A self-management programme to reduce falls and improve safe mobility in people with secondary progressive MS: the BRiMS feasibility RCT

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Scientific summary

The BRiMS feasibility RCT

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Scientific summary

Background

Multiple sclerosis (MS) is an incurable, unpredictable but typically progressive, life-long neurological condition, affecting approximately 100,000 people in the UK (Royal College of Physicians. *The National Audit of Services for People with Multiple Sclerosis 2011*. London: Royal College of Physicians; 2011). Although most people start with a relapsing–remitting disease course, approximately two-thirds move to a progressive phase, with a steady rise in the total percentage of progressive cases as the disease advances.

Within approximately 15 years of a MS diagnosis, an estimated 50% of people are unable to walk unaided, and eventually 25% are dependent on a wheelchair. An important contributor to difficulties in mobility is impaired balance, which is reported by roughly 75% of people and has been shown to be more compromised in those with secondary progressive multiple sclerosis (SPMS) than in those with relapsing–remitting multiple sclerosis (RRMS). Rehabilitation interventions that improve balance and physical activity and decrease the risk of falls may slow this deterioration, providing a persuasive argument for ensuring that optimal physical management is a clinical priority. With only limited medical interventions available for this patient group, such rehabilitation programmes are considered key to the treatment of SPMS but currently lack a robust evidence base.

In partnership with service users, providers, other key stakeholders (including commissioners) and international collaborators, our ongoing research programme systematically developed Balance Right in MS (BRiMS), an innovative evidence-based, user-focused self-management programme designed to improve safe mobility and reduce falls for people with MS. BRiMS is a novel 13-week, therapy-led personalised education and exercise programme structured to maximise the development of self-efficacy and support participant engagement. It addresses modifiable risk factors, enabling self-management through the use of individualised mobility, safety and falls risk management strategies.

The National Institute for Health Research commissioning brief (Health Technology Assessment commissioning call reference number 15/47) requested applications for studies undertaking primary research in rehabilitation therapies to improve quality of life (QoL) in patients with SPMS. Having previously developed BRiMS, it was critical, and timely, to assess the feasibility of the delivery of this programme and proposed evaluation methods before undertaking a definitive trial to assess the clinical effectiveness and cost-effectiveness of the programme.

Research questions

- Is it feasible and acceptable to conduct a multicentre randomised controlled trial of the BRiMS intervention?
- Is it feasible and acceptable to deliver the BRiMS programme for ambulant people with SPMS who live in the community?

Aim

This feasibility trial aimed to obtain the necessary data and operational experience to finalise the planning of an intended future definitive multicentre randomised controlled trial to compare a manualised 13-week education and exercise programme (BRiMS) plus usual care with usual care alone in improving mobility and

QoL and reducing falls in people with SPMS. The intention was to learn lessons to enable a definitive trial to be successfully delivered with confidence. The objectives were grouped into four clusters:

- trial feasibility
- trial outcomes
- process evaluation
- health economics analysis.

Methods

The trial recruited from four UK sites: Cornwall, Plymouth, East Devon and Ayrshire. The sample size was set at 60 to ensure that the feasibility objectives could be achieved with a sufficient degree of certainty. Participants were identified through several sources: local and national advertising through MS centres, MS Society (www.mssociety.org.uk) branches and support groups, websites and newsletters; adoption onto the local Clinical Research Network portfolio and via the caseload of local MS neurologists, MS nurse specialists and NHS therapists.

Potentially eligible participants were screened by telephone interview undertaken by a research therapist linked to the recruiting site. As each delivery of BRiMS was pre-scheduled to ensure the availability of staffing and facilities, potential participants were assigned to a specific BRiMS delivery at this point (if they were randomised to the BRiMS intervention plus usual-care group). Final eligibility checking, informed consent and baseline measures were undertaken at a single face-to-face meeting at a health-care venue local to the participant, at a time point no more than 2 weeks before the pre-scheduled randomisation date for each BRiMS delivery.

Randomisation was undertaken by the Peninsula Clinical Trials Unit after the baseline assessments were completed for all participants in a block (block size 8–12 participants). Participants were individually randomised on a 1 : 1 basis, blocked within each site.

Participants were followed up on two occasions: 13 weeks ($\pm$ 1 week) and 27 weeks ($\pm$ 1 week) following randomisation. This reflected an assessment at the end of the intervention period and a further follow-up 3 months later.

