concepts

3.2.1 Reflexivity

The process of reflexivity has been described as one that is often ambiguous in nature and can be a challenge to the researcher (Finlay, 2002). This resonates as a researcher whose previous research experience was a small clinical effectiveness trial conducted from a positivist perspective and a single systematic review. Reflexivity was a new process to learn, different, more considered perhaps, than previous reflective clinical practice. Working as a fit and active physiotherapist, previously in the NHS and now at a MS centre, brought assumptions about the value of PA, provision of accessible PA opportunities and the importance of offering interventions that people could adhere to long-term. Additionally, roles as a mum, daughter and friend and accompanying personal values around the importance of PA could also add potential bias to data collection, interpretation and reporting. Researcher interest in the topic and personal values were central to the aim of the portfolio and reflection on the work challenged previous assumptions about PA resulting in a broader awareness of a range of issues impacting on engaging with and sustaining PA.

The critical realism (Bhaskar, 1989) ontology underpinning both qualitative studies (papers 2 and 4) enabled the research to consider the web-based intervention and standing programme in terms of what worked, for whom, in what situation and why. Additionally, collection of that data (knowledge) through exploration of the individual’s perception via audio diary and interview, within the context of their own social experience ensured the research was conducted within a pragmatic epistemology. Whilst suggesting these philosophical assumptions fitted well with the research, the researcher acknowledges her limited experience in this area.

A particular benefit of this work being co-authored is that it encompasses a range of personal assumptions about PA, not solely those of this author. Strategies were incorporated to minimise researcher bias which included: independent coding of data by several members of the research team who then met to discuss their findings; sharing themes that had been developed from the data with other members of the trial management group who were not physiotherapists and who included a person with MS, and sending summaries of findings to study participants for member checking. Findings from the study were also shared with members of the University's Rehabilitation Research Group which provided opportunity for discussion with a broader audience. Additionally, the interview schedule used in paper 2 was piloted with pwMS not involved in the study and finally, findings of paper 4 were triangulated with the exit interview data from paper 3. On a personal level, keeping a 'reflexive diary' that was discussed in supervision sessions helped to acknowledge opinions, assumptions and judgements made and separate them as much as possible from the data analysis process. This was done for each of the qualitative studies but it is acknowledged that this could have been continued more thoroughly during the write up of this portfolio.

3.2.2. Reflection on use of the Behaviour Change Wheel Framework

A range of potential frameworks to reflect on and synthesise this work were considered. Given the focus of the work on adherence, initial reflection used the WHO "five dimensions of adherence" framework (WHO, 2003). However, whilst researching the use of the framework it became apparent that only a very limited number of other authors had used it previously; a factor that could potentially limit opportunity for collaboration and discussion. The aim was not to blindly "do what everyone else is doing", but pay attention to one of the findings of this body of work; the importance of speaking a clear and transparent common language to facilitate improved communication regarding behaviour change. Some authors raise and discuss potential issues of the Behaviour Change Wheel Framework. For example, Ogden notes that "systematisation" (Ogden, 2016) of frameworks and theories to reduce variability may in fact be detrimental to the way behaviour change research is conducted and implemented where patient, clinician and environment variability should be supported and celebrated (Ogden, 2016; Peters and Kok, 2016). Although this notion resonates with the value of personalised care discussed throughout this summary, the role of a framework in this instance was to bring together a variety of works, recognising and acknowledging the variability of the work, yet assimilating it into a single, coherent portfolio for which the Behaviour Change Wheel Framework was considered appropriate.

Use of the framework posed some challenges, the main being recognising and accepting that the process of retro fitting highlighted "gaps" in the work where not all components of the framework were addressed. Initially this was perceived as a failure of the works, but the process of supervised reflection and writing enabled appreciation that using the framework retrospectively had, as designed, enabled effective reflection on the "big picture" of the work. Further, it had helped assimilation of findings both within the context of the current evidence base and the clinical landscape.

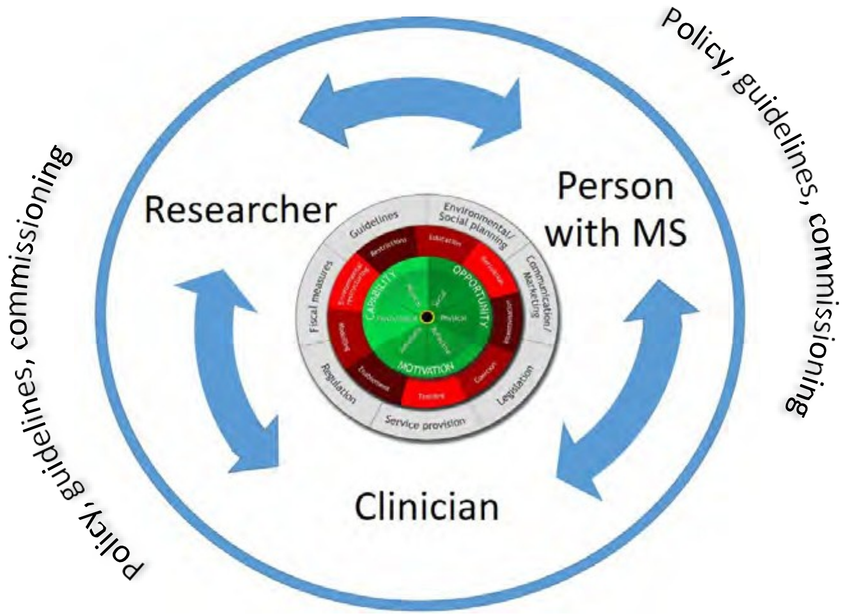
The reflection process enabled systematic development of two over-arching concepts: The 'Behaviour Change Triad' and 'Right intervention, right support, right time'. These concepts, which may resonate with people affected by MS, clinicians and researchers will be discussed further in section 3.3 and represent areas of new understanding which merit further exploration. Briefly, although current research in the field focuses on supporting pwMS to change their behaviour, this synthesis proposes a more complex interaction, requiring behaviour change of a number of parties.

3.2.3 Development of concepts

3.2.3.1 Behaviour Change Triad

Key to the fresh perspective presented is the concept that supporting pwMS adhere to PA requires behaviour change of (at least) three parties: pwMS, clinician(s) and researchers in the field. These complex and inter-related behaviour changes are referred to as a 'Behaviour Change Triad' as conceptualised in figure 4.

Figure 4: The Behaviour Change Triad



It is suggested that each party could use the Behaviour Change Wheel Framework to explore opportunities for a change in their own behaviour, hence the image of the Wheel at the centre of the process.

This concept was developed whilst reflecting on what had been learned from each of the works. The research journey began by focusing on what a physiotherapist, could do to support adherence to PA, thinking, in the main, about types of intervention that could be offered to pwMS so that they could change their PA behaviour. During this research journey a bigger picture has become apparent that, not only the pwMS but the physiotherapist needs to change behaviour. Not only is the role of a physiotherapist to support others to change behaviour, to do this most effectively there is a responsibility for clinicians and researchers to also change practice. Yes, the web-based and standing studies have demonstrated the value of such interventions for people with diverse levels of disability and technology literacy/ preference and the experiences shared have highlighted that every individual will want or require different support depending on a variety of personal factors. However, further to these factors this work has resulted in a realisation that the way in which people are supported to adhere to PA can be influenced more effectively if clinician and researcher behaviours are also modified in a number of ways. For example, ensuring that open and honest conversations are always part of often time-pressured clinical sessions, that a range of supported interventions are offered to accommodate those who access physiotherapy, and that targeted behaviour change techniques are consistently taught and used within clinical practice.

As a researcher this work has provided a challenge to ensure research findings are reported in a clear and transparent manner and in line with guidelines despite the confines of journal word counts. Paper 5 particularly has provided motivation to encourage the research community to modify behaviour specifically in terms of how aspects of adherence are collected and reported so that the information is more useful to clinicians and people affected by MS.

The Behaviour Change Triad conceptualises the interaction that each of these changes can have on each other. For example, a clinician discussing a trial of a standing frame programme with an individual supports implementation of evidence-based practice (clinician behaviour change). The person feeling supported to use this intervention is then more likely to feel motivated to sustain that new behaviour and go on to experience benefits as demonstrated in papers 3 and 4 and the films (person with MS behaviour change). This implementation of research into clinical practice then affords the researcher opportunity to evaluate the intervention (including adherence to it) in a real world setting and then report the findings transparently, clearly a benefit to all those affected by MS (researcher behaviour change). It is suggested that the potential interactions of the triad (including research from the fields of implementation and patient and public involvement) are numerous and offer a range of ways to positively impact the overall goal of supporting adherence to PA in pwMS.

When presenting the Behaviour Change Triad, 'at least' three parties were suggested, being involved mindful of the considerable influence that guideline and policy writers, and service commissioners have on UK healthcare provision. Although beyond the scope of this integrative summary further work could explore the interaction of these complex, interacting behaviour changes.

3.2.3.2 ‘Right intervention, right support, right time’

A theme running through this work is the importance of providing and valuing personalised opportunities for PA to optimise adherence; the ‘right intervention with the right support at the right time’. This forms the basis of a second over-arching ‘concept’. Every individual’s condition, life experience and current environment is different, as are their hopes, expectations and preferences (Papers 2 and 4). There is a wealth of research evidence supporting personalised care for pwMS (Donkers et al., 2020a, Mayo et al., 2020, NHS England, 2019, Richardson et al., 2020) and this work (Papers 2, 3, 4 and films) adds understanding regarding personalising opportunities for PA in this group of people. In addition, this work highlights the importance of personalising both the type and timing of support. Examples include modifying a web-based physiotherapy programme in response to changes in ability (Papers 2) or supporting pwMS problem solve how to alter their programme when standing is challenging (Papers 3, 4 and films). Further, the fluctuating nature of MS and progression of symptoms and disability over time means it is important that people are provided with the opportunity to re-access advice about suitable, meaningful and enjoyable opportunities for PA when they need it as exemplified by the experiences shared in the qualitative studies (Papers 2 and 4).

Recent research adds further weight to the importance of providing pwMS the ‘right intervention at the right time’. Researchers in the United States report data from a secondary analysis of PA intervention effectiveness outcomes from several previous studies (Baird and Motl, 2019). They suggest a ‘response heterogeneity’ in relation to factors such as MS disease characteristics, nervous system damage, and MS-related disability. It may be that future research could develop a response prediction model based, for example, upon ideas from Jeong and colleagues' "adherence prediction model" (Jeong et al., 2019). This, crucially, would enable clinicians to target interventions more effectively, resulting in enhanced benefits for pwMS, a crucial factor to consider in our resource-limited healthcare environment.

Finally, it is encouraging to see that many of the issues raised throughout this body of work (such as providing choice of intervention, level and timing of support and opportunities to use a hybrid (blended) approach to provision and having open and honest conversations) are supported by other research groups and are currently being evaluated in a number of trials across Europe, Australia and the US (Baird et al., 2020, Casey et al., 2019, Latchem- Hastings et al., 2021, Learmonth et al., 2017, Silviera et al., 2019). I look forward to readingthe results of these studies, being part of future research and exploring the concept of the Behaviour Change Triad within the field.

3.3 Next Steps

There are a number of next steps currently being developed that follow on from the work included in this research portfolio. Building on the successes of the SUMS study (paper 3 and 4 and films) a study to develop and evaluate an implementation intervention, co-created with stakeholders, to facilitate the supply and use of standing frames for people with MS is being planned. In addition it is hoped to further develop the adherence work from paper 5. Currently this has been limited to discussions with the MoXFo study design group regarding incorporating, as standard practice, comprehensive measurement of adherence within future study design. It is hoped this work may be incorporated and further developed by the adherence group of MoXFo. Another area that has potential to add significantly to the 'adherence debate' is an exploration of the perception and understanding of the term adherence by clinicians, researchers and pwMS. This work could look to incorporate the concept of the behaviour change triad and involve all parties in its co-production.

In addition to the direct results of this portfolio of work, this author's current role is closely aligned to its findings. Working as a Researcher in Residence (RiR) provides opportunity to be part of a team of clinicians, patients, carers and researchers co-producing and assessing the feasibility of a peer-coaching intervention for people with long-term health conditions. The RiR model enables the researcher to be embedded within the clinical team and together develop and action research that is relevant and implementable by the Trust's decision makers (Gradinger et al., 2019). This has additionally provided the opportunity to informally observe and reflect on roles and relationships within the team and consider factors that may be important to explore with regard to the behaviour change triad.

3.4 Summary

This integrative summary has brought together peer-reviewed, published work from three related streams all of which involved pwMS. Each output has provided new knowledge, much of which is at the forefront of the field. The work streams have discussed potential factors to support people with a range of disabilities adhere to PA. Critical analysis of the work has acknowledged areas where challenges were experienced, contextualised the findings within the current evidence base and has facilitated consideration of areas for future work. It is hoped that this research portfolio will help support pwMS, (especially those who, for whatever reason, find PA challenging) become and remain more active, experience the associated benefits and then share their story to inspire others to do likewise.

Chapter 2: Published Works

2.1 Web-based Interventions Stream

2.1.1 Paper 1

Dennett R, Gunn H and Freeman J. Effectiveness of and user experience with web-based interventions in increasing physical activity levels in people with multiple sclerosis: A systematic review. Physical Therapy. 2018. 98 (8) 679-690.

https://doi.org/10.1093/ptj/pzy060

Review

Effectiveness of and User Experience With Web-Based Interventions in Increasing Physical Activity Levels in People With Multiple Sclerosis: A Systematic Review

Rachel Dennett, Hilary Gunn, Jennifer A. Freeman

Background. Supporting people with multiple sclerosis (MS) to achieve and maintain recommended levels of physical activity is important but challenging. Web-based interventions are increasingly being used to deliver targeted exercise programs and promote physical activity.

Purpose. The purpose of this study was to systematically review current evidence regarding the effectiveness and user experience of web-based interventions in increasing physical activity in people with MS.

Data Sources. MEDLINE, EMBASE, CINAHL, AMED, PEDro, PsychInfo, Web of Sciences, The Cochrane Library, and gray literature were searched from 1990 to September 2016.

Study Selection. English language articles reporting the use of web-based interventions to increase physical activity in adults with MS were included. Eligible quantitative studies were of any design and reported a measure of physical activity. Qualitative studies exploring users' experiences in any context were included. Of the 881 articles identified, 9 met the inclusion criteria.

Data Extraction. Two reviewers independently assessed methodological quality and extracted data using standardized critical appraisal and data extraction tools from the Joanna Briggs Institute Meta Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI).

Data Synthesis. Meta-analysis of self-reported physical activity questionnaire data from 4 studies demonstrated a standardized mean difference of 0.67 (95% CI = 0.43–0.92), indicating a positive effect in favor of the web-based interventions. Narrative review of accelerometry data from 3 studies indicated increases in objectively measured physical activity. No qualitative studies met the inclusion criteria.

Limitations. In the 9 included articles, only 2 different interventions (used with people who were ambulant) were reported.

Conclusions. Web-based interventions had a short-term positive effect on self-reported physical activity in people who had MS and were ambulant. Evidence is not currently available to support or refute their use in the long-term or with people who are not ambulant.

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[Dennett R, Gunn H, Freeman JA. Effectiveness of and user experience with web-based interventions in increasing physical activity levels in people with multiple sclerosis: a systematic review. *Phys Ther.* 2018;98:679–690.]

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Multiple sclerosis (MS) is a progressive neurological condition that can result in wide-ranging impairments that may impact negatively upon activity and participation levels. Evidence demonstrates that people with MS are more sedentary and physically inactive than those in the general population, even in the early stages of the disease.[1,2] This is thought to be due to a combination of factors which include the direct effect of MS-related impairments (such as fatigue and weakness), and the general deconditioning and functional deterioration which occurs as the disease progresses.

It is now well established that targeted exercise and increased levels of physical activity can result in a range of physical[3–7] and emotional[8,9] benefits for people in the early stage of MS, although this is yet to be established for those in the progressive phase of the disease.[10,11] Such increases in physical activity are important to minimize the complications and comorbidities associated with living a more sedentary lifestyle.[12] Furthermore, recent literature has suggested possible neuroprotective properties of exercise in people with MS.[13] Accordingly, there has been an increased emphasis within clinical practice to incorporate exercise programs and facilitate engagement with physical activity.[14] This approach aligns with public health guidelines,[15] developed to promote physical activity participation in the general population at a sufficient level to achieve health benefits.

Evidence based physical activity guidelines recommend that people with MS who have mild to moderate disability should aim to participate in 30 minutes of moderate intensity aerobic activity twice a week and progressive resistance training involving major muscle groups twice a week.[16] There are no current guidelines regarding the prescription of physical activity levels for people with MS who have higher levels of disability.

Ensuring that adequate levels of physical activity are sustained in the long term is challenging, both for people with MS and for those involved in their management.[17] Choice of activity, advice and support, control over level of engagement,[18] and the ability to develop "self-support"[19] have been identified as key factors to facilitate participation with physical activity. The low levels of physical activity in people with MS[20] has also prompted researchers to identify the barriers to participation that people with MS experience. Fatigue, lack of time, and the effort and travel distance required to access rehabilitation venues are reported as barriers.[21,22] In parallel, health services across the world face ever-increasing financial pressures, enforcing reconsideration of cost effective, evidence-based service delivery.

Remote provision of health care using telecommunications technology is now widely used and is often described under an umbrella term of Telehealth. Such technologies may: facilitate real-time, interactive communication between the patient and professional; use "store and forward" technology where information related to the patient is gathered, stored and forwarded to the professional at a later date; or facilitate the patient to use technology for health benefits without the requirement to share information. Innovations in web-based technologies are increasingly being used as a method for delivering rehabilitation programs or promoting increased physical activity, where the term telerehabilitation may be used. Reviews of such interventions in the general population, as well as in conditions such as obesity, rheumatoid arthritis and diabetes, have indicated promising results.[23,24] More recently, 2 systematic reviews of randomized controlled trial studies in MS, evaluating a broad spectrum of telerehabilitation interventions, suggest that these distance-based interventions may be effective in increasing physical activity,[25,26] but that further robust research in this area is needed. However, these reviews of telerehabilitation are broad, including not only studies using technology in the form of real-time or store and forward innovations but also studies using technology in the form of gaming (such as the Wii) or pedometers to encourage increased engagement with physical activity. It is therefore not possible to evaluate the effectiveness of each specific type of telerehabilitation intervention. Qualitative work[27] and process evaluation questionnaires[17] have been undertaken to explore the feasibility and acceptability of web-based interventions, and provide helpful information to guide their on-going development. User feedback is important to optimise their effectiveness in enabling people with MS to increase and sustain physical activity levels in the long term.

This systematic review focused on studies of any design that investigated the use of interventions delivered via the internet that aimed to increase physical activity (as defined by Caspersen et al[28]) in people with MS. It sought to establish their effectiveness in increasing physical activity, over the short term (≤3 months) and the long term (>3 months),[25] and whether levels of activity met MS-specific guidance.[16] This systematic review was conducted according to an *a priori* published protocol, which was registered with PROSPERO (ref CRD42016054084).[29]

The original aim of this systematic review was to comprehensively explore the use of web-based interventions in increasing physical activity levels in people with a diagnosis of multiple sclerosis (MS), including both qualitative and quantitative data. As the literature search yielded quantitative papers, it was not possible to address the qualitative objectives. Therefore, only the quantitative elements of the review are reported in this paper.

The quantitative objectives were to identify the effectiveness of web-based interventions in enabling people with MS to increase their physical activity levels, as evaluated by measures of physical activity; to examine whether short- or long-term web-based interventions enable people with MS to achieve the physical activity levels recommended in guidelines for adults with MS while they are being used; and to examine whether the use of web-based interventions enable people with MS to maintain recommended levels of physical activity after the intervention has ceased, at short- and long-term follow-up.

Methods

Data Sources and Searches

Searches aimed to find both published and unpublished studies. A 3-step search strategy was utilized. An initial limited search of MEDLINE, AMED, and CINAHL was undertaken followed by an analysis of the text words contained in the title and abstract, and of the index terms used to describe articles. A second search using all identified keywords and index terms was then undertaken across all 8 included databases. Thirdly, the reference list of all identified reports and articles was searched for additional studies. Studies published in English since 1990 were considered for inclusion. This date restriction is in place as the World Wide Web was established in 1989, and, therefore, web-based interventions were not possible prior to this. Two independent reviewers screened abstracts and full text articles for eligibility for inclusion, and any duplicates were removed.

The initial keywords used were as follows:

> Web-based OR internet-based OR www OR world wide web OR e-learning OR telerehabilitation OR telemedicine OR eHealth
>
> Multiple sclerosis OR MS OR neurological condition OR neurolog*
>
> Physical activity OR exercise OR physical fitness OR walking OR motor activity OR rehabilitation OR physiotherapy

The full search strategy is provided in the Appendix.

Databases searched were MEDLINE (Ovid), EMBASE (Ovid), CINAHL (EBSCO), AMED (EBSCO), PEDro, PsychInfo, Web of Sciences, The Cochrane Library, and The Cochrane Central Register of Controlled Trials (CENTRAL). The search for unpublished studies included hand searches of reference lists of all identified articles and searches using Google Scholar, Conference Papers Index, and clinical trials registers via www.controlled-trials.com and http://clinicaltrials.gov. Authors of abstracts were contacted via email where possible, and on 2 occasions the full papers were provided, one of which was included in the review.[30]

Study Selection

This review considered studies that included adults over the age of 18 with a diagnosis of MS, regardless of MS type, time since diagnosis, or level of disability. It considered both experimental and epidemiological study designs, including randomized controlled trials, nonrandomized controlled trials, quasi-experimental studies, before and after studies, prospective and retrospective cohort studies, and case control studies.

Studies that investigated the use of web-based interventions that were exercise or lifestyle activity based, and/or incorporated a behavior change or coaching approach to increase physical activity were reviewed. Studies reporting an active comparator, usual care or waiting list control, and those without such comparators were included. Interventions describing any regimen of frequency or intensity of delivery were included. Studies that described use of the Internet to deliver virtual assessments or gaming interventions (such as Wii or Xbox) were not included to enable a focused, manageable, but in-depth review of this topic drawing upon evidence from a wide range of research methodologies.

Studies were considered if they included measures of physical activity such as accelerometer, pedometer or global positioning system data, or physical activity questionnaires. Participation outcomes, when measured alongside physical activity data, were also included (eg, by recorded numbers of log-ins to web-based interventions or completion of activity diaries). The purpose of this review was not to evaluate the effectiveness of web-based interventions at the level of impairment; therefore, outcomes such as weight loss, reduced blood pressure, increased cardiovascular fitness, and muscle strength were not considered.

Data Extraction and Quality Assessment

Papers selected for retrieval were evaluated by 2 independent reviewers using a 2-stage process to assess relevance and quality. Standardized critical appraisal instruments from the Joanna Briggs Institute Meta Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) were used (accessed via https://www.jbisumari.org/). Any disagreements that arose between the reviewers were resolved through discussion, or with a third reviewer on 2 occasions. The outcomes of the quality assessments were summarized by calculating the number of items that were marked as present for each study. In keeping with the aim to be as comprehensive as possible, a cutoff point for inclusion was not set for the quality review stage; however, the outcome of the quality assessment was considered when making inferences from the data synthesis.

Data were extracted from papers using the standardized data extraction tool from JBI-MAStARI. The data extracted included specific details about the interventions, populations, study methods, and outcomes of significance to the review question and specific objectives.

Data Synthesis and Analysis

Where possible, data were combined in statistical meta-analysis to obtain a pooled standardized mean difference with 95% CI. Where standard deviations were not reported, they were imputed from the reported standard error using the formula $SD = SE \times \sqrt{N}$.[31] Because of the small sample sizes and variability of sample characteristics within the studies,[32] a random-effects generic inverse variance analysis was undertaken. The pooled data set was analyzed for heterogeneity using a combination of visual inspection and consideration of the chi-squared statistic, setting a P value of .10.[33] Publication bias was not assessed as recommended[34] due to the low numbers of included studies.

Where statistical pooling was not possible, the findings are presented in narrative form, including tables and figures to aid in data presentation.

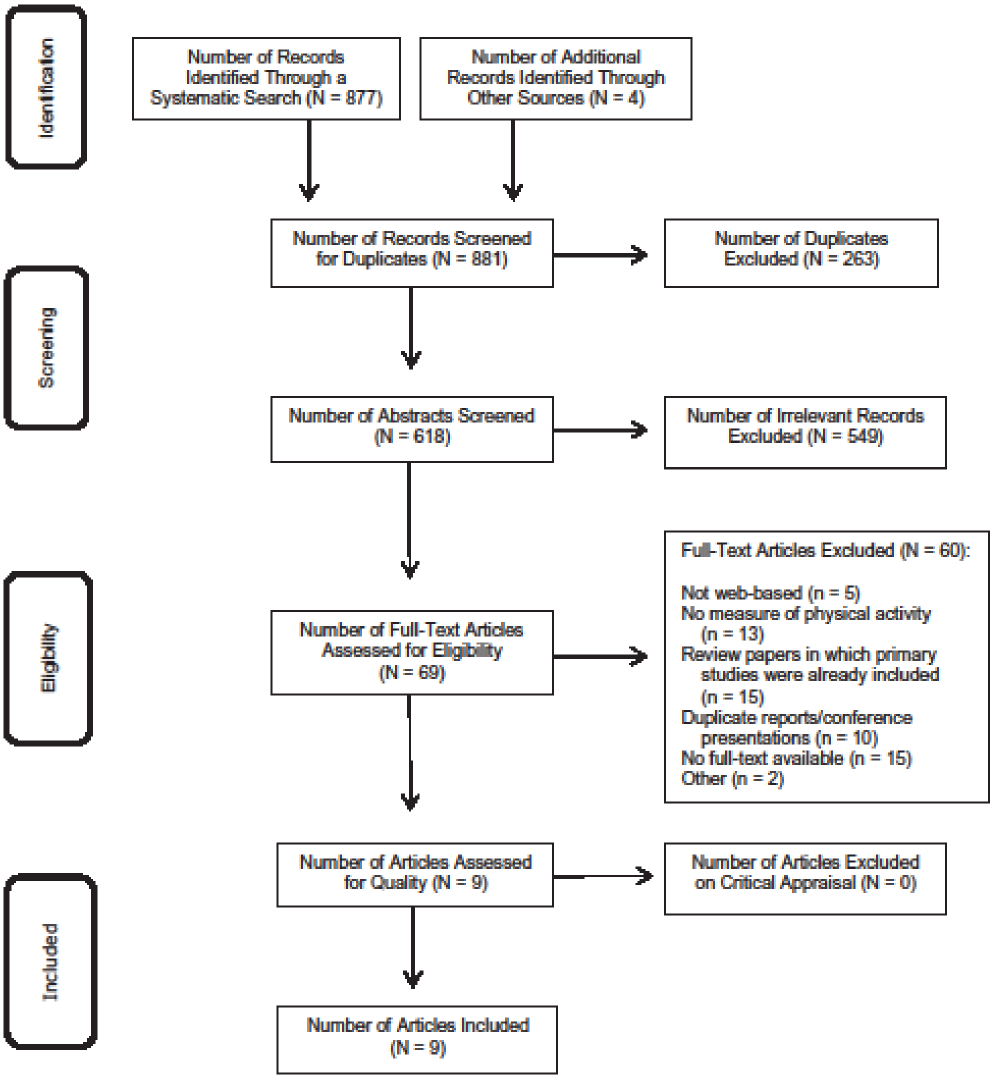

Figure 1.
Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[57] flow diagram of search and study selection.

Results

Study Selection

One reviewer (RD) performed the searches in September 2016. In total, 881 records were identified, which after removal of duplicates resulted in 618 titles and abstracts being screened for eligibility, and 9 studies subsequently being included in the review. The results of the searches are presented in the study selection flow chart (Fig. 1), with specific details of the included studies in Table 1.

Critical Appraisal Results

Methodological quality. Summaries of the appraisal of study quality are included in eTables 1 and 2 (available at https://academic.oup.com/ptj). Standards of reporting were generally good with both case series articles being marked as "yes" for all questions. Within the randomized controlled trials, the median number of "yes" scores was 10 of a possible 13 items (interquartile range = 8.75–10.25). The most frequently omitted methodological items related to masking of research assessors and management of incomplete outcome data. Masking of both participants and treating therapists was not reported to have been undertaken in any trial, a common finding in reviews of rehabilitation trials.[35]

Description of participants. The total number of participants recruited from the included studies was 346. Baseline characteristic data were available for 340 participants, of whom 68% were women, with a mean age of 45.7 years (SD = 9.4 years) and disease duration of 8.9 years (SD = 7.0 years). Participants were ambulant, with the majority (75%) walking unaided. Disability status was described using the Patient Determined Disease Steps scale[36] in all but 1 study[30] where the Expanded Disability Status Scale[37] was used. Only 4 studies included participants with a classification of relapsing-remitting MS.[17,38–40] The remaining studies included people with both progressive and relapsing-remitting subtypes[1,2,30,41,42] (4 of which reported on the same study sample). Tallner[30] excluded those with a primary progressive disease course. Eight of the 9 studies were based in the United States, and 1 was based in Germany.[30]

Study designs. Seven of the included articles report on randomized controlled trials of internet-based interventions with waiting list controls (Tab. 1).[1,2,17,30,38,41,42] Four of these[1,2,41,42] report different aspects of the same study, and hence to avoid double counting of data, of these only Pilutti et al[41] has been used within the meta-analysis. The other 2 included studies are single-group design where participants are the waiting list controls from previously reported studies.[39,40] Only 1 of the studies[30] described their sample size calculation.

Description of web-based interventions. Eight of the 9 articles report on studies that were part of the development process of a behavioral intervention designed to increase physical activity by promoting additional walking as part of everyday life. The intervention was initially trialled as a 12-week multimedia internet intervention[38,39] that focused on 4 information modules based on the Social Cognitive Theory: Getting Started, Planning for Success, Beating the Odds, and Sticking With It. Content of the modules was made accessible during the intervention period in a titrated fashion and was supported with group chat sessions and a telephone line and email address to provide direct contact with the study team. The professional background of the study team is not described. Subsequent studies[17,40] described the addition of 7 one-to-one video coaching sessions via Skype with the aims of increasing participant website log-in, and reinforcing and clarifying website content with them. The coach was a doctoral student with expertise in behavior change and experience in conducting physical activity research in people with MS. In these 5- to 10-minute sessions, the participant and coach reviewed and progressed goals and discussed strategies to aid behavior change based on the website content that had already been accessed.[17,40] In the latest reported study,[41] the intervention was delivered over 6 months and included 15 of the video coaching sessions. Intervention group participants in this study also wore a pedometer and completed a logbook and goal tracker spreadsheet to motivate and record physical activity as part of the program.

Tallner et al[30] describe a different intervention approach delivered via the internet: a 6-month, individually prescribed, twice-weekly strength training and weekly endurance training (jogging, walking, cycling, or swimming) program. The trainers were physical therapists or exercise therapists with experience of rehabilitation of people with MS and trained in the exercise prescription and study processes. Participants received supervision, and had their exercise programs progressed online using a standardized progression scheme, delivered via a messaging service in the web-based software (not in real time) with further email and telephone support if required. None of the articles published after the development of the Template for Intervention Description and Replication (TIDieR) guidelines[43] made reference to them in reporting their interventions,[2,30] although a summary of the intervention components is provided within each article.

