

Participation restriction in people with multiple sclerosis: prevalence and correlations with cognitive, walking, balance and upper limb impairments

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Running title: Participation restrictions in MS

1 Objective

2 To calculate percentage of participation restrictions according to disability level in Multiple
3 Sclerosis (MS) and to assess relationship between participation restriction, and cognitive, gait,
4 balance and upper limb deficits.

5 Design

6 Cross sectional study

7 Setting

8 Rehabilitation unit

9 Participants

10 105 people with MS and 20 healthy subjects (HS) were screened in Belgium and Italy.

11 Interventions

12 Not applicable

13 Main outcome measures

14 The Community integration questionnaire was used to assess participation in Home, Social and
15 Productive Activities. Percentages of people with MS scores lower than the 10th percentile of
16 those of HS were calculated for each sub scale to categorize the persons with participation
17 restrictions.

18 Cognitive deficits (Symbol Digit Modalities Test), walking disability (25-foot walking test /
19 EDSS), balance disorders (Bohannon Standing Balance Test) and manual dexterity (Nine Hole
20 Peg Test), were recorded.

21 Results

22 77% of participants showed participation restrictions, which increased with higher EDSS scores
23 from 40% (EDSS<4) to 82% (EDSS>5.5). Social participation was more restricted than home
24 integration with less than 20% of participants doing shopping for groceries alone. Cognitive
25 deficits were more highly associated ($r=0.60$) with participation restrictions than balance
26 ($r=0.47$), gait ($r=-0.45$) and hand dexterity ($r=0.45$) limitations.

27 Conclusions

28 Participation restrictions are present in MS and increase with disability level. However, the
29 results also show that multiple sclerosis does not restrict participation in all domains.

30 Participation restriction at home is less restricted compared to social participation. Cognitive
31 disorders are more associated to participation restrictions than physical limitations

32

33 Keywords: Participation; Gait; Posture; Upper extremity; Cognition.

34

35 Participation, defined as involvement in life situations, is often considered to be associated with
36 quality of life and has been proposed as one determinant of health status.¹ Indeed, participation
37 is recently suggested as a primary outcome of interventions aiming to improve quality of life.^{2,3}
38 Participation restrictions, defined as ‘problems an individual may experience in involvement in
39 life situations,⁴ can result from a combination of personal factors, impairments, activity
40 limitations and environmental factors⁵ that can differently impact on the execution of home,
41 social and productive activities.

42

43 Although participation has its own definition and should be viewed as an independent
44 construct, quality of life and independency in activity of daily living are often used to measure
45 participation restriction. An early survey reported that two-thirds of 166 people with multiple
46 sclerosis (PwMS) had limitations in performing activities without assistance and having an
47 independent social/lifestyle.⁶ A later study similarly revealed that 47% of 240 PwMS were not
48 completely independent in their domestic life⁷. Finally, a study by Argento et al⁸ reported
49 differences between MS and healthy subjects in time spent at home with other people and use
50 of domestic help.

51 Several studies have also been conducted to investigate the relationship between variables
52 related with quality of life and activity limitation and multiple sclerosis (MS) related disorders.
53 Mikula et al. found that health related quality of life is associated with disease severity and age
54 in MS.⁹ Ben Ari et al. found a correlation between activity limitation measured as restriction in
55 outdoor activities and depression, cognitive disorders and leisure and domestic activities.¹⁰
56 Finally, Yorkston et al. inquired on satisfaction with participation and found that participation is
57 associated with fatigue, pain, depression, stress, anxiety, and well-being in MS¹¹. Furthermore,

58 the frequency with which participants reported participating in active leisure, was associated
59 with mobility impairments¹².

60

61 While it is known that gait impairments can lead to limitations in activity and potentially
62 restrict participation, also balance disturbances¹³, hand dexterity dysfunctions^{14,15} and cognitive
63 deficits¹⁶ have a potentially deleterious effect on different domains of participation. However,
64 the relationship between cognitive deficits, disorders at activity level and participation
65 restrictions are not well understood. Moreover, physical and cognitive parameters have not been
66 studied together in connection with participation in life domains, such as, home activities,
67 social participation and work activities.

68 The study of the relation between participation restrictions and physical and cognitive factors
69 is important since they are mostly modifiable factors that might respond to rehabilitation.
70 Further, investigation of the magnitude of these relationships with tools commonly used in
71 rehabilitation to measure attention and activity limitation might indicate their appropriateness as
72 predictors of participation restrictions, Altogether, this may contribute to our developing more
73 focused clinical rehabilitation protocols that can lead to improved participation in home and
74 social situations, as well as better chances of participating in productive activities.

75

76 Until now participation restrictions have been mainly studied using scales addressing quality of
77 life⁹, amount of performed activities¹⁰ or life satisfaction¹² while a test specifically addressing
78 participation might give a better picture of restriction in different domains of life participation.
79 Furthermore the use of a standardized test on participation and the collection of data from a
80 reference group of healthy subjects made it possible to calculate the true prevalence of
81 participation restrictions.

82 The Community Integration Questionnaire (CIQ) was developed for people with traumatic
83 brain injury.¹⁷ It is a test specifically designed to assess participation restrictions, including
84 home, social and productive activities and has also been used.^{18, 19,2,20,21} for PwMS

85
86 The primary aim of this study was to use the home, social and productive activities domains of
87 the CIQ to calculate the prevalence of global and domain specific participation restrictions in
88 MS according to disability level and in relation to healthy persons. The secondary aim was to
89 assess the relationship between participation restrictions in these three domains and activity
90 disorders in terms of walking and balance disturbances, hand dexterity and cognitive deficits.

91

92 **Method**

93 A convenience sample of 105 people was recruited from inpatients and outpatients treated at the
94 Rehabilitation and MS Center, Overpelt, Belgium; and the Department of Neurorehabilitation,
95 Don Carlo Gnocchi Foundation Onlus, IRCCS, Milan, Italy. The inclusion criteria were:
96 confirmed MS diagnosis (McDonald criteria²²), age>18 year old, free from relapses or relapse-
97 related treatments for one month before the study, and the ability to touch the chin at least with
98 one hand. Subjects unable to follow test instructions or having other diseases interfering with
99 the execution of tests were excluded, further information on the sample is available in Bertoni
100 et al¹⁵.