Participants

The target population was English-speaking men and women, aged $\geq$ 18 years, with a confirmed diagnosis of SPMS, who reported having walking difficulties and experiencing falls.

Inclusion criteria

The patient:

- had a confirmed diagnosis of MS as determined by a neurologist; and, in the secondary progressive phase, as confirmed by a MS specialist clinician
- was aged $\geq$ 18 years
- was willing and able to understand/comply with all trial activities
- had an Expanded Disability Status Scale (EDSS) score of between $\geq$ 4.0 and $\leq$ 7.0 points
- had self-reported two or more falls in the past 6 months
- was willing and able to travel to and participate in BRiMS group sessions at local sites and to commit to undertaking their individualised home-based programme
- had access to a computer or tablet and to the internet.

Exclusion criteria

The patient:

- Had reported relapse or receiving steroid treatment within the past month {patient-reported relapse was defined as 'the appearance of new symptoms, or the return of old symptoms, for a period of 24 hours or more – in the absence of a change in core body temperature or infection' [MS Society. *Relapsing Remitting MS (RRMS)*. 2016. URL: www.mssociety.org.uk/what-is-ms/types-of-ms/relapsing-remitting-rrms (accessed 21 December 2016)]}.
- Had any recent changes in disease-modifying therapies. More specifically, patients were excluded if they:
  - had ever had previous treatment with alemtuzumab (Lemtrada®, Sanofi Genzyme, Cambridge, MA, USA); or
  - had ceased nataluzimab (Tysabri®, Biogen, Cambridge, MA, USA) in the past 6 months; or
  - were within 3 months of ceasing any other MS disease-modifying drug.
- Had participated in a falls management programme (e.g. for older people) within the past 6 months.
- Had comorbidities that may have influenced their ability to participate safely in the programme or that were likely to have an impact on the trial (e.g. uncontrolled epilepsy).
- Had been recruited to a concurrent interventional trial.

Interventions

Participants were randomised to one of two groups: BRiMS plus usual care or usual care alone. Those allocated to undertake the BRiMS programme were invited to attend two one-to-one sessions (an initial assessment and a home visit), to undertake a home exercise programme and falls prevention education programme supported by online resources and a paper manual, and to attend three group sessions for peer support, group exercise and interactive learning activities. Participation in the attended sessions was recorded by the treating therapists, and engagement in the online activities was captured by website log-in and usage. Participants were asked to record their adherence to the home exercise programme, and details of the progression of exercises undertaken, in a weekly diary that was integrated into the online exercise platform.

Outcomes

Trial feasibility

The outcomes were participant recruitment, retention and completion rates, trial acceptability and feasibility (via participant interviews), measures of trial safety and adverse events.

Trial outcomes

In addition to those on participant demographics, clinical characteristics and medication use, data were collected to inform the potential primary and secondary outcomes for a future definitive trial.

Potential primary outcomes

- MS Walking Scale (12-item) version 2 (MSWS-12vs2).
- EuroQoL-5 Dimensions, five-level version.
- MS Impact Scale (29-item) version 2 (MSIS-29vs2).

Potential secondary outcomes

- Falls frequency and injury rates (from participant self-report daily paper diaries).
- Physical activity [measured for 1 week after each trial assessment using an activPAL™ (Paltechnologies Ltd, Glasgow, UK) activity monitor].
- Two-Minute Walk Test.
- Mini-Balance Evaluation Systems Test.
- Functional Reach and Lateral Reach Tests.
- Falls Efficacy Scale – International.
- Community Participation Indicators.

BRiMS programme feasibility (process evaluation)

This included an assessment of programme acceptability and utilisation (from participant and therapist interviews), records of attendance at face-to-face sessions, online exercise diary completion and web-based programme log-in data.

Health economics

Evaluation of the feasibility of the proposed methods for assessing health, social care and other resource use in a future definitive trial was undertaken, plus evaluation of the intervention delivery costs for the BRiMS programme.

Results

A total of 56 participants (mean age 59.7 years, standard deviation 9.7 years; 66% female; median EDSS score of 6.0 points, interquartile range 6.0–6.5 points) were recruited in 5 months; 30 were block randomised to the intervention group.

Trial feasibility objectives

A total of 11 participants (19.6%) withdrew or were lost to follow-up, seven of whom were in the intervention group. Worsening of MS-related symptoms unconnected to the trial was the most common reason ($n = 5$) for withdrawal.