Description of Outcomes

Physical activity. Physical activity was measured using both self-report and objective measures. Three different standardized and validated self-report measures were used. The Godin Leisure Time Exercise Questionnaire (GLTEQ) was reported in 6 articles,[2,17,38–41] the International Physical Activity Questionnaire (IPAQ) was reported in 5 articles,[1,2,37,40,42] (3 of which reported the same sample[1,2,42]), and the Baecke Questionnaire was reported in 1 article.[30] The GLTEQ[44] includes 3 items that measure the frequency of light, moderate, and vigorous leisure-time physical activity completed for at least 15 minutes over the previous 7 days, which are weighted and summed (0–119). The IPAQ[45] has 6 items that measure the frequency and duration of vigorous, moderate, and walking physical activity over a 7-day period which are then weighted and summed (0–117). The sport score of the Baecke Quesionnaire[46] is the product of the frequency, intensity, and duration of a participant's reported sports activities. In each of these measures, higher values indicate increased levels of physical activity.

Accelerometers, worn at the waist during waking hours, were used to collect objective physical activity data over 7 days in 3 studies[39–41] and are reported as part of a composite measure in a secondary analysis article.[2] The activity counts per day (for days when the accelerometers were worn for at least 10 hours) were converted into minutes of moderate to vigorous physical activity (MVPA) per day using validated cutoff points.[47,48] In addition, pedometer steps-per-day data, as a descriptive measure of change in physical activity, were available from intervention group participants in 4 studies[17,39–41] where higher numbers of steps per day demonstrate greater levels of activity. Although no MS-specific step

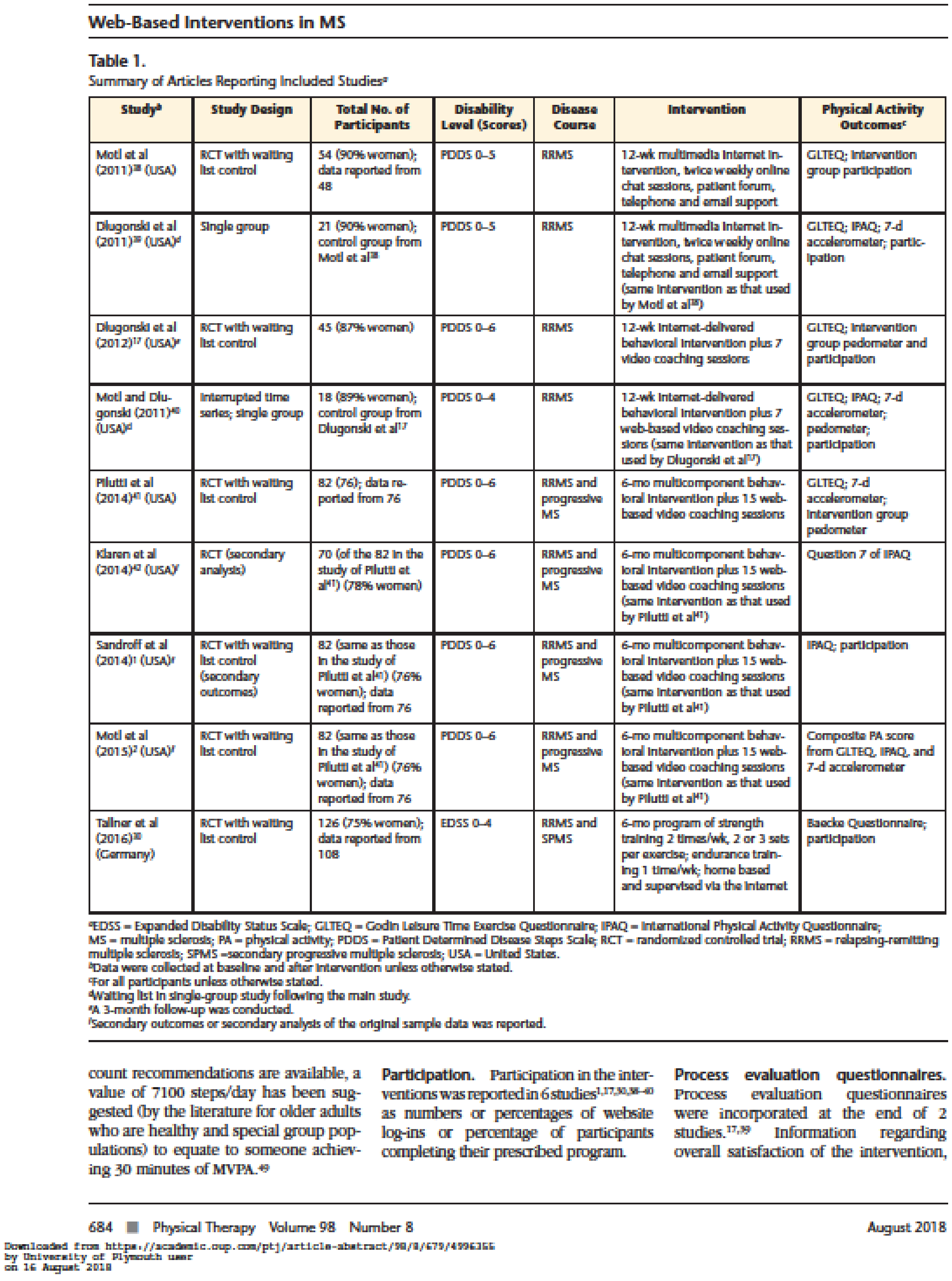

Table 1.
Summary of Articles Reporting Included Studies[a]

Study[b]	Study Design	Total No. of Participants	Disability Level (Scores)	Disease Course	Intervention	Physical Activity Outcomes[c]
Motl et al (2011)[38] (USA)	RCT with waiting list control	54 (90% women); data reported from 48	PDDS 0–5	RRMS	12-wk multimedia Internet intervention, twice weekly online chat sessions, patient forum, telephone and email support	GLTEQ; intervention group participation
Dlugonski et al (2011)[39] (USA)[d]	Single group	21 (90% women); control group from Motl et al[38]	PDDS 0–5	RRMS	12-wk multimedia Internet intervention, twice weekly online chat sessions, patient forum, telephone and email support (same intervention as that used by Motl et al[38])	GLTEQ; IPAQ; 7-d accelerometer; participation
Dlugonski et al (2012)[17] (USA)[e]	RCT with waiting list control	45 (87% women)	PDDS 0–6	RRMS	12-wk Internet-delivered behavioral intervention plus 7 video coaching sessions	GLTEQ; intervention group pedometer and participation
Motl and Dlugonski (2011)[40] (USA)[d]	Interrupted time series; single group	18 (89% women); control group from Dlugonski et al[17]	PDDS 0–4	RRMS	12-wk Internet-delivered behavioral intervention plus 7 web-based video coaching sessions (same intervention as that used by Dlugonski et al[17])	GLTEQ; IPAQ; 7-d accelerometer; pedometer; participation
Pilutti et al (2014)[41] (USA)	RCT with waiting list control	82 (76); data reported from 76	PDDS 0–6	RRMS and progressive MS	6-mo multicomponent behavioral intervention plus 15 web-based video coaching sessions	GLTEQ; 7-d accelerometer; intervention group pedometer
Klaren et al (2014)[42] (USA)[f]	RCT (secondary analysis)	70 (of the 82 in the study of Pilutti et al[41]) (78% women)	PDDS 0–6	RRMS and progressive MS	6-mo multicomponent behavioral intervention plus 15 web-based video coaching sessions (same intervention as that used by Pilutti et al[41])	Question 7 of IPAQ
Sandroff et al (2014)[1] (USA)[f]	RCT with waiting list control (secondary outcomes)	82 (same as those in the study of Pilutti et al[41]) (76% women); data reported from 76	PDDS 0–6	RRMS and progressive MS	6-mo multicomponent behavioral intervention plus 15 web-based video coaching sessions (same intervention as that used by Pilutti et al[41])	IPAQ; participation
Motl et al (2015)[2] (USA)[f]	RCT with waiting list control	82 (same as those in the study of Pilutti et al[41]) (76% women); data reported from 76	PDDS 0–6	RRMS and progressive MS	6-mo multicomponent behavioral intervention plus 15 web-based video coaching sessions (same intervention as that used by Pilutti et al[41])	Composite PA score from GLTEQ, IPAQ, and 7-d accelerometer
Tallner et al (2016)[30] (Germany)	RCT with waiting list control	126 (75% women); data reported from 108	EDSS 0–4	RRMS and SPMS	6-mo program of strength training 2 times/wk, 2 or 3 sets per exercise; endurance training 1 time/wk; home based and supervised via the Internet	Baecke Questionnaire; participation

[a] EDSS = Expanded Disability Status Scale; GLTEQ = Godin Leisure Time Exercise Questionnaire; IPAQ = International Physical Activity Questionnaire; MS = multiple sclerosis; PA = physical activity; PDDS = Patient Determined Disease Steps Scale; RCT = randomized controlled trial; RRMS = relapsing-remitting multiple sclerosis; SPMS =secondary progressive multiple sclerosis; USA = United States.
[b] Data were collected at baseline and after intervention unless otherwise stated.
[c] For all participants unless otherwise stated.
[d] Waiting list in single-group study following the main study.
[e] A 3-month follow-up was conducted.
[f] Secondary outcomes or secondary analysis of the original sample data was reported.

count recommendations are available, a value of 7100 steps/day has been suggested (by the literature for older adults who are healthy and special group populations) to equate to someone achieving 30 minutes of MVPA.[49]

Participation. Participation in the interventions was reported in 6 studies[1,17,30,38–40] as numbers or percentages of website log-ins or percentage of participants completing their prescribed program.

Process evaluation questionnaires. Process evaluation questionnaires were incorporated at the end of 2 studies.[17,39] Information regarding overall satisfaction of the intervention,

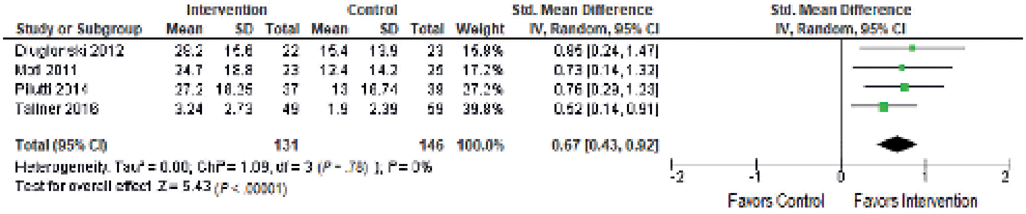

Figure 2.

Meta-analysis of self-reported physical activity questionnaire data. df = degrees of freedom; IV = inverse variance; Std. = standardized.

the website, and the staff delivering the program was collected.

Effectiveness of Interventions in Increasing physical activity levels. Both self-reported and objective data were available from the included studies and will be presented separately. All effect sizes are presented as the Cohen *d*.

Self-report physical activity questionnaires. Self-reported physical activity questionnaire data were available from 4 different study samples (n = 277 [complete data set]). Participants in the intervention groups participated in significantly more self-reported physical activity than controls: $P = .001$, $d = 0.77$[41]; $P = .01$, $d = 0.72$[38]; $P = .001$, $d = 0.33$[39]; and, for the fourth sample, $P < .001$, $d = 0.98$,[17] which remained statistically significant at the 3-month follow-up ($P < .001$, $d = 0.79$). These data were pooled in a meta-analysis (Fig. 2). The pooled standardized mean difference of 0.67 (95% CI = 0.43–0.92) indicated a positive effect in favor of the web-based interventions.

Self-reported physical activity questionnaire data were also available from the 2 single-group studies. One,[39] the waiting list control group from the initial pilot study, demonstrated a small and nonsignificant increase in GLTEQ scores ($P = .07$, $d = 0.34$) and a significant improvement in IPAQ scores ($P = .03$, $d = 0.43$). In the second follow-up single-group study,[40] a statistically significant and large increase in GLTEQ scores ($P < .0015$, $d = 0.83$) and IPAQ scores ($P < .001$, $d = 1.12$) was demonstrated on completion of the treatment period, which had not been seen in the period of no treatment.

Accelerometry data. Accelerometry data were available from only 1 randomized controlled trial[41] and the 2 single-group studies[39,40] and is therefore reported here narratively. Pilutti et al[41] presented accelerometry data which indicated that participants in the intervention group achieved a moderate but nonsignificant increase in time spent undertaking MVPA compared with controls ($P = .07$, $d = 0.43$). This equated to an average increase of just under 6 minutes a day of extra MVPA compared with controls. Reporting on the same study, Motl[2] conducted a secondary analysis in which a composite score of PA was created combining GLTEQ, IPAQ, and accelerometry. This composite physical activity data were analyzed using a 1-way analysis of covariance, controlling for baseline physical activity scores, and demonstrated that the intervention group had significantly higher levels of physical activity compared with those in the waiting list control group after the 6-month intervention ($P < .001$, ηp^2 [partial eta-squared effect size] = 0.12), which the authors reported to be a "practically meaningful effect."[2] The preintervention and postintervention accelerometer data from 2 single-group studies[39,40] demonstrated statistically significant increases in both total activity counts per day ($P = .002$, $d = 0.68$[39]; $P < .001$, $d = 0.92$[40]) and total step counts per day ($P < .001$, $d = 1.03$[40]).

Intervention group pedometer data were reported from 3 studies[17,40,41] all of whom report increases in weekly pedometer step counts. Two of the studies note that the increases occurred during the first 6 weeks of the 12-week interventions and were maintained to the end.[17,40] The magnitude of these increases ranged from 22%, or an average of 1387 steps per day,[38] to 46% (1869 steps)[40]—both in excess of the minimal clinically important difference; these data would indicate a change in ambulation and clinical/health outcomes in people with MS.[50] As there were no control-group pedometer data, it is not possible to comment on whether these increases were due to the intervention.

Achievement of recommended levels of physical activity. Although all articles describe the importance of physical activity in people with MS and one[30] makes direct reference to exercise prescription recommendations,[51] none report physical activity levels in line with recommendations for either the general[52] or MS[16] populations. However, 4[17,38–40] of the 9 articles were published before the publication of the MS-specific guidelines. Detailed information regarding the type and intensity of physical activity undertaken is reported in only 1 study,[30] in which participants were individually prescribed strength and self-selected endurance-training programs based on their fitness level. A standardized progression scheme was used to facilitate strength training overload, and guidance was given regarding endurance training intensity levels in line with recommendations.[51] There is no detail provided as to whether this was achieved or whether these data were collected.

Dlugonski et al[17] report intervention group pedometer data that demonstrated that the sample walked an average of 6368 steps per day in the final week of the 12-week intervention. However,

Table 2.
Participation Data Reported in Six Included Studies[a]

Study	Participation Measure	Outcomes	Conclusions
Motl et al (2011)[38]	% of participants logged in/wk	96% in weeks 1 and 2; declined throughout 12 wk; 52% in weeks 8, 10, and 11; 71% (SD = 15%) over 12-wk period	Very weak correlation with change in PA ($r = 0.10$, $P = .64$)
	Average no. of weeks participants were logged in	8.6 (SD = 3.0)	
Dlugonski et al (2011)[39]	% of participants logged in/wk	76% in week 1; 81% in week 2; 52% in weeks 10–12	Significant correlation between no. of weeks logged in and changes in accelerometer data ($r = 0.42$, $P = .03$) but not with changes in IPAQ ($r = 0.10$, $P = .32$) or GLTEQ ($r = 0.08$, $P = .36$)
	Average no. of weeks participants were logged in	7.5 (SD = 4.3) over 12 wk	
Dlugonski et al (2012)[17] (7 video coach sessions)	% of participants logged in/wk	~73% of participants logged in for ≥10 wk of 12-wk intervention	Weekly log-in was moderately and significantly correlated with change in weekly pedometer step counts between weeks 1 and 12 ($r = 0.43$, $P = .05$)
	Average no. of weeks participants were logged in	10 (SD = 2.7)	Negligible and nonsignificant correlation with weekly log-in and change in self-reported PA ($r = -0.03$, $P = .90$)
	Average no. of video coaching sessions attended	6.8 (range = 6–7) (77% of participants attended all 7)	
Motl and Dlugonski (2011)[40] (7 video coach sessions)	Average no. of weeks participants were logged in	10.6 (SD = 3) wk of 12-wk intervention	Moderate and significant correlations between weekly log-in and no. of coaching sessions attended ($r = 0.45$, $P < .05$) and between weekly log-in and change in GLTEQ score ($r = 0.51$, $P < .05$) but nonsignificant correlation between weekly log-in and change in IPAQ score ($r = 0.35$, $P = .08$)
	Average no. of video coaching sessions attended	6.6 (SD = 0.6) scheduled sessions	
Sandroff et al (2014)[1] (15 web-based video coach sessions)	% of participants who participated in:	Overall participation:	No further information regarding time points or possible correlations
	All intervention features	88.6%	
	Website log-in	80%	
	Uploading step counts	88.8%	
	Video coaching sessions	97%	
Tallner et al (2016)[30]	% of participants who documented at least 80% of the prescribed training program during:		
	Months 0–3	73%	Gradual decrease in participation from week 4 on
	Months 4–6	36%	Along with reduced participation, there was an increase in the dropout rate (14% during months 0–3; 39% during months 4–6)

[a] GLTEQ = Godin Leisure Time Exercise Questionnaire; IPAQ = International Physical Activity Questionnaire; PA = physical activity.

data from the follow-up single-group study[38] showed that 67% of the participants exceeded 7100 steps/day over 1 week—above the value suggested[42] to be required for accumulating 30 minutes of MVPA each day for older adults and special populations.

Participation in and maintenance of physical activity levels in the short and long term. Participation data were collected by 6 of the included studies and is summarized in Table 2. In the US behavioral intervention studies, participation in the early stages of the intervention[38,39] decreased during the intervention periods, but this was demonstrated to be improved by the addition of video coaching sessions during development of the intervention program.[1,17,40] These sessions were delivered one-to-one, online, in real-time, initially weekly and then with decreasing frequency over the intervention period. However, in the German exercise-based study, although web-based one-to-one support was available for each participant, participation in documented training sessions in the online activity journal declined after 4 weeks, falling to 36% of documented sessions after 3 months. However, it is not possible to establish if participants were continuing to exercise and not documenting their engagement with the program, or if they were no longer adhering to their exercise program.

Only 1 study[17] collected follow-up physical activity data (self-reported physical activity at 3 months) which demonstrated that the increase in physical activity after intervention ($P < .001$, $d = 0.98$) was sustained at 3 months ($P < .001$, $d = 0.79$).

Process Evaluation

Twelve of the 21 participants provided feedback in 1 study[39] and 21 of the 22 who completed the intervention in another.[17] Participants in both studies reported a high degree of satisfaction with the program as a whole, the staff involved, and an overall willingness to recommend the intervention to others. They reported less satisfaction with the intervention website, citing disinterest[39] in the online group chat sessions, and difficult to use forum section, as reasons for this and suggested that the program would benefit from more interaction with other participants.

Discussion

The purpose of this systematic review was to examine the effectiveness of web-based interventions in enabling people with MS to increase their physical activity levels. Further, to ascertain if any increases were in line with recommended levels for adults with MS[16] and were maintained at short- and long-term follow-up.[25] The review also set out to include a qualitative component, but as no studies were found that met the inclusion criteria, it is not possible to achieve this aim of the review. This finding is of interest in view of the potential benefit gained from engaging with intervention users when designing and developing effective interventions that people want to use long term.

Effectiveness in Enabling Increased Physical Activity Levels

The results of the meta-analysis of self-reported physical activity data demonstrated that web-based interventions had a moderate positive effect on physical activity in participants with mild disability. Self-report measures are recognized to have limitations in terms of social desirability and recall biases in their use.[53] Further, the GLTEQ measures only leisure-time exercise of longer than 15-minute duration and the Baecke Questionnaire sports score, only time in recognized sports; neither therefore capture the important shorter bursts of activity that people engage in as part of their usual activities of daily living throughout their day, or to accommodate disabling symptoms such as fatigue. To our knowledge, there are no established minimal clinically important differences for self-report measures of physical activity, and, hence, understanding the meaningful change also remains difficult. These issues highlight the importance of collecting more complete, objective data to accurately picture a person's daily lifestyle activity and help provision of the most appropriate physical activity advice.

Participants in all included studies had minimal disability, with a high percentage reporting no limitations to walking. Hence, it is not possible to comment on whether such interventions would be effective for people with higher levels of disability. Indeed, results from a secondary analysis of data from Pilutti et al[2] demonstrated a disability x time effect suggesting that their 6-month intervention was most effective for those whose mobility was least affected. Other analyses went further, suggesting a greater effect for people with relapsing-remitting MS and normal weight. In many countries, the population of people with MS who access health care systems have typically higher levels of disability and as such, this raises the question whether web-based interventions can also be beneficial for this group. Further, it may also challenge current practice, pointing to provision of physical activity promotion and rehabilitation input at earlier stages of the disease.

Participants from most of the included studies completed the Physical Activity Readiness Questionnaire,[54] a tool designed to help people evaluate their medical fitness prior to engaging in physical activity. Whilst fitness to exercise is very important, none of the studies asked participants about their attitude or readiness to engage in increased physical activity. It may be important to incorporate such questions prior to using such interventions in practice, where targeting a population ready to engage may have greater clinical and cost benefits.

Walking was the most common type of physical activity encouraged in the included studies. In order to describe the amount of activity undertaken at recommended levels, data were presented as steps per day or time spent undertaking MVPA. Those that reported time spent in MVPA calculated this according to defined cutoff points[1] of numbers of steps/minute that would equate to MVPA. It is suggested that for people whose disability levels are higher, the increased effort of walking[55] may mean that the number of steps/minute to reach MVPA is lower.[2,48] There is no available data regarding required numbers of steps per day for people with MS to achieve 30 minutes of MVPA, so reference is made to 7100 steps per day over 1 week, the figure obtained from the older adult and special groups literature.[49] For those people where it is too challenging to engage in sufficient walking to achieve health benefits, accessing other types of physical activity to achieve an adequate duration and intensity of activity is important.[1] This was incorporated into the Tallner[30] intervention, where choice of endurance activity included activities such as cycling, swimming, and cross training.

Achievement of Recommended Levels of Physical Activity

Physical activity guidelines for people with MS with mild to moderate disability recommend that people should aim to undertake 30 minutes of moderate intensity aerobic activity twice a week and progressive resistance training involving major muscle groups twice a week.[16] The findings of this review are such that it is not possible to suggest whether web-based interventions facilitate people with MS to meet these guidelines. Although some[17,39–41] of the 8 articles describing the US behavior intervention development included accelerometer or pedometer data (that could be used to estimate time undertaking MVPA), none report whether any of the web-based modules or coached sessions discussed or prescribed strength training. The final article[30] described a targeted exercise program including both strength and endurance components that could therefore have facilitated meeting recommendations, but do not present data as to whether prescribed levels were achieved, sufficiently intensive, or performed for long enough.

One of the potential benefits of a web-based intervention is that it may be used to help people maintain activity levels in the long term. As such, the issue of participation is an important one to consider. The importance of appropriate support to facilitate engagement with exercise is well recognized.[30,56] In the included studies, such support was provided by: experienced doctoral students (whose clinical background is not stated) in the behavioral intervention studies[17,40,41]; and physical therapists or exercise therapists in the targeted exercise intervention study.[30] The opportunity to engage with web-based support through a messaging service, with email and telephone options as required, did not appear to help participants adhere to the program in the latter study,[30] in which participation in documenting training sessions had already begun to decline after 4 weeks. However, during the development of the US behavioral intervention, the addition of web-based individual coaching sessions as part of the intervention was demonstrated to be instrumental in increasing participation.[17] It is perhaps the case, therefore, that planned, face-to-face sessions were key to the delivery of successful online support. This gives rise to the question as to whether it was the coaching itself or its role within the intervention package that made the difference. A further area of note is whether measuring participation as numbers of log-ins or attendance at a coaching session truly represents the level of engagement with an exercise program or indeed participation in increased physical activity.

Maintenance of Physical Activity Levels in the Short and Long Term

It is not possible to comment on whether the web-based interventions enabled people to sustain recommended levels of physical activity in the long-term due to the lack of data. Only 1 study[17] included any follow-up beyond the postintervention assessment and that was short term, at 3 months. The statistically significant increases in self-reported physical activity that remained at 3 months are promising, but longer-term follow-up data are required to enable thorough discussion of this issue.

Strengths and Limitations of This Review

One of the strengths of the review was that it set out to include both qualitative and quantitative studies of any design, not just randomized controlled trials. This systematic review has enabled clarification of the existing body of literature, which can be sometimes difficult given the wide-ranging publication sources. It has identified that, of the 9 articles published, there is multiple secondary reporting of a single study, resulting in 6 independent data sets (2 of which were single-group studies). It has identified that the included studies, in essence, report on just 2 different interventions. The web-based intervention inclusion criterion was chosen because of the very distinct role such interventions can provide and the specific challenges they present. This was in contrast to 2 previous technology based systematic reviews in MS[25,26] and resulted therefore in this focused review including only a small number of studies, which could be considered a limitation.

A further limitation of this study was that we chose not to include measures of effectiveness such as reduced blood pressure or weight loss. Although this was in keeping with our desire for the review to remain functionally focused, given the opportunity afforded by telehealth for remote monitoring of vital signs by patients, studies evaluating potential impact may have provided interesting additional evidence, specifically in relation to remote physical activity prescription, facilitation of participation, and progression of activity.

Conclusion

This systematic review suggests that web-based interventions have a positive effect on self-reported physical activity in the short term in people who have MS and are ambulant. There is insufficient evidence to comment on their effectiveness on objective physical activity data or whether increases in physical activity equate to disease specific or worldwide physical activity recommendations. Due to the lack of follow-up data, it is also not possible to suggest whether such interventions can have an effect on physical activity levels in the long-term. Similarly, it is not possible to comment on whether they can be effective for people with higher levels of disability, but it may be that web-based interventions have greatest impact on physical activity when used in the early stages of the disease.

Web-based interventions may be helpful in facilitating an increase in physical activity levels in people who have MS and are ambulant, at least in the short term. Evidence is not currently available to either support or refute the use of web-based interventions in enhancing physical activity levels in people who have MS and are not ambulant. The importance of the user experience should be considered in the on-going development and evaluation of web-based interventions in the MS population. Research into the short- and long-term effectiveness of such web-based interventions, especially for those with higher levels of disability, is required. Finally, determining the most effective support methods to maximize participation in web-based interventions is vital.

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Concept/idea/research design: R. Dennett, J.A. Freeman
Writing: R. Dennett, H. Gunn, J.A. Freeman
Data collection: R. Dennett
Data analysis: R. Dennett, H. Gunn, J.A. Freeman
Consultation (including review of manuscript before submitting): H. Gunn, J.A. Freeman

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Systematic Review Registration

Protocol CRD42016054084 was registered at http://www.crd.york.ac.uk/PROSPERO/.

Disclosure

The authors completed the ICJME Form for Disclosure of Potential Conflicts of Interest. The authors declared no conflicts of interest.

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Appendix.

Search Strategy[a]: Medline (Ovid) Search on September 22, 2016

Search	Query
1	multiple sclerosis [tiab] OR multiple sclerosis [Mesh] OR MS [tiab] OR neurological condition [tiab] OR neurology* [tiab]
2	Internet [mesh] OR "web based" [tiab] OR "Internet based" [tiab] OR telerehabilitation [tiab] OR telemedicine [tiab] OR www [tiab] OR "world wide web" [tiab] OR elearning [tiab] OR eHealth [tiab]
3	1 AND 2
4	"Physical activity" [tiab] OR exercise [tiab] OR "physical fitness" [tiab] OR walking [tiab] or "motor activity" [tiab] OR rehabilitation [tiab] OR physiotherapy [tiab]
5	3 AND 4

[a]Limits from 1990–current and English language.

2.1.2 Paper 2

Dennett R, Coulter E, Paul L Freeman J. A qualitative exploration of the participants' experience of a web-based physiotherapy program for people with multiple sclerosis: Does it impact on the ability to increase and sustain engagement in physical activity? Disability and Rehabilitation. 2019:1-8, 2019 https://doi.org/10.1080/09638288.2019.1582717

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ORIGINAL ARTICLE

A qualitative exploration of the participants' experience of a web-based physiotherapy program for people with multiple sclerosis: Does it impact on the ability to increase and sustain engagement in physical activity?

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ABSTRACT

Background: Web-based exercise and physical activity interventions are being developed as a potential way to help people with multiple sclerosis achieve and maintain increased physical activity levels. Seeking feedback from people who have used such interventions will help guide the development process.

Methods: In-depth interviews were used to explore the experiences of participants who used a web-based physiotherapy intervention as part of a feasibility randomized controlled trial. Interviews were audio-recorded, transcribed verbatim and analyzed using thematic analysis.

Results: Eleven people (age 28–68) were interviewed. Most perceived that their physical activity had increased, primarily due to completing twice-weekly web-based physiotherapy sessions. Three key themes were identified. 'It's all in one place' encompasses the value of having a convenient and portable program. 'Keeping an eye' captures people's thoughts regarding the supervision offered by the physiotherapist, through the website, and 'Hopes and expectations' reflects the importance of having opportunity to discuss what may be gained from using such a program.

Conclusions: This intervention offered a convenient, flexible and portable physiotherapy program which most people perceived helped them achieve and sustain increased levels of physical activity. Talking with people about expectations is important, particularly if a person's condition is deteriorating.

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Exercise; rehabilitation; telerehabilitation; internet-based; e Health

➤ IMPLICATIONS FOR REHABILITATION

- When discussing the potential benefits of exercise programs with people with multiple sclerosis it is important to have honest and open conversations about the expectations of what may be achieved. This is particularly important for people with progressive disease.
- Web-based interventions may be most valuable to people who are technology literate, seek flexibility regarding where and when to exercise, prefer to exercise independently and have the confidence and skills to self-manage.

Introduction

Achieving and maintaining recommended levels of physical activity is important yet challenging for many people with multiple sclerosis (MS). The use of targeted exercise programs and physical activity promotion have been demonstrated to lead to a range of physical [1–5] and emotional [6,7] benefits which may also extend to minimizing the complications and comorbidities associated with living a more sedentary lifestyle [8]. This has encouraged an increased emphasis within clinical practice to incorporate targeted exercise programs, and facilitate engagement with increased levels of physical activity [9]. In this study physical activity is considered in line with the Caspersen definition as 'any bodily movement produced by skeletal muscles that requires energy expenditure' [10] and as such enables participants to discuss all types of activity such as structured exercise and sport, but also lifestyle activity such as housework, gardening and employment.

Disease specific guidelines for people with MS [11] have helped guide physical activity prescription, particularly for those with mild to moderate disability, but the challenge to ensure adequate levels are sustained in the long term remains for individuals and those involved in their care. Current physical activity levels in people with MS remain low [12] and this concern has prompted research to identify factors that may have a positive influence on long-term participation. These include: choice of activity [13]; control over level of engagement; advice and support received; self-efficacy [14,15] and use of goal setting [16]. Evidence also describes some of the barriers to participation that people with MS experience, such as the effort and travel distance required to access rehabilitation venues, fatigue and lack of time [17].

The use of technology, such as the internet as a mode of delivery of exercise and physical activity interventions, is being increasingly trialed in many areas of healthcare to address some of these barriers. Two systematic reviews evaluating a wide variety of telerehabilitation interventions in MS provide a broad overview of their content, design and outcomes [18,19]. They suggest that this approach may be effective in increasing physical activity [18,19] in the short term, although compliance remains a significant issue [20–22] and an important factor to further explore.

