

1 **The effects of prolonged wear of textured shoe insoles on gait, foot sensation**  
2 **and proprioception in people with Multiple Sclerosis: protocol for a**  
3 **randomised controlled trial**

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27 **Abstract**

28

29 **Background:** Many people with Multiple Sclerosis experience problems with  
30 walking, which can make daily activities difficult and often leads to falls. Foot  
31 sensation plays an important role in keeping the body balanced whilst walking  
32 however, people with Multiple Sclerosis often have poor sensation on the soles of  
33 their feet. Wearing a specially designed shoe insole, which enhances plantar  
34 sensory information, could help people with Multiple Sclerosis to walk better. This  
35 study will explore whether long-term wear of a textured insole can improve walking in  
36 people with Multiple Sclerosis.

37 **Methods:** A prospective randomised controlled trial with two parallel groups will be  
38 conducted aiming to recruit 176 people with Multiple Sclerosis living in the  
39 community (Brisbane, Australia). Adults with a clinical diagnosis of Multiple  
40 Sclerosis, Disease Steps score 1-4, who are ambulant over 100m and who meet  
41 specific inclusion criteria will be recruited. Participants will be randomised to a  
42 smooth control insole (N=88) or textured insole (N=88) group. The allocated insole  
43 will be worn for 12-weeks within participants' own footwear, with self-report wear  
44 diaries and falls calendars being completed over this period. Blinded assessors will  
45 conduct two baseline assessments and one post-intervention assessment. Gait  
46 tasks will be completed barefoot, wearing standardised footwear only, and wearing  
47 standardised footwear with smooth and textured insoles. The primary outcome  
48 measure will be mediolateral base of support when walking over even and uneven  
49 surfaces. Secondary measures include: spatiotemporal gait parameters (stride  
50 length, stride time variability, double-limb support time, velocity), gait kinematics (hip,  
51 knee, ankle joint angles; toe clearance; trunk inclination; arm swing; mediolateral

52 pelvis/head displacement), foot sensation (light touch-pressure, vibration, two-point  
53 discrimination) and proprioception (ankle joint position sense). Group allocation will  
54 be concealed and all analyses based on an intention to treat principle.

55 **Discussion:** This study will explore the effects of wearing textured insoles over 12-  
56 weeks on gait, foot sensation and proprioception in people with Multiple Sclerosis.  
57 The study has the potential to identify a new, evidence-based footwear intervention  
58 which has the capacity to enhance mobility and independent living in people with  
59 Multiple Sclerosis.

60 **Trial registration:** Australian New Zealand Clinical Trials Registry  
61 ACTRN12615000421538. Registered 4 May 2015.

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63 **Key words:** Gait; Shoe insoles; Foot sensation; Proprioception; Multiple Sclerosis;

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77 **Background**

78 Falls are a major threat to the health and well-being of people with Multiple Sclerosis  
79 (pwMS)[1, 2]. Up to 50% of pwMS report falling within the past 6 months, and 50% of  
80 these falls result in injuries [3]. Impaired mobility and balance are two major risk  
81 factors for falls in people with pwMS [2]. In one study 85% of pwMS report gait  
82 disturbances as their main complaint [4], and continued loss of mobility amongst  
83 their greatest concerns for the future [5]. Impaired walking in pwMS is typically  
84 characterised by an increased mediolateral (ML) base of support, reduced stride  
85 length, step length and velocity, and prolonged double-limb support time during level  
86 ground walking, relative to healthy individuals [6-8]. Incipient signs of deteriorating  
87 walking ability can even be observed in the early stages of the disease [6-8].  
88 Therefore, interventions that effectively preserve or enhance walking capacity are  
89 paramount to improving quality of life and maintaining independence.

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91 Current rehabilitation strategies to improve gait and balance in pwMS, predominantly  
92 involve exercise participation to address deficient motor function, with some  
93 consideration given to sensory training [9-13]. These multimodal approaches have  
94 been shown to significantly improve several clinical and functional measures in  
95 pwMS, including dynamic balance, rate of falls, physical activity levels, perceived  
96 balance confidence, walking ability, and quality of life [9-13]. However, there is an  
97 urgent need to develop additional methods to complement exercise, which target MS  
98 sensory impairments [14-19] to a greater extent, in particular tactile sensation and  
99 proprioception, in order to preserve and enhance mobility for as long as possible.

