Safety, feasibility, acceptability and effects of a behaviour-change intervention to change physical activity behaviour among people with multiple sclerosis: results from the iStep-MS randomised controlled trial.

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Abstract

Background: There is limited information regarding the safety, feasibility and acceptability of behaviour-change interventions to increase physical activity (PA) and reduce sedentary behaviour among people with MS. Prior to evaluating efficacy, it is important to identify problems with feasibility and acceptability, which may undermine effectiveness.

Objective: To examine the safety, feasibility and acceptability of a behaviour-change intervention to increase PA and reduce sedentary behaviour among people with MS.

Methods: Sixty people received a three-month intervention or usual care. Fatigue, pain and adverse events (AEs) were assessed. Feasibility and acceptability were explored through focus groups with physiotherapists and interviews with participants. Fidelity to intervention content, delivery skills, programme receipt and programme task were assessed.

Results: There was no difference in AE event rate between groups (p=0.965). Fatigue and pain were not higher in the intervention group at 3 or 9 months. Therapists reported the intervention was feasible to deliver and fidelity was acceptable. Twenty-nine participants (97%) attended at least 75% of sessions. Participants found the intervention acceptable but suggested some amendments were required to intervention components.

Conclusion: The intervention was safe, feasible and acceptable. Although modifications are required to intervention components, the intervention warrants further evaluation in a future trial.

Trial registration: Changing physical activity behaviour in people with MS: the iStep-MS trial; https://doi.org/10.1186/ISRCTN15343862; ISRCTN15343862

Introduction

Physical activity (PA) and reduced sedentary behaviour are associated with milder disability, better mental health and less fatigue among people with multiple sclerosis (MS).[1-3] However, people with MS are insufficiently active and spend prolonged time in sedentary behaviour.[4,5] Behaviour-change interventions are a potential method for increasing PA and reducing sedentary behaviour in people with MS.

A recent meta-analysis concluded that behaviour-change interventions for people with MS improved self-reported PA.[6] However, as self-reported PA is only weakly correlated with objectively measured PA in people with and without MS,[7-9] it is recommended that objective measures of PA and sedentary behaviour are used to determine the effectiveness of behaviour-change interventions.[6,8] Of four studies that assessed effects on objectively measured PA,[6] only one found a between-group difference in favour of the intervention immediately post-intervention but not at 6 months post-intervention.[1] One study has examined the effect of a behaviour-change intervention on self-reported sitting time in people with MS with positive results.[10] However, as PA and sedentary behaviour are distinct concepts, and guidelines recommend both increasing PA and reducing sedentary behaviour for health benefits,[11] interventions targeting both PA and sedentary behaviour are required.

Prior to evaluating efficacy of such interventions, it is important to identify problems with feasibility, acceptability and fidelity to the intervention, which may undermine effectiveness. This is an important step in evaluating a complex intervention that can enable differentiation between true ineffectiveness and implementation failure,[12] and has not been well described in this context to date. Of the 14 studies included in the meta-analysis of behaviour change interventions,[6] one reported fidelity to content[13] and

another reported fidelity to delivery.[14] No study explored the feasibility of delivering behaviour-change interventions to change PA behaviour from the perspective of the intervention provider. Only two studies asked participants for feedback on the intervention, both using a questionnaire with open-ended questions.[15,16] Additionally, the safety of behaviour-change interventions to change PA behaviour is unclear. Seven of the 14 studies did not mention adverse events (AEs),[14,17-19] five stated no AEs were recorded without providing information on how this was assessed,[1,16,20] one assessed AEs in the intervention group only,[15] and one reported related-AEs only.[13]

We therefore aimed to examine the safety, feasibility, acceptability and effects of a behaviour-change intervention to increase PA and reduce sedentary behaviour among people with MS, and to explore the feasibility of conducting a larger trial to evaluate effectiveness.