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Table 1. Interview guide.

It has been a little while since you finished using the web based physiotherapy program … perhaps you can start by telling me what you thought of it?
Have you seen a physiotherapist before?
Prompt: One-to-one? Exercise program? Group? National Health Service?
Did web-based physiotherapy differ? How? Why?
As part of the WEBPaMS study you were asked to follow your program twice a week. Did you find you could stick to that? Prompt: What stopped/ helped you?
Did you manage to do any other physical activity as well as this?
Prompt; What do you do? Day to day routine? Around the house/ elsewhere?
Has using the web-based program made any difference to how active you are now?
Prompt: compare with activity prior to starting the program i.e. what did you do day to day? Exercise/ general activity? At home? Out and about? What do you think may have affected this?
Do you imagine using the website long term?
Prompt- key points in condition/ stepping stone/ with/out online support
Is there anything else you like to tell me about your experience of web-based physio?

Telephone interviews [23] and process evaluation questionnaires [23,24] have been previously used to explore the feasibility and acceptability of different web-based interventions and have provided researchers with areas of development on which to focus. Continuing to capture the user experience about issues broader than the operational aspects of the program, is likely to provide a deeper understanding of the factors that impact on the use of web-based interventions and may be instrumental in their further development.

This study aimed to explore the user experience of a web-based intervention which was part of a multi-centre randomized controlled feasibility trial of web-based physiotherapy ((WEBPaMS), registered at ClinicalTrials.gov (Identifier: NCT02508961)), and specifically, whether or not users perceived that it had impacted on their ability to increase and sustain engagement in physical activity.

Materials and methods

Ethical approval

Ethical approval for this study (15/WS/0030) was obtained from the West of Scotland Research Ethics Service, Glasgow. All participants gave written informed consent prior to taking part.

Research approach and methodology

A qualitative research approach was selected to address the aim of the study using a general qualitative inquiry design, underpinned by a pragmatic epistemology and a critical realism ontology. In-depth, individual, face-to-face interviews were undertaken with the participants allocated to the web-based program at one of the three main WEBPaMS study sites (Plymouth). Interviews were selected to gain depth of understanding about each participant's unique experience of the intervention and in order to explore this in light of their own individual circumstances. They were conducted at the participant's home (or preferred venue) using an interview guide (Table 1) which was developed and piloted with a person with MS who was unrelated to either this sub-study or the main WEBPaMS study. Open questions, with prompts as required, were used with sufficient flexibility to enable participants to raise issues they considered important. Interviews were conducted by the (female) primary researcher (RD, a PhD student and physiotherapist with 20 years clinical experience). Interviews lasted up to one hour, were audio recorded and transcribed verbatim. This study is reported in line with the COREQ guidelines [25].

Participants and intervention

Each of the WEBPaMS [26] intervention group participants at the Plymouth site were invited to participate in this sub-study. The entire WEBPaMS sample was not investigated for pragmatic reasons. This study was undertaken as part of the primary researcher's doctoral work exploring adherence to physical activity and physiotherapy programs and Plymouth was her location of residence. An invitation letter and participant information sheet were sent to the potential participants within one month of their final WEBPaMS follow-up assessment. Each gave consent and were interviewed within six weeks (range 1–6 weeks) of that final assessment. Inclusion criteria for the WEBPaMS study included; adults with a confirmed diagnosis of MS, known to an MS consultant in the study recruiting areas, an Expanded Disability Status Scale (EDSS) score of 4–6.5 (indicating mild to moderately impaired walking) and access to a personal computer/tablet or smart television with an email address and internet connection. Potential participants had been excluded if they were already taking part in regular exercise or physiotherapy (two or more times per week), had poor cognitive function as assessed by a Mini Mental State Examination Score (MMSE <24), had any significant change in medication or a relapse requiring treatment within the last 3 months, or any significant co-morbidities for which exercise was contra-indicated. They were also excluded if they were unwilling to be randomized to intervention/control group or were currently participating in another clinical trial (rehabilitation or pharmacological).

The main WEBPaMS study was a single blind randomized controlled feasibility study. Ninety participants from three centers were randomized to receive either a six-month individualized web-based exercise program ($n = 45$) (intervention) or a paper based exercise program ($n = 45$) (active comparator). All participants were assessed by a physiotherapist, had an individualized exercise program devised and were asked to complete it twice weekly. A range of outcome measures were completed at baseline, three months, six months and nine months (three month follow up). The active comparator group received their exercise program in paper format (www.physiotherapyexercises.com) and were asked to complete a paper exercise diary. The intervention group accessed their exercise program via a website (www.webbasedphysio.com). The website included exercises in video format with audio and text description along with MS specific exercise advice. Participants were requested to complete a diary entry after every session to indicate which of the exercises had been completed and to comment on any issues such as if the exercises were too hard or easy. The physiotherapist remotely reviewed the diaries every two weeks and was able to modify the exercise program in line with any feedback they had received. Participants were informed of any changes to their program via email and could contact the physiotherapist through the diary or via email or telephone at any point if required. Further information regarding the intervention can be found in the pilot [23] and main study [26] publications.

Data analysis and ensuring rigour

Data were analyzed using thematic analysis according to the six phase method of identifying and analyzing patterns in qualitative data described by Braun and Clarke [27] using a general inductive approach. Initially the audio recordings of each interview were listened to twice and transcripts were read and re-read in order for the researcher to become familiar with the data. Observations were noted on the transcriptions as appropriate during this stage and relevant codes were generated along with appropriate data extracts. The next stage of analysis involved the primary researcher considering and collating the codes by hand, rather than through use of a software package and making note of meaningful patterns in the data that were relevant to the research question. These were discussed with the other members of the research team (JF, LP and EC) on a number of occasions and used to create themes and subthemes that captured the essence of the participants' voice and worked in relation to the data set.

Themes and subthemes are presented using pseudonym quotes (with participant age and EDSS) to illustrate the participant view.

Rigour was enhanced during the process by ensuring an audit trail of the primary researcher's (RD) process. A second researcher (JF) independently coded and discussed in detail three of the transcripts with RD and the whole team was involved in reviewing each of the themes and subthemes. The principles of credibility, transferability and dependability were followed throughout [28]. Reflexivity was promoted by the primary researcher who is an experienced neuro-physiotherapist. Steps, such as completing a reflexive diary and regularly meeting with the research team were put in place to try and minimize the bias this would bring to interpretation of the data. A summary of the main themes was sent to participants for member checking. Responses indicated that the summary provided an accurate reflection of the interviews content.

Results

Eleven out of a possible 12 people were interviewed. One person did not respond to the initial invitation letter or to three further attempts to make contact by letter, email and telephone. Participants were 90% female with an age range 28– 68 years; time since diagnosis range 1–40 years and EDSS range 4–6.5. Disease course was: Relapsing Remitting [$n = 4$], Primary Progressive [$n = 1$] and Secondary Progressive [$n = 6$]. Three participants were employed, two unemployed and six were either retired or medically retired. Demographic information of participants is presented in Table 2.

Table 2. Demographic information of interview participants ($n = 11$).

Participant pseudonym	Gender	Age	EDSS	Disease course	Employment status
Mary	F	61	6.0	SPMS	Part time employed
Hannah	F	28	5.5	RRMS	Unemployed
Debbie	F	45	5.0	RRMS	Unemployed
Simon	M	63	6.5	SPMS	Retired/medically retired
Becky	F	54	6.5	SPMS	Retired/medically retired
Fay	F	68	6.5	SPMS	Retired/medically retired
Wendy	F	60	4.0	RRMS	Part time employed
Claire	F	65	6.0	SPMS	Retired/medically retired
Emily	F	48	6.0	RRMS	Retired/medically retired
Jane	F	59	4.5	SPMS	Retired/medically retired
Sarah	F	51	4.0	PPMS	Part time employed

EDSS: Expanded Disability Status Scale; F: female; M: male; RRMS: relapse remitting multiple sclerosis; SPMS: secondary progressive multiple sclerosis; PPMS: primary progressive multiple sclerosis.

Perceived impact on physical activity level

Nine of the 11 participants felt that their physical activity levels had increased over the study period. This was attributed to a variety of reasons including improved balance, confidence and general fitness, increased motivation to exercise, and being committed to the study protocol of completing the exercise program twice-weekly. One participant described an example of when she was more physically active which she attributed to the benefits she had experienced from engaging in the web-based program.

> "I picked up my daughter and we drove to [local town]; I got lost on the way but we got there. It took ages to get there … we walked all the way round [local town]. Oh my God. It is like really narrow, there's that little high street. So I had to walk up there. I probably stopped about three times. That's good for me. That is really good for me and that's quite a steep road and I made it all the way to the top."
>
> *Debbie (age 45, EDSS 5.0)*

Further exploration of the potential reasons for her improvement revealed that completing her exercise program had helped her to feel fitter and be able to achieve more, which in turn provided motivation to continue.

> Well that's [using web-based physio] what started me off isn't it? I wouldn't have bothered otherwise, would I, so yeah, I wouldn't honestly truthfully I wouldn't have bothered. That's what made me get up and go, "what, I can do it!"
>
> *Debbie (age 45, EDSS 5.0)*

Not everyone felt that their activity levels improved however. Two participants shared their thoughts regarding the impact that disease progression had had over the duration of the WEBPaMS study. Both noted a deterioration in their activity level, with one person, to the point that she was no longer able to walk. In this case the participant explained that although she was now not walking, having been able to make direct contact with the physiotherapist by reporting her difficulties on the online diary page, she was able to seek advice early, have her exercise program modified and was enabled to continue to exercise at a level she could manage. Without this, when her primary activity (walking) was no longer possible she would have had to contact her doctor and wait for referral for a physiotherapy appointment to discuss her situation. The participant's perception was that the program helped her to be more active than she would otherwise have been and noted that it was the timely remote support through the intervention that had facilitated this.

> Things had got to the point that I wasn't able to take my son to school, a friend was picking him up and another friend bringing him back because I was finding it too difficult to walk … so I was glad to have the exercise programme as well to make up for the lack of exercise that I was getting by not doing the school run, so that was quite good.
>
> *Becky (age 54, EDSS 6.5)*

Only two of the nine participants who perceived that their physical activity levels had improved described this in terms of walking further or more frequently. The majority reported that they had increased physical activity by completing the two web-based exercise sessions in addition to their usual weekly activity.

Themes and subthemes

Three key themes were identified from the participant experience data with specific regard to perceived impact on physical activity. They are: (1) "It's all in one place", (2) "Keeping an eye" and (3) "Hopes and expectations". Subthemes were also developed, some of which were linked to more than one of the themes.

Theme 1 "It's all in one place"

"It's all in one place" encompasses the value placed on having an easily accessed, portable and flexible individualized exercise program. These benefits were reported as important in helping participants use the intervention regularly, which in turn facilitated the increased physical activity they described.

Subtheme: Accessibility

Five participants reported that the ease of accessibility provided by having their exercise program accessed on their electronic device (e.g. computer, tablet, or phone) made it much more convenient. This meant they were more likely to complete their program, and in turn increase their physical activity that day. One participant [Hannah (age 28, EDSS 5.5)] commented: "the web is part of my life", reflecting that she used her electronic devices regularly.

Additional reasons were reported as to why ease of access was a benefit to participants. One participant described previous experience of having written paper exercise programs, which on occasions she had lost. She noted that having the program in one place (on her computer) not only meant she didn't have to worry about losing it, she had the added benefit of not having to physically struggle around the house to find where she had put it.

> I just find it quite difficult to manage lots of bits of paper which seems silly but I do, so having it online actually I found easier way to keep on track with it … papers do easily get lost, or dog-eared, or thrown away by mistake so it was good to have it all on computer in one place so you always know where your laptop is … Because it's there and easier to find and you're not faffing [colloquialism, struggling to get things together] around because of not being able to move very easily, I don't know, you value it more in a way.
>
> *Becky (age 54, EDSS 6.5)*

In some cases, when using their electronic device as part of their daily life, simply seeing the link website address to web-based physio prompted access to the site and completion of their exercise program.

> Well, if I'd have had a bit of paper and there wasn't the incentive to look on the website and um you know, I am fairly computer literate and I use the computer a lot and then you know it just becomes second nature to check and um and if I hadn't had that incentive it would have just been a bit of paper exercises I'd have put them or pinned them up on the wall and um then said oh I better do some exercises today as an after-thought. It wouldn't have been at the front of my mind … When I am on the computer, I see that and it incentivises me.
>
> *Simon (age 63, EDSS 6.5)*

One person reported that seeing the website link on her iPad motivated her to get out and walk more, so increasing her overall level of physical activity. At no point other than the very start of the study did she choose to access her web-based physio program on the website. For her, simply the visual prompt to exercise played a significant role.

> I've done a little bit more walking um, perhaps like popped into town on a day when I wouldn't have normally gone into town because I've seen it [the website link] and I've thought "oh, yeah, you know, I'd like to do that today" that's kind of helped me; reminded me to do some exercise … rather than sitting there like perhaps going on Facebook or something, going "well it's actually quite sunny and nice today, go out and take a walk".
>
> *Hannah (age 28, EDSS 5.5)*

One aspect of the program that some participants were less positive about was being asked to complete the online exercise diary to show what exercises had been done. Although the purpose was to enable the physiotherapist to remotely monitor and progress the exercise program this was not always completed, especially as people became more familiar with their exercises and did not rely as much on this aspect of the intervention. Two participants commented that once they had got to a stage where they were confident with their exercise program, they did not feel the need to access the website and as such it would have been helpful to have been able to go back to the website and add comments retrospectively rather than every time. These views were also reported by some of the participants who took part in exit interviews following the main study as part of the process of exploring the intervention feasibility and acceptability [26].

> Sometimes I did feel it was a bit annoying having to go back and do the ticking when you'd done your exercises like "oh right! Yes, need to do that part" as well so sometimes it could be a bit of a nuisance to think you had to do the filling in as well.
>
> *Becky (age 54, EDSS 6.5)*

The vast majority of the participants reported the intervention was easy to access however one noted difficulties setting up a link on her computer and suggested having an app to click on would have been easier.

> When I first started going on it I kept forgetting what the web address was and I kept having to go into the, I think it was in the email to the link to get on it cuz I couldn't remember what it was.
>
> *Debbie (age 45, EDSS 5.0)*

Subtheme: Flexibility

The opportunity to choose when and where to access the website was also reported as a benefit of this approach to delivering physiotherapy programs. Some people reported a preference to exercise in the privacy of their own home where they didn't experience embarrassment they had previously felt when exercising in front of others, In addition, flexibility in terms of exercising at a time that fitted with family life or around the presence of symptoms was described.

> If I was doing it in a group session, I would be conscious of being clumsy and messing up and something like that. At least at home, I am more comfortable at doing it at my own pace and my own way and then monitoring it. So I feel better doing it that way.
>
> *Simon (age 63, EDSS 6.5)*

> I don't particularly want to be part of a group um, I'm much happier doing at my own level and my own pace really um, and so that was good for me and it was good for me because I'm reasonably computer literate so it was easy, I did it on my phone …. It's difficult for me, not physically, to get to the same place regularly in the course of a week cos I just find work's quite, encroaches on my free time and also the children.
>
> *Sarah (age 51, EDSS 4.0)*

Literature suggests that to achieve the potential benefits of exercise, people with MS should be completing exercises at a challenging level [29]. For some people, the web-based program provided an opportunity to exercise in a safe and familiar environment where they felt able to challenge themselves and perhaps achieve increased benefits.

> I was in familiar surroundings, so I was able to push myself a bit more as well because of the surroundings I felt happy in my home … I knew where things were. You know, I did have wobbles when I was doing them [balance exercises] but it was great because I knew where everything was, so I could stop myself … whereas if I was doing that in a group and especially if I'd been in the middle of a group somewhere or something I'd have been right down on the floor. I didn't have to think, "oh I have to make the effort or I have got to make myself look presentable before I go out the door". I could just you know be in my jimjams [colloquialism pyjamas] if I wanted to do it, which was great, you know, it didn't really matter, you know. If I couldn't do one for any reason, or did it stupidly, or lost my balance or anything, it wasn't a problem because I was at home.
>
> *Emily (age 48, EDSS 6.0)*

For another participant, the flexibility of being able to exercise at home and with her children, was an important factor that helped her remain motivated to exercise.

> Me and my littlies [colloquialism, children], because they love exercising, they're really sporty and they've done it with me before when I've been upstairs in the bedroom and I've had it on and they've been doing exercises with me so they give me more incentive to do it then because they want to do it, "oh do your exercises mummy!"
>
> *Debbie (age 45, EDSS 5.0)*

In contrast, others reported missing the rapport and social aspect of exercising with others.

> I did miss the action of the [local MS exercise group], I do like the interaction with the group, it's the social side as much as anything isn't it?
>
> *Mary (age 61, EDSS 6.0)*

> There's nothing negative about it apart from the fact that it's just not social is it?
>
> *Debbie (age 45, EDSS 5.0)*

As such, it is perhaps the flexibility in choice of environment in which to exercise which is important. Facilitating choice of exercise was also reported as a benefit by some participants who liked being able to choose from their individualized program which exercises to do and when (perhaps encouraging self-management and reflection).

Subtheme: Portability

Portability was an issue raised as a benefit by three people. They each described situations where they had been able to continue using their exercise program when working away from home or traveling on holiday. Each suggested that their program worked well away from the house and that they would have been much less likely to have chosen to take a paper exercise program with them.

> You can take it with you because it's on your phone, and the first time I did it I put it on the iPad and we went away for the weekend and I thought it was great because I could do it, take it with me. It's been to Malta …. Tenerife, been to France.
>
> *Wendy* (age 60, EDSS 4.0)

> Having the website there, like I said at the beginning, is an incentive, whereas if you see a physio, you see the physio for a period and then you are left to go away and then it is up to you to ring them up again if you want more help and then again it is difficult to get appointments. It is accessible wherever I am. So even if you are travelling you can still access it.
>
> *Simon (age 63, EDSS 6.5)*

Theme 2: "Keeping an eye"

There were mixed views regarding the type and level of remote support provided by the physiotherapist through the website. Around half of the participants felt it was sufficient, suggesting that the support enabled discussion and progression of their exercise program and potentially facilitated longer-term engagement with it.

> I liked the fact that someone was keeping an eye so I wasn't doing something stupid [exercise technique] that, you know, I shouldn't have been doing, and also so that I knew that I would carry on doing it.
>
> *Mary (age 61, EDSS 6.0)*

> I always knew if I wanted to change something, all I had to do was contact the physio or write something in [the online diary] and they would respond. I'm quite independent in that way [choosing and modifying exercises], maybe that doesn't work for everybody but I think I'm quite, er, self-critical, you know, I can appraise what I'm doing quite well, quite honestly I think.
>
> *Sarah (age 51, EDSS 4.0)*

Others however did not feel that the support was sufficient to keep them engaged and resulted in them only accessing the site for four of the possible six months.

> [I needed someone] saying "Debbie, get on the website, you're doing really well, you need to exercise, don't give up". I'm one of those that needs a push all the time; that's the sort of person I am. It's the contact isn't it, it's the interaction I suppose [that wasn't enough].
>
> *Debbie (age 45, EDSS 5.0)*

One person discussed the importance of building a relationship with someone who could support and encourage them to continue to be active long-term. Her experience was that this did not happen for her through the website.

> When you're having like regular [face to face] physio more often, I think you're more likely to, or I personally am more likely to engage in your activities because you're, you're being reminded on a weekly basis by a, by a physio. but when you're not seeing a physio so often, it's hard to self-motivate yourself to do your exercises.
>
> *Hannah (age 28, EDSS 5.5)*

A related issue raised by three participants was that of the website allowing immediate access to a physiotherapist for advice regarding difficulties with an exercise or symptom. Each described previous experience of having to wait a considerable length of time to see a physiotherapist.

> If you see a physio, you see the physio for a period and then you are left to go away and then it is up to you to ring them up again if you want more help and then again it is difficult to get appointments.
>
> *Simon (age 53, EDSS 6.5)*

> Yeah some people would prefer that they don't have [only remote support] waiting perhaps several months for an appointment so they can have face to face contact. But for other people who are maybe more disabled and can't get there so easily or are perhaps working and haven't got the time they could just have a quicker contact with the physio.
>
> *Claire (age 65, EDSS 6.0)*

The most frequently reported aspects of the website that participants found helpful were the exercise videos, (in line with the pilot study [23]), and the opportunity to email for advice. This support enabled some participants to continue exercising without the need for face-to-face contact throughout the study.

> I think it's okay with the computer because as I say the videos are there for you to watch. If you didn't have that and you just had it written down as a diagram you might want to see the physio more in order that they could demonstrate to you what you are supposed to be doing.
>
> *Claire (age 65, EDSS 6.0)*

Further thoughts from participants suggested the potential benefit of such a system to the clinician, who could oversee and maintain close contact with many more patients rather than relying on face-to-face assessments.

> It would free up more time for the physio to see other people as well if they weren't constantly needing to have an appointment that lasted half an hour or something. If they could just be in touch with the person that had a problem they might be able to deal with it in five minutes rather than half an hour. They might know straight away what the problem is and say just do it this way instead and then it could be sorted out. I think it would free up their time more.
>
> *Claire (age 65, EDSS 6.0)*

Theme 3: Hopes and expectations

This particularly challenging theme highlighted that clinicians and researchers need to openly discuss and better understand people's hopes and expectations of the potential benefits of exercise and physical activity for them. Sarah described the emotional impact that not achieving what she had hoped for during the study.

> If I'm being brutally honest with myself, I think I've gone down even though I've been working quite hard and that has been quite hard [emotionally] I think. I think I'm quite good at burying my head in the sand … I didn't expect to feel the way I felt when I started doing it. I didn't expect that to be the way I would be feeling at say six, seven, eight months … maybe it's because I was coming to the end [of the study] and I haven't achieved what I thought I might.
>
> *Sarah (age 51, EDSS 4.0)*

One participant in particular clearly explained how disappointed she was in not seeing the improvements she had hoped for and how this had affected her motivation to continue. She challenged clinicians to consider how to manage her expectations more effectively.

> I thought that by doing the exercises I'd build up some stamina and I wouldn't have noticed it [fatigue] quite so much … but it was the fatigue … that was the annoying bit if you like, you know, I had hoped that I'd go through a barrier and come out the other side. I think it's the nature of the beast, perhaps it was my expectations that needed to be managed … because I carried on with it and did everything, but … .I always feel that I could be doing more, and then on some days when I try and do more I get disappointed because I haven't actually been able to do it. And I don't know whether that's because I'm judging myself on too high a standard or whether somebody should be behind me going "go on"," keep on" … . "Am I giving in to this?" "Should I be going that extra mile?" … do you know what I mean, how, how far do you push yourself?
>
> *Mary (age 61, EDSS 6.0)*

In contrast, being motivated to exercise and walk more in one case, and stick to, and progress their web-based program in another, helped two participants exercise beyond their own hopes and expectations.

> … it's um the like a rewarding process that when you get home you're like "actually I've done this today, I've walked this far" rather than just, kind of like, staying at home and perhaps watching something on tele so it's, it's been, yeah it, it's been quite nice actually.
>
> *Hannah (age 28, EDSS 5.5)*

> I've got the feeling that I'm actually doing more than I thought I could do.
>
> *Wendy (age 60, EDSS 4.0)*

Discussion

The purpose of this research was to explore the user experience of the web-based physio intervention and further, whether or not participants perceived it had impacted on their ability to increase and sustain engagement in physical activity. The interview data demonstrated that the majority of participants felt that the intervention had helped them achieve increased physical activity levels, typically by the addition of the twice-weekly web-based exercise sessions. This perception of having increased physical activity levels contrasts however with the objective accelerometry data from the main study which demonstrated a decline in steps per day over the nine month study period [26]. Such disparity between self-report and objective measures is well reported [30] and underlines the complexity of this issue, particularly in a progressive condition such as MS where physical activity levels fluctuate and where people's perspectives are constantly recalibrated as they adjust expectations within their changing context.

It is important to consider the role that factors other than the intervention itself may have played when considering perceived increase in activity. Some participants in this sub-study reported that it was their commitment to the study that was the motivator. However, having not interviewed the active comparator group participants it is not possible to know whether committing to the study provided a positive influence on their exercise behavior. Further research is required to better understand this.

Some strengths of this study are that it sought the experiences of people with all MS disease types and that of those with moderate as well as mild disability. Participants reported a variety of experiences of the intervention that do not appear to be related to disability level or indeed age, as demonstrated by the quotes from participants across the age spectrum (28, 54 and 63 years) regarding the accessibility of this intervention. The different opinions represented in this study highlight the importance of acknowledging that a variety of models of service delivery may be required to meet differing needs. Further, that discussing with people their preferences with respect to intervention and delivery type within the constraints of health service funding challenges is crucial.

In the first theme "All in one place", the subthemes of accessibility, flexibility and portability describe some of the benefits that participants in this study felt they gained from this intervention and go some way to address some of the reported barriers to exercise [13,15,17]. The qualitative data supports the notion that the intervention made it easier for some people to integrate regular exercise into their daily lives. The accounts of the participants also suggest that this mode of exercise program delivery may be particularly helpful for people who are technology literate, value flexibility in terms of location, time of day and choice of exercise, and who are confident to exercise at a challenging level independently. It may be that the ability to modify and progress exercise programs online result in these interventions being better able to deliver the ongoing change and challenge that is required to achieve positive clinical outcomes. This is yet to be determined in a definitive randomized controlled trial.

"Keeping an eye" was the second theme identified. For an intervention such as this to be effective in supporting people to be more physically active long-term, it is important for people to remain engaged. In this study, some participants reported that having their exercise diary monitored remotely and receiving timely support from the physiotherapist were important in maintaining adherence. Although each participant's web-based program was reviewed every two weeks, the amount of support each individual received depended upon the feedback they provided via their online diary, email or telephone. It is likely that this will have influenced their experience of the supervision received. Other studies describing the development of a different web-based intervention have demonstrated an improvement in adherence by the addition of video coaching sessions [24,31,32].

Whilst the views expressed by our participants regarding satisfaction with the level and type of support provided were mixed, with those most satisfied tended to also describe feelings of confidence in self-managing their condition. It appears that this intervention helped some people develop the confidence to exercise at a challenging level. Results from a nominal group study conducted as part of the development of a balance, safe mobility and falls management program for people with multiple sclerosis [33] identified that people may need significant encouragement and support to develop the confidence to undertake highly challenging balance exercise. For some people, this intervention may have facilitated this.

The important issues regarding the theme “hopes and expectations” draw focus on how best to support people with MS to be as physically active as possible. For some people this may be to achieve improvements such as getting fitter, walking further or gaining confidence but for others achievement may be in terms of minimizing the effects of disease progression on mobility. It is therefore imperative that clinicians and researchers attend to this range of expectations and consider carefully choice of outcomes when establishing programs such as this. In this study, some participants described the disappointment, frustration and distress experienced by not meeting their own, or what they perceived to be the clinician’s expectations. Similar issues were raised in other explorative studies in people with MS. One [34], in relation to a gaming intervention where some participants reflected negatively on their physical abilities and limitations in light of Nintendo Wii Fit feedback, and a second [35] evaluating a physical activity program, where issues of disappointment and frustration were described concerning the way in which their MS prevented them from being able to engage in pre-morbid activities. It is likely that on some occasions in this study, discussion regarding the expectations of the intervention by both the person with MS and the physiotherapist would have highlighted differences that could have been talked through and may not have led to the individuals becoming disappointed and demotivated by their lack of improvement.

Effective strategies are required to enable honest and open discussions especially when introducing the idea of exercise and its benefits to people with progressive disease. This is a key clinical area that warrants further exploration.

Limitations

There are a several limitations of this study. Firstly, participants knew the primary researcher (RD) through her role as the Plymouth site WEBPaMS intervention physiotherapist. This potentially may have resulted in participants feeling they needed to share experiences that were more positive. Secondly, all of the researchers are physiotherapists which will have influenced the reading and interpretation of data. Every attempt was made to explore all participant experiences through use of the interview guide and ensure the trustworthiness and credibility of the interpretation of the data by using several strategies to ensure decisions could be evaluated and defended [36]. Thirdly, only intervention group participants at one site were interviewed in this study as it was conducted as part of the doctoral work of the primary researcher. There is no reason to suggest however that there would be notable differences in data from either of the other two sites, and this was confirmed by the results of the process mapping exercise, which was undertaken as part of the feasibility trial [26]. Because the aim of the study was to explore user experience of the web-based physio intervention only intervention group participants were interviewed. Finally, the small numbers of participants in this study has the potential to limit its findings, however, the last two interviews did not add new themes to the data and as such, it is likely that data saturation had been reached.

Conclusion

The findings of this study demonstrate that most of the participants, perceived that the web-based physio had facilitated an increase in their day-to-day physical activity. Also highlighted is the importance of building in conversations with people with MS about expectations of exercise and its potential benefits, particularly for those whose condition is deteriorating. Finally, it is important to consider who will benefit most from a remotely delivered and monitored exercise program such as web-based physio. This data suggests that the target population may be those who are technology literate (or have a significant other who are), value the flexibility that such interventions can offer, prefer to exercise independently in an environment of their choice and have confidence and skills to self-manage without face to face contact.

Disclosure statement

No potential conflict of interest was reported by the authors.

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2.2 Standing frame programme stream

2.2.1 Paper 3

Freeman J, Hendrie W, Jarrett L, Hawton A, Barton A, Dennett R, Jones B, Zajicek J, Creanor S. Assessment of a home-based standing frame programme in people with progressive multiple sclerosis (SUMS): A pragmatic, multi-centre, randomised, controlled trial and cost-effectiveness analysis. The Lancet Neurology. 2019:18(8) 736-747.

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Assessment of a home-based standing frame programme in people with progressive multiple sclerosis (SUMS): a pragmatic, multi-centre, randomised, controlled trial and cost-effectiveness analysis

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Summary

Background People severely impaired with progressive multiple sclerosis spend much of their day sitting, with very few options to improve motor function. As a result, secondary physical and psychosocial complications can occur. Effective and feasible self-management strategies are needed to reduce sedentary behaviour and enhance motor function. In this study, we aimed to assess the clinical and cost effectiveness of a home-based, self-managed, standing frame programme.

Methods SUMS was a pragmatic, multicentre, randomised controlled superiority trial of people with progressive multiple sclerosis and severe mobility impairment, undertaken in eight centres from two regions in the UK. The study had assessor-blinded outcome assessments with use of clinician-rated and patient-rated measures at baseline, 20 weeks, and 36 weeks. After baseline assessment, participants were randomised (1:1) by computer-generated assignment to either a standing frame programme plus usual care or usual care alone. The intervention consisted of two home-based physiotherapy sessions (60 min each) to set up the standing frame programme, supported by six follow-up telephone calls (15 min per call). Participants were asked to stand for 30 min, three times per week over 20 weeks, and encouraged to continue in the longer term, although no further physiotherapy support was provided. The primary clinical outcome was motor function measured by the Amended Motor Club Assessment (AMCA) score at week 36, analysed in the modified intention-to-treat population (excluding only patients who were deemed ineligible after randomisation, those who withdrew from the trial and were unwilling for their previously collected data to be used, or those who did not provide baseline and week 36 measurements). A 9-point AMCA score change was considered clinically meaningful a priori. Adverse events were collected through a daily preformatted patient diary throughout the 36 weeks and analysed in the modified intention-to-treat population. An economic assessment established the resources required to provide the standing frame programme, estimated intervention costs, and estimate cost effectiveness. This trial is registered with the International Standard Randomised Controlled Trials, number ISRCTN69614598.