100 Previous evidence has shown that a strong relationship exists between foot  
101 sensation and standing balance performance in pwMS [15]. Similarly, a loss of lower

102 limb proprioception, including joint position sense at the ankles and feet in pwMS can  
103 detrimentally affect gait and standing balance, leading to greater dependence on  
104 compensatory motor mechanisms in order to remain upright [17, 19]. An increasing  
105 body of literature suggests footwear interventions may be another treatment option  
106 to help improve gait performance in pwMS [20-22].

107

108 Textured shoe insoles, designed to enhance plantar sensory information, have been  
109 shown to consistently alter gait patterns in the short-term, potentially improving  
110 walking stability in a range of clinical populations including older fallers [23], adults  
111 with Parkinson's disease [24] and pwMS [20, 21]. To date, exploratory studies  
112 indicate that textured insoles can lead to beneficial alterations in spatiotemporal gait  
113 parameters such as a reduced ML base of support [20], improved gait kinetics, and  
114 kinematics [21] in pwMS. Significant increases in lower limb muscle activity during  
115 both stance and swing phases of gait, changes in knee and hip excursion and  
116 ground reaction forces, have been found immediately after pwMS wore textured  
117 insoles, with these changes attributed to enhanced stimulation of plantar  
118 mechanoreceptors [21]. Furthermore, after wearing textured insoles for two weeks,  
119 significant increases have been also observed in stride and step length, and  
120 significant decreases in the size of the ML base of support during level-ground  
121 walking: interpreted to represent a more confident gait pattern. These changes were  
122 observed independent of wearing the textured insoles, again supporting the theory  
123 that a sensory training effect may have occurred during the intervention period [20].  
124 However, recent evidence reports no significant changes either in spatiotemporal  
125 gait measures during treadmill walking or plantar sensitivity after wearing textured  
126 insoles over a longer, 4-week intervention period in pwMS [25]. It is possible that any

127 effects of textured insoles on gait may only be identified when walking in conditions  
128 that emulate everyday life [25]. Further, whilst no changes were observed in plantar  
129 sensitivity, alterations may have occurred in other measures of sensory function,  
130 such as foot proprioception [25]. As such, the short-term effects of textured insoles  
131 on mobility, and their proposed underlying mechanisms in pwMS, remain unclear. It  
132 is possible that the benefits of textured insoles in pwMS may accrue, and additional  
133 benefits may be observed, with prolonged wear over 4-weeks, but this has not yet  
134 been explored. Previous work has shown limited effects of textured insoles on gait  
135 and balance measures in pwMS immediately after wearing the insoles for the first  
136 time, with subsequent improvements observed following 2-weeks wear [20].

137

138 This randomised controlled trial will determine whether wearing textured shoe  
139 insoles for 12-weeks can improve gait when walking over even and uneven surfaces,  
140 in pwMS. The primary aim of this study is to explore whether prolonged wear of  
141 textured insoles alters ML base of support (as a measure of walking stability) from  
142 baseline assessment 2 to the post-intervention assessment. Secondary aims are to  
143 explore whether prolonged wear of textured insoles alters other spatiotemporal gait  
144 parameters including stride length, stride time variability, double-limb support time,  
145 and gait velocity; gait kinematics (specifically lower limb joint and trunk movement)  
146 and; changes in the perception of foot sensation or proprioception, as underlying  
147 mechanisms associated with improvements in spatiotemporal gait parameters.

148

## 149 **Methods**

### 150 *Design*

151 A prospective, parallel group, single blinded, randomised controlled trial with 176  
152 pwMS living in the community will be conducted, conforming to the Consolidated  
153 Standards of Reporting Trials guidelines [26] (Figure 1).

154

#### 155 *Sample size*

156 Sample size has been calculated for the primary outcome measure, ML base of  
157 support during even surface walking, based on our pilot data [20]. Our preliminary  
158 study reported mean (SD) readings at baseline for base of support of 13.78 (5.11)  
159 cm and a significant mean change of -1.66 cm ( $P=0.02$ ) at 2-weeks post. With a  
160 power of 80%, and alpha level of 0.05, a calculation for two related groups indicated  
161 that  $n=76$  were required in each group. In our pilot study we recruited 46 pwMS, with  
162 no loss to follow-up across two visits (although completion of all test procedures was  
163 limited by fatigue in some participants). As this randomised controlled trial involves a  
164 longer intervention period, we will allow for a 15% attrition rate. An 85% retention  
165 rate over a 16-week period (Baseline assessments at Week 0 and Week 4,  
166 intervention 12-weeks, Post-intervention assessment at Week 16) is appropriate  
167 based on previous MS intervention studies. Three randomised controlled trials with  
168 12-week intervention periods conducted in pwMS, report retention rates of 82% [27],  
169 88% [11], and 90% [28]. Therefore, 88 participants per group will be recruited, giving  
170 a total of 176 participants.

