**Developing an intervention to promote physical activity engagement for people with multiple sclerosis living in rural settings: a feasibility study**

**Background**

Many studies (1-14) have demonstrated that exercise and physical activity can improve symptoms, increase cardiopulmonary health and improve quality of life for people with Multiple Sclerosis (MS). Thus, interventions which encourage people with MS (pwMS) to be more physically active are increasingly being investigated.

The experience of physical problems in pwMS is common because of MS exacerbations and disease progression, which result in secondary impairments, such as diffuse muscle weakness and poor cardiovascular fitness (15). These, coupled with low exercise self-efficacy (16, 17), fear of exercising, and high levels of fatigue, can lead to a progressively sedentary lifestyle (18). It was previously thought that physical exercise would aggravate MS symptoms. Therefore, patients were advised to rest and reduce their physical activity level (19). More recent research has shown that controlled physical activity can increase muscle power and strength, decrease fatigue and improve the quality of life in people with MS (12, 20). Many studies have looked at physical exercise provision for people with MS in the context of a laboratory-based or health provider-based clinic and their effectiveness in this respect (3, 11-14, 21-25), but few studies have explored exercise / physical activity participation and adherence in a home setting, let alone a rural home setting.

Three major types of MS are recognised: relapse-remitting (RRMS), primary progressive (PPMS) and secondary progressive (SPMS)(26). Regarding disability severity, the Expanded Disability Status Scale (EDSS)(27) is used to categorise pwMS where scores below 3 represent mild levels of disability, between 3.5 to 7 as moderate and 7.5 or more as severe levels of disability. The first symptoms of MS are typically noticed between the ages of 20-40 years. Over time, there is a marked loss of employment productivity and an increased health care cost (28-30), as well as marked impact on family relationships and socio-economic status (31). Furthermore, the apparent dependence on experienced rehabilitation specialists (32) increases costs (30) and limits accessibility to health promoting practices for many (33), particularly those living in rural areas (33-35). Recently studies have been conducted to illustrate the different characteristics of urban and rural healthy mostly young people physical activity (36-39), however, it is not determined clearly(37). Also, it is not known whether there are differences in the physical activity profiles of people with MS who live in rural versus urban areas. Interventions for pwMS to promote and support self-efficacy to engage and adhere to exercise and physical activity are required (40, 41). Two such interventions have been developed and trialled in feasibility studies and have been found to be acceptable to people with MS and potentially beneficial. One intervention is a Web-based physiotherapy (WBP) programme, and the other is a physiotherapy intervention known as Blue Prescription (BP)(42, 43). Qualitative and Objective findings illustrated that web-based physiotherapy for 12 weeks was feasible and acceptable intervention, and had a significant effect on the Multiple Sclerosis Impact Scale (physical subscale)(p=0.048)(43). Also, it seems that using BP as a behaviour change intervention is feasible and encourages pwMS to be more engaged in physical activity(42).

According to the Transtheoretical Model(44), behaviour change is a process that occurs in stages: precontemplation, contemplation, preparation, action, maintenance. While it is understood that transition through these phases is not necessarily linear, combining Blue Prescription and a web-based exercise programme may facilitate sustained physical activity engagement for people with MS living in a rural setting. The Web Based Physiotherapy intervention may help the person to progress from the precontemplation or contemplation stages to the action stage (in other words encourage the person to start an exercise programme in their homes). This intervention can then be followed by the Blue Prescription intervention which might encourage the person to go through the Action stage to the Maintenance stage. Also, these interventions deliver behaviour change techniques (BCTs) such as shaping knowledge, social supporting, goal setting, by WBP and then tailored by barrier identifying and problem-solving by BP part. This combination may address the potential problems that make pwMS less physical active.

Face-to-face BCIs showed promising results to increasing fitness in healthy people as well as pwMS; however, these interventions were costly and required expertise in delivering (45). Also, rural setting means more cost regarding physiotherapist recruitment to run face-to-face consultations. Therefore, use of telecommunicational devices such as website, Skype™ or Zoom meetings, telephone calls, and text messages may help to decrease the costs.

**Web-based exercise programme**

Web-based physiotherapy (WBP) may be an efficient alternative for those unable to access traditional hospital or community-based physiotherapy, such as those who work, live in rural locations, are housebound, have transport problems or for whom the effort/stress of getting to the therapy location outweighs the benefits gained (46). A pilot randomised qualitative and quantitative study on the use of WBP in 30 people with MS with moderate disability (EDSS 5-6.5) was funded by the Scottish Government(47). Objective findings suggested that twice-weekly home based physiotherapy for 12 weeks had a significant effect on the Multiple Sclerosis Impact Scale (physical subscale)(p=0.048). More importantly, interview findings demonstrated that people with MS found the website was easy to use, convenient, motivating and one which they would be happy to use in the future(47). It is not known how effective this WBP intervention would be in the longer term or across a range of disabilities.