101 A convenience sample of twenty healthy subjects (HS) matched for age and gender were also
102 tested to provide CIQ comparative data. We recruited all eligible subjects having the same age
103 range and sex as PwMS in a two weeks window. Seven were men (35%), mean age (SD) was
104 51.9 (11.5) years with none of them reporting any musculoskeletal or neurological conditions.

105

106 All subjects received information regarding the study and were included after signing the
107 informed consent forms. The study was approved by the ethical committee of each participating
108 centre.

109 *Descriptive variables*

110 Expanded Disability Scale (EDSS), type of MS, disease duration, gender and age were
111 retrieved from medical records as determined by the treating neurologist. Participants were
112 asked their employment status.

113 *Cognitive function and Activity predictors*

114 The cognitive level and psychomotor speed was determined by the Symbol Digit Modalities
115 Test (SDMT).²³ The SDMT requires individuals to identify nine different symbols
116 corresponding to the numbers 1 through 9, and to practice writing the correct number under the
117 corresponding symbol. Then they manually fill in the blank space under each symbol with the
118 corresponding number. A score was calculated by totalling the number of correct answers over
119 90s.

120 Manual dexterity was measured with the Nine Hole Peg Test (NHPT);²⁴ The time needed to
121 place and remove 9 pegs was recorded and averaged over 2 trials. Manual dexterity speed was
122 calculated as pegs per second and used in the analyses.¹⁴ Participants who were not able to
123 place any peg within a time limit of 300 seconds received a score of 0 pegs per second.

124

125 Walking speed (seconds), was assessed with the Timed 25 foot walking test (T25FW).²⁵
126 According to standardized instructions an average of the 2 trials was computed.

127 Upright balance was assessed with Bohannon Standing Balance Test (BSBT)²⁶, ranging from 0
128 (unable to stand) to 6 (stand on one foot for 30'').

129

130 *Participation*

131 The CIQ was used to assess participation. CIQ is scored to create a total score ranging from 0 to
132 29 representing from none to excellent community integration. It also provides scores from
133 three subscales assessing:

134 Home Integration (10 points) that refers to participation in activities such as preparing the meal,
135 doing house-work and planning social meeting in the home.

136 Social Integration (12 points), which refers to participation in outdoor activities including
137 shopping, visiting friends and aspects of interpersonal relations.

138 Productive Activities (7 points). Including items inquiring employment, educational and
139 volunteer activities.

140

141 Percentages of PwMS having CIQ scores lower than the 10th percentile of those of HS were
142 calculated for each sub scale of the CIQ and for the total score to categorize the persons as
143 having problem or no problem with participation.

144 Two physical therapists experienced in the assessment of PwMS performed all tests. To ensure
145 standardization between centres an instruction booklet was used and two practice sessions in
146 the two countries were held to minimize the differences between assessors. Data coming from

147 these preliminary assessments were analysed to verify if there were any statistically significant
148 differences between the two centres.

149 Data Analysis

150 A T test (two-tailed) was used to calculate statistically significant differences between HS and
151 PwMS.

152 Pearson's correlation coefficients were calculated to investigate the correlations between CIQ,
153 demographic and clinical variables. T25WT and EDSS showed a high level of redundancy
154 (Pearson's correlation coefficients > 0.8), thus only EDSS was entered in the subsequent models.

155 For multivariate analysis statistical manuals suggest at least 10 subjects for each independent
156 predictor²⁷. We included 98 subjects in the model to account for missing data. Generalized
157 linear models were used to assess the relationship between participation (dependent variable)
158 and the other variables used as predictors. The first analysis containing demographic and
159 clinical characteristics showed that only Type of MS and not age or disease duration was
160 statistically significantly associated with the dependent variable thus only MS type and
161 cognitive and activity deficits were entered in the final models.

162 Receiver Operating Characteristic curves were calculated to obtain cut off values for the
163 statistically significant predictors that best distinguished participation restrictions in total CIQ
164 or sub-domains of CIQ. Area Under the Curve (AUC) demonstrating accuracy of the cutoff
165 value was calculated.

166 To manage and analyze the data, we used Statistica 8 with the significance level set at $p < 0.05$.

167

168 Results

169 Seven subjects with incomplete data were excluded.

170

171 Table 1 shows the characteristics of the remaining 98 PwMS tested with all relevant tests.

172 People with relapsing remitting, secondary progressive or primary progressive types of MS

173 were: 32(33%), 56(57%) and 10(10%) respectively and 67 subjects (68.3%) used a walking aid.

174 Out of the whole group 17 (16.2%) were retired, 46 (43.8%) stopped working prematurely, 18

175 (17.1%) had never been employed, 6 (5.7%) worked part time and 18 subjects (17.1%) worked

176 full time.

177

178 Table 2 reports comparisons between HS and PwMS in terms of mean CIQ scores. As expected

179 HS had statistically significantly higher level of participation compared to PwMS This was very

180 evident in the productive activity domain where the score for HS were double compared to that

181 of PwMS.

182 Table 3 reports the percentages of PwMS having a total CIQ scores below the 10th percentile of

183 HS scores from which to calculate proportion of participation restrictions according to

184 disability level. Participation restriction increased with an increasing EDSS. Forty% of PwMS

185 with EDSS <4 had scores below the cut-off, thus denoting participation restrictions, and up to

186 82% of the subjects with EDSS 6+ had scores below the cut off (Table 3). Noteworthy, 90% of

187 wheelchair bound people (n=38) had scores below the cut-off.

188

189

190 Figure 1 depicts CIQ items and percentages of PwMS doing activities of daily living without

191 help or more than 5 times/month. Less than 10% of PwMS did shopping alone and less than

192 25% of PwMS did shopping more than 5 times a month.

193

194 Table 4 shows bivariate correlations assessing the relationship between participation
195 restrictions of the CIQ total score, its various domains and activity disorders. Highest
196 correlations were observed between CIQ total score and SDMT($r=0.60$) and between the home
197 integration section of the CIQ and EDSS($r=-0.57$) and NHPT($r=0.55$).

198

199 Results from the multivariate analyses are reported in Table 5 to show the simultaneous
200 relationship between participation restrictions, activity disorders and cognitive deficits. Models
201 predicting overall participation restrictions (CIQ Total score) and home participation
202 restrictions explained a larger proportion of variance than those predicting social integration
203 and productive activities.