Findings Between Sept 16, 2015, and April 28, 2017, 285 people with progressive multiple sclerosis were screened for eligibility, and 140 were randomly assigned to either the standing frame group (n=71) or the usual care group (n=69). Of these, 122 completed the primary outcome assessment (61 participants in both groups) for the modified intention-to-treat analysis. The use of the standing frame resulted in a significant increase in AMCA score compared with that for usual care alone, with a fully adjusted between-group difference in AMCA score at 36 weeks of 4·7 points (95% CI 1·9–7·5; p=0·0014). For adverse events collected through patient diaries, we observed a disparity between the two groups in the frequency of short-term musculoskeletal pain (486 [41%] of 1188 adverse events in the standing frame group *vs* 160 [22%] of 736 adverse events in the usual care group), which was potentially related to the intervention. The musculoskeletal pain lasted longer than 7 days in five participants (two in the standing frame group and three in the usual care group). No serious adverse events related to the study occurred. The standing frame group had a mean 0·018 (95% CI −0·014 to 0·051) additional quality-adjusted life-years (QALYs) compared with those of the usual care group, and the estimated incremental cost-per-QALY was approximately £14 700.

Interpretation The standing frame programme significantly increased motor function in people with severe progressive multiple sclerosis, although not to the degree that was considered a priori as clinically meaningful. The standing frame is one of the first physiotherapy interventions to be effective in this population. We suggest that the programme is feasible as a home-based, self-managed intervention that could be routinely implemented in clinical practice in the UK.

Funding UK National Institute of Health Research.

Research in context

Evidence before this study

We searched electronic databases (MEDLINE, AMED, CINAHL, Embase, PsycINFO, and PEDro) for manuscripts published in English and with study populations aged older than 18 years, from database inception to Aug 1, 2018. Search terms were "multiple sclerosis" and "standing frames", "standing tables", or "standing wheelchairs". We also checked the reference lists from identified papers and searched ClinicalTrials.gov and the International Standard Randomised Controlled Trials registry. No adequately powered randomised controlled trials assessing the clinical or cost effectiveness of a standing intervention were identified. Our search revealed one systematic review of standing in people with upper motor neuron disorders that cited a small pilot randomised trial in people with multiple sclerosis (n=6) and one mixed-methods study (AB case study design plus interviews, n=9), neither of which exclusively recruited people with progressive multiple sclerosis. To our knowledge, no randomised controlled trials of standing frame use in people with multiple sclerosis have been undertaken since our literature search.

Added value of this study

To our knowledge, the SUMS study is the largest randomised controlled trial assessing physical rehabilitation in people with progressive multiple sclerosis. It is the first assessor-blinded, multicentre, randomised trial to investigate the clinical and cost effectiveness, safety, and tolerability of a supported standing frame programme plus usual care versus usual care alone in people with progressive multiple sclerosis whose standing balance and walking is severely impaired. The standing frame programme was well tolerated in people with multiple sclerosis who were unable to walk or whose mobility was limited to a maximum of 20 m with a bilateral walking aid. The standing programme significantly increased motor function in people with progressive multiple sclerosis, although not to the degree that was considered a priori as clinically meaningful.
The response of participants varied regarding standing but, on average, longer standing times were associated with significantly greater improvements in motor function, with the confidence intervals containing the a priori clinically meaningful improvement. Our cost-effectiveness analysis showed that the standing frame programme had an estimated incremental cost of approximately £14 700 per quality-adjusted life-year (QALY) and a 0·52 to 0·61 probability of being cost effective at the National Institute of Health and Care Excellence threshold of £20 000–30 000 per QALY.

Implications of all the available evidence

The use of a home-based, self-managed standing frame programme could improve motor function in individuals with progressive multiple sclerosis. Our study is an important addition to the evidence-base for supported standing, for which high-level evidence is currently lacking.

Introduction

Multiple sclerosis is a progressive, neurological condition that affects 2·5 million people worldwide. The disease impacts all aspects of patients' lives, having substantial and adverse effects on quality of life. Multiple sclerosis is associated with high direct and indirect costs to patients, their families, and society. These costs are highly correlated with increasing immobility.[1]

Mobility is a major concern for people with multiple sclerosis.[2] It is estimated that, within 10–15 years of diagnosis, approximately 80% of people will have impaired mobility. Eventually, an estimated 25% of patients are wheelchair dependent.[3] Mobility spans more than walking, including also standing, transferring, and moving in bed.[4] These are important activities for maintaining independence, particularly for people who are severely physically impaired. Individuals with progressive multiple sclerosis spend much of their day sitting,[5] often with reduced ability to change position. In response, insidious but preventable secondary complications can occur, including muscle wasting, reduced skin integrity, spasms, constipation, depression, and lowered self-esteem.[6] These problems can compound the primary neurological disability, accelerating loss of independence, and can even be mistaken for disease progression. Furthermore, long periods of sitting time are associated with increased risks of morbidity and mortality.[5] The clinical importance of these issues is underlined by their consistent prominence in policy documents for long-term neurological conditions.[6,7]

Strong evidence exists that increases in physical activity can improve mobility and minimise secondary health problems in people with mild to moderate multiple sclerosis,[8] and evidence suggests that this might also be the case for people with severe multiple sclerosis.[9,10] Despite this evidence, up to 78% of people with multiple sclerosis do not participate in meaningful physical activity.[11] There can be considerable barriers to keeping active when mobility impairment is severe.[12] Interventions have typically been resource intensive, entailing regular supervised sessions by a physiotherapist or sports therapist, in an outpatient or hospital setting, and relying on expensive equipment that cannot be used in the home environment.[9,10] Moreover, more data are needed regarding adherence when supervision ceases.

Finite health-care resources mean that ongoing supervision of physical activity programmes is rarely possible. Effective self-management strategies, which are low cost and realistic to implement, are needed for people with severe physical limitations to optimise their engagement in physical activity. Regular supported standing with use of standing frames, which can be used within people's homes, is one such option. Standing frames enable individuals with restricted mobility, balance, or lower limb or trunk control the opportunity to spend time in supported standing. Proposed benefits of standing include strengthening antigravity muscles, providing prolonged weight-bearing muscle stretch, enhancing respiratory function, and maintaining bone density.[8] Although preliminary evidence has shown benefit for their use in people with multiple sclerosis,[11–15] no appropriately powered randomised controlled trials have been done. In line with the conclusions of a systematic review[8] that such evidence was needed, we aimed to assess whether a home-based standing frame programme was clinically effective and to explore its cost-effectiveness in people with severe, progressive multiple sclerosis.

Methods

Study design and participants

The trial methods, previously published in detail,[16] are briefly described in line with existing guidelines.[17–20] The SUMS study was an individually randomised, controlled, pragmatic, multi-centre, superiority trial with masked outcome assessments in people with progressive multiple sclerosis. Participants were randomly assigned to receive either usual care or usual care plus a standing programme, with masked assessments done at baseline, 20 weeks post-randomisation (aligned with the end of the protocol intervention period for those allocated to the intervention group), and again 16 weeks afterwards (36 weeks post-randomisation).

For the Oswestry standing frame see http://www.oswestry-frames.co.uk/

Participants were recruited through eight health-care organisations, including the UK National Health Service (NHS) Trusts, social enterprises, and third sector multiple sclerosis therapy centres, in two regions (Devon–Cornwall and East Anglia) of the UK. Individuals were invited consecutively until the allocated number of standing frames (dependent on commissioning costs) at each health-care organisation had been reached. Key inclusion criteria were age older than 18 years, a diagnosis of progressive multiple sclerosis (primary or secondary) according to McDonald's criteria,[21] and a score of 6·5–8·0 on the Expanded Disability Status Scale (EDSS). Key exclusion criteria were being within 3 months of ceasing a multiple sclerosis disease-modifying drug, receiving steroid treatment within the preceding month, or participating in another clinical trial. Full inclusion and exclusion criteria are reported in the protocol paper.[16]

This study was ethically approved by the NHS Health Research Authority Committee South West—Frenchay Research Ethics Committee (15/SW/0088). Participants provided written informed consent before enrolment or undertaking any study-related procedures.

People with multiple sclerosis were actively involved throughout the study, including in the development of the research questions, study design, trial management and steering groups, writing of study materials, and dissemination activities.

Randomisation and masking

The 1:1 allocation sequence was done with random-sized permuted blocks, stratified by region (Devon–Cornwall or East Anglia) and baseline EDSS score (≤7·0 or ≥7·5). The sequence was computer generated in conjunction with an independent statistician who had no further involvement in the trial. The randomisation list and the programme that generated it were stored in a secure network location within the Peninsula Clinical Trials Unit, registered with the UK Clinical Research Collaboration, accessible only to those responsible for providing the system. Participants were randomly assigned after baseline assessment, with the masked assessor inputting the participant details directly into the randomisation website.

It was not possible to mask trial participants, carers, or treating physiotherapists because of the nature of the intervention. However, outcome assessors (research therapists) were masked to treatment allocation, and all assessments were done independently and away from the participant's home. At each assessment timepoint, research therapists were asked whether they were unmasked to group allocation; 114 (89%) of 128 answers at week 20 and 110 (87%) of 126 at week 36 were "no". The trial statisticians were masked for the primary analysis of the primary outcome.

Procedures

Participants allocated to the standing frame group were issued with a wooden Oswestry standing frame (Theo Davies & Sons, Wrexham, UK), funded through the UK NHS commissioning process and delivered to the participant's home before the first physiotherapy session. The person with multiple sclerosis and their standing assistant (typically their spouse) engaged in two face-to-face, home-based, 60-min physiotherapy sessions, aimed at setting up, implementing, and progressing the standing programme according to ability, supplemented by online advice and DVDs. These were supported by six scripted telephone calls (15 min per call) that used a behaviour-change approach[22] to increase the participant's self-efficacy, intended to enhance long-term engagement.

In line with previous research,[14] participants were asked to stand in the frame for 30 min three times per week over 20 weeks, and to record the frequency and duration of each stand in a daily diary. This allowed for a graduated introduction to standing. At the end of the 20-week period, participants were encouraged to continue to regularly stand, although no further physiotherapy support was provided. On trial completion, participants were able to keep the frame, providing they used it at least once per week.

The use of standing frames is a recognised core skill for UK-trained neurological physiotherapists. To standardise and optimise implementation of the intervention, we provided educational materials and assessed fidelity to them.[16] All participants received their usual health and social service input throughout the study period.[16] This input was recorded on a self-report health-care and social-care resource form, which included changes in medication.

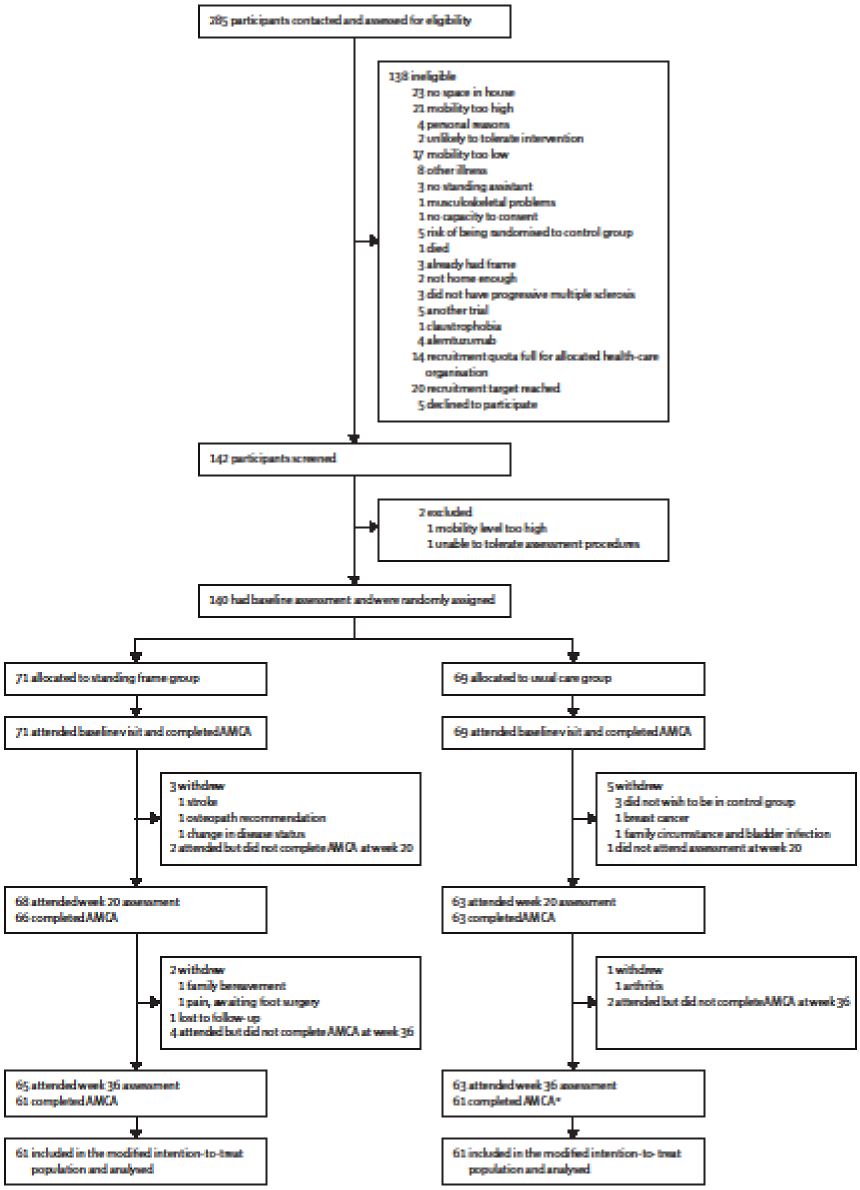

Figure 1: Trial profile
AMCA=Amended Motor Club Assessment. *One participant did not attend the 20-week assessment but resumed for week 36.

	Standing frame group (n=71)	Usual care group (n=69)	All (n=140)
Age, years	58·5 (51·3–66·4)	60·1 (54·1–66·0)	59·6 (52·6–66·2)
Mean EDSS score (SD; range)	7·3 (0·6; 6·5–8·0)	7·2 (0·6; 6·5–8·0)	7·3 (0·6; 6·5–8·0)
6·5	24 (34%)	18 (26%)	42 (30%)
7·0	11 (15%)	17 (25%)	28 (20%)
7·5	11 (15%)	16 (23%)	27 (19%)
8·0	25 (35%)	18 (26%)	43 (31%)
Sex			
Men	31 (44%)	19 (28%)	50 (36%)
Women	40 (56%)	50 (72%)	90 (64%)
Type of multiple sclerosis			
Primary progressive	28 (39%)	16 (23%)	44 (31%)
Secondary progressive	43 (61%)	53 (77%)	96 (69%)
Most recent relapse			
>1 year	62 (87%)	63 (91%)	125 (89%)
Within 3 months	2 (3%)	2 (3%)	4 (3%)
Within 6 months	2 (3%)	0	2 (1%)
Within 12 months	1 (1%)	2 (3%)	3 (2%)
Unknown	4 (6%)	2 (3%)	6 (4%)
Occupation			
Unemployed	5 (7%)	3 (4%)	8 (6%)
Student	0	1 (1%)	1 (1%)
Part-time work	2 (3%)	7 (10%)	9 (6%)
Full-time work	1 (1%)	1 (1%)	2 (1%)
Retired due to age	7 (10%)	8 (12%)	15 (11%)
Medically retired	56 (79%)	49 (71%)	105 (75%)
Indoor walking aid			
One stick	3 (4%)	2 (3%)	5 (4%)
Two sticks	7 (10%)	8 (12%)	15 (11%)
Frame	27 (38%)	30 (43%)	57 (41%)
Wheelchair	47 (66%)	48 (70%)	95 (68%)
Outdoor walking aid			
One stick	2 (3%)	2 (3%)	4 (3%)
Two sticks	6 (8%)	6 (9%)	12 (9%)
Frame	11 (15%)	15 (22%)	26 (19%)
Wheelchair	67 (94%)	64 (93%)	131 (94%)
Wheelchair use			
None	4 (6%)	4 (6%)	8 (6%)
Occasionally	4 (6%)	3 (4%)	7 (5%)
Monthly	2 (3%)	1 (1%)	3 (2%)
Weekly	13 (18%)	10 (14%)	23 (16%)
Daily	48 (68%)	51 (74%)	99 (71%)
Medical History			
None of note	14 (20%)	13 (19%)	27 (19%)
Osteoarthritis	6 (8%)	9 (13%)	15 (11%)
Coronary heart disease or hypertension	15 (21%)	9 (13%)	24 (17%)
Diabetes	8 (11%)	1 (1%)	9 (6%)
COPD	6 (8%)	1 (1%)	7 (5%)
Migraine	7 (10%)	5 (7%)	12 (9%)
Other neurological condition	4 (6%)	3 (4%)	7 (5%)
Depression	27 (38%)	30 (43%)	57 (41%)
Osteoporosis	5 (7%)	8 (12%)	13 (9%)
Other	25 (35%)	23 (33%)	48 (34%)

Data are n (%) or median (IQR), unless otherwise specified. EDSS=Expanded Disability Status Scale. COPD=chronic obstructive pulmonary disease.

Table 1: Demographic data and baseline characteristics

Outcomes

Validated outcome measures included clinician-rated assessments and self-reported questionnaires. The primary outcome was motor function as measured by the Amended Motor Club Assessment (AMCA) score[22] at the primary endpoint of 36 weeks post-randomisation. This score was developed for use by physiotherapists in a clinical setting to assess motor function in people with multiple sclerosis and has shown validity, reliability, and responsiveness.[14,23,24] The AMCA score (range 0–76) is the sum of two subscores. The functional activity subscore (16 items, each scored 0–3) comprises key functional activities of the trunk and lower limbs, such as rolling in bed, sit-to-stand, and sitting and standing balance. The lower limb movement subscore (14 items, each scored 0–2) rates motor impairment by grading hip and knee flexion and knee flexion and dorsiflexion in lying, sitting, and standing positions.

The secondary outcomes, at weeks 20 and 36, were measurements of explanatory physical impairments (length of hip flexors, hamstrings and ankle plantar flexors [manual goniometry], knee extensor strength [hand-held dynamometer], spasm frequency [Penn Spasm Frequency Scale], and forced expiratory volume at 1 s [hand-held spirometer]);[8] clinical outcomes (bowel and bladder control [bladder and bowel control scales], sitting balance [modified functional reach in sitting], and falls frequency); and quality of life (29-item Multiple Sclerosis Impact Scale [MSIS-29, version 2]). AMCA score at week 20 and the two AMCA subscores at week 36 were also measured as secondary outcomes. Participants were classified as fallers if they self-reported falling on 2 or more days during three different periods: up to week 20, up to week 36, and between weeks 21 and 36.

All participants were asked to record new symptoms, falls, and medication changes in a daily preformatted diary. Intervention participants were asked to record frequency and duration of standing sessions and any adverse events they had. A serious adverse event was defined as an untoward occurrence that resulted in death, was life-threatening, required hospital admission, or was

	AMCA score for standing frame group (n=71)		AMCA score for usual care group (n=69)		AMCA score for compliers		AMCA score for non-compliers plus usual care group		Fully adjusted analysis, mean difference (95% CI)*	Analysis adjusted for baseline alone, mean difference (95% CI)
	Baseline	Week 36	Baseline	Week 36	Baseline	Week 36	Baseline	Week 36		
mITT analysis	26·1 (13·9; 3·0–59·0; n=71)†	29·3 (17·2; 1·0–68·0; n=61)†	30·2 (14·6; 6·0–66·0; n=69)†	28·2 (17·0; 0·0–68·0; n=61)†	..	..	..	..	4·7 (1·9–7·5); p=0·0014	4·6 (1·6–7·6); p=0·0030
CACE analyses										
Best 16 weeks	..	..	..	..	26·2 (13·7; 3·0–56·0; n=49)†	29·9 (16·0; 6·0–65·0; n=46)†	29·1 (14·6; 6·0–66·0; n=91)†	28·4 (17·5; 1·0–68·0; n=76)†	6·1 (2·5–9·8); p=0·00094	6·1 (2·2–9·9); p=0·0020
Worst 16 weeks	..	..	..	..	28·2 (13·4; 8·0–56·0; n=36)†	31·6 (16·4; 8·0–65·0; n=35)†	28·1 (14·7; 3·0–66·0; n=104)†	27·9 (17·1; 1·0–68·0; n=87)†	7·9 (3·1–12·8); p=0·0013	7·9 (2·8–13·0); p=0·0025
Weeks 5–20	..	..	..	..	26·7 (14·0; 3·0–56·0; n=46)†	30·5 (15·9; 6·0–65·0; n=43)†	28·8 (14·5; 6·0–66·0; n=94)†	28·1 (17·5; 1·0–68·0; n=79)†	6·5 (2·6–10·4); p=0·0010	6·5 (2·3–10·6); p=0·0022
Best 32 weeks	..	..	..	..	26·6 (14·0; 3·0–56·0; n=46)†	32·4 (16·6; 6·0–65·0; n=43)†	32·4 (16·6; 6·0–65·0; n=43)†	28·0 (14·5; 6·0–66·0; n=94)†	6·5 (2·7–10·4); p=0·00077	6·5 (2·4–10·5); p=0·0016
Worst 32 weeks	..	..	..	..	28·4 (13·9; 8·0–56·0; n=36)†	32·4 (16·6; 6·0–65·0; n=35)†	28·0 (14·5; 3·0–66·0; n=104)†	27·5 (16·9; 1·0–68·0; n=87)†	7·9 (3·1–12·7); p=0·0013	7·8 (2·8–12·9); p=0·0025
Weeks 5–36	..	..	..	..	27·3 (13·8; 3·0–56·0; n=42)†	31·9 (15·7; 6·0–65·0; n=41)†	28·5 (14·6; 4·0–66·0; n=98)†	27·5 (17·4; 1·0–68·0; n=81)†	6·8 (2·8–10·8); p=0·00078	6·8 (2·6–11·0); p=0·0016

Data are mean (SD; range), unless otherwise specified. Mean differences in both analyses are between the standing and usual care group. *Adjusted for baseline AMCA Score, region and Expanded Disability Status Scale category. †n is the total number of participants who provided data at that timepoint.

Table 2: Primary outcome of Amended Motor Club Assessment (AMCA) scores at 36 weeks: primary modified intention-to-treat (mITT) analysis and Complier Average Causal Effect (CACE) sensitivity analyses

considered medically significant by the investigator. An embedded qualitative component explored the contemporaneous subjective experiences of using a standing frame within daily life through audio-recorded diaries by a subgroup of intervention participants. These data will be reported in a future publication.

Statistical analysis

The target sample size was based on comparing AMCA scores at week 36 between allocated groups, adjusting for baseline AMCA score, and detecting a minimal clinically important difference of 9 points, assuming an estimated SD 20 for AMCA score and estimated correlation of 0·55 between baseline and week 36 AMCA scores.[illegible] The detection of a 9-point between-group difference with 80% power and at a 5% significance level required follow-up data from 55 participants per group. We allowed for 20% loss to follow-up or non-completion of primary outcome and set the recruitment target at 140 participants.

The analyses were pre-specified in a statistical analysis plan approved by the trial steering committee before analysis started, except for the analysis method for spasm frequency. Primary analyses were adjusted for the stratification factors (region and baseline EDSS) as fixed effects and baseline scores where appropriate (ie, fully adjusted models); results adjusted for baseline scores alone are also presented. Estimated between-group differences are presented with two-sided 95% CIs, with the two-sided significance level for hypothesis testing set at 5%. The analyses were done with Stata SE (version 14.2).

The primary analysis population was defined as all participants who completed baseline and 36-week assessments. The primary analysis of the primary outcome, AMCA score at 36 weeks, followed a modified intention-to-treat approach, regardless of compliance to the intervention, but did exclude patients who were deemed ineligible after randomisation, those who withdrew from the trial and were unwilling for their previously collected data to be used, or those who did not provide baseline and week 36 measurements (ie, there was no imputation of missing baseline or week 36 scores for the primary analysis), and used an analysis of covariance (ANCOVA) approach. As prespecified in the statistical analysis plan, Complier Average Causal Effect (CACE) sensitivity analyses were done on the 36-week AMCA scores. This method provides an unbiased estimate of the intervention effect, based on participants who complied with the standing intervention protocol.[illegible] The agreed statistical analysis plan listed six compliance definitions that could trigger a CACE analysis[illegible] (appendix p 2). If at least 20% of participants allocated to the intervention group were classed as non-compliers in the definition. The CACE analysis, triggered

For the statistical analysis plan see https://www.plymouth.ac.uk/research/surrs

See Online for appendix

	Standing frame group (n=71)	Usual care group (n=69)
Adverse events lasting <7 days	1188	736
Pain	551	180
Categorised according to organ classification*		
Musculoskeletal	486	160
Neurological	16	12
Abdominal	9	6
Gynaecological	0	2
Renal	2	0
Respiratory	1	0
Spasms	231	197
Fatigue	60	184
Urinary tract infection	45	36
Numbness or sensory disturbance	41	33
Tremor or shaking	7	24
Weakness	24	23
Constipation or diarrhoea	7	17
Vertigo	22	9
Virus	31	5
Chest infection	16	5
Leg or back stiffness or tightness	23	2
Headache	3	3
Visual disturbance	3	3
Seizures	0	2
Balance problems	5	2
Loss of bladder control	0	2
Slurred speech	0	1
Multiple sclerosis relapse	1	1
Confusion	0	1
Rash	0	1
Toe infection	0	1
Shingles	0	1
Bladder spasms	2	1
Blood in urine	0	1
Nausea or vomiting	2	1
Low sodium	1	0
Ankle swelling	4	0
Depression	1	0
Shortness of breath	3	0
Tennis elbow	1	0
Low blood pressure	3	0
Bruising	1	0
Participants reporting adverse events lasting ≥7 days (number of participants)	28	21
Urinary tract infection	10	4
Chest infection	10	5
Nervous system	4	6
Spasms	2	4
Fatigue	2	1
Weakness	0	1
Stiff legs	1	0
Bowel difficulties	0	3
Infection	1	0
Psychiatric (depression)	1	0
Musculoskeletal pain†	2	3

*Pain categorised according to the MedDRA organ classification system. †Usual care group: coccyx pain (lasting 18 days), heel pain (9 days), and hip pain (22 days); standing frame group: back pain (lasting 11 days) and joint ache (14 days).

Table 3: Self-reported adverse events (new symptoms) according to allocated group

for all six definitions, used two-stage least squares instrumental variable regression, with treatment allocation as the instrument for the binary compliance variable and adjustment for baseline AMCA score, region, and EDSS category.[23]

A repeated-measures model was fitted to the post-baseline AMCA scores, including adjustment for baseline AMCA score, stratification variables, and the interaction term between allocated group and timepoint. Between-group pairwise comparisons at 20 and 36 weeks were calculated with use of marginal linear predictions and CIs from the fitted model.

All secondary outcomes were analysed on a modified intention-to-treat basis, with an ANCOVA approach, for both fully adjusted models and models with adjustment for baseline measures alone, except spasm frequency and falls. Ordinal logistic regression was prespecified for the analysis of the 5-level Penn Spasm Frequency Scale; however, because of insufficient numbers in some of the response categories, a dichotomisation of no spasms–mild spasms versus infrequent spasms–more than 1 per h–more than 10 per h was agreed. We used logistic regression to analyse the dichotomised Penn Spasm Frequency Scale and the binary outcome of fallers–non-fallers with adjustment for stratification factors.

We did a within-trial cost-effectiveness analysis. This estimated the additional costs of delivering the intervention, costs associated with health, social care, carer and patient resource use, and quality-adjusted life-years (QALYs) over the 36-week trial period. QALYs were estimated with use of self-report EQ-5D-5L (the five-level version of EQ-5D, a standardised generic instrument for measuring health status) data collected at baseline and at 20-week and 36-week follow-up, and by applying the so-called cross-walk algorithm[3] to provide QALY weights from the UK general population valuation survey of the three-level version of EQ-5D.[4] The primary perspective was the UK NHS and Personal Social Services (PSS), with a broader societal perspective considered in sensitivity analyses. Detailed methods are provided in the appendix (pp 3–9).

This trial is registered with the International Standard Randomised Controlled Trials, number ISRCTN69614598.

Role of the funding source

This was an investigator-initiated study. The sponsor and funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to all the data in the study and responsibility for writing the manuscript. The corresponding author had final responsibility for the decision to submit for publication.

Results

Between Sept 16, 2015, and April 28, 2017, we screened 285 potential participants. After screening, 140 participants were randomly assigned to either use a standing frame in addition to usual care (n=71) or to usual care alone (n=69; figure 1). Baseline characteristics were broadly consistent across the allocated groups (table 1). Some imbalances in sex and type of multiple sclerosis were observed: the proportion of men allocated to the standing frame group was higher than that allocated to the usual care group, and the proportion of participants with primary progressive multiple sclerosis was higher in the standing frame group than in the usual care group (table 1). Additionally, there was an imbalance in baseline AMCA score, with a lower mean score in the standing frame group compared to that in the usual care group (table 2).

At the primary endpoint, 36 weeks post-randomisation, the pooled (ie, across both groups) SD of the AMCA score was 16·9 points, with a correlation between baseline and week 36 AMCA score of 0·86. Individual-level changes in the score between baseline and week 36 assessments by allocated group are shown in appendix (p 10). The AMCA score at week 36 was significantly higher in the standing frame group than the usual care group, with a fully adjusted between-group mean difference of 4·7 points (95% CI 1·9–7·5, p=0·0014; table 2). Results of the analysis adjusted for baseline AMCA score alone were similar.

Analyses of 36-week AMCA subscores and short-term AMCA scores at 20 weeks showed significant fully adjusted between-group mean differences in favour of the standing frame group (appendix pp 11, 14). We observed short-term, statistically significant differences in favour of the standing frame group at 20 weeks in hip goniometry, knee extensor strength, and in both the physical and psychological components of the MSIS-29 scale (appendix pp 11–13). We also observed longer term significant differences, at 36 weeks, in hip and ankle goniometry in favour of the standing frame group; the short-term differences in MSIS-29 scale were not sustained at 36 weeks (appendix pp 14–16). The proportion of participants having two or more falls during weeks 21–36 was significantly lower in the standing frame group, with odds ratio of 0·43 (95% CI 0·20–0·94, p=0·035), but there was no significant between-group difference over weeks 1–20 or the full 36-week study period. Falling days per person-year, pooled across both groups, was 9·9 during 36 weeks.