171

#### 172 *Location and setting*

173 All assessments will be conducted in the Gait Laboratory within the Institute of  
174 Health and Biomedical Innovation at Queensland University of Technology,  
175 Brisbane, Australia.

176

177 *Participants*

178 Men and women with a diagnosis of MS will be identified through a pool of sampling  
179 frames including MS Queensland, local MS health care providers and community  
180 organisations across the Brisbane, Gold Coast, and Logan regions, Australia.

181 Participants will be recruited through mainstream media advertisements and written  
182 materials distributed to individuals listed on the MS Queensland database and those  
183 attending local MS Clinics. Recruitment procedures will be centrally coordinated by  
184 clinical staff working within each organisation to maintain patient confidentiality.

185 Participants will be invited to voluntarily contact the Principal Investigator for further  
186 information. Participants will be eligible to take part if they meet the following criteria:  
187 aged over 18 years; clinical diagnosis of MS; ambulant over 100 metres with or  
188 without the use of an assistive device; and Disease Step rating of 1-4 [29].

189 Participants rated as Disease Step 1 (Mild disability: Mild symptoms and/or signs) to  
190 4 (Late cane: Unable to walk 25 feet without a cane/unilateral support) will be eligible  
191 to take part in this study, ensuring they have sufficient ambulatory capacity to  
192 complete the gait trials. Exclusion criteria are: neurological conditions other than MS;  
193 peripheral neuropathy; currently being prescribed over-the-counter or custom-made  
194 foot orthoses; cardiovascular or orthopaedic conditions including recent injury to the  
195 back or legs limiting ambulation; unstable psychiatric condition or cognitive  
196 impairment (Short Form Mini-Mental State Examination [MMSE] score <24) [30].

197 Furthermore, enrolled participants who report an exacerbation of MS symptoms  
198 persisting >24hrs, four weeks prior to, or at any time during, the intervention period  
199 will also be excluded from the study. All participants will initially be screened via  
200 telephone interview, and invited to attend a clinical examination, to confirm eligibility.



201 Written informed consent will be obtained from all participants. This study was  
202 approved by the Medical Research Ethics Committee at The University of  
203 Queensland (#2014000781) and University Human Research Ethics Committee at  
204 Queensland University of Technology (#1500000615).

205

#### 206 *Randomisation and blinding*

207 The concealed randomisation schedule will be established using a computer  
208 generated random number sequence, and maintained by an offsite investigator who  
209 is neither involved with the enrolment nor assessment of participants. Consecutively  
210 numbered, randomly ordered, opaque envelopes containing group allocation (in a  
211 1:1 ratio), will be opened consecutively after baseline assessment 2, by a second  
212 research assistant who is only responsible for administering the insoles. All  
213 investigators and the first research assistant, who are involved in the enrolment or  
214 assessment of participants over the duration of the trial, will remain blinded to group  
215 allocation. Following baseline assessment 2, the Principal Investigator and first  
216 research assistant will leave the gait laboratory to ensure blinding to the insole  
217 condition. The second research assistant will then fit the participant with their  
218 allocated insole, and provide advice regarding; frequency of wear, completion of  
219 insole wear diaries, and emergency contact details for local podiatry care.  
220 Participants will be instructed not to divulge their group allocation. As it is not  
221 possible for participants to be blinded to their allocated group (those in the  
222 intervention group will be able to perceive the textured material against the sole of  
223 their foot), the full aims of the study will be concealed. Participants will not be told  
224 that the intervention is designed to provide enhanced plantar sensory information  
225 which could potentially lead to changes in gait. Such knowledge could influence how

226 participants walk and they could purposefully alter their walking patterns between-  
227 conditions: debriefing will occur upon completion of the study. Furthermore, coding of  
228 participants will not refer to group.