204 The SDMT was the best predictor in all participation domains and CIQ total score. Total CIQ
205 scores were also negatively associated with BSBT and Type of MS (score of 14, 16 and 13
206 respectively for RR, PP and SP type). Meaning that people with higher cognitive and balance
207 disorders and secondary progressive type of MS had higher participation restrictions compared
208 to PwMS with primary progressive MS. Finally, decreased hand dexterity was positively
209 associated with home participation restrictions.

210 The AUC (CI) and cut off scores for total CIQ were: 0.76 (0.64-0.87) and 34.5 points for
211 SDMT, and 0.74 (0.63-0.84) and 2.5 points for BSBT respectively. AUC (CI) and cut off scores
212 for home integration CIQ for the NHPT were respectively 0.73 (0.60-0.84) and 0.27 peg/s
213 (around 33.3s to move 9 pegs).

214

215 **Discussion**

216 The aims of the study were to estimate the prevalence of participation restrictions in MS
217 according to disability level and to assess relationship between participation restrictions,
218 activity limitations and cognitive deficits.

219 This is the first study documenting that 77% of a sample of PwMS showed participation
220 restrictions, with integration in social participation tending to be more restricted than home
221 integration, and providing test cut off scores that discriminate between PwMS with or without
222 restriction in participation. However, the results also highlight the fact that multiple sclerosis
223 does not restrict participation in the whole population and in all domains. PwMS with mild
224 involvement reported no or only mild participation restriction at home, while the vast majority
225 of PwMS with EDSS>7 show participation restrictions in all domains. In addition, participation
226 restrictions were less prevalent in the productive domain compared to the social domain.

227 Overall participation restrictions were found to be more correlated with cognitive deficits than
228 balance and gait limitations while hand dexterity was predominantly associated to participation
229 in home activities. Finally, even controlling for disorders at activity and cognitive level subjects
230 with a secondary progressive type of MS had a higher level of participation restrictions than
231 those with primary progressive type.

232

233 PwMS showed a substantial decrease in participation compared to age-matched HS.

234 Restrictions in social participation were the most prevalent, more than 70% of participants did
235 not perform outdoor activities such as shopping and visiting relatives on a regular basis. One-
236 third of the participants showed participation restrictions in home and productive activities
237 which have been linked to reduced self-esteem, life satisfaction, mental health status^{28,29,30} and
238 perceived MS severity³¹.

239 Participation restrictions also increased burden for family members with 91% of participants
240 needing help for shopping and only 38% of them preparing the meal for themselves. Decreased
241 number of activities may further impact on level of physical capacity leading to a further
242 reduction in participation.³² It is, however, important to point out that the comparison with
243 healthy subjects scores and the analysis of subgroups showed that participation restriction are
244 unevenly distributed. All participants having an EDSS score less than 4 had a normal level of
245 participation in home activities and more than 60% of the sample reported normal levels of
246 participation in productive activities irrespective of the EDSS score.

247

248 Cognitive deficits were the best predictor of participation restrictions in MS, results
249 corroborated by Rao et al³³ that found that PwMS with cognitive deficits had restrictions in
250 social, vocational, routine household activities and work. Huges et al³⁴ similarly found that
251 cognitive impairment measured with a self-reported questionnaire was associated to a lower
252 level of participation.

253 Our results and results from other studies^{10,35} underscore the importance of neurocognitive
254 assessment in MS and the use of cognitive tests preceding interventions aimed at improving
255 community integration. We can also speculate that multimodal interventions, including
256 treatments for cognitive disorders, might improve participation of PwMS.

257 Balance disorders were associated to participation restrictions. Balance disorders interfere with
258 basic activities of daily living and may increase social isolation, fear of falling and consequent
259 activity curtailment.³⁵ Petterson found that one third of PwMS were concerned about falling³⁵
260 with majority of them reporting activity curtailment. The above results underline the
261 importance of considering fall risk factors such as balance and fear of falling in interventions to

262 enhance participation.³⁵
263 Limited hand dexterity was associated with participation restrictions and in particular to
264 restrictions in home activities, where upper limb control is essential for activities like dressing
265 and cooking. Our results corroborate preceding studies that revealed a high percentage of
266 bilateral hand dexterity deficits and correlations between the community integration Index and
267 impairment in upper limb strength and sensibility.^{14,15}

268 In agreement with other studies^{7,36} bivariate correlation was found between walking and
269 participation restrictions but walking did not reach a significant threshold in the predictive
270 model after controlling for other factors. Results did not change when gait speed was
271 substituted by EDSS. Sample characteristics may have played a role since more than half used
272 an assistive device and one quarter had severe walking restriction. The use of assistive device
273 may aid in reducing participation restrictions even in participants with severe walking
274 disturbances.

275 Social integration and productive activities were limited in our sample; more than two-third of
276 PwMS were retired and 43 % of them stopped working prematurely due to MS thus markedly
277 increasing the burden on society. Association between functional status and social/protective
278 activities was, however, unclear and deserves further studies. We found that a cognitive deficit
279 was the only predictor associated with the social integration and productive domains of the
280 CIQ. However, the explained variance was moderate, indicating that these domains cannot be
281 explained solely by the deterioration of cognitive deficits and activity-related performances. It
282 is known that interaction between cognitive disorders and social policy factors contributes to
283 employment status³⁷. This may have influenced our analysis since 16% of the sample was
284 already of retirement age irrespective of activity limitations. Further, we did not evaluate social

285 support which has been reported as being important for quality of life in PwMS³⁸. Results also
286 imply that EDSS, NHPT and BSBT, cannot by themselves inform clinicians on potential
287 participation restrictions in social and productive activities. It should be noted that the social
288 integration and productive activities domains of the CIQ have been shown to have a low level
289 of internal consistency and dimensionality¹⁹ which may reduce the quality of information
290 provided by these two subscales.

291

292

293 Finally PwMS with secondary progressive type of MS had increased participation restrictions
294 compared to persons with the primary progressive form. This difference was consistent also
295 when age, disease duration and clinical characteristics were controlled for. Several studies have
296 revealed that depression, mood and anxiety are more prevalent in people with secondary
297 progressive type of MS than primary progressive³⁹. It is possible that these factors can explain
298 observed differences between groups.