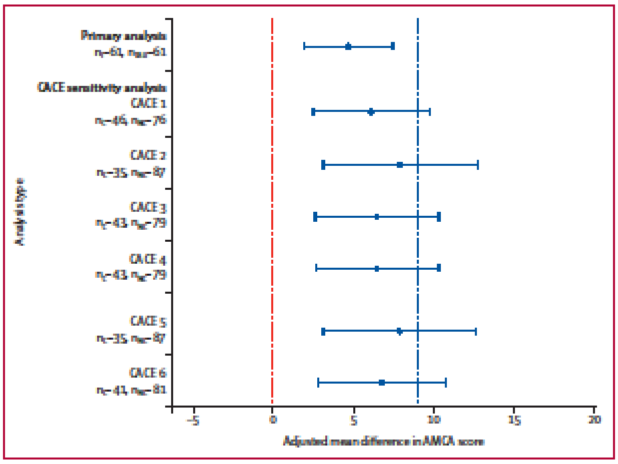

Figure 2: Fully adjusted mean difference in Amended Motor Club Assessment (AMCA) score at 36 weeks for the primary analysis and Complier Average Causal Effect (CACE) sensitivity analyses

CACE sensitivity analyses done under the six compliance definitions (numbered 1–6). Error bars represent 95% CIs. The blue dashed line represents the pre-specified minimal clinically important difference of 9 points on the AMCA scale. n_{sf}=number of participants in the standing frame group. n_{uc}=number of participants in the usual care group. n_c=number of compliers. n_{nc}=number of compliers plus participants in the usual care group.

18 serious adverse events were reported in 15 participants (seven participants in the usual care group and eight in the standing frame group; three participants each had two serious adverse events), none of which occurred during or in relation to the standing frame intervention. These serious adverse events were in line with expectations: urinary tract infections (n=8), cardiovascular events (stroke [n=2] and arrhythmia [n=1]), breast cancer (n=1), falls (n=3, of whom two participants fractured a hip), respiratory infections (n=2), and burns (n=1). In two individuals, pressure sores on the heels developed after hospital admission. For one of these participants, this resulted in the inability to continue using the frame after hospital discharge, despite regular use pre-hospitalisation.

Our adverse event reporting was based on so-called new symptoms, recorded with pre-formatted daily diaries, and is distinct from the serious adverse event data. Overall, 1924 symptoms were recorded (1188 in the standing frame group and 736 in the usual care group; table 3). These were expected in people with multiple sclerosis.[3] We observed a disparity between the groups in the frequency of short-term musculoskeletal pains, such as aching leg muscles, which was potentially related to the intervention. The musculoskeletal pain lasted for longer than 7 days in five individuals (two in the standing frame group and three in the usual care group).

Prespecified sensitivity analyses of the primary outcome with additional adjustment for variables with observed

	Standing frame (n=71)	Usual care (n=69)	Difference adjusted for baseline covariates*†
Resource item			
Primary care	£594·58 (831·29); n=65	£470·46 (681·94); n=62	15·79 (–199·74 to 248·23)
Secondary care	£1787·40 (4155·02); n=65	£2074·17 (3836·70); n=62	–284·82 (–1368·04 to 1077·62)
Personal social services	£477·58 (1359·09); n=65	£947·28 (3086·93); n=62	–10·78 (–408·81 to 369·46)
Total NHS-PSS (excluding standing frame intervention)	£2859·56 (4958·43); n=65	£3491·91 (5408·15); n=62	–539·27 (–1953·60 to 1138·40)
Standing frame intervention	£807·74; n=54	–	–
Total NHS-PSS	£3667·30 (4958·43); n=65	£3491·91 (5408·15); n=62	268·47 (–1093·79 to 2051·38)
Patient personal costs	£2999·25 (6951·45); n=65	£2117·50 (3437·69); n=62	709·07 (–998·70 to 2469·58)
Informal care	£16 047·16 (9944·57); n=65	£18 624·35 (13 589·22); n=62	–3643·34 (–6020·19 to –1348·18)
Total costs (NHS, PSS, and patient and informal care)	£21 905·97 (12 147·65); n=65	£24 233·75 (13 464·93); n=62	–2192·41 (–5755·23 to –1163·43)
EQ-5D-5L values by timepoint			
Baseline	0·224 (0·272, range –0·352 to 0·813); n=71	0·251 (0·274, range –0·265 to 0·778); n=69	–
20 weeks	0·294 (0·269, range –0·256 to 0·813); n=68	0·271 (0·304, range –0·319 to 0·779); n=63	–
36 weeks	0·266 (0·303, range –0·307 to 0·767); n=65	0·262 (0·293, range –0·358 to 0·836); n=62	–
QALYs (based on EQ-5D-5L) over the 36-week follow-up	0·189 (0·174, range –0·125 to 0·549); n=65	0·183 (0·182, range –0·142 to 0·544); n=62	0·018 (–0·014 to 0·051)

Data are mean (SD) or mean (95% CI), unless otherwise specified. *Cost (specific to each cost component) or EQ-5D-5L value at baseline, Expanded Disability Status Scale category (≥7·5 to <7·5) at baseline, and region. †Mean (95% CI) from bootstrap with 10 000 replication.

Table 4: Estimated costs and EQ-5D-5L values by group, and adjusted cost and adjusted quality-adjusted life-years (QALYs) differences, over a 36-week follow-up

baseline imbalance (sex and type of multiple sclerosis) were consistent with the primary analysis results. The planned CACE sensitivity analyses yielded results consistent with the primary analysis, although, under the CACE approach, the average between-group mean differences were larger and all the CIs included 9·0 (figure 2). The repeated-measures modelling gave similar results to the primary analysis, with a significant between-group difference in mean AMCA score at week 20 of 3·7 points (95% CI 1·2–6·2, p=0·004) and at week 36 of 4·5 points (2·0–7·0, p<0·001).

The estimated mean intervention cost per participant was £808 (SD 91; appendix p 17). The main cost drivers were the standing frame (£504) and physiotherapist home visits (£76). Mean costs to the NHS–PSS over the follow-up period (adjusted for cost at baseline, EDSS category, and region) were approximately £539 less for the standing frame group than for the usual care group, excluding the cost of the intervention itself. With the addition of the intervention cost, adjusted mean costs to the NHS–PSS were approximately £268 greater for the standing frame group (table 4, and appendix pp 18–26). The amount of informal care used by our study population was substantial, and application of a national average hourly rate to this time gave an adjusted informal care cost of approximately £3643 less in the standing frame group than in the usual care group (table 4; appendix pp 18–26). The mean EQ-5D-5L increase from baseline to 36-week follow-up was 0·042 for the standing frame group and 0·01 for the usual care group. This equated to an adjusted mean of 0·018 (95% CI –0·014 to 0·051) additional QALYs over the period of follow-up (table 4).

The cost-per-QALY of the intervention from the perspective of the NHS–PSS was approximately £14700 (appendix pp 27). Uncertainty around this estimate is illustrated in the cost-effectiveness plane of bootstrapped replicates of incremental costs and incremental QALYs (appendix pp 28). These simulations suggested that, on 87% of occasions, the standing frame group would have greater QALYs over the period of follow-up than those of the usual care group. The bootstrap replicates also indicated a 0·52 probability of the intervention being considered cost-effective at a willingness-to-pay threshold of £20 000 per QALY and a 0·61 probability at a threshold of £30 000 per QALY. Broadening the analysis perspective beyond health and social care, in line with the recommendations of the Second Panel on Cost-Effectiveness in Health and Medicine,[illegible] increased the apparent cost-effectiveness of the intervention.

There were few missing data and thus, we did not use multiple imputation. Sensitivity analyses explored the broader societal perspective and also took into account the 10-year life of the frames and the NHS's policy of equipment re-use. For both scenarios, the intervention appeared dominant in terms of cost-effectiveness (appendix pp 27–28).

Discussion

Our results provide high-quality evidence that, compared with usual care alone, regular use of frame standing plus usual care provides significant improvements in motor function (our primary outcome) in people severely physically impaired with progressive multiple sclerosis, although not to the degree that was considered a priori as clinically meaningful. We also found evidence for differences in favour of the standing frame group regarding hip and ankle joint range and quality of life (secondary outcomes). This standing frame intervention was shown to be feasible for people with progressive multiple sclerosis to self-manage with the help of a standing assistant and for physiotherapists to implement within routine clinical practice.

Less clearcut is whether the outcome of the standing frame intervention was clinically meaningful. Interpretation is difficult because of the insufficient evidence to define what constitutes a minimal clinically important difference on the AMCA score. We relied on the only two physiotherapy studies we were aware of that had used the AMCA score; both suggested that a 9-point improvement was clinically relevant in people with severe multiple sclerosis.[14,24] A 9-point change could mean, for example, that a person could have improved so that they could balance in sitting to dress themselves (3 points), transfer independently (3 points), and stand without having to use their hands for balance (3 points). However, an improvement in any single one of these functional activities might constitute a clinically meaningful change. This view is supported by the audio narrative accounts of the changes undergone by SUMS study participants. When considering the design of future studies, further exploration is needed regarding the minimal clinically important difference on this measure for severely impaired individuals.

Our CACE analysis showed that accounting for compliance to the intervention resulted in a larger estimated intervention effect, with the prespecified minimal clinically important difference of 9 points on the AMCA score contained within the 95% CIs of all six compliance definitions. This suggests a positive association between compliance with the intervention and the motor benefits gained. This is consistent with theoretical expectations and with the results of (low methodological quality) studies of standing frame use in populations with other neurological conditions.[8]

To sustain any benefits gained from physical activity, individuals need to maintain long-term engagement, which is a particular challenge for people with a disability.[27] Evidence is scarce regarding long-term adherence in people with multiple sclerosis to physical activity interventions; however, non-adherence rates are as high as 80% for individuals with chronic conditions for which interventions might aim to slow down decline rather than to cure.[27] Two thirds of the participants in the standing frame group continued to stand regularly in the frame during the 36-week period, which, in light of the literature, we consider to be a high proportion. Furthermore, 70% of participants who had a standing frame during the study requested to keep the frame on completing the study, thus further supporting the feasibility and acceptability of the intervention.

Behavioural change techniques were an integral component of the standing frame intervention. To complement the physiotherapy advice and support, individuals had access to paper-based, DVD, and online resources, designed to equip them and their standing assistants with the knowledge and skills necessary to undertake this activity within their own homes. Aimed at enhancing self-efficacy,[22] this approach was considered essential because self-efficacy is a key determinant of physical activity behaviour in people with multiple sclerosis[28] and is typically low.[23]

Tolerability of an intervention is important for adherence and thus, capturing adverse events potentially associated with the intervention was important. We achieved this by using daily, self-reported, preformatted diaries. However, free-text description of adverse events was often ambiguous, making it difficult to determine whether they were new symptoms. Therefore, it is challenging to precisely state what proportion of these broad-ranging symptoms are related to the standing frame intervention. Bias in reporting of adverse events is also possible because the standing frame group recorded both details of each standing session and any new symptoms in the same diaries, potentially triggering reporting of new symptoms more comprehensively than in the usual care group. However, overall, the data suggest that this intervention is well tolerated; the adverse events were typically transient (lasting less than 7 days), musculoskeletal in nature (aches and pains), and occurred early in the programme when participants were probably adjusting to recommencement of regular standing. Importantly, physiotherapists should inform people that short-term musculoskeletal aches and pains might occur and provide education about how to manage this. From a methodological perspective, effective and reliable systems for collecting adverse event data in rehabilitation trials should be further investigated.

For the audio narratives of the SUMS study participants see https://www.plymouth.ac.uk/research/sums

Our study has several strengths. To our knowledge, this is the largest randomised controlled physical rehabilitation study to date undertaken in severely impaired people with progressive multiple sclerosis. It was the first definitive multicentre randomised controlled trial to assess the clinical and cost effectiveness, safety, and tolerability of a home-based, self-managed standing frame programme in this population. The study was originally planned to have 80% power, on the basis of conservative assumptions;[18] with our observed SD being lower and the correlation between baseline and week 36 AMCA scores higher than anticipated, we were able to estimate the intervention effect with increased precision. Our cost-effectiveness analysis assumed that a new standing frame would be purchased for everyone in the intervention group; however, given the NHS policy of equipment re-use, and the average 10-year life of a frame, our cost-effectiveness estimate is likely to be conservative.

Another strength of our study is that it was a pragmatic trial. To maximise generalisability of the results, we minimised our exclusion criteria. The intervention was delivered by physiotherapists working within the NHS, who did not undergo specific training for this intervention, making it likely that similar results would be gained on implementation within usual practice. However, we should note that our findings cannot automatically be generalised to other countries that do not have a similar organisational context. The publication of our educational resources on a freely available website aims to enhance shared, evidence-based, decision making about the effect of introducing this intervention to people's daily lives.

For the SUMS educational resources see https://www.plymouth.ac.uk/research/sums

Our study has several limitations. Our primary economic outcome measure was QALYs, in line with guidance by the National Institute for Health and Care Excellence. The difference in EQ-5D-5L scores (used to calculate QALYs) between the standing frame and usual care groups at 36-weeks did not reach the minimal clinically important difference for the EQ-5D-5L score described by Marra and colleagues.[28] Therefore, it could be argued that the QALY gain was not perceptibly different from zero, implying that the intervention was not cost-effective. However, the standing frame intervention did appear effective from the patient's perspective when considered across outcome measures, specifically according to the primary clinical outcome measure. Our main analysis might have been restrictive in identifying benefits of the intervention, and a broader societal perspective might have been preferable.

The usual care group was not offered an intervention and hence, we could not exclude that placebo effects might have contributed to the benefits experienced by the standing frame group. However, the primary outcome was clinician-rated and measured by a masked assessor, which should reduce the effect of this. Nevertheless, further research is needed to disentangle the intrinsic effects of standing from non-specific effects due to, for example, attention. It is also possible that drug interventions might have contributed to any of the changes observed. However, participants were excluded if there had been any recent changes in disease-modifying therapies, and they were asked to record any medication changes throughout the study period; the two groups were balanced in terms of medication changes, therefore, this is unlikely to account for the between-group differences.

In conclusion, there is a paucity of evidence-based, self-management interventions that are recommended for people severely impaired with progressive multiple sclerosis who have few treatment options available. We hope this intervention can now be offered and reimbursed more widely as a management option for this population.

Contributors

JF, WH, LJ, SC, and AB developed the study. JF, WH, LJ, SC, AB, AH, and JZ contributed to trial design, data interpretation, and writing of the report. RD contributed to data acquisition, data interpretation, and writing of the report. SC and BJ were responsible for the statistical analysis and data interpretation. All authors approved the final draft of the manuscript.

Declaration of interests

We declare no competing interests.

Data sharing

The SUMS study protocol and statistical analysis plan are publicly available at https://www.plymouth.ac.uk/research/sums. Individual participant data that underlie the results will be made available (after de-identification) on a controlled access basis, subject to suitable data sharing agreements. Requests for data sharing should be made to the Chief Investigator (CI; J Freeman) in the first instance. Requesters will be asked to complete an application form detailing specific requirements, rationale, and proposed usage. Requests will be reviewed by the CI and study sponsor, who will consider the viability and suitability of the request and the credentials of the requester. Where access to requested data is granted, requesters will be asked to sign a data sharing agreement. Requested data will be made available, along with supporting documentation (eg, data dictionary) on a secure server or through other secure data transfer method.

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2.2.2 Paper 4

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BMJ Open

“I’m in a very good frame of mind”: a qualitative exploration of the experience of standing frame use in people with progressive multiple sclerosis

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ABSTRACT

Objectives The study aim was to explore the experiences of people with progressive multiple sclerosis (MS) and their standing assistants during their participation in Standing Up in Multiple Sclerosis, a randomised controlled trial (RCT) of a home-based, self-managed standing frame programme.

Design A qualitative approach, using audio diary methodology was used to collect data contemporaneously. Diary data were transcribed verbatim and analysed using thematic analysis.

Setting Participants were recruited from eight healthcare organisations in two regions of the UK. The intervention was home-based.

Participants As part of the RCT, 140 participants were randomly allocated to either usual care or usual care plus a standing frame programme. Using a sampling matrix 12 people with progressive MS (6 female, aged 35–71 years, Expanded Disability Status Scale 6.5–8.0) and 8 standing assistants (4 female) kept audio diaries of their experiences.

Intervention The standing frame programme involved two face-to-face home-based physiotherapy sessions to set up the standing frame programme, supplemented by educational material designed to optimise self-efficacy. Participants were encouraged to stand for at least 30 min, three times a week for the 36-week study period.

Results Four main themes were identified: “Feeling like the old me”; ‘Noticing a difference’; “I want to do it right” and “You have a good day, you have a bad day”.

Conclusions Supported standing helped people with progressive MS feel more like their old selves and provided a sense of normality and enjoyment. People noticed improvements in physical and psychological symptoms, which were often associated with increased participation in activities they valued. Provision of support from a physiotherapist and recognition of the variable nature of the condition were highlighted as factors to consider when establishing a standing programme.

Trial registration number ISRCTN69614598.

Strengths and limitations of this study

- Audio diary methodology enabled data to be collected contemporaneously and longitudinally.
- Data include the perspectives of both the person with multiple sclerosis (MS) and their assistant.
- This qualitative data complement and support findings from our randomised controlled trial that demonstrated standing frame use to be beneficial for people with severe progressive MS.
- Some practical difficulties were encountered when using the audio recorders.

INTRODUCTION

Multiple sclerosis (MS) is a progressive, neurological condition where inflammation and neurodegeneration in the central nervous system can result in a wide variety of symptoms.[1] Approximately 1 000 000[2] people worldwide live with progressive MS, where increasing disability can negatively impact on function and quality of life. With symptom onset commonly in early adulthood and survival rates improving, years lived with disability are increasing.[3] Consequently, people with MS are likely to have an increasing requirement for rehabilitation over the course of their lives to help manage symptoms and maximise independence. Higher levels of disability can make it difficult for people to engage in sufficient physical activity to achieve recognised health benefits,[4–7] with many people with progressive MS spending most of the day sitting down.[4 5 8] This prolonged immobility places them at risk of developing preventable secondary complications, which may include muscle wasting, spasms, constipation and depression.[5]

Effective long-term, physical activity strategies, which can be self-managed and implemented relatively easily and cheaply within people’s homes, are needed. The use of a standing frame is one option that enables people with severe MS to increase their physical activity through regular supported standing. Standing frames are devices which allow people who have limited or no ability to stand upright independently, to do so safely, with good postural alignment and for extended periods of time. We have provided robust evidence, from a definitive, multicentre, randomised controlled trial (RCT) with cost-effective analysis, that a home-based, self-managed standing frame programme, set up by a physiotherapist and supported using behavioural interventions can significantly increase motor function in people with severe progressive MS, is feasible to implement and appears cost-effective.[9] Of importance, at 6 months follow-up, the majority of people allocated to the standing frame group (66%) were continuing to use the frame regularly.

Understanding the subjective perspective of using supported standing devices is also important. This has been explored in a small number of studies. Two cross-sectional surveys of frame users with spinal cord injury included questions about the perceived benefits of standing,[10 11] both finding that the vast majority of participants (76% and 87%, respectively) reported improved well-being and quality of life, and that standing had a positive impact on self-esteem and self-image.[10] This improvement in well-being increased to 88% for respondents who stood more than once a day.[12] Similar findings have been reported in surveys of mixed neurological populations, including people with MS.[13 14]

Nordström *et al*[15] interviewed 15 people (7 of whom had a progressive neurological condition including MS), who had used a variety of standing devices for between 1 and 10 years. The authors described how the upright standing position alters the person's sense of self, augments their availability to the outside world, strengthens social interplay and changes a person's motivation and expectations over time. They concluded that standing unites body to self and emphasised that therapists should understand both the subjective and physiological impacts. Similar conclusions were drawn by Hendrie *et al*,[16] who used a mixed-methods approach involving nine single-case studies of people with MS who participated in a home-based standing-frame programme. In this study, in-depth interviews were undertaken on three occasions: at baseline (before standing began) and again at 36 and 48 weeks postbaseline. Respondents' stories revealed how regular frame standing enabled them to reconnect with their body, regain skills, re-engage with relationship roles and develop a sense of optimism for the future.

To our knowledge, no previous study has explored the contemporaneous experience of using a standing frame from the initial stand onwards, either from the perspective of the participant or the individual assisting with frame use (referred to here as the 'standing assistant' and typically their spouse). There are a number of important factors to consider in order to optimise any impact of the intervention and subsequently increase the likelihood that this self-managed activity is sustained over the long term. These include: understanding the immediate experiences of using the frame; changes experienced over time; factors which impact on its everyday use and how standing frames can be integrated into people's everyday lives. We embedded a qualitative component within our RCT,[9] which explored participants' subjective experience of self-managing this standing frame programme, over the 36-week trial period, from the moment the person with MS first stood in the frame. Capturing the personal experience and impact of using a standing frame within daily life was considered important to complement the objective data gathered, and to provide a richer understanding of both the benefits and drawbacks of this intervention.

MATERIALS AND METHODS

Our multicentre RCT involved 140 people with progressive MS. Abilities ranged from being able to walk 20 m with bilateral assistance to full-time wheelchair users (graded 6.5–8.0 on the Expanded Disability Status Scale (EDSS)). Here, we focus on reporting the embedded qualitative component; the RCT methodology and results have been previously described.[9 17]

The qualitative component reported here is described in line with the standards for reporting qualitative research.[18]

PATIENT AND PUBLIC INVOLVEMENT

People with MS and their family members were actively involved in development of the research questions, study design, trial management and steering groups, writing study materials and dissemination activities.

Research approach and methodology

We conducted this qualitative study from a critical realist perspective[19] and explored people's experiences of a particular phenomenon (frame standing) in a particular context (the home environment). We chose the audio diary method to capture data about participants' day-to-day experiences because of its potential ability to reveal people's ongoing, everyday experiences longitudinally by offering 'multi-occasional windows' for data collection.[20 21] We considered this important since people's views and experiences of undertaking an activity alter over time; the mastery of a skill such as standing within the frame is an ongoing process, and MS symptoms fluctuate. The hope, therefore, was that the diaries would enable the immediacy of the moment to be reflected, rather than participants recollecting these feelings later, at a single point in time distant to the event, as would have been the case using interview or focus group methods. Other advantages of the unstructured nature of this approach is that it allows people flexibility over when, where and what to record, and being able to erase files they do not wish to share.[22] Furthermore, the participant is not required to write down their thoughts, which may be problematic for people with progressive MS where upper limb dexterity issues are commonplace.[23] In addition, such a method reduces the bias that may be introduced due to an interviewer's questioning.[21] Exploring the experiences of both people with MS and standing assistants was considered important due to the invaluable role assistants play in the lives of many people with MS. For many people with significant disability, participation in this standing activity would only be possible with help from an assistant. Understanding both perspectives of the frame use therefore was recognised as crucial for successful integration of a standing programme into everyday life.

The standing intervention

Briefly, the standing frame programme involved provision of an Oswestry standing frame (Theo Davies & Sons, Wrexham, UK), at home to 71 participants who were allocated to the standing group. A physiotherapist visited the person in their home on two occasions, 1 week apart, to teach the person with MS and their standing assistant how to use the frame. This was complemented by the provision of educational materials, via written and video mediums, designed to optimise self-efficacy (for details, see https://www.plymouth.ac.uk/research/sums). These face-to-face sessions were followed up with six short phone calls interspersed over 3 months. Behavioural change strategies such as goal setting and facilitated problem-solving were used to progress the exercise programme in the frame and optimise adherence. Participants were asked to progress the time they spent standing in the frame so that, by the end of 4 weeks, they were standing for at least 30 min, three times a week. This approach was individualised according to the ability of the person with MS.

Qualitative study sampling and recruitment

Purposive sampling was used to select participants from those allocated to the intervention group to take part in this embedded qualitative study with the aim of achieving maximum variation. A sampling matrix informed the selection in terms of gender, age, disability level, home environment (eg, from one bedroom flats to houses) and people with and without a standing assistant. Participants were excluded if they did not have the physical capacity to operate an audio recorder or a carer to assist them with this, or had severe communication difficulties preventing them from verbally recording their experiences. From the pilot study by Hendrie *et al*,[16] it was considered that 20 participants would provide a broad representation of people using the frames under different circumstances so that as much in-depth information as possible about the experience of using a standing frame in the home could be obtained. The decision was made to recruit more people with MS than standing assistants to reflect the possibility that some participants would be living alone, self-managing without an assistant. In total, 12 participants allocated to the standing intervention arm of the RCT, together with 8 standing assistants were invited to participate, and written consent was obtained.

Data collection

Data were collected using portable, hand-held, audio digital recorders. Participants (people with MS and standing assistants) were provided with, and shown how to operate the recorder and given an opportunity to practise using it. To supplement this, they were provided with illustrated instructions on its use and a written summary to remind them about the purpose of the audio diaries. They were requested to record their experiences of how it felt to stand and use the frame from the first moment they tried it. They were also asked to describe any changes they experienced or witnessed, and include any other comments they wished to make. As our intention was to gather contemporaneous data, participants were asked to record these experiences, if possible, during each stand or as near to the completed standing period as possible. Participants were free to record as many times as they wanted and when they wanted. No further prompts regarding this were given. The audio recorders were collected after the participants had completed the final 36-week RCT assessment. The audio files were downloaded and stored securely. They were transcribed verbatim, dated and anonymised.

Data analysis

Data were analysed using thematic analysis according to the Braun and Clarke six-phase method of identifying and analysing patterns in qualitative data.[24] In the initial stages, the audio recordings were listened to alongside reading of the transcripts to ensure accuracy. Two members of the research team (WH and RD) read and re-read the transcripts several times and independently assigned relevant initial codes to the data using comment boxes on word versions of the transcripts. To further ensure rigour, a third researcher (JAF) independently listened to, read, re-read and checked the coding of each of the transcripts. In addition, the narrative trajectories were considered over time, exploring whether and how the narratives changed across the trajectory by viewing the diary entries as a whole series rather than solely as fragmented entries.

The next stage of analysis involved reviewing and revising the codes and combining them into themes by looking for meaningful patterns that were relevant to the research aim. This stage was completed longhand rather than using a computer software programme. The assigned codes were considered and critically discussed on several occasions by WH, JAF and RD. Disagreements were resolved through discussion until consensus was obtained. Using this iterative process, themes and subthemes were agreed on, supported by associated key extracts of data that captured the participant voice. Preliminary results were shared with the trial management group, including people with MS, and the extended research team, who were able to reflect and comment on the findings.

The data were analysed as a whole as it was considered that the experiences of the people with MS and their standing assistants were interdependent and entwined.

Trustworthiness and credibility

The trustworthiness and credibility of the analytical process was optimised through several strategies. The transcripts were independently coded by several members of the research team who were experienced in undertaking qualitative data analysis and detailed discussions were held to ensure decisions could be defended. Triangulation was undertaken with field data gathered from informal, voluntary, exit interviews with all RCT standing group participants who completed the study (61 of the 71 participants allocated to the standing frame group). A summary of the main themes was sent to participants for member checking to ensure credibility of the findings. WH, RD and JAF are all experienced neurological physiotherapists working in the field of MS. In order to minimise the bias this may have brought to the analysis, and to enhance reflexivity, regular trial management meetings were held to enable discussions with the broader research team and MS representatives.

RESULTS

Twelve people with progressive MS (six female, aged 35–71 years, EDSS 6.5–8.0) and eight standing assistants (four female) kept audio diaries of their experiences of using the Oswestry standing frame. All participants who were invited to participate accepted and none dropped out. Two of the participants encountered technical difficulties using the recorders and, instead, chose to write accounts of their experiences over the duration of the study. Demographic information of participants is presented in table 1.

A total of 155 (range 1–36) diary entries were recorded. More entries were recorded by the individuals with MS (median 8, range 1–36) than the standing assistants (range 1–16 entries). All data were analysed.

Four overarching quoted themes were developed: "Feeling like the old me"; 'Noticing a difference'; "I want to do it right" and "You have a good day, you have a bad day". A number of subthemes were also identified and are presented below, supported by quotes using pseudonyms.

"Feeling like the old me"

This theme describes how standing reconnected people with their old, more able selves in a positive way, either through changed behaviours brought about by physical improvements or the feelings that were elicited by standing safely upright in the frame. The participants with MS described the enjoyment of standing. As a result, standing made them feel more like the person they used to be. Two subthemes were identified.

'Being upright is really most enjoyable'

Participants talked about the enjoyment they felt standing fully upright again and the feelings that standing evoked. Most commented specifically about the positive impact of supported standing, sometimes from as early as the very first stand.

> Simon has had his standing frame for a week and it has just been the most fantastic thing. He just really enjoys standing up…It seems to have completely changed his life. He is just really excited about life looking forward now, so brilliant…he just loves being upright. *Sophia, standing assistant of Simon EDSS 8.0*

Table 1 Demographic information of participants (12 people with MS and 8 standing assistants)

pwMS pseudonym	Gender of pwMS	Age of pwMS	Baseline EDSS of pwMS	Standing assistant pseudonym	Home setting
James	M	63	6.5		Three bed house
Justin	M	68	6.5		One bed flat
Jamie	M	41	6.5	Claire	Two bed flat
Mandy	F	43	6.5	Keith	Three bed bungalow
Sam	F	69	6.5	Rob	Two bed flat
	F	66	6.5	Thomas	Three bed bungalow
Jane	F	62	7.0		Three bed house
	M	64	7.5	Liz	Two bed house
Joyce	F	71	7.5	Peter	Three bed house
Henry	M	58	8.0		Four bed house
David	M	54	8.0		Three bed house
Simon	M	51	8.0	Sophia	Three bed old cottage
	M	54	8.0	Penny	Four bed house
Sarah	F	53	8.0		Three bed house
Ellen	F	35	8.0		Two bed flat

EDSS, Expanded Disability Status Scale; F, female; M, male; MS, multiple sclerosis; pwMS, person with MS.

Enjoyment from standing was reported throughout the 36 weeks of the trial, even after any potential novelty of using this new piece of equipment had passed. For many, it gave them a feeling of being in control and doing something to help themselves.

> It gives me a different kind of freedom because I don't have to cling onto everything … usually I have total lack of confidence, I cling onto everything as I walk, but in the frame it's like a kind of freedom. Although I am strapped in, I am able to move and it's really very enjoyable… it really has given me a sense of liberation. *Jane, EDSS 7.0*

Participants also reported a positive psychological impact of standing even when physical improvements did not appear to have been gained. The pleasure of being upright in standing in itself was a motivator for them to continue.

> I don't think the standing frame has helped as far as the MS symptoms are concerned. As far as stretching my muscles, stretching my body and the psychological effect that I am standing which is fantastic. All those side issues are great. *Henry, EDSS 8.0*

'A sense of normality'

For some people, the impact of standing upright in the frame gave them a feeling of being 'normal'. People described enjoying the sensation of standing to their full height again and of engaging with previous life roles in standing: a dad listening to his daughter practising her violin, a husband and wife talking in the kitchen.

> It gives you a sense of normality…It has been really nice standing in the standing frame looking out of the conservatory watching all the birds on the feeders. *Henry, EDSS 8.0*

> And

> It's a major, major plus being able to stand up because everything looks the size it always used to and I don't feel like a little tiny seven year old (standing assistant added) [insignificant] boy. *Simon, EDSS 8.0*

On occasions, people provided illustrations of how using the frame had enabled them to achieve something they may not otherwise have managed. For some, this was due to an improvement in symptoms or function (described in the next theme), but for others it was purely standing in the frame itself that facilitated the sense of achievement.

> I have been building up for my daughter's wedding, and when it was time for me to make my father-of-the-bride speech they brought the frame in and my carer who was there for the day for me strapped me in, and no problem, I stood for about 13 minutes … read the whole speech, got everyone in tears… *David, EDSS 8.0*

For some, the experience of standing in the frame appeared to give an opportunity to reflect on their past identity,

> My friends and I were surfing a lot, that's what we did, we surfed in the summer, surfed in the winter, whenever… the reason I am saying that is that now on the standing frame if I let go of the table or the side arms and lean backwards a little bit I can balance… I can imagine myself standing on the surfboard with my arms down by my side and I just move my body around a little bit in the straps as if I'm moving the board… I am enjoying it tremendously. *Henry, EDSS 8.0*

Family and friends were also affected by seeing their loved ones standing again.