Materials and Methods

We conducted a randomised controlled trial with parallel process evaluation comparing a physiotherapist-led behaviour-change intervention to usual care. Participants were recruited from an MS Therapy Centre in England, and the MS Society UK website from April-September 2017. Inclusion criteria were a self-reported diagnosis of MS, ability to independently walk within the home with or without a walking aid, relapse-free for the past 3 months, and free of unstable medical conditions such as unstable angina that would make it unsafe to participate in PA. Participants had to be able to travel to the centre, converse in English and have sufficient cognition to complete assessments and participate in the intervention. Exclusion criteria were pregnancy and ongoing participation in other trials. Assessments were conducted at baseline, 3 and 9 months. Further details on the recruitment and assessment are described in the

protocol.[21] Approval was obtained from Brunel University London's Research Ethics Committee. Participants gave informed written consent prior to completing the baseline assessment.

Following baseline assessments, participants were randomly allocated to the intervention or usual care control group in a 1:1 ratio. Allocation was performed by an individual independent to the study according to a computer-generated random schedule in random permuted blocks of 2 or 4. The allocation sequence was placed in sequentially numbered, opaque, sealed envelopes. Following each baseline assessment, an envelope was drawn sequentially by a researcher who informed the participant of their group allocation.

Participants and therapists were not blind to group allocation. Although assessors were also not blind, self-reported questionnaires were used and participants received standardised instructions to minimise detection bias. Assessment of objective PA and sedentary behaviour is unlikely to be influenced by the assessor being aware of group allocation. Data were processed and analysed by a researcher blind to group allocation.

Intervention

Participants in the intervention group received four face-to-face sessions, each lasting 30-45 min, with a physiotherapist at the centre over three months, supported by a handbook and *Yamax SW-200 digiwalker* pedometer.[22] The intervention, which was delivered by four therapists, is described in the protocol[21] and supplemental material. Briefly, physiotherapists discussed increasing PA and step-count and reducing sedentary behaviour with participants using behaviour-change techniques,[23] guided by the handbook. The handbook contained pre-reading and reflection to be completed by the participant prior

to each session. Therapists received a specific handbook with additional comments. Participants set and recorded PA, sedentary behaviour, and step-count goals in sessions 1-3, and monitored and recorded these behaviours between sessions using diaries included in the handbook (examples provided in supplemental material). Therapists received three half-day training sessions led by a behaviour-change technique trainer; two prior to delivering the intervention and one feedback session after they had each completed at least one intervention session. We video-recorded an example of the trainer delivering a session to a person with MS on our advisory group and used this to support training. The trainer reviewed audio-recordings of one session for each therapist, and provided feedback on this in the third training session. Brief cognitive-behavioural strategies, which were targeted at addressing perceived stress and coping with negative emotions in relation to adjusting to MS,[24] were included in both the training and handbook.

Procedures

Data on sociodemographic characteristics, MS-specific characteristics, anthropometric measures, and the MS Impact Scale were collected at baseline.

Safety was determined by assessing pain, using the pain item on the EQ-5D-5L, and fatigue, using the Modified Fatigue Impact Scale (MFIS), at each assessment. The EQ-5D-5L asks people to identify the best description of their pain on a five point scale, from no pain or discomfort to extreme pain or discomfort. The EQ-5D-5L is linearly related to EDSS score in people with mild-to-moderate disability.[25] Specifically, the pain item on the EQ-5D-5L demonstrates excellent discriminatory capacity and no ceiling effect among people with MS.[25] At 3 and 9 months, participants were asked if they had experienced a fall,

relapse or other AE, the number of events experienced, and a description of the event, using standardised questioning.

MVPA and step-count were measured with the Actigraph GT3X accelerometer. Non-wear-time was defined as ≥90 consecutive minutes of 0 counts[26] and validated against participants' wear-time diaries. Participants with at least 3 days of 10 hours wear-time were included in analysis.[27] MVPA was indicated by a cut-point of ≥1745 counts/minute.[28] Sedentary (sitting and lying), standing and stepping time, respectively, were measured using the activPAL3µ activity monitor, which was worn on the person's thigh for 7 days. Identification of non-wear time is described in supplemental material. Participants had at least 2 days of 10 hours of wear-time.