299

300 The results of the study underline the association of activity and cognitive deficits on
301 participation, especially in moderately to severely disabled PwMS. This is important since they
302 are factors that can potentially respond to intervention. Reducing activity limitations and
303 cognitive deficits might thus lead to better participation. This, however, remains to be studied in
304 future intervention studies. Further, the cut off scores provided can be used as guidance for the
305 physician to detect PwMS having participation restrictions and potentially intervene to reduce
306 the impact of the deficits in order to improve their participation.

307 Study Limitations

308 While the present study has strengths, such as, the number of participants and the inclusion of
309 modifiable factors such as mobility, hand function and cognition that influence participation it

310 does have some limitations. First, recruitment of participants attending rehabilitation centers
311 led to an overrepresentation of PwMS with moderate to severe disability. In addition, mild
312 cognitive disorders may have reduced the reliability of patient-reported outcomes. Second, this
313 study featured a cross sectional design with correlation and regression analyses making
314 definitive causation impossible.

315 Lastly, we did not measure specific factors that may have a direct impact on participation, such
316 as depression, anxiety, fatigue, sensory disorders, presence of caregiver and internal-external
317 barriers.

318

319 Conclusions

320 Participation restrictions are present in MS and increase with disability level. However,
321 multiple sclerosis does not restrict participation in all domains. Participation restriction at home
322 is less restricted compared to social participation. Cognitive disorders are more associated to
323 participation restrictions than balance, gait and hand dexterity impairments. Finally, the results
324 of this study provided cut off scores that will enable clinicians to evaluate the risk that a PwMS
325 can have of participation restrictions.

326

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Figure Legend

Figure 1. Community Integration Questionnaire Items. Percentages (and numbers) of PwMS performing activities of daily living without help (scored 2 points on Items 1-6) or more than 5 times/month (scored 2 points on Items 7-12).

1 Objective

2 To calculate percentage of participation restrictions according to disability level in Multiple
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29 results also show that multiple sclerosis does not restrict participation in all domains.

30 Participation restriction at home is less restricted compared to social participation. Cognitive
31 disorders are more associated to participation restrictions than physical limitations

32

33 Keywords: Participation; Gait; Posture; Upper extremity; Cognition.

34

35 Participation, defined as involvement in life situations, is often considered to be associated with
36 quality of life and has been proposed as one determinant of health status.¹ Indeed, participation
37 is recently suggested as a primary outcome of interventions aiming to improve quality of life.^{2,3}
38 Participation restrictions, defined as ‘problems an individual may experience in involvement in
39 life situations,⁴ can result from a combination of personal factors, disabilities impairments,
40 activity limitations and environmental factors⁵ that can differently impact on leading to
41 difficulties in the execution of home, social and productive activities.

42
43 Although participation has its own definition and should be viewed as an independent
44 construct, quality of life and independency in activity of daily living are often used to measure
45 participation restriction. People with multiple sclerosis (PwMS) tend to have limitations in
46 activities of daily living with a An early survey reporting ing that two-thirds of 166 people with
47 multiple sclerosis (PwMS) had limitations in performing activities without assistance and
48 having an independent social/lifestyle.⁶ A second later study similarly revealed that 47% of 240
49 PwMS reported restrictions were not completely independent in their domestic life⁷. Finally, a
50 study by Argento et al⁸ reported differences between MS and healthy subjects in time spent at
51 home with other people and use of domestic help.

52 Several studies have also been conducted to investigate the relationship between variables
53 related with quality of life and activity limitation and multiple sclerosis (MS) related disorders.
54 Mikula et al. found that health related quality of life is associated with disease severity and age
55 in MS.⁹ Ben Ari et al. found a correlation between activity limitation measured as restriction in
56 outdoor activities and depression, cognitive disorders and leisure and domestic activities.¹⁰
57 Finally, Yorkston et al. inquired on satisfaction with participation and found that participation is
58 associated with fatigue, pain, depression, stress, anxiety, and well-being in MS¹¹. Furthermore,

59 the frequency with which participants reported participating in active leisure, was associated
60 with [gait mobility](#) impairments¹².

61

62 While it is known that gait impairments can lead to limitations in activity and potentially
63 restrict participation, also balance disturbances¹³, hand dexterity dysfunctions^{14,15} and cognitive
64 deficits¹⁶ have a potentially deleterious effect on different domains of participation. However,
65 the relationship between cognitive deficits, disorders at activity level and participation
66 restrictions are not well understood. Moreover, physical and cognitive parameters have not been
67 studied together in connection with participation in life domains, such as, home activities,
68 social participation and work activities.

69 The study of the relation between participation restrictions and physical and cognitive factors
70 is important since they are [mostly](#) modifiable factors that might respond to rehabilitation.

71 Further, investigation of the magnitude of these relationships with tools commonly used in
72 rehabilitation to measure attention and activity limitation might indicate their appropriateness as
73 predictors of participation restrictions, Altogether, this may contribute to our developing more
74 focused clinical rehabilitation protocols that can lead to improved participation in home and
75 social situations, as well as better chances of participating in productive activities.

76

77 Until now participation restrictions have been [mostly-mainly](#) studied using scales addressing
78 quality of life⁹, amount of performed activities¹⁰ or life satisfaction¹² while a test specifically
79 addressing participation might give a better picture of restriction [in life's](#) in different domains [of](#)
80 [life participation](#). Furthermore the use of a standardized test on participation and the collection
81 of data from a reference group of healthy subjects made it possible to calculate the true
82 prevalence of participation restrictions.

83 The Community Integration Questionnaire (CIQ) was developed for people with traumatic
84 brain injury.¹⁷ It is a test specifically designed to assess participation restrictions, including
85 home, social and productive activities and has also been ~~validated~~ used.^{18, 19,2-and-used,20,21} for
86 PwMS

87
88 The primary aim of this study was to use the home, social and productive activities~~three~~
89 domains of the CIQ to calculate the prevalence of global and domain specific participation
90 restrictions in MS according to disability level and in relation to healthy persons. The secondary
91 aim was to assess the relationship between participation restrictions in home, social and
92 productive activities~~these three domains~~ and activity disorders in terms of walking and balance
93 disturbances, hand dexterity and cognitive deficits.

