

by establishing large international biomarker cohorts is another priority.⁵ Accuracy of early clinical diagnosis is still an issue, with a high frequency of misdiagnosis particularly in the early stages of disease. Clinical criteria that were last revised more than 10 years ago are still in use. The need to revise these criteria to enable accurate diagnosis early in the disease course has been identified, and a revision is planned.⁶

Levin and colleagues' study showed that these unresolved issues could be crucial hurdles on the way to identification of a neuroprotective treatment for multiple system atrophy. Despite the positive aspects and gains of their trial, an efficacious treatment for patients with this devastating disease is still not available.

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Restoring function in progressive multiple sclerosis

The use of frames and tilt tables to support passive standing for people with lower limb paralysis has been part of the entry-level training of physiotherapists for more than 60 years. In 1955, Marjorie Farnbach¹ described such practice of passive standing in patients with poliomyelitis, stating that “the length of time spent in this standing frame varies from a few minutes at first with increasing periods as they can be tolerated up to several hours daily.” In a paper² published in the preceding year, Willhite and colleagues outlined the development of an apparatus used to place the patient “in the standing position for weight-bearing purposes”, to “prevent demineralisation” of bone and obtain “better postural control alignment”. But, despite the many reports of the advantages of supported standing, research examining this approach in people with chronic neurological conditions has been inconclusive, with some studies suggesting that the intervention provided no meaningful benefits to mobility or lower extremity range of motion.^{3–6}

In *The Lancet Neurology*, the Standing Up in People with Progressive Multiple Sclerosis (SUMS) study done by Jennifer Freeman and colleagues,⁷ with a randomised controlled trial design, provides the first high-quality evidence that using a standing frame for 20 weeks

at home can reduce lower extremity contracture and enhance mobility in people with disability related to severe multiple sclerosis.⁸ In the trial, participants had two home-based physiotherapy sessions to set up the standing frame and six follow-up telephone calls. Participants were asked to stand for 30 min, three times per week over 20 weeks, and encouraged to continue in the longer term, but without further physiotherapy support provided. Participants who used the standing frame (n=71) had a significant increase in Amended Motor Club Assessment (AMCA) score compared with that in participants who had usual care alone (n=69), with a fully adjusted between-group difference in AMCA score at 36 weeks of 4.7 points (95% CI 1.9–7.5; p=0.001). The frequency of short-term musculoskeletal pain was higher in the standing frame group than in the usual care group (486 [41%] of 1188 adverse events vs 160 [22%] of 736 adverse events), which was potentially related to the intervention.

This positive outcome begs the question: “how does the intervention provided in Freeman and colleagues' study differ from other supported standing programmes described in previous research”? The following are probably some of the features that made a difference in the supported standing intervention provided in the SUMS trial.



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First, the SUMS trials included specific instructions provided to participants regarding how to incorporate upper-limb exercises, balance activities, and stretching within the frame.⁸ The exercises, along with instruction on how to progress and intensify the programme, were available online. In fact, several of the exercise activities were subcomponents of the functional tasks that were tested in the primary outcome, AMCA score, such as reaching and standing balance.

Second, patients were extensively supervised by experienced physiotherapists who implemented behavioural change methods. Interestingly, the subjective lessening of the physical and psychological effect of multiple sclerosis reported by participants in the standing frame group at 20 weeks was lost at 36 weeks, once therapist contact was discontinued. We could surmise that the therapist's interaction during the active treatment phase might have contributed to participants' more positive outlook and, perhaps, their willingness to adhere to the standing programme.

Third, the target dose of the standing intervention in the SUMS trial, lasting 1800 min over 20 weeks, was double the dose provided in a negative trial⁶ of tilt-table standing in people after traumatic brain injury. In the SUMS trial, mobility benefits were most robust in participants who achieved more than 1152 min of standing over a 20-week period. However, participants who increased the standing time beyond this level (>2304 min over 32 weeks) had similar outcomes to those achieving half that amount (1152 min). This finding suggests there is probably a plateau or ceiling effect whereby standing beyond 1200 min over 20 weeks provides no further enhancement of mobility.

Fourth, an optimal responder group was potentially chosen. Several trials^{9,10} of supported standing in patients after stroke suggested that the method does not accelerate recovery of standing and walking in people with acute paralysis. Freeman and colleagues⁸ recruited participants who were long-term users of gait aids or wheelchairs, and many of them had lower limb contracture and muscle weakness in the legs—two of the main targets of the SUMS intervention. Therefore, supported standing has the potential to overcome some of the learned non-use of the lower limbs. Because of

the severity and chronicity of disability, it was perhaps not surprising that participants in the standing group had some musculoskeletal pain.

In summary, the SUMS trial is an important guidepost in rehabilitation research. Not only were benefits sustained over time (16 weeks after cessation of the trial), but also the restoration of function was observed in patients with a chronic progressive neurological disease in whom worsening, rather than improvement, would be expected. The findings support that some of the impairment and functional losses observed in people with progressive multiple sclerosis are indeed reversible, and rehabilitation interventions, such as home-based standing, can stabilise or even restore lost abilities.

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