Self-reported time in moderate, vigorous, and walking activity were assessed using the International Physical Activity Questionnaire short-form. Walking capability was assessed using the Twelve Item MS Walking Scale (MSWS-12); higher scores indicated poorer walking capability. Fatigue was assessed using the MFIS; higher scores indicated greater impact of fatigue on a person's activities. Self-efficacy was assessed using the Multiple Sclerosis Self-Efficacy Scale (MSSE); higher scores indicated higher self-efficacy. Participation over four domains (autonomy indoors, family role, autonomy outdoors, social life and relationships) was assessed using the Impact on Participation and Autonomy Questionnaire (IPA); higher scores represented poorer participation. Data on health service use over 9 months was obtained using a modified version of the Client Service Receipt Inventory (CSRI). Information on psychometric properties of measures is provided in the protocol.[21]

Feasibility of training therapists and therapists' experience of delivering the intervention was assessed by recording attendance at training sessions and via a focus group. Informed consent was obtained from therapists prior to conducting the focus group. A random selection of each therapists' sessions were audio-recorded. Fidelity to intervention content and delivery skills was assessed by one person using a standardized tool.[21] Percentage of expected content delivered was assessed; ≥70% was deemed acceptable.[21] Therapists' use of seven key skills, including empathic listening, partnership working and use of open-ended questions was rated as competent or not.

Fidelity to programme receipt and programme task, respectively, were evaluated though attendance at sessions and percentage of sections completed in the handbook, including diaries. Semi-structured interviews were conducted with 15 and 10 participants from the intervention and control groups, respectively, to explore acceptability of the intervention and feasibility of a definitive trial.

Data analysis

Primary analyses were intention-to-treat. Secondary "per-protocol" analyses were conducted using data from participants who attended ≥75% of intervention sessions and completed follow-up to 9 months. Analyses were conducted using Stata (version 15.0). To examine the effect and safety of the intervention mean scores were compared between groups, at 3 and 9 months respectively, using ANCOVA adjusting for baseline score, and gender and type of MS as groups were unbalanced on these baseline characteristics. Logistic regression was used to compare the number of people with an AE at 9 months between groups. A negative binomial model, which accounts for overdispersion in the outcome, was used to compare the incidence of AEs over 9 months between groups. The focus group and interviews were analysed through Framework Analysis.[29]

Results

Sixty people were randomly allocated to receive the intervention or usual care (figure 1). The groups were mostly similar on baseline characteristics (table 1). There were more women and more people with relapsing remitting MS in the control group. More people in the intervention group had secondary progressive MS. Outcomes at baseline are described in table 2. Twenty-nine participants (97%) attended at least 75% of sessions. Fifty-five (92%) and fifty-two people (87%) attended the 3 and 9 month assessments. Health service use in both groups over 9 months is described in supplemental material. Activity data were obtained from between 84% and 93% of participants (table 2 and 3). Wear-time for activity monitors is presented in supplemental material.

Safety

Fatigue was lower in the intervention group at 3 (mean difference [MD]: -6.19, 95% CI -12.06 to -0.31) and 9 months (MD: -8.97, 95% CI -16.21 to -1.72; table 4). There was no difference in pain between groups at 3 months (MD: -0.20, 95% CI -0.56 to 0.17). Pain was lower in the intervention group at 9 months (MD: -0.53, 95% CI -0.96 to -0.10). Twenty-two participants in each group experienced at least one AE (table 5). There was no difference between groups in the proportion of people who experienced an AE (odds ratio 0.83, 95% CI 0.22 to 3.14, p=0.788) or the incidence of an AE (rate ratio 0.98, 95% CI 0.47 to 2.07, p=0.965). Two participants in the intervention group experienced unrelated serious AEs; one person was admitted to hospital for a planned procedure and another person was admitted to hospital with pleurisy.

Feasibility and acceptability

Training was deemed adequate in relation to content and approach. The therapists' handbook, use of a videoed example of delivering a session, and feedback on their delivery of the first face-to-face session were particularly valued. Therapists reported that the programme was feasible to deliver within their current workload, although flexibility around timing of sessions and time for familiarisation was required. This required a commitment to invest 'out of study' time to consolidate their own learning and peer-support to clarify aspects between and after sessions, which improved their confidence to deliver the intervention.