94

95 **Method**

96 A convenience sample of 105 people was recruited from inpatients and outpatients treated at the
97 Rehabilitation and MS Center, Overpelt, Belgium; and the Department of Neurorehabilitation,
98 Don Carlo Gnocchi Foundation Onlus, IRCCS, Milan, Italy. The ~~405 people meeting the~~
99 following inclusion criteria were ~~recruited~~: confirmed MS diagnosis (McDonald criteria²²),
100 age>18 year old, free from relapses or relapse-related treatments for one month before the
101 study, and the ability to touch the chin at least with one hand. Subjects unable to follow test
102 instructions or having other diseases interfering with the execution of tests were excluded,
103 further information on the sample is available in Bertoni et al¹⁵.

104 A ~~convenient~~ convenience sample of twenty healthy subjects (HS) matched for age and gender
105 were also tested to provide CIQ comparative data. We recruited all eligible subjects having the

106 same age range and sex as PwMS in a two weeks window. Seven were men (35%), mean age
107 (SD) was 51.9 (11.5) years with none of them reporting any musculoskeletal or neurological
108 conditions.

109

110 All subjects received information regarding the study and were included after signing the
111 informed consent forms. The study was approved by the ethical committee of each participating
112 centre.

113 *Descriptive variables*

114 Expanded Disability Scale (EDSS), type of MS, disease duration, gender and age were
115 retrieved from medical records as determined by the treating neurologist. [Participants were](#)
116 [asked their employment status.](#)

117 *Cognitive function and Activity predictors*

118 The cognitive level and psychomotor speed was determined by the Symbol Digit Modalities
119 Test (SDMT).²³ The SDMT requires individuals to identify nine different symbols
120 corresponding to the numbers 1 through 9, and to practice writing the correct number under the
121 corresponding symbol. Then they manually fill in the blank space under each symbol with the
122 corresponding number. A score was calculated by totalling the number of correct answers over
123 90s.

124 Manual dexterity was measured with the Nine Hole Peg Test (NHPT);²⁴ The time needed to
125 place and remove 9 pegs was recorded and averaged over 2 trials. Manual dexterity speed was
126 calculated as pegs per second and used in the analyses.¹⁴ Participants who were not able to
127 place any peg within a time limit of 300 seconds received a score of 0 pegs per second.

128

129 Walking speed (seconds), was assessed with the Timed 25 foot walking test (T25FW).²⁵

130 According to standardized instructions an average of the 2 trials was computed.

131 Upright balance was assessed with Bohannon Standing Balance Test (BSBT)²⁶, ranging from 0

132 (unable to stand) to 6 (stand on one foot for 30'').

133

134 *Participation*

135 The CIQ was used to assess participation. CIQ is scored to create a total score ranging from 0 to

136 29 representing from none to excellent community integration. It also provides scores from

137 three subscales assessing:

138 Home Integration (10 points) that refers to participation in activities such as preparing the meal,

139 doing house-work and planning social meeting in the home.

140 Social Integration (12 points), which refers to participation in outdoor activities including

141 shopping, visiting friends and aspects of interpersonal relations.

142 Productive Activities (7 points). Including items inquiring employment, educational and

143 volunteer activities.

144

145 Percentages of PwMS having CIQ scores lower than the 10th percentile of those of HS were

146 | calculated for each sub scale of the CIQ and for the total score to categorize the persons as

147 | having problem or no problem with participation.

148 Two physical therapists experienced in the assessment of PwMS performed all tests. To ensure
149 standardization between centres an instruction booklet was used and two practice sessions in
150 the two countries were held to minimize the differences between assessors. Data coming from
151 these preliminary assessments were analysed to verify if there were any statistically significant
152 differences between the two centres.

153 Data Analysis

154 A T test (two-tailed) was used to calculate statistically significant differences between HS and
155 PwMS.

156 Pearson's correlation coefficients were calculated to investigate the correlations between CIQ,
157 demographic and clinical variables. T25WT and EDSS showed a high level of redundancy
158 (Pearson's correlation coefficients > 0.8), thus only EDSS was entered in the subsequent models.

159 For multivariate analysis statistical manuals suggest at least 10 subjects for each independent
160 predictor²⁷. We included 98 subjects in the model to account for missing data. Generalized
161 linear models were used to assess the relationship between participation (dependent variable)
162 and the other variables used as predictors. The first analysis containing demographic and
163 clinical characteristics showed that only Type of MS and not age or disease duration was
164 statistically significantly associated with the dependent variable thus only MS type and
165 cognitive and activity deficits were entered in the final models.

166 ~~To manage and analyze the data, we used Statistica 8 with the significance level set at~~
167 ~~p < 0.05. We calculated Receiver Operating Characteristic curves~~ were calculated to obtain cut
168 off values for the statistically significant predictors that best distinguished participation
169 restrictions in total CIQ or sub-domains of CIQ-. Area Under the Curve (AUC) demonstrating
170 accuracy of the cutoff value was calculated.

171 | To manage and analyze the data, we used Statistica 8 with the significance level set at p<0.05.

172

173 Results

174 Seven subjects with incomplete data were excluded.

175

176 Table 1 shows the characteristics of the remaining 98 PwMS tested with all relevant tests.

177 People with relapsing remitting, secondary progressive or primary progressive types of MS

178 were: 32(33%), 56(57%) and 10(10%) respectively and ~~57~~ sixty-seven subjects (68.3%) used

179 a walking aid. Out of the whole group 17 (16.2%) were retired, 46 (43.8%) stopped working

180 prematurely, 18 (17.1%) had never been employed, 6 (5.7%) worked part time and ~~68-18~~

181 subjects (~~69~~17.1-3%) were unemployed~~worked full time.~~

182

183 Table 2 reports comparisons between HS and PwMS in terms of mean CIQ scores. As expected

184 HS had statistically~~ly~~ significantly higher level of participation compared to PwMS This was very

185 evident in the productive activity domain where the score for HS were double compared to that

186 of PwMS.

187 Table 3 reports the percentages of PwMS having a total CIQ scores below the 10th percentile of

188 HS scores from which to calculate proportion of participation restrictions according to

189 disability level. Participation restriction increased with an increasing EDSS. Forty% of PwMS

190 with EDSS <4 had scores below the cut-off, thus denoting participation restrictions, and up to

191 82% of the subjects with EDSS 6+ had scores below the cut off (Table 3). Noteworthy, 90% of

192 wheelchair bound people (n=38) had scores below the cut-off.

193

194

195 Figure 1 depicts CIQ items and percentages of PwMS doing activities of daily living without
196 help or more than 5 times/month. Less than 10% of PwMS did shopping alone and less than
197 25% of PwMS did shopping more than 5 times a month.