229

### 230 *Intervention*

231 In this randomised controlled trial we will investigate two different shoe insoles:  
232 textured insoles and smooth (control) insoles. Both insoles have been implemented  
233 in previous research strategies in pwMS [20], older fallers [23], and middle-aged  
234 adults [31]. The textured insole (Evalite Pyramid ethyl vinyl acetate [EVA], 3mm  
235 thickness, shore value A50, black, OG1549; Algeos PTY Ltd., Liverpool, UK) was  
236 selected from a range of EVA soling materials, and has small, pyramidal peaks with  
237 centre-to-centre distances of approximately 2.5mm. The smooth control insole  
238 (Medium Density EVA, 3mm thickness, shore value A50, black, OG1304; Algeos  
239 PTY Ltd., Liverpool, UK) was chosen from a range of plain EVA materials and has a  
240 flat surface with no indentations. Insoles will be tailored to each participant's shoe  
241 size. An experienced podiatrist will oversee and advise on the delivery of insoles,  
242 and any podiatry-related issues including insole fit, durability, and dermatological or  
243 peripheral changes at the foot during the intervention period. Participants will be  
244 instructed to wear their allocated insoles, in their own shoes, as much as possible.  
245 All assessments of balance and gait will be conducted with the participants wearing  
246 standardised footwear (Donated by Pacific Brands Australia Pty Ltd), comprising a  
247 basic construct rubber-soled shankless shoe with a soft canvas upper [32], into  
248 which the insoles will be inserted. This standardisation will control for any possible  
249 insole/shoe interactions across participants, which could impact the findings. To

250 allow for familiarisation to the footwear, participants will be instructed to walk for 5  
251 minutes in the standardised shoes prior to testing.

252

### 253 *Primary outcome measures*

254 *Spatiotemporal gait variables:* The primary gait measure will be ML base of support,  
255 when walking over an even and uneven surface. Our pilot study demonstrated that  
256 after 2-weeks wear of the textured insoles, the significant mean reduction in base of  
257 support was 1.7cm ( $P=0.02$ ) compared to baseline measures [20]. The magnitude of  
258 this effect is highly clinically relevant as previous research indicates a mean  
259 difference of ~2cm in base of support exists between pwMS and healthy controls [6,  
260 7]. This suggests that the textured effect is clinically significant, and may be of  
261 sufficient magnitude to reduce base of support to a level similar to healthy adults.

262

### 263 *Secondary outcome measures*

264 *Spatiotemporal gait variables:* Additional measures of walking stability will include  
265 stride length, stride time variability, double-limb support time, and gait velocity, when  
266 walking over an even and uneven surface. Our pilot study reported that wearing  
267 textured insoles for 2-weeks led to significant increases in mean stride length (Right  
268 leg: 5.8cm [ $P<0.01$ ]; Left leg: 4.4cm [ $P<0.01$ ]), compared to baseline assessment  
269 [20]. Details of specific methods underpinning all measures are provided in the  
270 assessment section below.

271

272 *Gait kinematics:* During both even and uneven surface walking trials, lower limb gait  
273 kinematics will be collected using a 3D motion capture system and will include hip,  
274 knee, ankle joint angles (and their inter-relationships), and foot-to-floor angle to

275 determine maximum toe clearance. Segmental measures of trunk inclination, as well  
276 as arm swing, mediolateral pelvis and head displacement will also be collected.  
277 Specific details are presented below.

278

279 *Sensory measures:* Light touch-pressure sensation will be determined by recording  
280 the smallest monofilament that the participant can perceive at five locations on the  
281 foot as detailed below [15]. Vibration sense will be measured using a digital stop  
282 watch, started when the tuning fork touches the participant's skin at two sites on the  
283 feet, then stopped when the participant indicates the vibration can no longer be felt.  
284 The average of three trials will be recorded for both feet (seconds) [15]. For two-point  
285 discrimination, when the participant perceives two stimuli as one, the distance will be  
286 recorded in mm [15]. Ankle joint position sense will be determined by the participant  
287 performing the ankle joint position sense test [33].

288

289 *Insole wear and falls:* Participants will be followed for 12-weeks with insole wear self-  
290 reported diaries and falls calendars to determine: i) number of hours insoles are  
291 worn and ii) frequency, time, location of any falls and injuries. In this study, a fall will  
292 be defined as an unexpected event in which the participant comes to rest on the  
293 ground, floor or lower level [34].

294

#### 295 *Clinical screening examination*

296 Prior to enrolment, all individuals will undergo a clinical screening examination,  
297 conducted by a Specialist Neurological Physiotherapist (KW), which will include the  
298 assessment of disease stage, and symptoms including spasticity and ataxia. Stage  
299 of disease will be determined using Disease Steps [29]. This tool is an assessment

300 of disability in patients with MS, which has low inter-rater variability, correlates  
301 strongly to the Expanded Disability Severity Scale at initial assessment (EDSS), and  
302 can be used to monitor disease progression [35]. Spasticity will be assessed using  
303 the Tardieu Scale [36], and ataxia scored using the Brief Ataxia Rating Scale [37].

