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

Davide Cattaneo<sup>1</sup>, Ilse Lamers,<sup>2</sup> Rita Bertoni,<sup>1</sup> Peter Feys<sup>2</sup> and Johanna Jonsdottir<sup>1</sup>

<sup>1</sup>LaRiCE lab: Gait and Balance Disorders Laboratory; Don Gnocchi Foundation I.R.C.C.S. Rome, ITALY

<sup>2</sup>REVAL – Rehabilitation Research Institute, BIOMED – Biomedical Research Institute, Faculty of Medicine and Life Sciences, Hasselt University, Hasselt, Belgium

Address for Correspondence:

Davide Cattaneo; LaRiCE. Servizio riabilitazione neurologica adulti (Int. 282); Don Gnocchi Foundation I.R.C.C.S. V. Capecelatro 66 – 20148 Milan, ITALY

Tel: 00390240308814; Fax: 00390240308498;

e-mail: [dcattaneo@dongnocchi.it](mailto:dcattaneo@dongnocchi.it)

Running title: Participation restrictions in MS

1 Participation, defined as involvement in life situations, is often considered to be associated with  
2 quality of life and has been proposed as one determinant of health status.<sup>1</sup> Indeed, participation  
3 is recently suggested as a primary outcome of interventions aiming to improve quality of life.<sup>2 3</sup>  
4 Participation restrictions, defined as ‘problems an individual may experience in involvement in  
5 life situations,<sup>4</sup> can result from a combination of personal factors, impairments, activity  
6 limitations and environmental factors<sup>5</sup> that can differently impact on the execution of home,  
7 social and productive activities.

8

9 Although participation has its own definition and should be viewed as an independent  
10 construct, quality of life and independency in activity of daily living are often used to measure  
11 participation restriction. An early survey reported that two-thirds of 166 people with multiple  
12 sclerosis (PwMS) had limitations in performing activities without assistance and having an  
13 independent social/lifestyle.<sup>6</sup> A later study similarly revealed that 47% of 240 PwMS were not  
14 completely independent in their domestic life<sup>7</sup>. Finally, a study by Argento et al<sup>8</sup> reported  
15 differences between MS and healthy subjects in time spent at home with other people and use  
16 of domestic help.

17 Several studies have also been conducted to investigate the relationship between variables  
18 related with quality of life and activity limitation and multiple sclerosis (MS) related disorders.  
19 Mikula et al. found that health related quality of life is associated with disease severity and age  
20 in MS.<sup>9</sup> Ben Ari et al. found a correlation between activity limitation measured as restriction in  
21 outdoor activities and depression, cognitive disorders and leisure and domestic activities.<sup>10</sup>  
22 Finally, Yorkston et al. inquired on satisfaction with participation and found that participation is  
23 associated with fatigue, pain, depression, stress, anxiety, and well-being in MS<sup>11</sup>. Furthermore,

24 the frequency with which participants reported participating in active leisure, was associated  
25 with mobility impairments<sup>12</sup>.

26

27 While it is known that gait impairments can lead to limitations in activity and potentially  
28 restrict participation, also balance disturbances<sup>13</sup>, hand dexterity dysfunctions<sup>14,15</sup> and cognitive  
29 deficits<sup>16</sup> have a potentially deleterious effect on different domains of participation. However,  
30 the relationship between cognitive deficits, disorders at activity level and participation  
31 restrictions are not well understood. Moreover, physical and cognitive parameters have not been  
32 studied together in connection with participation in life domains, such as, home activities,  
33 social participation and work activities.

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

41

42 Until now participation restrictions have been mostly studied using scales addressing quality of  
43 life<sup>9</sup>, amount of performed activities<sup>10</sup> or life satisfaction**Error! Bookmark not defined.** while a  
44 test specifically addressing participation might give a better picture of restriction in different  
45 domains of life participation. Furthermore the use of a standardized test on participation and the  
46 collection of data from a reference group of healthy subjects made it possible to calculate the  
47 true prevalence of participation restrictions.

48 The Community Integration Questionnaire (CIQ) was developed for people with traumatic  
49 brain injury.<sup>17</sup> It is a test specifically designed to assess participation restrictions, including  
50 home, social and productive activities and has also been used.<sup>18, 19,2,20,21</sup> for PwMS

51

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

57

## 58 **Method**

59 A convenience sample of 105 people was recruited from inpatients and outpatients treated at the  
60 Rehabilitation and MS Center, Overpelt, Belgium; and the Department of Neurorehabilitation,  
61 Don Carlo Gnocchi Foundation Onlus, IRCCS, Milan, Italy. The inclusion criteria were:  
62 confirmed MS diagnosis (McDonald criteria<sup>22</sup>), age>18 year old, free from relapses or relapse-  
63 related treatments for one month before the study, and the ability to touch the chin at least with  
64 one hand. Subjects unable to follow test instructions or having other diseases interfering with  
65 the execution of tests were excluded, further information on the sample is available in Bertoni  
66 et al<sup>15</sup>.