198

199 Table 4 shows bivariate correlations assessing the relationship between participation
200 restrictions of the CIQ total score, its various domains and activity disorders. Highest
201 correlations were observed between CIQ total score and SDMT($r=0.60$) and between the home
202 integration section of the CIQ and EDSS($r=-0.57$) and NHPT($r=0.55$).

203

204 Results from the multivariate analyses are reported in Table 5 to show the simultaneous
205 relationship between participation restrictions, activity disorders and cognitive deficits. Models
206 predicting overall participation restrictions (CIQ Total score) and home participation
207 restrictions explained a larger proportion of variance than those predicting social integration
208 and productive activities.

209 The SDMT was the best predictor in all participation domains and CIQ total score. Total CIQ
210 scores were also negatively associated with BSBT and Type of MS (score of 14, 16 and 13
211 respectively for RR, PP and SP type). Meaning that people with higher cognitive and balance
212 disorders and secondary progressive type of MS had higher participation restrictions compared
213 to PwMS with primary progressive MS. Finally, decreased hand dexterity was positively
214 associated with home participation restrictions.

215 [The AUC \(CI\) and cut off scores for total CIQ were: 0.76 \(0.64-0.87\) and 34.5 points for](#)
216 [SDMT, and 0.74 \(0.63-0.84\) and 2.5 points for BSBT respectively. AUC \(CI\) and cut off scores](#)
217 [for home integration CIQ for the NHPT were respectively 0.73 \(0.60-0.84\) and 0.27 peg/s](#)
218 [\(around 33.3s to move 9 pegs\).](#)

219

220 **Discussion**

221 The aims of the study were to estimate the prevalence of participation restrictions in MS
222 according to disability level and to assess relationship between participation restrictions,
223 activity limitations and cognitive deficits.

224 This is the first study documenting that 77% of a sample of PwMS showed participation
225 restrictions, with integration in social participation tending to be more restricted than home
226 integration, [and providing test cut off scores that discriminate between PwMS with or without](#)
227 [restriction in participation](#). However, the results also highlight the fact that multiple sclerosis
228 does not restrict participation in the whole population and in all domains. PwMS with mild
229 involvement reported no or only mild participation restriction at home, while the vast majority
230 of PwMS with EDSS>7 show participation restrictions in all domains. In addition, participation
231 restrictions were less prevalent in the productive domain compared to the social domain.
232 Overall participation restrictions were found to be more correlated with cognitive deficits than
233 balance and gait limitations while hand dexterity was predominantly associated to participation
234 in home activities. Finally, even controlling for disorders at activity and cognitive level subjects
235 with a secondary progressive type of MS had a higher level of participation restrictions than
236 those with primary progressive type.

237

238 PwMS showed a [relevant-substantial](#) decrease in participation compared to age-matched HS.
239 Restrictions in social participation were the most prevalent, more than 70% of participants did
240 not perform outdoor activities such as shopping and visiting relatives on a regular basis. One-
241 third of the participants showed participation restrictions in home and productive activities

242 which have been linked to reduced self-esteem, life satisfaction, mental health status^{28,29,30} and
243 perceived MS severity³¹.
244 Participation restrictions also increased burden for family members with 91% of participants
245 needing help for shopping and only 38% of them preparing the meal for themselves. Decreased
246 number of activities may further impact on level of physical capacity leading to a further
247 reduction in participation.³² It is, however, important to point out that the comparison with
248 healthy subjects scores and the analysis of subgroups showed that participation restriction are
249 unevenly distributed. All participants having an EDSS score less than 4 had a normal level of
250 participation in home activities and more than 60% of the sample reported normal levels of
251 participation in productive activities irrespective of the EDSS score.

252

253 Cognitive deficits were the best predictor of participation restrictions in MS, results
254 corroborated by Rao et al³³ that found that PwMS with cognitive deficits had restrictions in
255 social, vocational, routine household activities and work. Huges et al³⁴ similarly found that
256 cognitive impairment measured with a self-reported questionnaire was associated to a lower
257 level of participation.

258 Our results and results from other studies^{10,35} underscore the importance of neurocognitive
259 assessment in MS and the use of cognitive tests preceding interventions aimed at improving
260 community integration. We can also speculate that multimodal interventions, including
261 treatments for cognitive disorders, might improve participation of PwMS.

262 Balance disorders were associated to participation restrictions. Balance disorders interfere with
263 basic activities of daily living and may increase social isolation, fear of falling and consequent
264 activity curtailment.³⁵ Petterson found that one third of PwMS were concerned about falling³⁵

265 with majority of them reporting activity curtailment. The above results underline the
266 importance of considering fall risk factors such as balance and fear of falling in interventions to
267 enhance participation.³⁵

268 Limited hand dexterity was associated with participation restrictions and in particular to
269 restrictions in home activities, where upper limb control is essential for activities like dressing
270 and cooking. Our results corroborate preceding studies that revealed a high percentage of
271 bilateral hand dexterity deficits and correlations between the community integration Index and
272 impairment in upper limb strength and sensibility.^{14,15}

273 In agreement with other studies^{7,36} bivariate correlation was found between walking and
274 participation restrictions but walking did not reach a significant threshold in the predictive
275 model after controlling for other factors. Results did not change when gait speed was
276 substituted by EDSS. Sample characteristics may have played a role since more than half used
277 an assistive device and one quarter had severe walking restriction. The use of assistive device
278 may aid in reducing participation restrictions even in participants with severe walking
279 disturbances. ~~The protective role of walking aid on participation restriction warrants further~~
280 ~~studies.~~

281

282 Social integration and productive activities were limited in our sample; more than two-third of
283 PwMS were retired and 43 % of them stopped working prematurely due to MS thus markedly
284 increasing the burden on society. Association between functional status and social/protective
285 activities was, however, unclear and deserves further studies. We found that a cognitive deficit
286 was the only predictor associated with the social integration and productive domains of the
287 CIQ. However, ~~the~~ explained variance was moderate ~~in the models addressing social~~

288 | ~~integration and productive activities~~, indicating that these domains cannot be explained solely
289 by the deterioration of cognitive deficits and activity-related performances. It is known that
290 interaction between cognitive disorders and social policy factors contributes to employment
291 status³⁷. This may have influenced our analysis since 16% of the sample was already of
292 retirement age irrespective of activity limitations. Further, we did not evaluate social support
293 which has been reported as being important for quality of life in PwMS³⁸. Results also imply
294 that EDSS, NHPT and BSBT, cannot by themselves inform clinicians on potential participation
295 restrictions in social and productive activities. It should be noted that the social integration and
296 productive activities domains of the CIQ have been shown to have a low level of internal
297 consistency and dimensionality¹⁹ which may reduce the quality of information provided by
298 these two subscales.