304

#### 305 *Baseline assessments*

306 Demographics including gender, age, height, and body mass will be collected. To  
307 characterise the study sample, participants will be asked to complete questionnaires  
308 that address relevant medical history and medications, length of time since diagnosis  
309 of MS, current MS symptoms using the MS Impact Scale (MSIS-29) [38], and  
310 perceived walking ability using the MS Walking Scale (MSWS-12) [39]. Quality of life,  
311 the impact of fatigue and pain, and perceived disability will be assessed using four  
312 self-report questionnaires: MS Quality of Life Instrument (MS QoL-54) [40]; Modified  
313 Fatigue Impact Scale (a questionnaire which measures how MS-related fatigue  
314 affects everyday life including physical, cognitive and psychosocial functioning [41]);  
315 Medical Outcomes Study (MOS) Pain Effects Scale (a MS-specific questionnaire  
316 which assesses how pain and disturbing sensations, such as burning or tingling,  
317 affect everyday life [42]); and the Perceived Deficits Questionnaire (a MS-specific  
318 questionnaire which assesses several domains of cognitive function that are  
319 commonly affected by MS: attention; retrospective memory, prospective memory,  
320 planning and organization [43]). Number of self-reported falls experienced in the  
321 previous 12 months will be recorded, and current fear of falling assessed using the  
322 Falls Efficacy Scale-International [44].

323

324 Following the clinical screening examination, all participants will complete initial  
325 assessments of gait, foot sensation and proprioception (Baseline assessment 1).  
326 Standing balance and activity levels will also be measured at baseline assessment 1  
327 only. Each participant will receive a wireless activity monitor (activPAL, Glasgow,  
328 Scotland), to be worn every day for seven consecutive days; allowing us to  
329 characterise the activity of the study group, monitor habitual weekly activity levels  
330 and establish any relationships with gait performance at baseline. The increasing  
331 use of accelerometry in pwMS [45, 46] is accredited to its ability to allow monitoring  
332 of changes in walking impairments with disease progression (e.g. worsening of MS)  
333 or disease activity (e.g. acute relapse), over long periods of time [47]. Four weeks  
334 after baseline assessment 1, a second baseline assessment (Baseline assessment  
335 2) will be conducted. The purpose of this 4-week waiting period is to establish each  
336 participant's natural rate of MS disease progression, specifically the magnitude of  
337 change in the primary and secondary outcomes measures of gait, foot sensation and  
338 proprioception, prior to delivery of the intervention.

339

#### 340 *Gait*

341 Gait performance will be evaluated by completing a 12m walk over an even surface  
342 and an uneven surface. The even surface will consist of a level, vinyl material: the  
343 top cover of an instrumented walkway (GAITRite®, CIR Systems, Inc., Havertown,  
344 PA 19083, USA). The GAITRite® system is an electronic walkway, approximately  
345 8.2m long (the active area being 0.61m wide and 7.32m long), which has been  
346 shown to have high reliability [48, 49]. The uneven surface (placed directly on the  
347 laboratory floor, adjacent to the GAITRite® walkway) will consist of two layers of  
348 thick soft foam, over which small blocks of wood of uneven shapes and sizes will be

349 spread in a random manner; with a top layer of artificial grass covering the walkway,  
350 using previously described methods [50]. Maintenance of stability when walking  
351 requires individuals to control their centre of mass within a constantly changing base  
352 of support: this becomes even more challenging when the surface is uneven,  
353 increasing the risk of loss of balance, resulting in a fall. Deficits in balance control  
354 during walking, or conversely the therapeutic benefit of interventions (such as shoe  
355 insoles) on walking performance may only become apparent when the balance  
356 challenge is sufficiently demanding. The uneven walking surface will emulate a  
357 situation encountered in daily life. A start and finish line will be marked on the floor  
358 2m in front and 2m behind both the even and uneven surface walkways, allowing  
359 participants to accelerate and decelerate outside the walkways [48]. Participants will  
360 be positioned at the start line and instructed to walk at their comfortable, self-  
361 selected walking pace. Five walking trials will be completed on the even surface and  
362 5 trials on the uneven surface, each whilst barefoot, wearing standardised footwear  
363 only, and wearing two different shoe insoles (textured and smooth) within  
364 standardised footwear. The test sequence (footwear condition, surface) will be  
365 randomised. Spatiotemporal gait variables will be measured using the GAITRite®  
366 system (sampling rate 80Hz) when walking over the even surface, and using an 11-  
367 camera Vicon® motion capture system (Vicon, 6 x MX13 and 5 x T40 cameras,  
368 giganet control box, with a MX Net and Mx Link), sampled at 200Hz, when walking  
369 over the uneven surface. Participants will have multiple reflective markers attached  
370 to their body, following the Vicon PlugIn Gait full body model. The Vicon system  
371 records the position of reflective markers placed at standardised anatomical sites on  
372 the upper and lower body and will be used to measure spatiotemporal gait variables  
373 and gait kinematics.