**Facilitating long-term exercise engagement in multiple sclerosis (Blue Prescription)**

Many pwMS would like to exercise more but are not sure where to start and are fearful that exercise might exacerbate their MS (42). One approach that has attempted to tackle this problem is a novel physiotherapeutic approach called Blue Prescription (BP) (42, 48, 49). In a feasibility study, Blue Prescription significantly lessened the negative impact of MS on the lives of participants and appeared to strengthen the confidence of participants in their ability to adhere to exercise over a longer period. This approach, however, seemed to work best for people with MS, who were already considering a behaviour change with regards to exercise (50). Importantly, the study was carried out in two urban areas of New Zealand, meaning that physiotherapists could visit participants in their homes and even accompany participants to exercise venues. It also meant there were more exercise activities and venues to choose from (an important factor for potential exercisers). From an earlier stakeholder consultation process, we know that many people with MS living in New Zealand are based in rural areas where there is little support for or choice about their exercise plans (49).

**Aims**

The primary objective aim of this feasibility study is to explore whether a combination of a 12-week WBPweb-based exercise programme followed by the Blue Prescription intervention is acceptable to and feasible to those involved in the programme.

Secondary aims will include evaluating the potential benefits and/or success of the 1) the potential benefit of those interventions for pwMS, 2) the recruitment strategies, and 3) the outcome measures of the advantages tested.

Specifically, the research questions asked in this feasibility study are:

* Is the combination of WBP and BP interventions feasible and acceptable to pwMS?
* What are the potential benefits for pwMS regarding
  + Physical activity engagement
  + Quality of life
  + Fatigue
  + Anxiety and depression
  + Self-efficacy

Procedure:

This feasibility study will be a randomised mixed method design. In line with developing complex interventions, this feasibility study follows an earlier proof-of-concept study (51). Twenty PwMS will be recruited and randomly allocated to two groups. In this process, pwMS after matching of their essential characters such as sex, age, EDSS and type of MS, will be randomly allocated to the experimental group (WBP and BP in combination) or a waiting list control group by a research administrator (independent of testing and intervention delivery). Each participant in the experimental group will have four measurement sessions: 1) Baseline, one week before interventions 2) after 12 weeks 3) after 24 weeks and finally 4) 6-month follow-up ( one year after baseline). The control group will have five evaluation sessions: 1) Baseline 2) After 12 weeks 3) After 24 weeks, 4) After36 weeks (WBP part of their intervention) and 5) at the ends of their interventions at 48 weeks (after BP part of their intervention).

Sample size:

Twenty people with MS will be recruited and randomly divided into experimental groups. Because of nature of feasibility and pilot studies that mostly focused on checking of the conceivability of a conducted intervention rather than carrying out a full-power RCT and the interventions effectiveness, the estimation of sample size may not be necessary(52-54). However, one method to find sample size estimation is to use other similar studies(55). Therefore, the sample was decided based on the Lapshin et al. study (2008) that recruited 20 people with MS (56).

Recruitment:

Volunteers will be recruited via the Otago and Southland branches of the NZ Multiple Sclerosis Society. The branches will distribute study flyers to rural members identified by their residential postal address, and the researchers will also present the planned study at Society branch meetings within the Otago region. Furthermore, some local physiotherapists and GPs in Otago, Central Otago, and Southland will be asked to introduce their MS participants to this study. PwMS interested in participating will be asked to contact the research team via email. Where possible we will recruit both men and women with varying types of MS and different levels of disability to determine the feasibility of this approach across a heterogeneous sample. All participants will be asked to provide signed an informed consent before participation.

Inclusion and exclusion criteria:

Inclusion criteria: a diagnosis of MS of any type, aged 18 years or more, presenting with a moderate to high level of disability based on EDSS scale. Participants will be required to have computer and internet access (compatible with Zoom and the WBP) and have basic computer skills (or have a person who can help them to use a computer). Participants will live in a rural area as determined by their residential postal address.

Exclusion criteria: Current or recent disease relapse (< 3 months), currently participating in regular exercise or physical activity programmes, receiving regular rehabilitation or participating in other clinical trials, and the presence of co-morbidities, such as cardiac, orthopaedic or neurological conditions that prevent them from taking part in physical activity. The Physical Activity Readiness Questionnaire(PARQ) will be administered to assess the latter criteria(57) and any positive answer in participant’s PARQ will check with their GPs to omit any potential harm.