299

300

301 Finally PwMS with secondary progressive type of MS had increased participation restrictions
302 compared to persons with the primary progressive form. This difference was consistent also
303 when age, disease duration and clinical characteristics were controlled for. Several studies have
304 revealed that depression, mood and anxiety are more prevalent in people with secondary
305 progressive type of MS than primary progressive³⁹. It is possible that these factors can explain
306 observed differences between groups.

307

308 The results of the study underline the association of activity and cognitive deficits on
309 participation, especially in moderately to severely disabled PwMS. This is important since they
310 are factors that can potentially respond to intervention. Reducing activity limitations and
311 cognitive deficits might thus lead to better participation. This, however, remains to be studied in

312 future intervention studies. Further, the results cut off scores provided can be used as guidance
313 for the physician to estimate the difficulties detect PwMS having participation restrictions each
314 person with MS may have in different domains of participation and thus potentially intervene to
315 reduce the impact of the deficits in order to improve their participation.

316 Study Limitations

317 While the present study has strengths, such as, the number of participants and the inclusion of
318 modifiable factors such as mobility, hand function- and cognition that influence participation it
319 does have some limitations. First, recruitment of participants attending rehabilitation centers
320 led to an overrepresentation of PwMS with moderate to severe disability. In addition, mildly
321 cognitive disorders may have reduced the reliability of patient-reported outcomes. Second, this
322 study featured a cross sectional design with correlation and regression analyses making
323 definitive causation impossible.

324 Lastly, we did not measure specific factors that may have a direct impact on participation, such
325 as depression, anxiety, fatigue, sensory disorders, presence of caregiver and internal-external
326 barriers.

327

328 Conclusions

329 Participation restrictions are present in MS and increase with disability level. However,
330 multiple sclerosis does not restrict participation in all domains. Participation restriction at home
331 is less restricted compared to social participation. Cognitive disorders are more associated to
332 participation restrictions than balance, gait and hand dexterity impairments. Finally, the results
333 of this study provided cut off scores that will enable clinicians to evaluate the risk that a PwMS
334 can have of participation restrictions.

335

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Figure Legend

Figure 1. Community Integration Questionnaire Items. Percentages (and numbers) of PwMS performing activities of daily living without help (scored 2 points on Items 1-6) or more than 5 times/month (scored 2 points on Items 7-12).

Figure 1

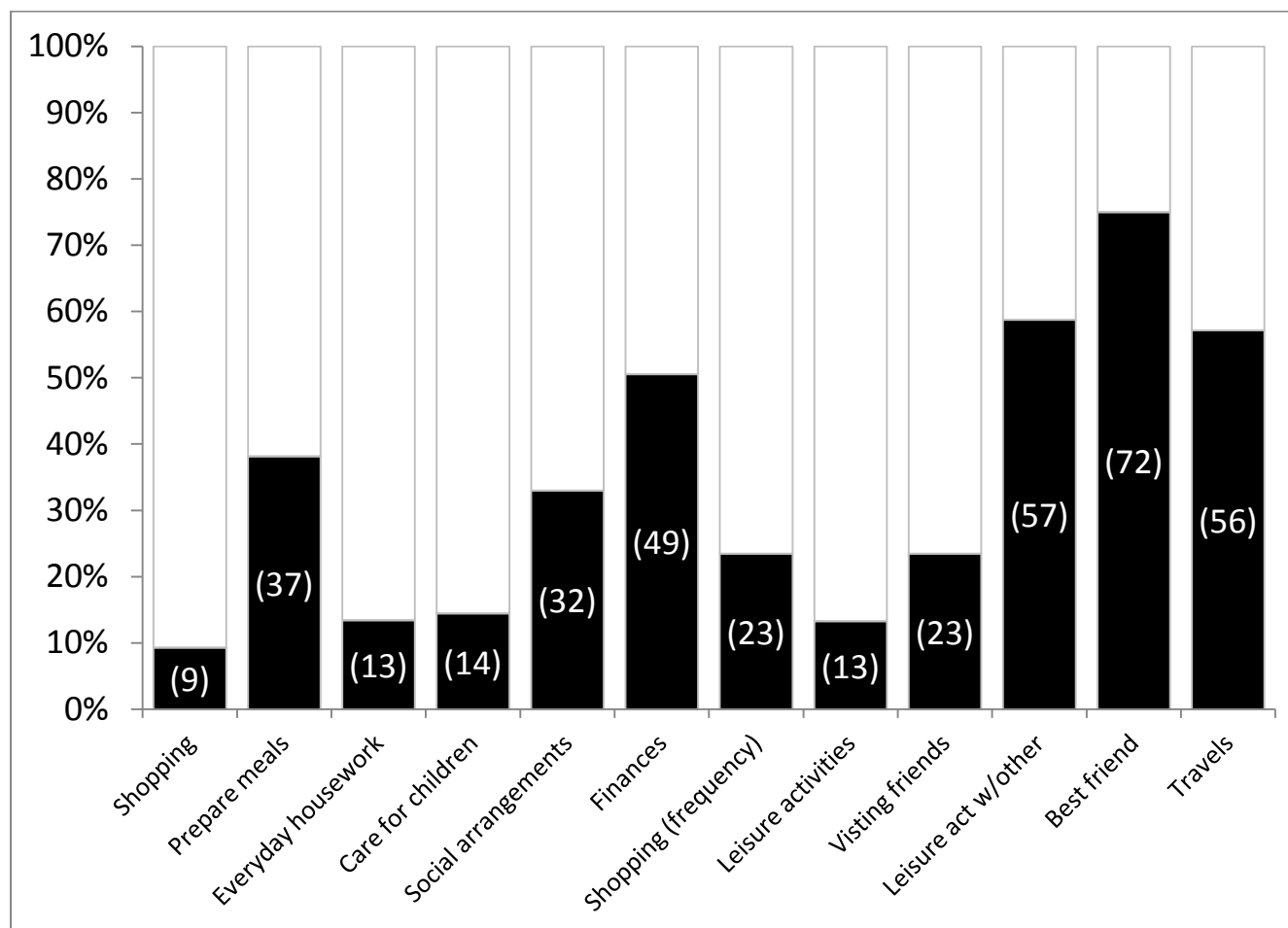


Figure 1. Community Integration Questionnaire Items. Percentages (and numbers) of PwMS performing activities of daily living without help (scored 2 points on Items 1-6) or more than 5 times/month (scored 2 points on Items 7-12).