374

375 *Balance*

376 Standing balance will be assessed to provide a measure of basic, unperturbed  
377 postural stability. Participants will stand on an AMTI force platform (sampling rate  
378 1000Hz), using a standardised foot position (heels placed  $1/10^{\text{th}}$  participants height  
379 apart and angled to  $14^{\circ}$  [51]), and arms hanging by their sides, for 30 seconds [52].  
380 Double-limb standing tests will be performed on a firm and foam surface, with their  
381 eyes open and eyes closed. To prevent vestibular disruption when standing with  
382 eyes open, participants will be instructed to look straight ahead and focus on the  
383 middle of a black circular visual target (10cm diameter), mounted onto a board  
384 positioned 3 metres from the centre of the force platform, and adjusted to the eye  
385 level of each participant. Standing balance will be assessed whilst barefoot, wearing  
386 standardised footwear only, and when wearing two different shoe insoles (textured  
387 and smooth) within standardised footwear. The test sequence (footwear condition,  
388 surface, vision) will be randomly presented. Measures of baseline standing balance  
389 will include centre of pressure (CoP) path velocity, range and standard deviation of  
390 CoP movement in the anterior-posterior and mediolateral directions.

391

392 *Foot sensation and proprioception*

393 Somatosensory function, including light touch-pressure sensation, vibration sense,  
394 and two-point discrimination will be assessed. Semmes-Weinstein monofilaments  
395 (smallest [1.65] to largest [6.65]) will be used to determine light touch-pressure  
396 sensation at five locations on the foot: plantar surface of the great toe; first  
397 metatarsal head; fifth metatarsal head; heel; and dorsum of the foot between the first  
398 and second toes [53]. The monofilaments will be applied perpendicular to the skin for



399 1.5 seconds, and the participant will be required to indicate whether the fibre can be  
400 felt. The smallest monofilaments (1.65-4.08) will be applied three times  
401 consecutively, whilst larger ones (4.17-6.65) will be applied only once [15]. Duration  
402 of vibration sense will be measured using a 128-Hz frequency tuning fork at the first  
403 metatarsal head and medial malleoli of both feet [15]. The ability to distinguish  
404 between two light-touch stimuli (two-point discrimination) will be measured using an  
405 aesthesiometer applied to the skin at three foot regions: tip of the great toe; first to  
406 second metatarsal interspace, fifth metatarsal head. Each region will be touched with  
407 either one point or two points simultaneously in a random order, with approximately 2  
408 seconds between each application of the stimuli. Assessment will begin with the two  
409 stimuli at the maximum distance apart, and decrease until the participant can no  
410 longer differentiate the two points [15]. Foot position awareness will be assessed  
411 bilaterally using the ankle joint angle reproduction test [33]. The investigator will  
412 passively set the participant's ankle joint to three pre-determined angles in  
413 plantarflexion and dorsiflexion directions, relative to a neutral foot position. A variable  
414 time and trajectory will be used when positioning the foot in order to eliminate  
415 extraneous cues and psychophysical processes. The participant will be asked to  
416 reposition the ankle joint at the target angle, by moving only the foot segment.  
417 Accuracy in joint positioning will be determined by measuring the difference between  
418 the target and actual angles using an internet-based goniometer [54]. This  
419 application has been shown to be a valid method for measuring joint angles and has  
420 a high level of inter- (ICC<sub>2,1</sub>=0.96 to >0.99) and intra- (ICC= all >0.99) rater reliability  
421 [54].

422

423 *Post-intervention assessment*

424 Gait, foot sensation and proprioception will be assessed within two weeks of the end  
425 of the 12-week intervention period, using the same procedures employed at  
426 baseline. A 12-week intervention period will provide maximal time to allow for the  
427 accrual of any sensory training effects and accumulation of meaningful changes in  
428 outcomes measures, in particular for participants with MS who show minimal gait  
429 disturbance at baseline and currently engage in an active lifestyle. This intervention  
430 period is consistent with previous randomised controlled trial intervention studies  
431 conducted in pwMS [11, 27, 28], and footwear intervention trials [55, 56]. This final  
432 point of assessment will: (i) quantify whether any immediate changes in gait,  
433 observed at baseline, have accrued over time, or if additional effects can be seen  
434 and; (ii) determine whether there are any alterations in the perception of foot  
435 sensation or proprioception, which may suggest the insoles have a sensory training  
436 effect. Participants will be asked to return their insole wear diaries and falls  
437 calendars at this time. Participants will also be asked to rate the level of comfort  
438 experienced when wearing the insoles by way of a series of 100mm visual analogue  
439 scales (VAS) used in previously published research [57].