Intervention:

WBP and BP combination group: The 12 weeks of WBP will be delivered via a website designed and evaluated for pwMS (52), containing a library of over 200 exercises, each exercise page consists of a video clip, audio, and text description of each exercise and a timer. Some local NZ registered physiotherapists will have one face-to-face visit with each participant. Based on this first visit, exercise goals with the participant will be agreed and an individualised exercise programme prescribed using the web-based resource. Participants will be asked to complete a digital diary of exercise participation via the internet, available for remote viewing by the physiotherapist who can alter the patient's programme, dependent on progress, and monitor adherence and adverse events. After 12 weeks of WBP, participants will then receive the BP approach for 12 weeks (42, 53). Participants will be have given a “Zoom visit”, Zoom is similar to Skype but has been found to be more user friendly and require less broadband, by the same physiotherapist and, using the technique of motivational interviewing, together decide on a programme of physical activity (the participant chooses a physical activity they would like to do), how often and for how long. The physiotherapist will conduct a second “Zoom visit” approximately two weeks later, providing further advice or information. In the third “Zoom visit” (12 weeks later), the physiotherapist will ask the participant to identify any barriers to ongoing physical activity participation, encouraging the participant to problem-solve to maintain engagement. During this 12 week period, the therapist and the participant will also be in contact via telephone, email or text message to enable the physiotherapist to support the participant’s engagement in physical activity. Also, the WBP website will be accessible for the participant to use until the follow-up session (one year after baseline). The control group will be asked to complete all the five questionnaires and send them to research assistance at baseline then they have to wait for six months. Within this six-month they will receive another same questionnaire packs in the weeks 12 and 24. Then, the control group will have the same interventions as the experimental group will receive. Their next assessments will be in the weeks 36 and 48.

**Outcome measures:**

Primary

The primary aim will be addressed in three ways:

1. Qualitative evaluation:

To explore participants’ perceptions of the combined interventions, outcome measures, and adverse events, semi-structured, in-depth interviews will be held once, via a Zoom meeting, at the completion of the interventions. The interviews will be recorded by Zoom application facilities and then transcribed word for word.

1. Diary:

Each participants’ diary on the WBP website (in WBP and BP combination group) will be used to address three items. Firstly, the number of days participants use the diary will be assumed to be an indicator of participation. Secondly, participants will report difficulties encountered on the WBP website diary as well as in their emails, text messages, emails or telephone calls. Thirdly, participants will record on the WBP site when the complete each exercise, this will be taken as their physical activity.

1. Completion and attrition ratios:

Completion and attrition ratios can be assumed as good indicators to evaluate the acceptability and feasibility. The participants will be assumed as a “complete case” if they finish 12 weeks each of their both interventions. Therefore, if some participants will not participate in the 24-week assessment, they pull out from the calculation. A completion level of greater than 95% will indicate the high feasibility/acceptability and between 80 to 95% an acceptable one reasonable feasibility/acceptability.

Secondary:

At the baseline measurement session, demographic data, such as sex, age, type of MS, medications and the duration of MS will be recorded. The five questionnaires will be sent to participants for the all of the measurement sessions points by email and will return by email too.

The five questionnaires are described below:

Questionnaires:

The Godin leisure-time Exercise Questionnaire (GLTEQ): measures physical activity participation(58). This instrument is simple to complete, and its validity and reliability for measuring physical activity in pwMS have been confirmed. It is moderately correlated to other physical activity questionnaires and pedometer and accelerometer measurements of physical activity participation (r= 0.51 to 0.53 respectively). The respondents answer questions about the amount of time they spend engaged in vigorous, moderate and low-intensity physical activity in a typical week.

Multiple Sclerosis Impact Scale 29 (MSIS-29) V2: evaluates the quality of life in multiple sclerosis(59). The reliability and validity of this instrument were previously shown to be significant; furthermore, a consensus suggested it to be an appropriate tool(60).

Modified Fatigue Impact Scale (MFIS): assesses fatigue(61). Previously, The validity and reliability of this instrument were showed significantly.(61) The association between fatigue and physical activity has been previously identified; therefore, improvement in physical activity by use of WBP and BP interventions may have an influence in this respect.

Exercise Self-efficacy Scale (EXSE): estimates the effect of the interventions on exercise and physical activity self-efficacy (62). Motl et al. have reported that people with a higher level of physical activity also have a higher degree of self-efficacy (63). The validity and reliability of this tool was illustrated by Motl et al and McAuley(18, 64).

Hospital Anxiety and Depression Scale (HADS): evaluates the level of depression(65). Also, the validity of this tool previously showed significantly(65). There is a high incidence of mood disorders in pwMS. There are conflicting results on the influence of physical activity and exercise on mood disorders, and more research is needed.

Data analysis:

A thematic framework analysis will be used to analyse participants’ interview data(66). After familiarization with the data, a coding and charting process will be used to identify potential patterns and associations in the data. Diary data will be analysed in two ways. First, the number of days that the intervention group participants used the diary. Second, all diary entries will be read carefully to identify difficulties encountered and adverse events as a result of participating in the programme. These findings will be reported narratively. The normality of continuous data (quantitative parts) will be tested and confirmed by the Kolmogorov-Smirnov test. Descriptive statistics, such as standard deviation, average, and range will be reported. Repeated measurement analysis will be used to investigate the between-group effects on the quantitative outcome measures with the simultaneous effect of time and group variables (interaction effect) analysed. The effect of other factors such as gender (male-female), age, and EDSS as confounding factors will be entered into the model. The significance level will be considered to be p< 0.05.

**Timetable:**

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