> It's really nice to be upright… my mum and her husband came today and she was absolutely amazed. It's a long time since she's seen me standing so we kind of reminisced about the days when I was walking and getting up and about, so that was nice… she had tears in her eyes, bless her…. *Sarah, EDSS 8.0*

'Noticing a difference'

This theme captures the variety of positive changes the participants reported in activities such as walking, transfers, posture and sitting balance and in a wide range of MS symptoms including spasms, weakness, muscle stiffness, fatigue and bladder and bowel function. These improvements appeared to increase participants' confidence and enable them to engage more in everyday life. The changes were from across the spectrum of impairments, activities and participations, as illustrated by the following subthemes:

"My muscles have woken up"

> I can truthfully say I felt as if I was using my muscles, the muscles in my calves and thighs were aching but pleasantly as if my body was saying to me 'hello you're using some more muscles that you're not used to using'… consequently I was standing more upright and feeling a little bit more confident about doing things around the house. So, as far as the standing frame is concerned, posture's improved, upper body movement has improved and I'm in a very good frame of mind. *James, EDSS 6.5*
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> I don't have the spasms I used to have by any means. In fact I have really cut down on the Baclofen, which is the anti-spasm drug. Bowels and things like that… within about a couple of weeks, I suppose, it is so much easier, I can go on demand, so that is really, really good… I've cut down on a load of my medicines. It's the best thing ever. *David, EDSS 8.0*

> ….we are already noticing a difference… His bowels are fantastic. I don't think he has been constipated in the last few months [since starting the standing programme]. I don't think he wees so much in the

> night… He's up for trying new things, going out doesn't seem to be such a problem. *Sophia, standing assistant of Simon EDSS 8.0*

"We suddenly noticed he was passing the salad bowl"

Participants often talked about functional improvements as they described the day-to-day impact of using the frame.

> I have been able to stand more confidently when I have got up from the toilet and I know that I am able to pull my trousers up… without feeling the need to hold onto anything, so little goals like that I am achieving already. *Jane, EDSS 7.0*
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> Just the last couple of days I felt my legs being a little bit stronger and consequently due to that, I've been able to walk a little bit further with less fatigue and it's quite nice feeling that sensation that you know the muscles in your legs are beginning to work. *Justin, EDSS 6.5*

Standing assistants also reported they had observed functional improvements of the person with MS, for example, those associated with increased trunk strength and sitting balance.

> We suddenly noticed he was passing the salad bowl and he reached in with the two salad servers and helped himself. He has never been able to do that before because he has always had to hold on with one hand. And then I caught him piling the plates, reaching across the table, picking up plates, putting them on top of each other and taking them out to the kitchen. *Sophia, standing assistant of Simon EDSS 8.0*

'Going out doesn't seem to be such a problem'

Many of the positive changes that people experienced appeared to impact on their confidence to participate with life in a new way which, in turn, gave enjoyment and a sense of achievement.

> I have had no falls since I have been using the standing frame and I have been feeling a little more confident with my balance… Yesterday I went to lunch at a friend's house…I decided to use my husband's arm and a crutch… the improved feeling that I can balance now, it was just really absolutely brilliant… I am so happy that I managed to do it. *Jane EDSS 7.0*
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> … I've just been to my [pheasant] shoot today and I'm absolutely amazed, I've been able to stand [perching on the seat of the electric scooter] for a good hour at least, at least 20 minutes at a time, and that's 3 lots for 20 minutes… and I've had a fantastic time. *James, EDSS 6.5*

"I want to do it right"

Initially, some participants lacked confidence in using the frame and wanted to make sure they were doing it correctly. With increased practise and support from the physiotherapist, however, their confidence grew and they were able to modify the standing programme to suit their own needs and manage difficulties that arose. This is illustrated by the following subthemes:

"The physio came round and set me right"

Participants commented that they valued the support and guidance from the physiotherapist in helping them establish a standing programme that worked for them.

> We were… floundering in it… was he standing up completely straight? Was it alright to be leaning back on the back strap? Anyway, so it was very comforting to have the physiotherapist here. *Sophia, standing assistant of Simon, EDSS 8.0*

One person would have preferred increased contact, remarking:

> You do feel left alone a little bit and wondering why you're doing them [the exercises in the standing frame], but I have persevered as far as I can. *Justin, EDSS 6.5*

Interestingly, however, this participant's audio diary entries illustrated how he independently problem-solved issues as they arose and he used the frame regularly over the entire course of the study.

"I am finding different things as I go along"

People found that they needed to modify their standing routine over time in order to maximise benefit, manage symptoms and gain the greatest enjoyment from it. Making these (often small) changes to the programme appeared instrumental in helping long-term adherence. A number of ideas were described: gradual progression of standing time; standing at different times of the day or on different days of the week; varying the exercises completed or adding functional tasks such as folding the washing.

> I started with a couple of minutes and then worked up to kind of ten minutes, then fifteen minutes, then I was doing my thirty and I am absolutely loving it. *Sarah, EDSS 8.0*
>
> Mandy decided to use it a little bit later. Normally she uses it mid-afternoon, about half past three, but decided to do it about half past six. She found it a lot easier because that is a better time of day for her. *Keith, standing assistant of Mandy, EDSS 6.5*

"My back gets a bit achy but it's early days yet"

An important area that some participants talked about was in relation to side-effects that they experienced. These were mainly back and leg aches and pains, which tended to occur early on in the programme, and either resolved completely or reduced in frequency as the individual became more accustomed to standing.

> Today I used the frame for the first time, knees and back a bit sore when standing, but the feeling disappeared when I was back in my chair. *Joyce, EDSS 7.5*

> My legs feel quite stiff immediately after I've got out of the frame but that soon passes. *Mandy, EDSS 6.5*

Experience of side effects, even in the early days, was not mentioned by everyone, with a couple of participants specifically noting their absence.

> At the moment [week three] there's no side effects for me personally doing them. *Justin, EDSS 6.5*

"We are definitely not giving the frame back"

At the end of the trial, several of the people with MS reflected on the value they placed on standing in the frame and on how they intended to use it in the long-term. This sentiment was also echoed by many of the standing assistants, and with particular enthusiasm by Sophia.

> All in all it has been the most fantastic thing and we are definitely not giving the frame back and he will be using it every day for the rest of his life! *Sophia, standing assistant of Simon, EDSS 8.0*

The acceptability of both the user and standing assistant may be important factors in facilitating long-term use of a frame. In this study, people reported that, after a period of adjustment to this new piece of equipment, they could incorporate this into their weekly routine.

> Just to say as a partner [of Simon] and having to help, it is no bother at all. I don't have to haul him up at all. I just wait for him to get in standing position, easily tie him in and sometimes rearrange his feet just to get them exactly right, and then leave him. *Sophia, standing assistant of Simon, EDSS 8.0*

The data revealed that a 'settling in' process was sometimes needed, as people became accustomed to the equipment.

> [day one] we had a couple of issues with the standing frame. It is our first time using it on our own…. we used the standing frame again today [day three] we found it much easier to use; we have got the straps set up pretty much where we want them now…. [day seven], so we are getting a lot quicker using it. *Keith, standing assistant of Mandy, EDSS 6.5*

This is an interesting example of the insight provided by the multi-occasion windows that the audio diaries enabled.

Another standing assistant raised two important issues for consideration for anyone contemplating using a frame in their home environment: having sufficient physical ability to move the frame if necessary and having adequate space for it.

> The frame itself is quite cumbersome to move so it is better left in situ. In our case it needed to be moved each time to allow a wheelchair or walker access past it. *Thomas, standing assistant of person with EDSS 6.5*

"You have a good day, you have a bad day"

This theme highlights the challenges faced by people living with a progressive and fluctuating condition when implementing a self-management programme and their expectations of standing. Three subthemes were identified.

'The ups and down of MS'

Many participants talked about how the unpredictability of their condition affected their ongoing ability to engage in the standing programme and that this could change on a day-by-day basis.

> I think it is just the nature of my illness, I just, I know only too well that you have a good day, you have a bad day. *Jane, EDSS 7.0*

"He really hasn't been feeling well"

This subtheme demonstrates the impact that other illness, infections and environmental conditions can have on someone's symptoms,[4] and in turn, on their ability to consistently engage in a standing programme.

> Yesterday for the first time, he couldn't even get up into the frame, which was really scary and thought oh well perhaps it's another bladder infection and we thought we would take another urine sample [to the doctor], and then suddenly yesterday evening he suddenly said 'oh, I am feeling better now'. He did a fifteen minute stand and then got up the bottom step to go to bed… today he seems to be back on track. *Sophia, standing assistant of Simon, EDSS 8.0*
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> I couldn't use the frame at all last week [week 5], as I had a bad cold and that always leaves me weak and tired as it seems to affect all my muscles. Today I am feeling better, so I used the frame in the afternoon… Last week [week 6] I hurried back into using the frame too quickly after being unwell. I felt comfortable with no pain so I did 35 minutes two days running and was exhausted with back ache. This week I am doing less time, but more often with rest days in between… I feel that the legs and the back are gaining more strength now. *Joyce, EDSS 7.5*

"I'm not expecting miracles"

Participants expressed different expectations of the standing frame programme both in terms of their hopes of improvement and the length of time changes may take to happen. In the main, participants appeared satisfied with their experience, although some described an internal dialogue regarding the struggles they had in balancing their aspirations with the reality of their achievements.

> I was hoping that by now [six months] I would have noticed something … that would be better, my balance or being able to stand or strengthening my legs or whatever. Maybe it is strengthening my legs, but because they don't work, which is nothing to do with that, it's just the MS damaging the nerves which I

> suppose the standing frame isn't going to help is it? I have tried to soldier on, as I usually do… as much as I possibly can… *Henry, EDSS 8.0*

Once again, the multiwindow nature of the audio diary methodology enabled the reader to realise that individuals continued to stand throughout the study timeline, despite the challenges they faced.

Exit interviews

Qualitative data were also captured in informal exit interviews with the 61 standing group participants who completed the RCT. Interviews were in the region of 10min duration, and were completed face-to-face at the end of the final study assessment by the research therapist. They were designed to ask briefly about participant experience of the study, aspects that could have been improved, things that they particularly liked and an opportunity to share any other thoughts regarding the study. The main points raised in the exit interviews about the use of the standing frame concurred with the themes and subthemes identified in the audio diary data but without the detail, depth or sense of personal journey. People reported specific physical and psychological changes they had noticed, how they established and modified their standing over time and described issues they faced in terms of both the practicalities of using the frame, and the impact that the variable nature of their symptoms had on maintaining a regular programme.

DISCUSSION

This embedded qualitative study is, to our knowledge, the first to explore the contemporaneous experience of self-managing a standing frame programme in the home, from the perspective of both the person with progressive MS and their standing assistant. The choice of using audio diaries to facilitate contemporaneous data collection has enabled the reader to gain an insight into both the immediate experience and the standing journey as it unfolded over time. This may help therapists to better understand the experiences of people living with a long-term, progressive and often unpredictable condition when they are asked to carry out a new, self-managed, physical intervention. Other studies have used surveys[10 11 13 14] or interviews[15 16] to explore standing frame use but this methodology has proven helpful in capturing the day-to-day experiences and has provided new detailed insights.

Participants and their standing assistants reported a variety of physical and psychological changes over the 6-month data collection period. Among the range of perceived benefits reported, one very commonly described was that of enjoyment. This was linked by some to feeling a sense of normality and/or freedom, experiences that have also been previously reported in other qualitative studies of supported standing.[13–15] The contemporaneous nature of the data collection revealed these feelings even from early on in the standing programme and sometimes in the absence of noticing any physical changes. Engagement with an activity is more likely to be sustained over the long-term if that activity is meaningful and enjoyable.[25 26] Our study showed that this was the case for many of the standing participants. Therapists, therefore, have an important role in identifying what the patient considers, for them, is a relevant activity and how they might integrate it into daily life.[27 28]

The subjective reports of improvements in symptoms complements and supports some of the objective results of the RCT, such as those relating to motor function.[9] It is noteworthy, however, that some of the perceived benefits highlighted in this qualitative component, such as improvements in bladder and bowel function and sitting balance were not supported by the objective trial data. There are a number of potential reasons for this: (i) the lack of responsiveness of the standardised measures in detecting small but meaningful improvements for an individual; (ii) the group-based nature of analyses in RCTs, where the focus is on *average* treatment effects[29] and (iii) the restricted range of outcomes that can feasibly be measured within a trial. These issues underline the added value of qualitative work in expanding our understanding of issues which are important to consider when implementing evidence-based interventions into clinical practice.

Gauging the type, timing and level of support that individuals need to sustain effective behaviour change when introducing new equipment is complex and requires careful consideration. For some participants in this study, the range of behaviour change strategies incorporated and level of support provided appeared sufficient to enable them to problem-solve and modify their programme from the outset. These individuals appeared successful in continuing to engage in their standing programme despite the challenging circumstances they faced, which included fluctuating symptoms and adverse events. Others, however, reported they would have valued additional support to gain confidence when learning to use the frame. An example of gaining additional support might be the opportunity to hear the experiences of people in similar circumstances. An output of this qualitative study therefore has been the production of four short films, compiled from these audio diary data, and a narrative account, which can be accessed at www.plymouth.ac.uk/research/sums. In addition, we suggest a number of 'top tips' compiled from the study data which may provide helpful guidance for therapists, people with MS, their family and friends (see box 1).

Strengths and limitations

Several methodological points have been highlighted by this qualitative study. The choice of using audio diaries enabled data to be collected contemporaneously and longitudinally at multiple windows over a period of time, rather than retrospectively. This approach captured the day-to-day experiences as well as the ongoing challenges faced over time by people when implementing a

Box 1 Top tips to maximise adherence to a standing frame programme

- Try to integrate the standing programme into a weekly routine.
- There will be a 'settling in' process which may include short-term aches and pains. This is a normal response to starting a new physical activity and usually improves after a few days.
- Find activities and exercises to do when standing that are enjoyable to undertake.
- There are many ways to modify the programme over time, even when MS symptoms are 'up and down'. Support from a physiotherapist can help with this. Sharing ideas with other people who use a frame can also be useful.
- Not everyone feels up to standing every day—that's ok.
- Frames are about the size of an armchair so space is a consideration. From a practical perspective, it is ideal if they are kept in one place, but they can be moved quite easily with help from an assistant.

self-managed programme while living with a progressive, fluctuating condition. The inclusion of standing assistants gave different perspectives on changes seen as a result of standing, as well as the practicalities of using a frame in the home.

Other strengths of the study are the clear audit trail and variety of strategies to enhance transparency and rigour. Although the findings represent a subsample of participants involved in the RCT, a comprehensive sampling approach was used to ensure representation of viewpoints from a range of participants. In addition, triangulation of the audio data with that obtained from the exit interviews supports the validity of the findings.

It is difficult to know how this audio diary approach fared compared with more traditional interviews. One might surmise, for instance, that the participants may have produced less sanitised accounts of their experiences given the opportunity they were afforded to provide, at their own discretion, a more immediate reaction to a situation in comparison to a more formal interview approach; there is scope for further research regarding this. At a practical level, however, the use of this methodology presented some challenges. Despite showing the person with MS and their standing assistant how to use the audio recorder, and providing written information to support this, some people experienced difficulties with using the audio recorder. Some people with dexterity problems found the small, portable recorder difficult to use and on two occasions, people chose to replace the audio with written notes. On other occasions, it was not until the recorders were returned at the end of the study, that it became apparent that for a few of the participants recordings had only been successfully completed on two or three occasions during the intervention period. Additional systems, such as telephone or email reminders to encourage use of the audio diary, may have helped to minimise this.

While other researchers using audio diary methodology have found ethical challenges in dealing with emotional distress, given the delay in listening to the diaries and thus the inability to offer immediate support in times of distress; we did not experience this when listening to the recordings, although it is an important consideration.[30]

CONCLUSION

Supported standing in the frame appeared to help people with severe progressive MS experience a sense of normality and enjoyment, which led to them feeling more like their old selves. People reported improvements in physical and psychological symptoms and impairments, which were associated with an increase in activities of daily living and (re-)engagement with activities which were important to them. These positive changes and the enjoyment they derived from standing meant that two-thirds of participants requested to keep the frame at the end of the 36-week trial period in order to continue to use it. Notably, people wanted to continue using the frame even if they had not seen many physical improvements as a result of standing. Physiotherapy support to establish the programme and educate the person with MS and their standing assistant about how to modify it according to their individual and varied needs and symptoms was considered key, as was a recognition of the ups and downs of living with a progressive and fluctuating neurological condition.

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Contributors JAF, WH, LJ, SC, AB and AH developed the study and contributed to trial design. RD, JAF and WH contributed to data collection, data analysis and writing of the manuscript. LJ, SC and AB contributed to drafts of the paper. All authors approved the final draft of the manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the 'Materials and methods' section for further details.

Patient consent for publication Not required.

Ethics approval Ethical approval was gained from the NHS Health Research Authority Committee South West-Frenchay Research Ethics Committee (15/SW/0088). All participants gave written informed consent prior to commencing study activity.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. The SUMS study protocol and statistical analysis plan are publicly available at: https://www.plymouth.ac.uk/research/sums. Individual participant data that underlie the results will be made available (after de-identification) on a controlled access basis, subject to suitable data sharing agreements. Requests for data sharing should be made to the Chief Investigator (JAF) in the first instance.

2.2.3 Films

Dennett R, Hendrie W, Jarrett L, Creanor S, Barton A, Hawton A, Freeman J. “I’m in a very good frame of mind”: A qualitative exploration of the experience of standing frame use in people with progressive multiple sclerosis. Four Short Films. 2019 on study website: https://www.plymouth.ac.uk/research/sums

In order to play these films with audio, please ensure your device is set to play sound from webpages. To do this, go to ‘control panel’, select ‘internet options’, ‘advanced’, scroll down to multimedia and tick ‘play sounds in webpages’. I hope you enjoy the films.

“Feeling like the old me”

In this short film people share the enjoyment they experienced from standing in the frame and some describe the opportunity it provided to reflect on their past and consider their present identity.

“Noticing a difference”

Here people talk about the positive differences they noticed from standing in terms of both physical changes and emotional well-being.

“You have a good day, you have a bad day”

In this film we learn more about the impact that the "ups and downs" of living with MS can have on using the standing frame as part of a daily routine, and how people's hopes and expectations influence their experience of standing.

“I want to do it right”

In the final film people share ways they found to modify their standing frame programme. Potential short-term issues such as aches and pains and managing fatigue are also highlighted as factors to consider when establishing a standing programme.

2.3 Adherence Stream

2.3.1 Paper 5

Dennett R, Madsen LT, Connolly L, Hosking J, Dalgas U, Freeman J. Adherence and drop-out in randomized controlled trials of exercise interventions in people with multiple sclerosis: A systematic review and meta-analyses. Multiple Sclerosis and Related Disorders. 2020: 43(8) 1-16 https://doi.org/10.1016/j.msard.2020.102169

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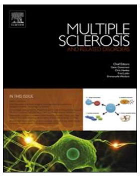

Adherence and drop-out in randomized controlled trials of exercise interventions in people with multiple sclerosis: A systematic review and meta-analyses

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ABSTRACT

Background: The short-term benefits of exercise in people with multiple sclerosis (MS) are well established. To sustain benefits exercise needs to continue long-term. Despite important clinical implications, no systematic reviews have synthesized evidence on adherence and drop-out in MS exercise interventions.
Objectives: 1) To summarize reported adherence and drop-out data from randomized controlled trials (RCTs) of exercise interventions, and 2) identify moderators related to adherence and drop-out.
Methods: Nine databases were electronically searched in October 2018. Included studies were RCTs of exercise interventions in adults with MS published from January 1993 to October 2018. Abstracts and full texts were independently screened and selected for inclusion by two reviewers. Methodological quality was assessed using the TESTEX rating scale.
Results: Ninety three articles reporting 81 studies were included. Forty one studies (51%) reported both adherence and drop-out data during the intervention period with three (4%) also reporting follow-up data. Of the 41 studies, < 25% pre-defined adherence or described how adherence was measured. Meta-analyses of 59 interventions (41 studies) showed a pooled adherence estimate of 0.87 (95% CI 0.83 to 0.90) and 0.73 (CI 0.68-0.78) when including drop-outs. Mean age, proportion of females and intervention duration were inversely associated with adherence.
Conclusion: Little consensus existed on definition of adherence or determination of drop-out in MS exercise studies, with reporting generally of poor quality, if done at all. Hence it is largely unknown what can moderate adherence and whether exercise continued following an exercise intervention. Researchers should ensure clear transparent measurement and reporting of adherence and drop-out data in future trials.

1. Introduction

Promoting exercise in people with multiple sclerosis (pwMS) is important since the short-term benefits of exercise are well documented (Edwards and Pilutti, 2017, Heine et al., 2015, Jorgensen et al., 2017, Latimer-Cheung et al., 2013) as are the low levels of physical activity within the population. (Kinnett-Hopkins et al., 2017) The international community of researchers (Motl et al., 2017) and clinicians continue to develop our understanding of exercise in pwMS and work towards identifying the most effective exercise interventions for people with a range of disability (Feinstein et al., 2015, Riemenschneider et al., 2018, Edwards and Pilutti, 2017, Garrett et al., 2013, Freeman et al., 2019) and in a range of settings. (DeBolt and McCubbin, 2004, Feys et al., 2019, Zimmer et al., 2018) For example, over the past twenty years interventions to enhance long-term engagement with activity (McAuley et al., 2007, Dennett et al., 2018, Emmerson et al., 2019) have been developed and evaluated and the value of incorporating behavioural interventions to support behaviour change has been investigated. (Casey et al., 2018, Motl et al., 2017, Motl et al., 2018) These developments are vital since sustained engagement in exercise is required to retain any benefits gained. (Twomey and Taylor J, 1984)

A key term used when considering long-term engagement with an intervention is "adherence". Within the field of exercise research this term is often used synonymously with that of compliance, concordance

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or participation but within this paper the term adherence as defined by the World Health Organisation (WHO) (see definitions section below) will be used.(World Health Organisation, 2003) It is of note that according to WHO, across diseases, adherence is the single most important modifiable factor that affects outcome. Despite the advances in MS exercise and rehabilitation research, poor exercise and physical activity levels are still reported in pwMS (Kinnett-Hopkins et al., 2017), highlighting the importance of continuing to gain greater depth of understanding regarding the factors that impact adherence in this population.

In addition, in order for any intervention to have a positive long-term impact it is imperative that its efficacy transcends the research setting into clinical practice and the daily lives of those people it is designed to help. As such, it is important that research is conducted and reported in a manner that allows clinicians and healthcare providers to be confident in the quality, replicability and relevance of the findings. It is also important that effective exercise interventions are suitable for implementation within the financial constraints of health service provision and are feasible and acceptable to the user in order to maximise adherence.

Many of these important factors, including intervention delivery, level of supervision, study retention and intervention adherence were considered by Allen et. al. (Allen et al., 2012) in a review of exercise interventions in people with Parkinson's disease. Interventions from the 53 included studies were typically of short duration and highly supervised, with less than half reporting adherence. They highlighted the challenge this presented to clinicians considering the cost-benefit balance when seeking to translate research into practice. It is not yet known whether similar issues are experienced in the field of MS or whether sufficient information exists to identify important moderators of long-term adherence and drop-out in exercise studies. Therefore, the objectives of this systematic review were to 1) summarize reported adherence and drop-out data from Randomized Controlled Trials (RCTs) of exercise interventions during the intervention and at follow up, and 2) identify moderators related to adherence and drop-out during the exercise intervention and at follow up.

2. Methods

This review is reported in line with the Preferred Reporting Items for Systematic Reviews and Meta- Analyses (PRISMA). (Moher et al., 2009) The protocol for this review was registered with PROSPERO ref CRD42018112866.

The following PICO question was formulated and guided the literature search and study inclusion: What adherence and drop-out data are reported by studies evaluating structured exercise interventions (according to the definition of Caspersen (Caspersen et al., 1985)) in pwMS, during both the intervention period and any follow-up period, and what moderators of adherence and drop-out can be identified, which relate to these exercise interventions?

2.1. Definitions

The following definitions are used within this review:

Exercise: As defined by Caspersen, a form of physical activity that is planned, structured and repetitive, and is undertaken with the objective of improving or maintaining at least one aspect of physical fitness; that is strength, flexibility or aerobic endurance. (Caspersen et al., 1985)

Physical activity: Any bodily movement produced by skeletal muscles that requires energy expenditure. (Caspersen et al., 1985)

Adherence: The World Health Organisation (WHO) define adherence as "the extent to which a person's behaviour; taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider". (World Health Organisation, 2003) Adherence is reported as the number of attended sessions expressed as a % of the total number of planned supervised sessions, and/or the percentage of completed prescribed home programme exercises/sessions where this was a component of the intervention. In addition, adherence can be reported according to pre-defined cut-offs as stipulated by study authors. Where possible distinction is made between adherence to session attendance (session adherence) and adherence to the specific exercise protocol (content adherence).

Drop-out: Participants that leave a study during the intervention period or during the follow up period expressed as:

% drop-outs during intervention period = (drop-outs during intervention period/ total number recruited participants) x100

% drop-outs during follow up = (drop-outs during follow up period/ total number recruited participants) x100

Study drop-outs could be related to a multitude of factors. Some, directly related to the exercise intervention itself such as time commitment, but others may be study related factors such as failure to attend follow up assessments

Adverse event: Any unfavourable and unintended symptom or disease that develops or worsens during the period of the trial, whether or not it is considered to be related to the trial intervention. (European Parliament, 2002)

2.2. Eligibility criteria

To be eligible for inclusion, studies were RCTs in adults over 18 years of age with a diagnosis of MS but regardless of gender, disease duration, MS phenotype or level of disability. Trials involved exercise interventions of any modality (location, group/ individual structure, level of supervision, intervention duration, session duration, intensity, frequency); content (aerobic, resistance, combined, other); with or without inclusion of a behavioural or home exercise component and with or without a follow up period.

Studies where the primary intention was to improve balance but the intervention was exercise (as defined by Caspersen (Caspersen et al., 1985)) were included. Studies reporting: balance gaming interventions (such as the Wii Fit); interventions specifically for the upper limb; gait re-education, where the primary intention was to impact on spatial or temporal parameters of gait; vestibular rehabilitation; and wheelchair propulsion interventions were not included. Studies reporting activities where the participant could be passive such as hippotherapy and robotic training were also not included. Control interventions could include passive controls, (often reported as usual activity/ care or a non-targeted exercise intervention such as relaxation or massage) or active controls where an active exercise comparator was included.

Included studies had to report at least one objective and/or self-report measure of either strength, aerobic capacity, endurance, fatigue, walking capacity or physical activity. Measures of walking capacity could include 10 metre, 25 foot, 2 minute and 6 minute walking tests and any type of accelerometry data.

Exercise interventions were categorised as either aerobic, resistance or combined training or as 'other' interventions, such as yoga, Pilates and inspiratory muscle training.

2.3. Data sources and search strategy

A search strategy was developed in liaison with an information specialist, based on the following key terms; "multiple sclerosis" OR MS AND exercise OR "physical activity" AND strength OR aerobic OR fitness OR training. The full search strategy can be found in appendix 1. Two reviewers (LM and RD) conducted electronic searches of MEDLINE, EMBASE, CINAHL, AMED, PEDro, SPORTDiscus, PsycINFO, Web of Sciences and SCOPUS from January 1993 to October 2018. This 25 year period was chosen to encompass the earliest of MS rehabilitation/ exercise randomized controlled studies. Electronic searches were supplemented by hand searches of reference lists. Duplicates were removed and records were imported into the Rayyan data management system. Titles and abstracts were independently screened for eligibility based on the inclusion criteria by two reviewers (RD or JF and LM). Finally, full texts of remaining articles were read by two reviewers (LM, LC or RD) and any disagreements were discussed with a fourth member of the research team (JF).

2.4. Data extraction

A customized Excel spreadsheet was used to collate the extracted data from included studies. Details extracted included participant characteristics (age, gender, disease duration, MS phenotype, disability level and fatigue as a symptom); modality of the intervention (setting, group/ individual structure, level of supervision, intervention duration, session duration, intensity, frequency); content of the intervention (aerobic/ resistance/ combined / other modality/ including a behavioral or home exercise program component); report of adverse events, % drop-out, and adherence during the intervention period and at any follow up. Where there was missing data, the median was used as a proxy for the mean and 0.75 times the interquartile range or 0.25 times the range as proxies for the standard deviation. (Hozo et al., 2005) Standard errors were converted into standard deviations by multiplying the standard error by the square root of the sample size. (Hozo et al., 2005)

Data extraction was completed by one reviewer (RD, LM or LC) and 10% of papers (n = 10) were also extracted by a second reviewer for quality assurance purposes (JF or UD) with a kappa of 0.639, $p < 0.0001$ indicating substantial agreement between reviewers. Adherence data from all studies that reported this was extracted by two reviewers (RD, LM or LC).

2.5. Quality Assessment

Methodological quality was assessed independently by two reviewers (LM, LC or RD) using the Tool for the assEssment of Study qualiTy and reporting in EXercise (TESTEX) rating scale; a novel tool designed for appraising methodological quality of exercise studies. (Smart et al., 2015) Any discrepancies were discussed, and on six occasions a third reviewer (JF) was consulted to reach consensus.

2.6. Synthesis of results

The adherence data were extracted in the form of proportion of participants 'adherent' to an intervention or mean number or percentage of sessions attended. Where adherence was reported as mean number or percentage of sessions attended, this was not always accompanied by a measure of variation. Consequently, and in line with McPhate et al. (McPhate et al., 2013) the data were converted to represent the proportion of participants 'adherent' in order to include all interventions in the analysis. In studies with an exercise comparator group, adherence data were reported separately for each different intervention evaluated in the same study; for example, Pilutti et al. 2016a (recumbent stepper), Pilutti et al. 2016b bodyweight support treadmill). For the purpose of clear reporting, in cases where study results were reported by more than one article, the paper reporting the primary outcome or with most complete adherence data was used.

A meta-analysis was conducted to estimate the pooled adherence across the 59 interventions (41 studies) using the Freeman-Tukey double arcsine transformation to transform the raw proportions. We hypothesised that intervention type (i.e. 'aerobic', 'resistance', 'combined' or 'other) would be a moderator of adherence and as such we calculated pooled adherence within these sub-groups as well as across all studies, taking into account this sub-grouping using a mixed effects model.

Heterogeneity was assessed using the I-squared statistic and meta-regression was used to examine the association between the a priori defined study intervention related variables (potential moderators including: intervention type, duration, and frequency, supervised or unsupervised, inclusion of a behavioural intervention or home exercise component and EDSS, disease duration, mean age and proportion of female participants, TESTEX score of study quality) and adherence.

Studies reported adherence data for participants who completed an intervention. As such, this did not take into account participants who dropped out of a study (for whatever reason). In this review therefore, in order to consider the impact of study drop-outs on adherence, analysis was repeated with percentage adherence recalculated to include drop-outs. Mindful that reasons for drop-out (exercise intervention or study process related) were not consistently provided, each drop-out was assumed a conservative adherence estimate of 0%.