67 A convenience sample of twenty healthy subjects (HS) matched for age and gender were also  
68 tested to provide CIQ comparative data. We recruited all eligible subjects having the same age  
69 range and sex as PwMS in a two weeks window. Seven were men (35%), mean age (SD) was  
70 51.9 (11.5) years with none of them reporting any musculoskeletal or neurological conditions.

71

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

75 *Descriptive variables*

76 Expanded Disability Scale (EDSS), type of MS, disease duration, gender and age were  
77 retrieved from medical records as determined by the treating neurologist. Participants were  
78 asked for employment status.

79 *Cognitive function and Activity predictors*

80 The cognitive level and psychomotor speed was determined by the Symbol Digit Modalities  
81 Test (SDMT).<sup>23</sup> The SDMT requires individuals to identify nine different symbols  
82 corresponding to the numbers 1 through 9, and to practice writing the correct number under the  
83 corresponding symbol. Then they manually fill in the blank space under each symbol with the  
84 corresponding number. A score was calculated by totalling the number of correct answers over  
85 90s.

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

90

91 Walking speed (seconds), was assessed with the Timed 25 foot walking test (T25FW).<sup>25</sup>  
92 According to standardized instructions an average of the 2 trials was computed.

93 Upright balance was assessed with Bohannon Standing Balance Test (BSBT)<sup>26</sup>, ranging from 0  
94 (unable to stand) to 6 (stand on one foot for 30’’).

95

#### 96 *Participation*

97 The CIQ was used to assess participation. CIQ is scored to create a total score ranging from 0 to  
98 29 representing from none to excellent community integration. It also provides scores from  
99 three subscales assessing:

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

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

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

106

107 Percentages of PwMS having CIQ scores lower than the 10<sup>th</sup> percentile of those of HS were  
108 calculated for each sub scale of the CIQ to categorize the persons as having problem or no  
109 problem with participation.

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

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

## 115 Data Analysis

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

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

121 For multivariate analysis statistical manuals suggest at least 10 subjects for each independent  
122 predictor<sup>27</sup>. We included 98 subjects in the model to account for missing data. Generalized  
123 linear models were used to assess the relationship between participation (dependent variable)  
124 and the other variables used as predictors. The first analysis containing demographic and  
125 clinical characteristics showed that only Type of MS and not age or disease duration was  
126 statistically significantly associated with the dependent variable thus only MS type and  
127 cognitive and activity deficits were entered in the final models.

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

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

133

## 134 Results

135 Seven subjects with incomplete data were excluded.



136

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

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

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

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

141 (17.1%) had never been employed, 6 (5.7%) worked part time and 18 subjects (17.1%) worked

142 full time.

143

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

145 HS had statistical significantly higher level of participation compared to PwMS This was very

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

147 of PwMS.

148 Table 3 reports the percentages of PwMS having a total CIQ scores below the 10<sup>th</sup> percentile of

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

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

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

152 82% of the subjects with EDSS 6+ had scores below the cut off (Table 3). Noteworthy, 90% of

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

154

155

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

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

158 25% of PwMS did shopping more than 5 times a month.

159

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

164

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

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

176 The AUC (CI) and cut off scores for total CIQ for the SDMT were respectively 0.76 (0.64-  
177 0.87) and 34.5 points; BSBT were respectively 0.74 (0.63-0.84) and 2.5 points. AUC (CI) and cut  
178 off scores for home integration CIQ for the NHPT were respectively 0.73 (0.60-0.84) and 0.27  
179 peg/s (around 33.3s to move 9 pegs).

180

181 **Discussion**

182 The aims of the study were to estimate the prevalence of participation restrictions in MS  
183 according to disability level and to assess relationship between participation restrictions,  
184 activity limitations and cognitive deficits.  
185 This is the first study documenting that 77% of a sample of PwMS showed participation  
186 restrictions, with integration in social participation tending to be more restricted than home  
187 integration and providing test cut off scores that discriminate between PwMS with or without  
188 restriction in participation. However, the results also highlight the fact that multiple sclerosis  
189 does not restrict participation in the whole population and in all domains. PwMS with mild  
190 involvement reported no or only mild participation restriction at home, while the vast majority  
191 of PwMS with EDSS>7 show participation restrictions in all domains. In addition, participation  
192 restrictions were less prevalent in the productive domain compared to the social domain.  
193 Overall participation restrictions were found to be more correlated with cognitive deficits than  
194 balance and gait limitations while hand dexterity was predominantly associated to participation  
195 in home activities. Finally, even controlling for disorders at activity and cognitive level subjects  
196 with a secondary progressive type of MS had a higher level of participation restrictions than  
197 those with primary progressive type.