There were nine reports of serious adverse events during the trial, none of which was assessed to be related to the BRiMS intervention. The adverse events reported were not unexpected for this sample of people with progressive MS, and are in line with other MS rehabilitation and exercise trials.

Qualitative feedback indicated that trial processes and participant burden were acceptable, although some areas for improvement were highlighted. For example, participants recommended that written pre-trial information be reviewed to ensure that the content and format are straightforward while remaining comprehensive.

Trial outcome objectives

The groups were broadly comparable at baseline, although the intervention group scored worse on the majority of the baseline outcome measures. Potential primary and secondary outcomes had excellent completion rates of > 98% for all those assessed at each time point. There were a number of issues with diary data, which meant that the overall return rate was 62%, with a rate of 58.6% of the expected total for falls, and 40.6% of the expected total for injurious falls.

After adjusting for baseline score, the differences between the groups (intervention compared with usual care) at week 27 were –7.7 on the MSWS-12vs2 [95% confidence interval (CI) –17.2 to 1.8], 0.6 on the MSIS-29vs2 physical (95% CI –7.8 to 9.0), –0.4 on the MSIS-29vs2 psychological (95% CI –9.9 to 9.0) and 0.0 on the EuroQol-5 Dimensions, three-level version (crosswalk) (95% CI –0.1 to 0.1).

After one outlier was removed, a total of 715 falls were reported over the 27-week trial period, with substantial variation between individuals (range 0–93 falls). Of these 715 falls, 101 (14%) were reported as injurious. The falls rate at week 27 was 25.9 falls per person per year in the usual-care group and 21.9 falls per person per year in the intervention group. The injurious falls rates at 27 weeks were 4.7 falls per person per year (usual care) and 2.2 falls per person per year (intervention).

Based on this feasibility study and other relevant data, with MSWS-12vs2 as the primary outcome and 27 weeks post randomisation as the primary end point, the estimated sample size for a definitive trial would be within a range of 575 to around 990.

Process evaluation objectives

Therapists and participants were generally positive when describing their engagement with the BRiMS programme. Therapists particularly valued the ethos of the programme, and the resources provided to them, which they felt enabled them to deliver a structured and comprehensive approach to support self-management, incorporating both educational and exercise activities.

Levels of participant engagement with the programme varied both over time and between participants, influenced by a range of condition- and context-related factors. A number of suggestions were made by therapists and participants to improve the utility and accessibility of the programme model and delivery methods.

Patterns of participant recorded exercise varied, with only six (21%) of the 28 participants who commenced the programme logging at least 100 of the advised 120 minutes of weekly exercise activity over the 12 weeks. Participants and treating therapists reported a number of technical and logistical issues with the recording of exercise activities.

Participants highlighted both physical and behavioural changes that they perceived had resulted directly from undertaking the BRiMS programme. These included changes in balance confidence and competence, an increased awareness of falls risk and the introduction of falls prevention strategies.

Health economics analysis objectives

As with the potential primary and secondary outcome measures, the health economics resource-use questionnaires and therapist contact sheets had excellent completion rates, at > 98% for all those assessed.

The estimated mean cost for the delivery of BRiMS was £400 per person, although qualitative feedback from treating therapists suggests that the time allocation should be increased in future deliveries by approximately 15%.

Participants reported relatively modest levels of resource use, predominantly focused on primary and secondary care. Provision of informal unpaid care was consistent between the groups at 24–25 hours per week. When applying a unit cost to hours of informal care, the estimated weekly cost of this care is approximately £445 per participant.

Conclusions and recommendations

This trial aimed to assess the feasibility of undertaking a definitive trial to compare BRiMS plus usual care with usual care alone in a sample of people with SPMS. The results suggest that the trial procedures are feasible and acceptable, and the retention, programme engagement and outcome completion rates were sufficient to satisfy the a priori trial progression criteria. Challenges were experienced in some areas of data collection, such as the recording of adherence to exercise activity and the completion of daily diaries; the lessons learnt in this feasibility trial will enable these processes to be refined for a future trial. Further

development of the BRiMS programme is required to address logistical issues and enhance user satisfaction and adherence. Following this, a definitive trial to assess the effectiveness and cost-effectiveness of the BRiMS intervention is warranted. Estimated sample sizes for this trial range from 575 to around 990 participants.

Trial registration

This trial is registered as ISRCTN13587999.

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