A further meta-analysis was also carried out including only those studies which reported mean adherence (with a measure of variation). All analyses were carried out using the 'metafor' (Viechtbauer, 2010) package in R. (CoreTeam, 2019)

3. Results

3.1. Study characteristics

Searches identified 10267 articles which after deduplication resulted in 6612 titles and abstracts being reviewed. Of these, 133 were included for full text review of which 93 met the inclusion criteria. For further detail please refer to figure 1.

The 93 included articles reported on 81 RCTs which involved 4007 pwMS, mean (SD) age 43.8 (8.2) years, disease duration 9.2 (6.3) years. Eleven of the included studies only involved people with relapsing remitting MS (RRMS), 19 included people with all types of MS (RRMS, secondary progressive MS, primary progressive MS and benign) and 11 did not state MS type. Disability level was reported using the Expanded Disability Status Scale (EDSS) in 59 studies. (Kurtzke, 1983) Other measures used were the Patient Determined Disease Steps (PDDS) (Learmonth et al., 2013) and the Guys Neurological Disability Scale (GNDS). (Sharrack and Hughes, 1999) The vast majority of studies included people who were ambulant with or without walking aids (EDSS 0-6.5) with only three studies (Aidar et al., 2018, Klefbeck and Hamrah Nedjad, 2003, Pilutti et al., 2016) including participants with an EDSS ≥ 7.

In eleven studies the RCT involved exercise comparator groups, seven included active controls and 31 enrolled passive controls. Of the passive controls, two were defined as relaxation exercises (Fox et al., 2016, Ozkul et al., 2018) and one as massage. (Duff et al., 2018) The remaining studies described the content of the passive control as "usual activity" or "usual care". Two studies gave some information about what usual activity could comprise of, for example 'recording in a diary all physical activity exceeding 20 minutes and occurring more than twice a week', [58] or 'usual care could include habitual exercise participants engaged in, or therapy, provided it did not include progressive resistance training. (Dodd et al., 2011) Importantly however, no authors defined, detailed or reported what usual activity included or stated adherence to that activity. As such it is not possible to comment on adherence to the passive control group content. Adherence data throughout this review, therefore, is reported for active exercise interventions, both the exercise comparator and active control groups.

3.2. Studies reporting adherence and drop-out

Of the 81 included studies, 41 (51%) reported adherence to an intervention (exercise comparator and/ or active control). Details regarding the study interventions can be found in table 1. The definitions of adherence used and methods of reporting were not consistent. In 38 cases adherence was defined as the proportion of prescribed sessions attended. On three occasions adherence was defined as the proportion of people who were adherent based upon a pre-defined cut-off; exercise on 45% (Conroy et al., 2018) of days during the study or 67% (Hosseini et al., 2018) or 80% (Tallner et al., 2016) of sessions attended.

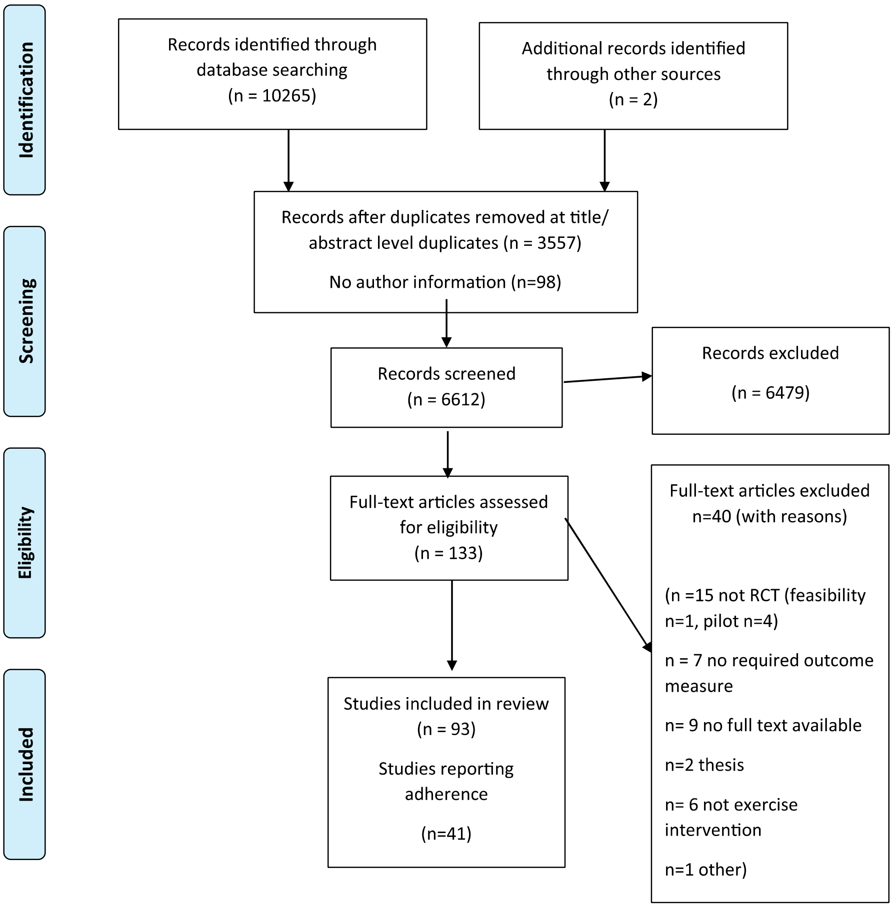

Figure 1. PRISMA Flow Diagram.

Nine (DeBolt and McCubbin, 2004, Zimmer et al., 2018, Tallner et al., 2016, Fox et al., 2016, Fry et al., 2007, Mutluay et al., 2007, Oken et al., 2004, Romberg et al., 2004, Wens et al., 2015) papers stated within their methods section that adherence was an outcome of interest. Sample size in the studies reporting adherence ranged from n = 14[47] to n = 314[9] with mean (SD) intervention participant age 46.1(8.4) years and control participant age 45.5 (7.8) years. Mean disease (SD) duration of intervention participants was 9.4 (7.1) years and EDSS score 3.8 (1.2) and controls was 9.5 (6.2) years and 3.3 (1.1) EDSS score.

Mean intervention duration was 12.2 weeks (range 3-26) and mean frequency 3.3 sessions a week (range 1-7). Of the included studies only 11 (14%) included a follow up assessment (range 4-26 weeks) of which three (4%) made reference to exercise adherence during this period.

3.3. Reporting of adherence and drop-out

Authors reported adherence in a variety of ways including: the number or proportion of participants attending a particular number of sessions (n = 7); the number or proportion of participants attending all sessions (n = 6); the total number of prescribed exercise sessions attended (n = 2); mean number of sessions attended by participants (either as a single average (n = 7) or as an average accompanied by a measure of variation (n = 19)).

With respect to adherence to the exercise protocol (content adherence), thirty-five of the forty-one studies did not provide any detail to confirm completion of the exercise program as prescribed. A further five studies reported only very briefly on intervention completion, by statements such as: "the intervention was completed as prescribed" (Sandroff et al., 2017, Hogan et al., 2014); participants "completed all the scheduled training sessions" (Medina-Perez et al., 2014); "affirmed full compliance with the programme" (Mutluay et al., 2007) or that "the intervention schedule was completed". (Collett et al., 2011) Only one study gave additional, although limited details, by reporting that adherence to the program was successful, with 95% of exercise sessions completed and participants in the exercise group successfully increasing the weight in their vests by 0.5% to1.0% of body weight during the 8-week intervention. (DeBolt and McCubbin, 2004)

Reported adherence to an exercise intervention (exercise comparator or active control) ranged from 50% (Conroy et al., 2018, Collett et al., 2011) -100% (Fimland et al., 2010, Hojjatollah et al., 2012) during the intervention period and 20% (Dalgas et al., 2009) - 88% (Kjolhede et al., 2015) in the three studies reporting this during follow up. Seventy eight percent of included interventions reported adherence of 80% or more. Eighty two percent of these were supervised interventions. In two studies, flexibility regarding time frame for completing the intervention was allowed within the protocol in order to attain 80% adherence. (Feys et al., 2019, Moradi et al., 2015) Methods used to measure adherence were stated in eleven studies, some of which included more than one method, and included session attendance monitoring (n = 5), self-report diary or logbook (paper; n = 9; electronic diary n = 1) or activity tracker (n = 1).

Table 1
Characteristics of included studies reporting adherence

Study	Active/passive control	Recruited (N)	Analysed (N)	Sex (% female)	Age (mean)	MS type (% RRMS)	EDSS	Disease duration (mean)	Individual/ group	Supervised/ unsupervised	Frequency (d/wk) and duration (wks)	Intensity	Length of training session (min)	Intervention %adherence	% Adherence Incl Drop out[+]
Aerobic															
Bicycle ergometer															
Collett et al, 2010*	Three comparator groups	Int 1: 20 Int 2: 21 Int 3: 20	20 18 17	53 80 78	55.0 52.0 50.0	40	NR	12.0 15.0 11.0	NR NR NR	Supervised Supervised Supervised	2d/wk*12 wks 2d/wk*12 wks 2d/wk*12 wks	Continuous: 45% PPO Interval: 30s on/30 s off at 90% of PPO Combined: 10 min HIIT + 10 min continuous	20 20 20	66 54 50	56 51 45
Mostert and Kesselring, 2002 (upper- and lower-limb cycling)	Active control (inpatient physical therapy)	Int: 18 Con: 18	13 13	77 85	45.2 43.9	31 39	4.6 4.5	11.2 12.6	NR NR	Supervised NR	5d/wk*4wk NR	NR NR	30 NR	65 NR	47 NR
Negaresh et al, 2018	Passive control (not defined usual activity)	Int: 36 Con: 30	34 27	64 67	31.7 30.6	100	1.7 1.5	7.3 7.4	NR NR	Supervised NR	3d/wk*8wk NR	Intermittent: 2 min on/2 min off at 60-75% of PPO NR	42-66 NR	92 NR	87 NR
Oken et al, 2004	Comparator (yoga) Passive Control (not defined waitlist control)	Int1: 21 Int2: 26 Con: 22	15 22 20	87 91 100	48.8 49.8 48.4	NR NR NR	2.9 3.2 3.1	NR NR NR	Group Group NR	Supervised Supervised NR	1d/wk*26wks 1d/wk*26wks NR	NR NR NR	NR 90 NR	65 68 NR	46 58 NR
Petajan et al, 1996 (combined arm and leg cycle ergometer)	Passive control (not defined usual activity)	Int: 27 Con: 27	21 25	71 67	41.1 39.0	NR	3.8 2.9	9.3 6.2	NR NR	Supervised NR	3d/wk*15wk NR	60% of VO_{2max} NR	45-50 NR	97 NR	75 NR
Zimmer et al, 2017 (HIT)	Comparator (moderate intensity cycling)	Int 1: 29 Int 2: 31	27 31	74 60	51.0 48.0	52 53	4.4 4.4	12.0 12.3	NR NR	Supervised Supervised	5d/wk*3wk 5d/wk*3wk	Interval: 5 x 3 min on/1.5 min off at 80% of VO_{2peak} Continuous: at 65% of VO_{2peak}	20 30	100 100	93 97
Running															
Feys et al, 2017	Passive control (not defined waitlist control)	Int: 21 Con: 21	18 17	95 86	36.6 44.4	NR	NR	8.1 9.2	Indiv NR	Unsupervised NR	3d/wk*12wk NR	NR NR	NR NR	94 NR	81 NR
Recumbent stepper															
Pilutti et al, 2016	Comparator (body weight support treadmill)	Int 1: 6 Int 2: 6	5 5	60 40	58.8 48.2	0 0	7.0 7.0	15.2 12.7	NR NR	Supervised Supervised	3d/wk*12wk 3d/wk*12wk	NR NR	Gradually increased to 30	89 89	74 74
Resistance															
Calisthenics															
Forsberg et al, 2016	Passive control (not defined waitlist control)	Int: 44 Con: 43	35 38	80 82	52.0 56.3	57 34	NR NR	15 16	Group NR	Supervised NR	2d/wk*7wk NR	NR NR	50-60 NR	86 NR	68 NR
Progressive resistance training															

(continued on next page)

Table 1 (*continued*)

Study	Active/passive control	Recruited (N)	Analysed (N)	Sex (% female)	Age (mean)	MS type (% RRMS)	EDSS	Disease duration (mean)	Individual/ group	Supervised/ unsupervised	Frequency (d/wk) and duration (wks)	Intensity	Length of training session (min)	Intervention %adherence	% Adherence Incl Drop out^{+}
Dalgas et al, 2009*	Passive control (waitlist control, not defined usual activity)	Int: 19 Con: 19	15 16	66 62	47.7 50.4	100	3.7 3.9	6.6 8.1	Group NR	Supervised NR	2d/ wk*12wk NR	3-4 sets of 8-12 repetitions at 8-15 RM NR	NR NR	100 NR	79 NR
DeBolt and McCubbin 2004	Passive control (not defined usual activity)	Int: 19 Con: 18	19 17	79 78	51.6 47.8	47 44	4.0 3.5	15.1 13.0	Indiv NR	Unsupervised NR	3d/wk*8wk NR	2-3 sets of 8-12 repetitions wearing a weighted vest (0.5% of BW) increasing by 0.5-1.5% of BW every 2 wk	35-50 NR	95 NR	95 NR
Dodd et al, 2011	Passive control (Usual activity + social program)	Int: 39 Con: 37	36 35	72 74	47.7 50.4	100	NR	NR	Group Group	Supervised Supervised	2d/ wk*10wk 1d/ wk*10wk	2 sets of 10-12 repetitions at 10-12 RM NR	45 60	92 NR	85 NR
Fimland et al, 2010	Active Control (conventional rehabilitation)	Int: 7 Con: 7	7 7	57 57	53.0 54.0	NR	4.6 3.5	8.0 8.0	Indiv NR	Supervised NR	5d/wk*3wk NR	4 sets of 4 repetitions at 85-90 % of 1RM NR	NR	100 NR	100 NR
Hosseini et al, 2018	Comparator Yoga Passive control (not defined usual activity)	Int 1: 9 Int 2: 9 Con: 8	8 8 8	55 55 50	32.9 31.3 33.0	NR	NR	NR	Indiv Indiv NR	Unsupervised Unsupervised NR	3d/wk*8wk 3d/wk*8wk NR	1% of BW fastened to body increasing by 0.5-1% every 2 wk NR NR	35-50 60-70 NR	100 100 NR	89 89 NR
Harvey et al, 1999	Comparator (mobility exercises) Passive control (not defined, usual activity)	Int 1: 7 Int 2: 7 Con: 5	6 5 5	83 83 80	38.0 49.0 43.0	100	NR	5 5 10	Indiv Indiv NR	Unsupervised Unsupervised NR	2d/*8wk 7d/wk*8wk NR	5 sets of 10 leg extensions using 0.5 or 1kg ankle weights NR NR	NR NR NR	69 69 NR	59 59 NR
Kjolhede et al, 2015*	Passive control (waitlist not defined usual activity)	Int: 18 Con: 17	17 15	NR	43.2	100	3	5	NR NR	Supervised NR	2d/wk* 24wk NR	3-5 sets of 6-10 repetitions at 6-15 RM NR	NR NR	93 NR	88 NR
Manca et al, 2017 *Contra lateral strength training*	Active control (direct strength training)	Int 1: 15 Int 2: 15	15 15	64 75	42.1 47.3	100 100	3.8 4.1	12.7 16.8	Indiv Indiv	Supervised Supervised	3d/wk*6wk 3d/wk*6wk	3 sets of 4 repetitions at 45°/s and 10°/s at 100% of 1RM 3 sets of 4 repetitions at 45°/s and 10°/s at 100% of 1RM	25 25	91 91	91 91
Medina-Perez et al, 2014	Passive control (not defined usual activity)	Int: 30 Con: 12	30 12	88 71	49.6 46.2	100 100	4.5 4.1	11.3 12.2	NR NR	Supervised NR	2d/ wk*12wk NR	3 sets of 8-12 repetitions at 35-70 % of MVC NR	NR NR	95 NR	95 NR
Medina-Perez et al, 2016	Passive control (not defined usual activity)	Int: 38 Con: 39	20 20	50 50	45.6 41.3	100 100	3.9 4.2	10.9 10.4	NR NR	Supervised NR	2d/ wk*12wk NR	3 sets of 4-10 repetitions at	NR NR	95 NR	50 NR

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Table 1 (*continued*)

Study	Active/passive control	Recruited (N)	Analysed (N)	Sex (% female)	Age (mean)	MS type (% RRMS)	EDSS	Disease duration (mean)	Individual/ group	Supervised/ unsupervised	Frequency (d/wk) and duration (wks)	Intensity	Length of training session (min)	Intervention %adherence	% Adherence Incl Drop out^{+}
Moradi et al, 2015	Passive control (not defined usual activity)	Int: 10 Con: 10	8 10	0 0	34.4 33.1	62 60	3.0 3.0	8.1 6.5	NR NR	Supervised NR	2d/wk*8wk NR	40-70 % of MVC NR 1 set of 6-15 repetitions at 50-80% of 1 RM NR	30 NR	100 NR	80 NR
Inspiratory muscle training															
Mutluay et al, 2007	Passive control (not defined usual activity)	Int: 20 Con: 20	20 20	60 60	40.3 38.1	20 40	4.8 4.2	9.8 9.0	Indiv NR	Unsupervised NR	7d/wk*6wk NR	NR NR	NR NR	94 NR	94 NR
Fry et al, 2007*	Passive control (not defined usual activity)	Int: 23 Con: 23	20 21	91 74	50 46.2	50 75	3.96 3.36	NR NR	Indiv NR	Unsupervised NR	7d/ wk*10wk NR	3 sets of 15 repetitions at 30% of pretest MIP NR	NR NR	81 NR	70 NR
Combined															
Aerobic and resistance															
Bjarnottir et al, 2007	Passive control (not defined usual activity)	Int : 11 Con: 12	6 10	50 80	38.7 36.1	100	2.1 1.8	8.7 8.3	NR NR	Supervised NR	3d/wk * 5wk NR	55% of VO_{2peak} NR	60 NR	80 NR	44 NR
Cakit et al, 2010	Comparator (strength and balance exs) Passive control (not defined usual activity)	Int 1: 15 Int 2: 15 Con: 15	14 10 9	60 80 66	36.4 43.0 35.5	NR	NR	9.2 6.2 6.6	Group Indiv NR	Supervised Unsupervised NR	2d/wk *8wk 2d/wk *8 wk NR	15 sets of 2 min at 40% of TMW + 2 min at 30-40 W NR NR	90 30 NR	93 60 NR	87 40 NR
Carter et al, 2014	Passive control (not defined usual activity)	Int: 60 Con: 60	50 49	72 72	45.7 46	78 85	3.8 3.8	8.4 9.2	Group NR	Supervised Unsupervised	2d/wk *12wk NR	5 sets of 3-4 min intervals at 50-69% of HR_{peak} interspersed with 2 min rest NR	60 NR	90 NR	75 NR
Hansen et al, 2015*	Passive control (not defined usual activity)	Int: 23 Con: 13	16 11	63 55	46.0 48.0	75 55	3.0 3.0	NR	NR NR	Supervised NR	5d/ 2wk*24wk NR	NR NR	1x6-3x10 NR	90 NR	63 NR
Hojjatollah et al, 2012	Passive control (not defined usual activity)	Int: 10 Con: 10	10 10	0 0	NR NR	NR	NR	NR	NR NR	Supervised NR	3d/wk*8wk NR	3 sets of 10 repetitions at 40-50% of 1 RM NR	60-90 NR	100 NR	100 NR
Kerling et al, 2015	Active control (cycle endurance)	Int: 38 Con: 39	19 18	80 66	42.3 45.6	NR	2.6 3.1	NR	NR	Supervised Supervised	2d/ wk*12wk 2d/ wk*12wk	50% of PPO and 2 sets of 10-15 repetitions at 10-15 RM 50% of PPO	40 40	92 92	58 55
Tallner et al, 2016	Passive control (not defined waitlist usual activity)	Int: 59 Con: 67	49 59	75 75	40.9 40.7	88 85	2.7 2.7	9.8 9.2	Indiv NR	Unsupervised NR	3d/ wk*12wk NR	NR NR	NR NR	73 NR	61 NR
								NR	NR						

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Table 1 (*continued*)

Study	Active/passive control	Recruited (N)	Analysed (N)	Sex (% female)	Age (mean)	MS type (% RRMS)	EDSS	Disease duration (mean)	Individual/ group	Supervised/ unsupervised	Frequency (d/wk) and duration (wks)	Intensity	Length of training session (min)	Intervention %adherence	% Adherence Incl Drop out+
Wens et al, 2015 (HIIT)	Comparator (continuous training) Passive control (not defined “sedentary” control)	Int 1 : 12 Int 2: 11 Con : 11	12 11 11	59 55 82	43.0 47.0 47.0	73 73 83	2.3 2.7 2.5			Supervised Supervised NR	5d/ 2wk*12wk 5d/ 2wk*12wk NR	80-100% of HR_{max} and 1-2 sets of 10-20 repetitions at 10-20 RM 80-90% of HR_{max} and 1-2 sets of 10-20 repetitions at 10-20 RM NR	Aerobic: 10-15 Aerobic: 6-20 NR	90 90 NR	90 90 NR
Wens et al, 2015*	Passive control (not defined usual activity)	Int: 30 Con: 15	29 15	59 53	48.0 49.0	59 73	3.25 3.36	NR	NR	Supervised NR	5d/ 2wk*24wk NR	NR NR	10-36 NR	90 NR	87 NR
Treadmill walking / cycle ergometer + Pilates															
Ozkul et al, 2018	Passive control (relaxation exs)	Int: 21 Con: 20	18 18	78 78	34.5 34.0	100 100	1.0 1.0	4.0 4.0	NR NR	Supervised NR	3x/ wk*8wks NR	60-80% of HR_{max} and 10-20 repetitions in Pilates NR	Aerobic: 30 and Pilates: 60 NR	85 NR	73 NR
circuit resistance training and aquatic aerobic training for 3 weeks then 23 weeks home resistance and aerobic of choice															
Romberg et al, 2004*	Passive control (not defined usual activity)	Int: 49 Con: 50	45 46	64 64	43.8 43.9	NR	2.0 2.5	6.0 5.5	Indiv NR	Supervised 3wks; unsupervised 23 wks NR	50 min 4-5d/ wk*26wk NR	NR NR	NR NR	93 NR	85 NR
Self-selected leg cycle ergometry, treadmill walking, and recumbent stepping exercise+ LL resistance training and balance exercises															
Sandroff et al, 2017	Active control (stretching and toning exs)	Int: 43 Con: 40	32 30	84 87	49.8 51.2	NR	PDDS 4.0 3.0	NR	Indiv NR	Supervised NR	30-60 min 3d/ wk*24wk NR	40–60% of VO_{2peak} and 40-70% of 1RM NR	30-60 NR	81 84	60 63
Other															
Pilates															
Duff et al, 2018	Passive control (massage)	Int: 15 Con: 15	15 15	80 73	45.7 45.1	93 73	PDDS 2.1 2.3	NR	Group Individual	Supervised Supervised	3d/ wk*12wk 1d/ wk*12wk	NR NR	50-60 min 60 min	85 NR	85 NR
Fox et al, 2016	Comparator and passive control (relaxation exs)	Int 1: 33 Int 2: 35 Con: 32	33 32 29	85 71 66	53.9 54.6 53.8	39 37 38	NR	13.2 13.9 12.4	Indiv Indiv NR	Supervised Supervised NR	1d/ wk*12wk 1d/ wk*12wk NR	NR	30 30 NR	66 84 92	56 72 72
Kalron et al, 2017	Active control (standard physiotherapy)	Int: 25 Con: 25	22 23	61 65	44.3 42.9	100	4.3 4.1	12.4 11.3	Indiv Indiv	Supervised Supervised	1d/ wk*12wk 1d/ wk*12wk	NR	30 30	83 83	73 76

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Table 1 (*continued*)

Study	Active/passive control	Recruited (N)	Analysed (N)	Sex (% female)	Age (mean)	MS type (% RRMS)	EDSS	Disease duration (mean)	Individual/ group	Supervised/ unsupervised	Frequency (d/wk) and duration (wks)	Intensity	Length of training session (min)	Intervention %adherence	% Adherence Incl Drop out[+]
Physiotherapy															
Garrett et al, 2012	Comparators (yoga)(fitness instructor) Passive control (not defined usual activity)	Int1 :80 Int2: 77 Int 3: 86 Con: 71	63 63 67 49	79 70 67 88	51.7 49.6 50.3 48.8	58	NR	9.8 11.6 10.5 10.6	Group Group Group NR	Supervised Supervised Supervised NR	1-2d/ wk*10wk Resistance 2-3/wk Aerobic 1d/ wk*10wk 1d/ wk*10wk NR	Resistance: 3 sets of 12 repetitions at 12 RM + Aerobic: at 65% of HR_{max} NR NR NR	Resistance: NR, Aerobic 30 NR NR NR	81 73 78 NR	64 60 61 NR
Hogan et al, 2014	Comparators (1:1 physio) (yoga) Passive control (usual activity)	Int 1: 66 Int 2: 45 Int 3: 16 Con: 19	48 35 13 15	63 57 62 87	57.0 52.0 58.0 49.0	27 20 31 33	NR	18 13 15 10	Group Indiv Group NR	Supervised Supervised Supervised NR	1d/ wk*10wk 1d/ wk*10wk 1d/ wk*10wk NR	NR	60 min 60 min 60 min 60 min	80 90 80 NR	58 70 65 NR
Conroy et al, 2018 (with internet programme)	Active control (paper home exercise programme)	Int: 26 Con: 25	16 8	44 63	50.4 54.3	25 50	PDDS 4.4 3.3	14.2 14.7	Indiv Indiv	Unsupervised Unsupervised	7d/ wk*26wk NR	NR	NR	50 NR	31 NR
Aquatherapy															
Sutherland et al, 2001	Passive control (not defined usual activity)	Int: 11 Con: 11	11 11	54 54	47.2 45.4	NR	NR	7.0 7.0	NR	Supervised NR	3x/ wk*10wk NR	NR	45 NR	90 NR	90 NR

Legend: *main study reported, also reported in following articles: 2009* Dalgas 2010, Dalgas 2010a, Dalgas 2013; Collett 2010* also in Feltham 2013; Hansen 2015* also in Hansen 2015a, Fry 20017* also in Pfalzer 2011; Kjolhede 2015* also in Kjolhede 2017; Romberg 2004* also in Romberg 2005, Surakka 2004; Wens 2015* also in Wens 2016.

[+] Adherence calculated to include drop-outs (drop-outs assigned 0% adherence)

Abbreviations: PPO: Peak power output achieved during incremental exercise test to exhaustion, VO_{2max}: maximal oxygen consumption, VO_{2peak}: peak oxygen consumption, RM: repetition maximum, BW: body weight, MVC: Maximal voluntary contraction, MIP: Maximal inspiratory pressure, TMW: Tolerated maximum workload, W: Watts; PDDS: Patient determined disease steps; Indiv: Individual; NR: not reported.

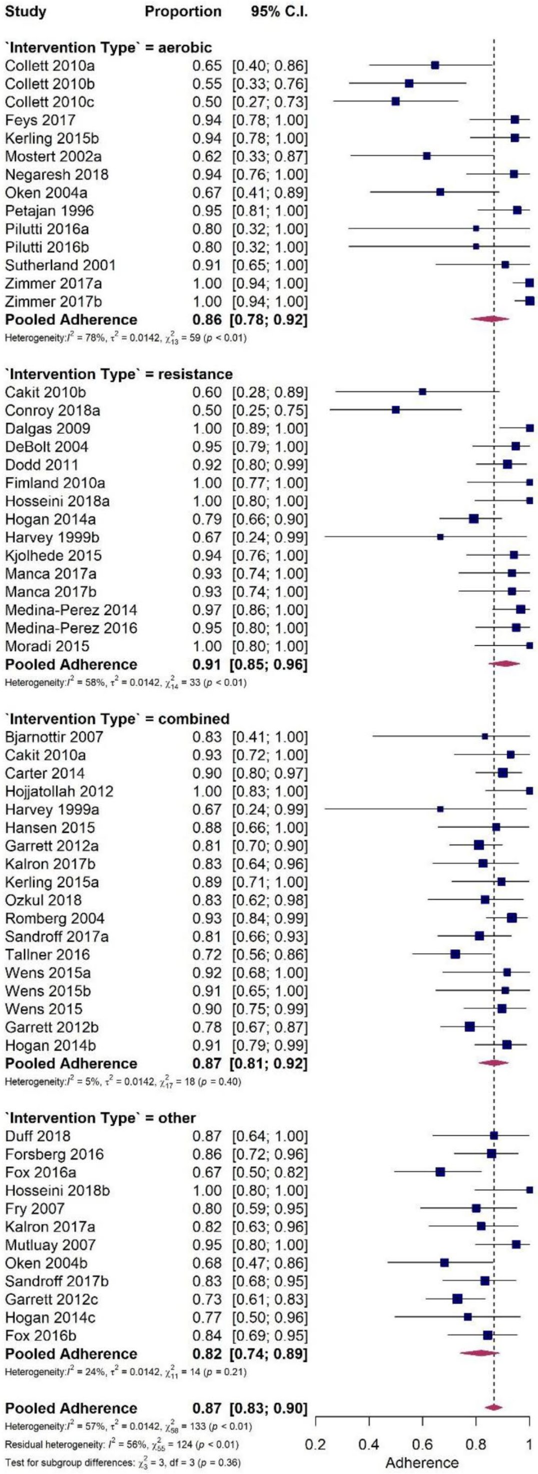

Figure 2. Pooled adherence (excluding drop-outs) according to intervention type.

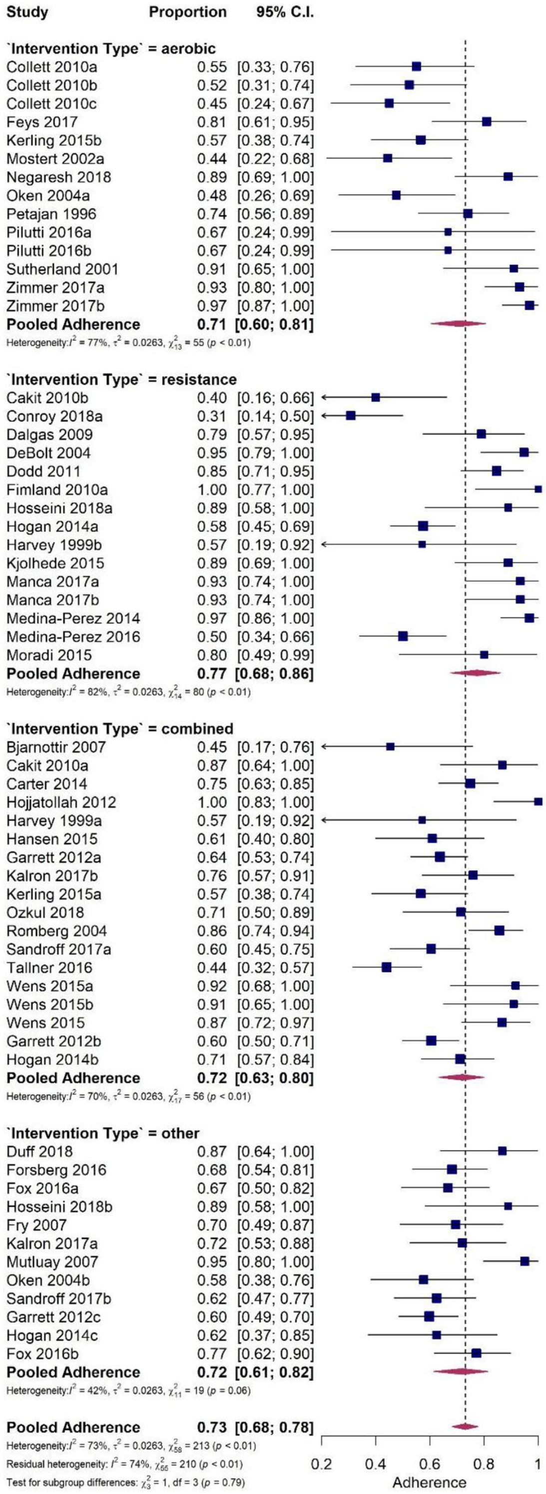

Figure 3. Pooled adherence (including drop-outs) according to intervention type.