198

199 PwMS showed a substantial decrease in participation compared to age-matched HS.  
200 Restrictions in social participation were the most prevalent, more than 70% of participants did  
201 not perform outdoor activities such as shopping and visiting relatives on a regular basis. One-  
202 third of the participants showed participation restrictions in home and productive activities  
203 which have been linked to reduced self-esteem, life satisfaction, mental health status<sup>28,29,30</sup> and  
204 perceived MS severity<sup>31</sup>.

205 Participation restrictions also increased burden for family members with 91% of participants  
206 needing help for shopping and only 38% of them preparing the meal for themselves. Decreased  
207 number of activities may further impact on level of physical capacity leading to a further  
208 reduction in participation.<sup>32</sup> It is, however, important to point out that the comparison with  
209 healthy subjects scores and the analysis of subgroups showed that participation restriction are  
210 unevenly distributed. All participants having an EDSS score less than 4 had a normal level of  
211 participation in home activities and more than 60% of the sample reported normal levels of  
212 participation in productive activities irrespective of the EDSS score.

213

214 Cognitive deficits were the best predictor of participation restrictions in MS, results  
215 corroborated by Rao et al<sup>33</sup> that found that PwMS with cognitive deficits had restrictions in  
216 social, vocational, routine household activities and work. Huges et al<sup>34</sup> similarly found that  
217 cognitive impairment measured with a self-reported questionnaire was associated to a lower  
218 level of participation.

219 Our results and results from other studies<sup>10,35</sup> underscore the importance of neurocognitive  
220 assessment in MS and the use of cognitive tests preceding interventions aimed at improving  
221 community integration. We can also speculate that multimodal interventions, including  
222 treatments for cognitive disorders, might improve participation of PwMS.

223 Balance disorders were associated to participation restrictions. Balance disorders interfere with  
224 basic activities of daily living and may increase social isolation, fear of falling and consequent  
225 activity curtailment.<sup>35</sup> Petterson found that one third of PwMS were concerned about falling<sup>35</sup>  
226 with majority of them reporting activity curtailment. The above results underline the  
227 importance of considering fall risk factors such as balance and fear of falling in interventions to

228 enhance participation.<sup>35</sup>  
229 Limited hand dexterity was associated with participation restrictions and in particular to  
230 restrictions in home activities, where upper limb control is essential for activities like dressing  
231 and cooking. Our results corroborate preceding studies that revealed a high percentage of  
232 bilateral hand dexterity deficits and correlations between the community integration Index and  
233 impairment in upper limb strength and sensibility.<sup>15, 36</sup>

234 In agreement with other studies<sup>7,37</sup> bivariate correlation was found between walking and  
235 participation restrictions but walking did not reach a significant threshold in the predictive  
236 model after controlling for other factors. Results did not change when gait speed was  
237 substituted by EDSS. Sample characteristics may have played a role since more than half used  
238 an assistive device and one quarter had severe walking restriction. The use of assistive device  
239 may aid in reducing participation restrictions even in participants with severe walking  
240 disturbances.

241 Social integration and productive activities were limited our sample; more than two-third of  
242 PwMS were retired and 43 % of them stopped working prematurely due to MS thus markedly  
243 increasing the burden on society. Association between functional status and social/protective  
244 activities was, however, unclear and deserves further studies. We found that a cognitive deficit  
245 was the only predictor associated with the social integration and productive domains of the  
246 CIQ. However, the explained variance was moderate, indicating that these domains cannot be  
247 explained solely by the deterioration of cognitive deficits and activity-related performances. It  
248 is known that interaction between cognitive disorders and social policy factors contributes to  
249 employment status<sup>38</sup>. This may have influenced our analysis since 16% of the sample was  
250 already of retirement age irrespective of activity limitations. Further, we did not evaluate social

251 support which has been reported as being important for quality of life in PwMS<sup>39</sup>. Results also  
252 imply that EDSS, NHPT and BSBT, cannot by themselves inform clinicians on potential  
253 participation restrictions in social and productive activities. It should be noted that the social  
254 integration and productive activities domains of the CIQ have been shown to have a low level  
255 of internal consistency and dimensionality<sup>19</sup> which may reduce the quality of information  
256 provided by these two subscales.

257

258

259 Finally PwMS with secondary progressive type of MS had increased participation restrictions  
260 compared to persons with the primary progressive form. This difference was consistent also  
261 when age, disease duration and clinical characteristics were controlled for. Several studies have  
262 revealed that depression, mood and anxiety are more prevalent in people with secondary  
263 progressive type of MS than primary progressive<sup>40</sup>. It is possible that these factors can explain  
264 observed differences between groups.

265

266 The results of the study underline the association of activity and cognitive deficits on  
267 participation, especially in moderately to severely disabled PwMS. This is important since they  
268 are factors that can potentially respond to intervention. Reducing activity limitations and  
269 cognitive deficits might thus lead to better participation. This, however, remains to be studied in  
270 future intervention studies. Further, the cut off scores can be used as guidance for the physician  
271 to detect PwMS having participation restrictions and thus reduce the impact of the deficits in  
272 order to improve their participation.

273

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

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

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

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