Fidelity to content delivery was ≥70% for all sessions (range 89% to 98%). All therapists were rated as competent across key delivery skills. Median completion of the handbook was 86.7% (range 23.3% to 100%); 75% of participants completed ≥70% of the handbook. While overall, the handbook was both well received and deemed useful, some participants suggested improvements to the usability of the handbook. These included an online version, a reduction in some of the pre-session content and clearer signposting between sections. Indicative quotes representing its acceptability and these suggestions are provided in supplemental material.

Participants with MS found the length of intervention, and frequency and length of sessions acceptable. Intervention structure and therapist continuity facilitated the development of a supportive participant-therapist relationship, which fostered a sense of relatedness and autonomy that was crucial to enhance self-efficacy for PA engagement. Self-management strategies such as pacing, goal-setting, setting graded tasks, self-monitoring and action-planning were well received. More detail on participants' experiences of the intervention is presented elsewhere.[30]

The pedometer provided visual, objective feedback, which enhanced participants' awareness of and motivation to increase PA. However, eight participants reported issues with attachment and accuracy of the pedometer, two expressed a desire for a monitor that could measure MVPA in addition to step-count, six purchased an alternative monitor, and two used their phone to measure step-count.

Feasibility of definitive trial

Communication with the research team was acceptable to participants. Study information was deemed adequate and understanding among participants about the randomisation process was good. Participants found the assessment process acceptable. In general, activity monitoring was well-tolerated. Specific issues with the Actigraph included forgetting to attach it (n=6), discomfort caused by the waistband or from the monitor shifting position (n=5), and difficulty removing the monitor in relation to bladder urgency (n=3). Skin irritation from wearing the activPAL3µ, visibility of the activPAL3µ under clothing, and the intrusiveness of wearing the monitor at night were each mentioned by one participant respectively.

Effects

Results from intention-to-treat analysis are presented in tables 3 and 4. There was no difference in sedentary time, step-count, MVPA, or self-reported walking or MVPA between groups. Stepping time differed between groups at 3 (MD: 0.17hr, 95% CI 0.04 to 0.31) and 9 months (MD: 0.27hr, 95% CI 0.06 to 0.48), in favour of the intervention group. In addition to improvements in fatigue and pain (table 4), there were between-group difference in scores for MSWS-12 (MD: -7.11, 95% CI -14.04 to -0.19) at 3 months, and MSSE (MD: 9.10, 95% CI 0.39 to 17.81), autonomy indoors (MD: -0.36, 95% CI -0.69 to -

0.04) and autonomy outdoors (MD: -0.46, 95% CI -0.90 to -0.02) at 9 months, in favour of the intervention group. Results from per-protocol analyses were nearly identical (supplemental material).

Discussion

Findings show that a physiotherapist-led behaviour-change intervention of four face-to-face sessions supported by a handbook and pedometer was safe, feasible and acceptable to people with MS. The following criteria were proposed *a priori* to determine if the intervention warrants further evaluation in a larger trial[21]: no evidence of a greater number of AEs or greater negative change in pain and fatigue in the intervention group in comparison to the control group; no indication of a dominant negative theme from interviews with participants and physiotherapists; attrition rate <20%. We found no evidence that the rate of AEs differed between groups or that pain or fatigue was higher in the intervention group at 3 or 9 months. Although the proportion of participants who experienced an AE was relatively high in both groups, this may be because we systematically assessed AEs, regardless of their relatedness. Reporting of AEs in studies of behaviour-change interventions for people with MS has been poor to date with many not reporting information on AEs or not describing how AEs were assessed.

Focus groups with therapists and interviews with participants indicated that the intervention was feasible to deliver and acceptable to receive. However, therapists committed additional time to consolidating their learning outside of formal training sessions and this likely contributed to the successful implementation of the intervention. Further, therapists used peer-support to clarify aspects between and after sessions, and consequently build their confidence. Therapists working in isolation may find it more difficult to deliver the intervention.