440

#### 441 *Data analysis*

442 All analyses will be conducted in a blinded manner, on an intention-to-treat basis,  
443 with the alpha set to 0.05. We will explore frequency distributions, percentages and  
444 calculate means and standard deviations for the outcome measures. Differences  
445 between intervention and control groups in spatiotemporal gait variables, gait  
446 kinematics, foot sensation or proprioception, over the intervention period will be  
447 explored using General Linear Models (repeated measures analysis of variance,  
448 ANCOVA), in a two group (smooth control insole; textured insole) x 3 phase

449 (Baseline assessment 1, Baseline assessment 2, Post-intervention) model. We will  
450 adjust for potential confounding variables (e.g. age, gender, disease duration) by  
451 using these as covariates. Non-parametric tests will be used where data is not  
452 normally distributed or violates the assumption of sphericity. Multiple regression  
453 modelling will be used to determine any relationships between foot sensation,  
454 proprioception and measures of gait performance. Data will be analysed using SPSS  
455 version 22 (SPSS Inc., Chicago, IL 60606, USA).

456

## 457 **Discussion**

458 Gait impairment is one of the most disabling and debilitating complaints reported by  
459 pwMS [5]. Deteriorating mobility observed in the early stages of disease [6-8] not  
460 only increases the risk of falling [1, 2], but frequently culminates in a complete loss of  
461 walking ability in the advanced stages [58]. The associated personal and societal  
462 burdens can have devastating implications for the individual, their families, and  
463 national health services. Physical rehabilitation strategies reported to improve gait in  
464 pwMS commonly involve short-term multi-component exercise programs [9-13].  
465 Maintenance of walking stability is attributed to optimal sensorimotor function,  
466 however therapeutic management of gait impairments in pwMS, largely focuses on  
467 addressing motor problems and poor aerobic capacity, and to a lesser extent  
468 sensory training, which is commonly addressed purely by way of balance tasks  
469 under a variety of sensory conditions. Interventions targeting sensory impairments at  
470 a more local level, including foot sensation and lower limb proprioception, are not  
471 frequently incorporated. This is a crucial area to address as loss of foot sensation  
472 and impaired lower limb proprioception are strongly associated with standing  
473 balance and gait performance in pwMS [15, 19]. Therefore, the effectiveness of

474 current strategies for managing mobility in pwMS could be further enhanced by using  
475 a wider range of treatment techniques.

476

477 Providing enhanced sensory input to the plantar surface of the feet has recently  
478 been considered a potential mechanism through which footwear interventions may  
479 improve gait [21, 22, 24, 59-63], by way of altering sensorimotor function. Underlying  
480 physiological mechanisms by which a textured insole may initiate changes in gait are  
481 suggested to include the provision of sufficient tactile stimulation to alter the rate of  
482 discharge from mechanoreceptors or firing patterns of populations of sensory  
483 afferents located in the feet. Textured shoe insoles appear to have the capacity to  
484 alter gait patterns, potentially improving gait stability in ageing, neurodegenerative  
485 and neuromuscular disease groups with known balance impairments. To date,  
486 exploratory studies report that wearing shoe insoles deigned to enhance plantar  
487 sensation can significantly increase single-limb support time [24], increase stride  
488 length and reduce double-limb support time [32] during walking in people with  
489 Parkinson's disease. Similar conclusions are emerging for pwMS, with exploratory  
490 work observing beneficial alterations in spatiotemporal gait parameters [20], gait  
491 kinetics and kinematics [21].