The pooled estimate of adherence was 0.87 (95% CI 0.83 to 0.90), as illustrated in Figure 2. This estimate represents the proportion of participants reported as adherent to the intervention when adherence data were combined in a meta-analysis. The I-squared statistic was 57% (95% CI 46.4% to 76.2%) indicating a moderate-to-high degree of heterogeneity.

The reported drop-outs from exercise interventions ranged from 0% (Fimland et al., 2010) to 47% (Medina-Perez et al., 2016) during the intervention period and 0-27[40]% at follow up. There was a lack of consistency in reporting adherence and drop-out numbers and reasons for drop-out. This was the case regardless as to whether or not studies reported adherence at follow up. For instance, some studies excluded people who did not reach a pre-defined cut-off level of adherence to an intervention, such as 75% (Medina-Perez et al., 2016) or 80% (Wens et al., 2015, Dalgas et al., 2009) of sessions attended and instead reported them as drop-outs.

When adherence was re-calculated to include drop-outs, the pooled adherence was 0.73 (95% CI 0.68 to 0.78) and I-squared was 73% (95% CI 66.0% to 84.7%) as illustrated in figure 3.

3.4. Moderators

Only mean age (estimate = -0.009, standard error = 0.003, p = 0.013), proportion of female participants (estimate = -0.003, standard error = 0.001, p = 0.017), and duration of intervention (estimate = -0.007, standard error = 0.003, p = 0.045) all showed statistically significant inverse associations with adherence and together explained 31% of the adherence heterogeneity.

A range of potential strategies to enhance adherence have been suggested. (Casey et al., 2018, Motl et al., 2017) Our moderator analysis however suggested that there was not a significant association with adherence in relation to the use of behavioural interventions or a home exercise component. Fifteen studies (Garrett et al., 2013, DeBolt and McCubbin, 2004, Feys et al., 2019, Conroy et al., 2018, Hosseini et al., 2018, Tallner et al., 2016, Fox et al., 2016, Fry et al., 2007, Mutluay et al., 2007, Oken et al., 2004, Romberg et al., 2004, Cakit et al., 2010, Carter et al., 2014, Harvey et al., 1999, Kalron et al., 2017) incorporated a home exercise element, eight of which were home based interventions. Fifteen studies (Garrett et al., 2013, DeBolt and McCubbin, 2004, Feys et al., 2019, Conroy et al., 2018, Tallner et al., 2016, Fox et al., 2016, Fry et al., 2007, Mutluay et al., 2007, Oken et al., 2004, Romberg et al., 2004, Cakit et al., 2010, Carter et al., 2014, Harvey et al., 1999, Bjarnadottir et al., 2007, Dodd et al., 2011) included a behavioural intervention component. These were reported as goal setting, (Feys et al., 2019, Carter et al., 2014) use of an activity tracker, (Feys et al., 2019) telephone support, (DeBolt and McCubbin, 2004, Fry et al., 2007, Romberg et al., 2004) face to face support, (DeBolt and McCubbin, 2004) peer support, (Feys et al., 2019) social support, (Carter et al., 2014, Dodd et al., 2011) education regarding benefits of exercise (Garrett et al., 2013, Fry et al., 2007, Carter et al., 2014, Bjarnadottir et al., 2007) and log or workbooks. (Fox et al., 2016, Oken et al., 2004) Only one (Carter et al., 2014) of the studies described the theoretical background of the behavioural component.

3.5. Quality

The mean TESTEX score of the included studies reporting adherence was 7.5/15. Details of the individual scores can be found in table 2. Sixty six (70%) studies scored below 10 points, which although not designed to be a cutoff point, is suggested by the scale's authors as indicative of poor study design and/ or reporting (personal communication). TESTEX score was not found to be a moderator of adherence.

4. Discussion

The results of this systematic review provide a novel synthesis of the measurement and reporting of adherence and drop-out from exercise interventions (both exercise comparators and active controls) in exercise studies in MS. Overall measurement and reporting is poor, with only half (41/81) of the identified RCT studies reporting adherence. The lack of data is particularly striking in the follow up period where only three of 81 studies reported whether participants continued to engage in exercise. Hence we cannot ascertain from the existing evidence whether or not pwMS continue to exercise in the medium or longer term following the initiation of an exercise programme. This potentially limits the translation of results to clinical practice, since clinicians cannot make evidence based decisions regarding which exercise approach is most effective in sustaining long-term engagement in exercise; this being known to be required to retain any immediate benefits gained. In addition, only a few weak adherence moderators were identified. It would have also been interesting to determine levels of adherence to the control group intervention, however this data was rarely recorded or reported.

On a more positive note, it is encouraging that adherence to the exercise interventions (based on attendance to supervised sessions and percentage completion of prescribed home programme exercises) was high in the 41 studies which reported adherence during the intervention period, with the majority (78%) reporting adherence in excess of 80%. It is noteworthy, that more than 80% of this data related to attendance at supervised sessions. It is possible however, that this level of adherence is an overestimation given half of the exercise studies did not report adherence which potentially may have been due to poor levels of adherence rather than lack of measurement. During follow up, when supervision had ceased, the three studies reporting adherence scored 20, (Dalgas et al., 2009) 36 (Tallner et al., 2016) and 88% (Kjolhede et al., 2015) although this data should be interpreted with caution given the very limited number of studies upon which this is based.

Drop-out during intervention ranged from 0-47% and 0-27% at follow up. Whilst it is possible that participants may have dropped out for reasons related to the exercise intervention, unfortunately, a lack of consistency and detail in reporting means that it is not possible to determine whether or not this was the case. The limited available data provided wide ranging reasons for drop-out, which include personal circumstances (e.g. family illness) which are not modifiable when considering potential changes to either study or intervention design. Of note, Pilutti et al. (Pilutti et al., 2014) has previously reviewed the literature and reported that the number of adverse events in, and drop-outs from MS exercise groups are comparable to those from the control groups. In addition, the exercise groups in general had a risk reduction of 27% for having a relapse thus, adverse events and an increased relapse rate are likely not major factors affecting adherence in MS exercise studies.

There are several major findings of this review. Firstly, the variety of adherence definitions reported by the identified studies suggests that trials do not consider adherence in consistent ways. Indeed the focus of a laboratory-based proof of concept intervention study will have different issues related to adherence than a pragmatic community-based physiotherapy intervention. It may therefore be that different definitions are appropriate for different trials, however their definition should clarify the specific elements of adherence that are being addressed. (Hawley-Hague et al., 2016)

The majority of studies in the review reported the proportions of available sessions *attended* as the measure of adherence. This data is informative for determining feasibility of the programme, particularly from a service delivery perspective. Another aspect of adherence relates to whether an exercise intervention is *completed* at the prescribed intensity and/or duration of the protocol (content adherence). This provides information as to whether an adequate training stimulus was

Table 2
TESTEX scores of all included studies

Paper	Eligibility criteria	Randomization	Allocation concealed	Baseline data	Blinded_assessor_primary OM	OM in > 85% patients	AE_reported	Exs_attendance	ITT	Between-group stats_primary OM	Between-group stats_secondary OM	Outcomes_point estimates	Control_PA	Exs_load_titrated	Ex_vol Energy_exp	Total score/15
Ahmadi 2010	0	0	1	1	0	1	0	0	0	0	0	1	0	0	0	4
Ahmadi 2010	1	0	1	1	0	1	0	0	0	0	0	1	0	0	0	5
Ahmadi 2013	1	0	1	1	0	1	0	0	0	0	0	1	0	0	1	6
Ahmadi 2013	1	0	1	1	0	1	0	0	0	0	0	1	0	0	1	6
Aidar 2018	0	1	0	0	0	1	0	0	0	0	0	1	0	0	0	3
Amiri 2018	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	2
Aydin 2014	0	1	0	1	0	1	0	0	0	0	0	1	0	0	0	4
Bansi 2012	1	1	0	1	1	1	0	0	0	0	0	1	0	0	1	7
Bansi 2013	1	1	0	1	0	1	0	0	0	1	1	1	0	0	1	8
Barrett 2009	1	1	0	1	0	0	1	0	0	1	1	1	0	0	0	7
*Bjarnadottir 2007	1	0	1	1	1	0	1	0	0	0	0	1	0	1	1	8
Bulguroglu 2017	1	0	0	1	1**	1	1	0	0	0	0	1	0	1	0	7
*Cakit 2010	1	1	1	1	1	0	0	1	0	1	1	1	0	1	1	11
*Carter 2014	1	0	1	1	0	1	1	1	0	1	1	1	0	1	0	10
Castro-Sánchez 2011	1	0	1	1	1	1	1	0	0	1	1	1	0	0	0	9
*Collett 2010	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	14
*Conroy 2018	1	0	1	1	1	0	0	0	0	1	1	1	0	0	0	7
*Dalgas 2009	1	1	1	1	0	0	0	1	0	1	1	1	0	1	1	10
Dalgas 2010	1	0	1	1	0	0	0	1	0	0	0	1	0	1	1	7
Dalgas 2010	1	1	1	1	0	1	0	1	0	0	1	1	0	1	1	10
Dalgas 2013	1	0	1	1	0	0	0	0	0	0	1	1	0	1	1	7
*DeBolt 2004	1	0	1	0	0	1	0	1	0	1	1	1	0	0	0	7
Dettmers 2009	1	0	0	1	0	1	0	0	0	1	0	1	0	0	0	5
*Dodd 2011	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	14
*Duff 2018	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	12
Ebrahimi 2012	1	0	0	1	1**	1	0	0	0	0	1	1	0	1	1	8
Eftekhari 2012	1	0	1	1	0	1	1	0	0	0	1	0	0	0	0	6
Eftekhari 2018	1	0	0	1	0	0	0	0	0	0	1	1	0	0	0	4
Escudero-Uribe 2017	1	1	1	1	1**	1	1	0	0	0	1	1	0	0	0	9
Feltham 2013	1	1	1	1	1	0	0	1	0	0	0	0	0	1	1	8
*Feys 2017	1	0	0	1	0	0	1	1	1	1	1	1	0	0	1	9
*Fimland 2010	1	0	1	1	0	1	1	1	0	0	1	0	0	1	1	9
*Forsberg 2016	1	1	1	1	1	0	1	1	0	1	1	1	0	0	0	10
*Fox 2016	1	1	1	1	1	0	1	1	1	1	1	1	0	0	0	11
Frevel 2015	1	1	1	1	0	1	0	0	0	1	1	1	0	0	0	8
*Fry 2007	1	0	1	1	1**	1	0	1	0	0	1	1	0	0	1	9
Gandolfi, 2014	1	1	1	1	1	1	1	0	1	1	1	1	0	0	0	11
*Garrett, 2012	0	0	0	0	1	0	0	0	0	1	1	1	0	1	1	6
Golzari, 2010	1	0	0	1	0	0	0	0	0	0	0	1	0	1	0	4
Hansen, 2015i	0	1	1	1	1	0	0	1	0	1	1	1	0	1	0	9
*Hansen, 2015ii	0	1	1	1	1	0	1	1	0	1	1	1	0	1	0	10

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Table 2 (*continued*)

Paper	Eligibility criteria	Randomization	Allocation concealed	Baseline data	Blinded_assessor_primary OM	OM in > 85% patients	AE_reported	Exs_attendance	ITT	Between-group stats_primary OM	Between-group stats_secondary OM	Outcomes_point estimates	Control_PA	Exs_load_titrated	Ex_vol Energy_exp	Total score/ 15
*Harvey, 1999	1	1	0	1	0	1	0	1	0	0	0	0	0	0	0	5
Hassanpour-Dekho, 2016	1	1	0	0	1**	1	0	0	0	0	0	1	0	0	0	5
Hayes, 2011	1	0	1	1	0	1	1	1	0	0	0	1	1	1	0	9
Hebert, 2011	1	1	1	1	1	1	1	1	1	1	1	1	0	0	1	13
Heine, 2017	1	1	0	0	1	0	0	1	1	1	1	1	1	1	1	11
*Hogan, 2014	1	1	1	0	1**	0	0	1	0	0	0	1	0	1	0	7
*Hojjatollah, 2012	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	2
*Hosseini, 2018	1	1	0	1	0	1	0	0	0	0	0	1	0	0	0	5
*Kalron, 2017	1	1	0	1	1**	1	1	1	0	0	0	1	0	1	0	9
Kargarfard, 2012	1	1	1	1	1**	0	1	0	1	0	0	1	0	0	0	8
*Kerling, 2015	1	0	1	1	1	0	0	1	1	1	1	1	0	1	1	11
*Kjolhede, 2015	1	1	1	0	0	1	0	1	1	0	0	1	0	1	1	9
Kjolhede, 2017	0	1	1	0	1**	0	0	0	0	0	0	1	0	0	0	4
Klefbeck, 2003	1	0	0	1	0	1	0	0	0	0	0	0	0	1	1	5
Kooshiar, 2014	1	1	1	0	0	1	0	0	0	0	0	1	0	0	0	5
Kucuk, 2016	1	1	0	1	0	0	0	0	0	0	0	1	0	0	0	4
Magnani, 2016	1	1	0	1	0	0	0	0	0	1	1	0	0	1	1	7
*Manca, 2017	1	1	1	1	1**	0	1	1	0	0	0	1	0	0	1	9
*Medina-Perez, 2014	1	0	1	1	0	1	1	1	0	1	1	1	0	1	1	11
*Medina-Perez, 2016	1	0	1	1	1**	0	1	1	0	0	1	1	0	1	1	9
Mokhtarzade, 2017	1	0	1	1	0	1	0	0	0	0	0	1	0	1	1	7
*Moradi, 2015	1	1	0	1	1**	0	1	0	0	0	0	1	0	1	1	8
Mori, 2011	1	0	1	1	1	0	0	0	0	0	0	1	0	0	0	5
*Mostert, 2002	1	0	1	0	0	0	0	1	0	0	0	0	1	0	0	4
*Mutluay, 2007	1	1	0	1	1**	1	0	1	0	0	1	1	0	0	0	8
Najafidoulatabad, 2014	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
*Negaresh, 2018	1	1	0	0	1	1	1	1	0	1	1	1	0	1	1	11
*Oken, 2004	1	0	1	1	1	0	1	1	0	1	0	1	0	0	0	8
*Ozkul, 2018	1	1	1	1	1	1	0	1	0	1	0	1	0	1	1	11
Pazokian, 2013	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
*Petajan, 1996	1	0	0	1	1**	1	0	1	0	0	0	1	0	1	1	8
Pfalzer, 2011	1	0	0	1	1**	0	0	1	0	0	0	1	0	0	0	5
*Pilutti, 2016	1	1	1	0	0	0	1	1	0	1	1	1	1	1	0	10

(*continued on next page*)

Table 2 (*continued*)

Paper	Eligibility criteria	Randomization	Allocation concealed	Baseline data	Blinded_assessor_primary OM	OM in > 85% patients	AE_reported	Exs_attendance	ITT	Between-group stats_primary OM	Between-group stats_secondary OM	Outcomes_point estimates	Control_PA	Exs_load_titrated	Ex_vol Energy_exp	Total score/ 15
Razazian, 2016	1	1	0	1	1**	1	0	0	0	0	0	1	0	0	0	6
Riksfjord, 2017	1	0	1	0	0	1	1	0	0	1	1	1	0	1	1	9
*Romberg, 2004	1	0	0	0	0	0	1	1	1	1	1	1	0	1	0	8
Romberg, 2005	1	0	0	1	0	1	0	0	1	0	0	1	0	0	0	5
Samaei, 2016	1	1	1	1	1	1	0	0	1	1	1	1	0	1	1	12
*Sandroff, 2017	1	1	1	1	0	0	0	1	1	1	1	1	1	1	1	12
Sangelaji, 2016	1	0	0	1	1**	1	0	0	1	0	0	1	0	1	1	8
Schulz, 2004	1	0	1	1	0	0	0	0	0	0	0	1	0	0	1	5
Smeltzer, 1996	0	0	1	1	0	0	0	0	0	0	0	0	0	1	0	3
Surakka, 2004	1	1	0	1	0	1	0	1	0	0	0	1	0	1	0	7
*Sutherland, 2001	1	0	0	1	0	1	0	1	0	0	0	1	0	0	0	5
*Tallner, 2016	1	1	1	1	1	0	0	1	0	1	1	1	1	0	0	10
Tarakci, 2013	1	0	1	1	1	1	1	0	1	1	1	1	0	0	0	10
Velikonja, 2010	0	0	0	0	1**	0	0	0	0	0	0	1	0	0	0	2
*Wens, 2015i	1	1	1	1	0	1	1	1	0	1	1	1	0	1	0	11
*Wens, 2015ii	1	1	1	1	0	1	1	1	1	1	1	1	0	1	1	13
Wens, 2016	1	1	1	1	0	1	1	1	0	1	1	1	0	1	0	11
Westerdahl, 2015	1	1	1	1	1	1	1	0	0	1	1	1	0	0	0	10
*Zimmer, 2017	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1	13

Legend: **no primary outcome but assessor blinded. *Study included in meta-analysis.
i/ii Two studies by the same author in the same year in referenced order where included in meta-analysis.

received, and whether the prescribed training is achievable for all participants. In this review only one study (DeBolt and McCubbin, 2004) was identified that provided any detail on this aspect of adherence and none explicitly reported details of how many people deviated from the prescribed training protocol with respect to intensity and/or duration. As exercise protocol deviations are likely to be present in most studies, future trials should optimally provide data on planned versus actual intensity (such as heart rate data confirming aerobic intensity or loading data from resistance training) and duration of exercise. This also highlights the issue that words often used synonymously may indicate different aspects of adherence, a finding also underlined by other reviews of adherence in different populations. (Ezzat et al., 2015, Frost et al., 2017) In addition, studies reported adherence of completer participants. Reporting adherence including that of those who dropped out of a study for an intervention related reason would add further transparency and accuracy of intervention adherence. Interestingly the Consensus on Exercise Reporting Template (CERT) only recommend that a detailed description is provided on how adherence to exercise is measured and reported, but do not provide any specific recommendation on *how* to report adherence. (Slade et al., 2016)

A second finding is that of how adherence is measured. To our knowledge there is no guidance available regarding the optimal method for measuring adherence in exercise studies in people with neurological conditions, although attempts have been made to make such recommendations within the musculoskeletal field. (Holden et al., 2014) In our review, the majority of studies measured adherence as session attendance. However, some studies measured adherence via self-report electronic or paper logbooks or self-report diaries. The use of different methods makes comparison between studies or inclusion within meta-analysis difficult. Furthermore, interpretation of the self-report data needs to be considered mindful of the widely recognised issues of over-inflation of exercise reporting, memory recall and social desirability. (Jansons et al., 2017) Thirdly, without a follow up period post intervention it is not possible to know whether people continued to engage in exercise or if any benefits resulting from a given intervention are maintained long-term, which is a key focus of current research. Only eleven of the studies in this review included such a follow up period and of these only three made comment as to whether exercise adherence continued over this time. The necessity of evaluating long-term follow up to determine whether short-term changes persist is emphasised in the Development and Evaluation of Complex Interventions guidance. (Mohler, 2015) Our review demonstrates that this recommendation is not yet being widely followed.

It is noteworthy that in this review, we have highlighted studies that include comprehensive behavioural interventions as well as those incorporating a component in line with Michie et. al. (Michie et al., 2011) such as follow up phone calls or completion of activity logs. Although the benefits of including a behavioural intervention are recognised in the literature, only around a third of studies reported inclusion of such and in the majority of cases the extent of this component appeared to be limited. Although not included in this review, it is encouraging that more recent pilot and feasibility studies (Coote et al., 2017, Hayes et al., 2017, Keytsman et al., 2019) are seeking to further evaluate the addition of such interventions which may provide useful future insights.

An objective of this review was to identify moderators related to adherence and drop-out during the exercise intervention and at follow up. Of the variables assessed, only age, proportion of females and duration of intervention were the significant moderators. This finding was unexpected. On the basis of clinical experience and studies investigating correlates and determinates of physical activity. (Streber et al., 2016) it was anticipated that disease duration and level of disability might also have been significant moderators. So too might programme related factors such as the exercise modality, mode of intervention delivery, and whether or not the programme was supervised, as has been the case in studies in other populations (McPhate et al., 2013, Reljic et al., 2019, Allen et al., 2015) however this was not the case. In addition, group allocation may have been a moderator but analysis of this was not possible due to the lack of passive control (usual activity) group adherence data.

As has been the finding of previous systematic reviews of rehabilitation interventions, (Hawley-Hague et al., 2016, McLean et al., 2017, Jordan et al., 2010) reporting of the study methods and results was not consistently of a high standard. In particular this was with respect to the transparency of reporting and incomplete or inaccurate reporting (such as of drop-out data). This makes both interpretation and implementation of the results more difficult for both researchers and clinicians. It underlines the necessity for authors to more closely follow the Consolidated Standards of Reporting Trials (CONSORT), (Page et al., 2017) CERT (Slade et al., 2016) and the Template for Intervention Description and Replication (TIDieR) (Hoffmann et al., 2014) guidelines in order to facilitate the translation of evidence to practice. In addition, future exercise studies should seek to report their work in line with the criteria for the development and evaluation of complex interventions, (Mohler et al., 2015) where process evaluation is considered important to exploring issues related to the delivery and uptake of an intervention, such as adherence.

4.1. Strengths and limitations

This is a comprehensive review of adherence to exercise interventions over the last 25 years. Conducted in line with PRISMA guidance and utilising an exercise specific methodological appraisal tool, it provides a robust overview of the MS specific exercise literature. The study, however has several limitations, which include possible bias as studies not published in English were not included. The grey literature was not searched in this systematic review which may be a further limitation. Finally, we did not go back to the original authors for raw data, since the focus of our review was on the measurement and reporting of adherence data. Whilst this may have provided additional information, poor response rates are common when attempting to retrieve such data. (Schroll et al., 2013) The results should therefore be interpreted in light of these.

5. Conclusions

Only half of the existing exercise RCT studies in MS report data on both adherence and drop-out during the intervention period, and it was very rare for this data to be gathered at follow up. In addition, only a few weak moderators of exercise adherence were identified. Researchers are urged to consider clear definitions and presentation of adherence data within future studies to enable the clinician to make a balanced cost-benefit decision regarding implementation.

CRediT authorship contribution statement

Rachel Dennett: Conceptualization, Investigation, Writing - original draft, Writing - review & editing, Project administration. **Laurits T Madsen:** Investigation, Writing - review & editing. **Luke Connolly:** Investigation, Writing - review & editing. **Joanne Hosking:** Formal analysis, Resources, Writing - original draft, Writing - review & editing. **Ulrik Dalgas:** Conceptualization, Methodology, Resources, Writing - review & editing. **Jennifer Freeman:** Conceptualization, Methodology, Investigation, Resources, Writing - original draft, Writing - review & editing, Supervision.

Declaration of Competing Interest

None.

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Supplementary materials

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Chapter 3: Evidence of contribution to published work

This research portfolio comprises co-authored published work. The bibliographical details of each work along with a description and an estimated percentage of my contribution (%) are listed below. Written support from a co-author of each output can be found on subsequent pages.

Paper 1

Dennett R, (90%) Gunn H and Freeman J. Effectiveness of and user experience with web-based interventions in increasing physical activity levels in people with multiple sclerosis: A systematic review. Physical Therapy. 2018. 98 (8) 679-690. https://doi.org/10.1093/ptj/pzy060

Rachel Dennett led the study concept and design, conducted the searches, study selection, data extraction, data analysis, quality assessment and manuscript write up.

Paper 2

Dennett R, (90%) Coulter E, Paul L Freeman J. A qualitative exploration of the participants' experience of a web-based physiotherapy program for people with multiple sclerosis: Does it impact on the ability to increase and sustain engagement in physical activity? Disability and Rehabilitation. 2019:1-8, 2019 https://doi.org/10.1080/09638288.2019.1582717

Rachel Dennett was responsible for the study concept and led the study design. She conducted the interviews and led the analysis and manuscript write up.

Paper 3

Freeman J, Hendrie W, Jarrett L, Hawton A, Barton A, **Dennett R, (20%)** Jones B, Zajicek J, Creanor S. Assessment of a home-based standing frame programme in people with progressive multiple sclerosis (SUMS): A pragmatic, multi-centre, randomised, controlled trial and cost-effectiveness analysis. The Lancet Neurology. 2019:18(8)736-747.

https://doi.org/10.1016/S1474-4422(19)30190-5

Rachel Dennett was involved in data collection, analysis and manuscript write up.

Paper 4

Dennett R, (60%) Hendrie W, Jarrett L, Creanor S, Barton A, Hawton A, Freeman J. “I’m in a very good frame of mind”: A qualitative exploration of the experience of standing frame use in people with progressive multiple sclerosis. British Medical Journal Open 2020:10:e037680 http://doi.org/10.1136/bmjopen-2020-037680

Rachel Dennett led the data analysis and manuscript write up.

Films

Dennett R, (80%) Hendrie W, Jarrett L, Creanor S, Barton A, Hawton A, Freeman J. “I’m in a very good frame of mind”: A qualitative exploration of the experience of standing frame use in people with progressive multiple sclerosis. Four Short Films. 2019 on study website: https://www.plymouth.ac.uk/research/sums

Rachel Dennett led the production of these short films. She was responsible for personally capturing several of the images, planning the photo shoots that provided many of the rest of the images, selecting the audio extracts and working with the creative team in creating and compiling these films to produce a coherent and accurate interpretation of the data.

Paper 5

Dennett R, (90%) Madsen LT, Connolly L, Hosking J, Dalgas U, Freeman J. Adherence and drop-out in randomized controlled trials of exercise interventions in people with multiple sclerosis: A systematic review and meta-analyses. Multiple Sclerosis and Related Disorders. 2020: 43(8) 1-16 https://doi.org/10.1016/j.msard.2020.102169

Rachel Dennett led this review. She was responsible for the concept and design, conducted the searches, study selection, data extraction, data analysis, quality assessment and manuscript write up.

Declaration from co-author: Contribution to publication (paper 1) 04/08/2021

Dear Hilary

I am in the process of compiling my research portfolio for Doctor of Philosophy by prior published works; health professions. The title is: "Supporting Adherence to Physical Activity in People with Multiple Sclerosis". The below co-authored paper is a part of my portfolio. Please can you confirm that my contribution to the following publication was 90%?

Dennett R, Gunn H and Freeman J. Effectiveness of and user experience with web-based interventions in increasing physical activity levels in people with multiple sclerosis: A systematic review. Physical Therapy. 2018:98 (8) 679-690. https://doi.org/10.1093/ptj/pzy060

Many thanks
With best wishes

Rachel

Please insert your signature below:

Dr Hilary Gunn

Declaration from co-author: Contribution to publication (paper 2) 04/08/2021

Dear Lorna

I am in the process of compiling my research portfolio for Doctor of Philosophy by prior published works; health professions. The title is: "Supporting Adherence to Physical Activity in People with Multiple Sclerosis". The below co-authored paper is a part of my portfolio. Please can you confirm that my contribution to the following publication was 90%?

Dennett R, (90%) Coulter E, Paul L Freeman J. A qualitative exploration of the participants' experience of a web-based physiotherapy program for people with multiple sclerosis: Does it impact on the ability to increase and sustain engagement in physical activity? Disability and Rehabilitation. 2019:1-8, 2019 https://doi.org/10.1080/09638288.2019.1582717

Many thanks
With best wishes

Rachel

Please insert your signature below:

Lorna Paul

Prof Lorna Paul

Declaration from co-author: Contribution to publication (paper 3 and films) 04/08/2021

Dear Jenny

I am in the process of compiling my research portfolio for Doctor of Philosophy by prior published works; health professions. The title is: "Supporting Adherence to Physical Activity in People with Multiple Sclerosis". The below co-authored paper and films are part of my portfolio. Please can you confirm that my contribution to the following publication was 20%, and films, 80%?

Freeman J, Hendrie W, Jarrett L, Hawton A, Barton A, **Dennett R,** Jones B, Zajicek J, Creanor S. Assessment of a home-based standing frame programme in people with progressive multiple sclerosis (SUMS): A pragmatic, multi-centre, randomised, controlled trial and cost-effectiveness analysis. The Lancet Neurology. 2019:18(8)736-747. http://doi:10.1016/s1474-4422 (19)30190-5

Dennett R, Hendrie W, Jarrett L, Creanor S, Barton A, Hawton A, Freeman J. "I'm in a very good frame of mind": A qualitative exploration of the experience of standing frame use in people with progressive multiple sclerosis. Four Short Films. 2019 on study website: https://www.plymouth.ac.uk/research/sums

Many thanks
With best wishes

Rachel

Please insert your signature below:

J Freeman

4.8.21
Prof Jenny Freeman

Declaration from co author: Contribution to publication (paper 4) 04/08/2021

Dear Wendy

I am in the process of compiling my research portfolio for Doctor of Philosophy by prior published works; health professions. The title is: "Supporting Adherence to Physical Activity in People with Multiple Sclerosis". The below co-authored paper is a part of my portfolio. Please can you confirm that my contribution to the following publication was 60%?

Dennett R, Hendrie W, Jarrett L, Creanor S, Barton A, Hawton A, Freeman J. "I'm in a very good frame of mind". A qualitative exploration of the experience of standing frame use in people with progressive multiple sclerosis. British Medical Journal Open 2020;10:e037680 http://doi.org/10.1136/bmjopen-2020-037680

Many thanks
With best wishes

Rachel

Please insert your signature below:

W Hendrie

Dr Wendy Hendrie

Declaration from co-author: Contribution to publication (paper 5) 04/08/2021

Dear Ulrik

I am in the process of compiling my research portfolio for Doctor of Philosophy by prior published works; health professions. The title is: "Supporting Adherence to Physical Activity in People with Multiple Sclerosis". The below co-authored paper is a part of my portfolio. Please can you confirm that my contribution to the following publication was 90%?

Dennett R, (90%) Madsen LT, Connolly L, Hosking J, Dalgas U, Freeman J. Adherence and drop-out in randomized controlled trials of exercise interventions in people with multiple sclerosis: A systematic review and meta-analyses. Multiple Sclerosis and Related Disorders. 2020: 43(8) 1-16 https://doi.org/10.1016/j.msard.2020.102169

Many thanks
With best wishes

Rachel

Please insert your signature below:

Prof Ulrik Dalgas

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