Some amendments to intervention components are recommended prior to further evaluation. Some participants documented aspects covered in the handbook, specifically monitoring, in self-designed electronic spreadsheets. These were not included in the assessment of fidelity suggesting we underestimated handbook completion. The choice to document elsewhere as well as some people's requests for an online version of the handbook, suggests an online version is required. However, there was no consensus regarding the "best" format, and alternative formats may be required depending on participant choice. While some participants suggested reducing pre-session content, the level of information required may depend on the individual. Clearer signposting between sections may improve the usability of the handbook without the need to reduce content. Although the pedometer was previously validated among adults with MS, several participants reported difficulties using it and doubts regarding its accuracy. As no study has examined the acceptability of behaviour-change interventions that incorporate an activity monitor for people with MS, it is unclear if these issues are specific to our sample or apply to the MS population more broadly. Additionally, the ability to monitor MVPA may contribute to greater changes in MVPA. However, the cost and accuracy of such a monitor needs to be considered against potential benefits.

Although the intervention was less intensive than other behaviour-change interventions in the literature,[31] it was delivered face-to-face, on a one-to-one basis, unlike previous interventions that delivered group sessions,[32,33] or delivered telephone[20,34] or internet interventions.[17-19] Participants emphasised the strong therapeutic relationship was key to developing confidence and competence for PA enactment. Therefore, the potential challenges of delivering face-to-face sessions should be balanced against the benefits of a relatively low-resource intervention.

Attrition was low at 3 and 9 months and missing data were minimal. Although a small number of participants reported issues with wearing the monitors such as forgetting to attach them or discomfort, monitoring was generally well-tolerated. The proportion of missing data was higher for activity monitors compared to other outcome measures, but not higher than levels of missing data reported in similar trials involving activity monitoring.[35] Given we found objective measurement of PA and sedentary behaviour to be acceptable, and that it is recommended over self-report,[8] we believe that accelerometers should be used in future trials examining effectiveness of behaviour-change interventions on PA and sedentary behaviour. However, the potential for up to 15% missing data should be considered when determining sample size.

We found no evidence of between-group differences in step-count, MVPA or sedentary behaviour at 3 or 9 months. However, our analysis was likely underpowered. Based on the standard deviation of 2,400 steps/day observed in our sample at baseline, we estimate a sample of 382 individuals is required to detect a between-group difference of 800 steps/day at 3 months with 90% power and 5% significance. Only one study has found a positive effect on objectively measured PA among people with MS. Carter observed a between-group difference of 688.5 steps/day in favour of the intervention following a 3-month intervention, but no difference at 9 months.[1] We observed a positive treatment effect on fatigue at 3 and 9 months. In contrast, a meta-analysis of behaviour-change interventions reported no effect on fatigue,[31] despite many of the interventions specifically targeting fatigue management.[36-39] We also found between-group differences in self-efficacy, walking capability and participation at 9 months. Although a measure of PA self-efficacy may be more sensitive to change following the intervention, the MSSE includes a number of items such as confidence in ability to mobilise, complete activities of daily living, and manage symptoms of MS, which we believe are important to evaluate when determining the effects of a behaviour-change intervention.

There are limitations to this study. We used the pain item on the EQ-5D-5L to assess bodily pain as we were unable to identify an instrument that specifically measured bodily pain in people with MS. Although the pain item on the EQ-5D-5L demonstrates excellent discriminatory capacity among people with MS,[25] it may provide only a crude indication of pain and does not provide information about pain frequency. Although we attempted to be as inclusive as possible by not indicating a specific distance that individuals should be able to walk for, findings are not generalisable to non-ambulatory individuals. Similarly, participants were largely recruited from a single MS Therapy Centre and thus may not be representative of the wider population of adults with MS in England. The effect of the intervention on an objective measure of function such as a timed walk test was not assessed because we were unable to conduct such a test in participants' homes. Analysis of efficacy was preliminary and should be interpreted with caution. The analysis lacked statistical power and the lack of an active comparator and blinding of participants potentially inflated the observed treatment effect. While there is currently no evidence as to what constitutes best practice to increase PA and reduce sedentary behaviour among people with MS, some form of active comparator should be included in a trial of clinical-effectiveness in order to control for the effect of attention and placebo on outcomes.

In summary, our results show that a behaviour-change intervention to increase PA and reduce sedentary behaviour in people with MS was safe, feasible, acceptable, and showed some positive effects. Comparison of findings against pre-determined criteria indicates that the intervention warrants further evaluation to determine effectiveness on PA and sedentary behaviour.

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Figure legend

Figure 1. Participant flow diagram