Table 1. Baseline characteristics of the patient sample, n=98, female=58 (59.2%).

	Mean	(SD)	Minimum	Maximum
Demographic characteristics				
Age (y)	53.4	(11.3)	25.0	82.0
Disease duration (y)	18.2	(11.2)	1.0	47.0
EDSS	6.0	(1.7)	1.5	8.5
Clinical variables				
T25FW (m/s)	0.5	(0.5)	0.0	2.0
SDMT	27.7	(11.2)	13.0	59.0
BSBT	2.8	(2.1)	0.0	6.0
NHPT (pegs/s)	0.3	(0.1)	0.0	0.5

EDSS: Expanded Disability Status Scale; T25FW: Timed 25 foot Walking test; SDMT: Symbol Digit Modality Test; BSBT: Bohannon Standing Balance Test; NHPT: Nine Hole Peg Test. Higher scores in clinical variables mean favourable outcomes.

Table 2. Comparisons between Healthy Subjects and People with Multiple Sclerosis

	Healthy Subjects		People with Multiple Sclerosis		t-value	p value
	Mean	(SD)	Mean	SD		
CIQ Total score	21.2	(3.2)	13.4	(5.0)	-6.6	<0.001
CIQ Home	6.3	(2.3)	3.6	(2.3)	-4.4	<0.001
CIQ Social	9.8	(2.1)	7.3	(2.3)	-4.4	<0.001
CIQ Productive Act	5.1	(1.6)	2.5	(2.0)	-5.5	<0.001

CIQ: Community Integration Questionnaire; Higher scores mean favourable outcomes.

Table 3. Numbers and percentages of CIQ scores lower than the 10th percentile of those of HS for the whole sample of PwMS and subgroups

	Whole sample (EDSS 1-8, n=98)		Mild (EDSS 1-3.5, n=15)		Moderate (EDSS 4-5.5, n=16)		Severe (ESDD 6+, n=67)	
CIQ Total score (<17)	75	76.5%	6	40.0%	13	81.3%	55	82.1%
CIQ Home (<3)	34	34.7%	0	0.0%	6	37.5%	28	41.8%
CIQ Social (<8)	54	55.1%	5	33.3%	12	75.0%	37	55.2%
CIQ Productive Act (<2)	36	36.7%	4	26.7%	5	31.3%	27	40.3%

CIQ: Community Integration Questionnaire; EDSS: Expanded Disability Status Scale. Numbers in parentheses represent cut-off scores used to calculate percentages of abnormal scores.

Table 4. Pearson's correlation coefficients between CIQ and clinical predictors

CIQ	EDSS	SDMT	BSBT	NHPT
Total score	-0.45*	0.60*	0.47*	0.45*
Home	-0.57*	0.49*	0.53*	0.55*
Social	-0.27*	0.46*	0.23*	0.23*
Productive Act	-0.14	0.36*	0.28*	0.20

CIQ: Community Integration Questionnaire; EDSS: Expanded Disability Status Scale; SDMT: Symbol Digit Modality Test; BSBT: Bohannon Standing

Balance Test; NHPT: Nine Hole Peg Test; *: P<0.05

Table 5. Summary of the results of the multivariate analysis with participation restriction (CIQ total score and sub-scores) as the dependent variable.

Dependent Variable	Multiple R ²	Adjusted R ²	F test	P Value	Intercept	Predictor	Coefficient b	SE b	β	SE β	t test	P Value t
Total score	0.47	0.44	13.65	<0.001	6.17	SDMT*	0.20	0.04	0.46	0.09	4.83	0.00
						EDSS	0.01	0.35	0.00	0.12	0.03	0.98
						BSBT*	2.05	1.01	0.23	0.11	2.03	0.05
						NHPT	2.53	4.29	0.06	0.10	0.59	0.56
						Type_of_MS	-0.38	0.67	-0.05	0.08	-0.56	0.58
						Type_of_MS*	-1.49	0.60	-0.20	0.08	-2.49	0.01
Home integration	0.53	0.50	17.25	<0.001	2.79	SDMT*	0.04	0.02	0.20	0.09	2.20	0.03
						EDSS	-0.26	0.16	-0.19	0.11	-1.63	0.11
						BSBT*	0.88	0.45	0.20	0.11	1.94	0.05
						NHPT*	3.84	1.93	0.20	0.10	1.99	0.05
						Type_of_MS	-0.39	0.30	-0.10	0.08	-1.30	0.20
						Type_of_MS*	-0.92	0.27	-0.26	0.08	-3.43	0.00
Social integration	0.25	0.20	5.06	<0.001	5.51	SDMT*	0.09	0.02	0.44	0.11	3.92	0.00
						EDSS	-0.07	0.20	-0.05	0.15	-0.37	0.72
						BSBT	0.31	0.57	0.07	0.13	0.56	0.58
						NHPT	-1.02	2.40	-0.05	0.12	-0.42	0.67
						Type_of_MS	-0.54	0.38	-0.14	0.10	-1.44	0.15
						Type_of_MS	-0.41	0.33	-0.12	0.10	-1.24	0.22
Productive Act	0.18	0.13	3.32	0.01	-1.82	SDMT*	0.07	0.02	0.37	0.12	3.11	0.00
						EDSS	0.31	0.18	0.26	0.15	1.72	0.09
						BSBT	0.81	0.52	0.22	0.14	1.57	0.12
						NHPT	-0.35	2.19	-0.02	0.13	-0.16	0.87
						Type_of_MS	0.57	0.34	0.17	0.10	1.67	0.10
						Type_of_MS	-0.17	0.31	-0.06	0.10	-0.55	0.58

SDMT: Symbol Digit Modality Test; EDSS: Expanded Disability Status Scale; BSBT: Bohannon Standing Balance Test; NHPT: Nine Hole Peg Test. *

P<0.05

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