492

493 This randomised controlled trial will use fundamental knowledge of sensory and  
494 motor function in MS to develop novel ways to improve gait by way of enhancing  
495 sensory information at the soles of the feet. Preliminary work in this clinical  
496 population [20] provides strong evidence of improvements in gait patterns when  
497 textured insoles were worn (as a single intervention) for two weeks. It is possible that  
498 the benefits of wearing textured insoles may accrue, and additional benefits may be

499 observed, over a longer period of time. Findings from this trial could have  
500 implications on the management of gait impairment in pwMS. The benefit for pwMS  
501 (and their families) is that this study may lead to the development of a new,  
502 evidence-based footwear intervention which is inexpensive, non-invasive, promotes  
503 self-management by the user, and has the capacity to enhance mobility and  
504 independent living. Furthermore, addressing problems with mobility, and  
505 subsequently quality of life, could have a major economic impact, through  
506 improvements in productivity or reducing working days lost. The benefit for health  
507 care professionals is that this study may generate vital evidence to inform the  
508 development of more effective, multi-faceted and multi-disciplinary rehabilitation  
509 programmes, which are tailored to address a greater range of MS-specific  
510 impairments that contribute to deteriorating gait. This could have major implications  
511 on current clinical guidelines and policy relating to physical rehabilitation strategies  
512 for pwMS.

513

#### 514 *List of abbreviations*

515 ANCOVA: analysis of covariance; CoP: Centre of pressure; EDSS: Expanded  
516 Disability Severity Scale; EVA: ethyl vinyl acetate; ICC: intraclass correlation  
517 coefficient; ML: mediolateral; MMSE: Mini-mental state examination; MOS: Medical  
518 Outcomes Study; MS: Multiple Sclerosis; MSIS-29: Multiple Sclerosis Impact Scale;  
519 MS QoL-54: Multiple Sclerosis Quality of Life Instrument; MSWS-12: Multiple  
520 Sclerosis Walking Scale; pwMS: people with Multiple Sclerosis; SD: standard  
521 deviation; SPSS: Statistical Package for the Social Sciences VAS: visual analogue  
522 scale

523

524 *Competing interests (non-financial)*

525 The textured insoles and smooth control insoles investigated in this study were  
526 supplied by Algeos PTY. Ltd. (Liverpool, UK). This company had no involvement in  
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529

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533 manuscript; and will not be involved in subsequent data acquisition, analysis or  
534 interpretation.

535

536 *Authors' contributions*

537 AH conceived the idea for the study and took primary responsibility for drafting the  
538 manuscript. All authors obtained funding for the study, contributed to the design of  
539 the trial protocol, intervention, and outcome measures, and preparation of the  
540 manuscript. All authors have read and approved the final manuscript.

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729

730

731 **Figure 1:** Trial Design

**Enrolment**

Initial contact through Multiple Sclerosis Queensland; Multiple Sclerosis community and health care services across the Brisbane, Gold Coast, Logan regions; local media

Assessed for eligibility via telephone screening  
**Eligible participants invited for clinical screening examination**

Clinical screening examination  
**Eligible participants recruited and consented**

- Excluded**
- Not meeting criteria
  - Declined to participate
  - Deceased
  - Other

**Baseline assessment 1 (Week 0)**

**Spatiotemporal gait variables & gait kinematics**

- Walking over even and uneven ground (2 surfaces, 4 footwear conditions)

**Sensory measures**

- *Foot sensation*: Light touch-pressure, vibration sense, two-point discrimination
- *Proprioception*: Ankle joint position sense

**Baseline assessments**

- Demographics, medical history, self-report questionnaires addressing quality of life, impact of symptoms, perceived disability, falls
- *Balance*: Quiet standing (2 surfaces, 2 visual conditions, 4 footwear conditions)

**Habitual activity monitoring (7 consecutive days)**

- Withdrawal
- Exacerbation of Multiple Sclerosis symptoms lasting >24hrs
- Lost to follow-up
- Deceased
- Other

**Baseline assessment 2 (Week 4)**

**Spatiotemporal gait variables & gait kinematics**  
**Sensory Measures: *Foot sensation, Proprioception***

**Allocation**

**Randomisation (N=176)**

**Smooth insole (N=88)**

**Textured insole (N=88)**

**12-week intervention period**

**Follow-up**

**Post-intervention assessment (Week 16)**

**Spatiotemporal gait variables & gait kinematics**  
**Sensory measures: *Foot sensation, Proprioception***  
**Insole wear diaries & falls calendars**

- Withdrawal
- Exacerbation of Multiple Sclerosis symptoms lasting >24hrs
- Discontinued intervention
- Lost to follow-up
- Deceased

**Post-intervention assessment (Week 16)**

**Spatiotemporal gait variables & gait kinematics**  
**Sensory measures: *Foot sensation, Proprioception***  
**Insole wear diaries & falls calendars**

- Withdrawal
- Exacerbation of Multiple Sclerosis symptoms lasting >24hrs
- Discontinued intervention
- Lost to follow-up
- Deceased

**Analysis**

**Analysed (Excluded from analysis)**

**Analysed (Excluded from analysis)**