



**HAL**  
open science

## **Time to be Ready to Void: A new tool to assess the time needed to perform micturition for patients with multiple sclerosis**

Claire Hentzen, Anaïs Villaumé, Nicolas Turmel, Gabriel Miget, Frédéric Le Breton, Camille Chesnel, Gérard Amarenco

### ► **To cite this version:**

Claire Hentzen, Anaïs Villaumé, Nicolas Turmel, Gabriel Miget, Frédéric Le Breton, et al.. Time to be Ready to Void: A new tool to assess the time needed to perform micturition for patients with multiple sclerosis. *Annals of Physical and Rehabilitation Medicine*, In press, 10.1016/j.rehab.2020.01.002 . hal-02485618

**HAL Id: hal-02485618**

**<https://hal.sorbonne-universite.fr/hal-02485618>**

Submitted on 20 Feb 2020

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

1 **Time to be Ready to Void: a new tool to assess the time needed to perform micturition**  
2 **for patients with multiple sclerosis**

3

4 C. Hentzen, MD<sup>1</sup>, A. Villaumé<sup>1</sup>, N. Turmel, MD<sup>1</sup>, G. Miget, MD<sup>1</sup>, F. Le Breton, MD<sup>1</sup>, C.  
5 Chesnel, MD<sup>1</sup>, G. Amarenco, PhD<sup>1</sup>

6

7 <sup>1</sup>Sorbonne Université, GRC 001, GREEN Groupe de Recherche Clinique en Neuro-Urologie,  
8 AP-HP, Hôpital Tenon, F-75020 Paris, France

9

10 **Abstract**

11 **Background.** Urgency urinary incontinence is one of the major disabling urinary symptoms  
12 in people with multiple sclerosis (PwMS). The warning time (time from first sensation of  
13 urgency to voiding or incontinence) only partially reflects the possibility of continence. Other  
14 factors such as mobility, difficulties in transfer or undressing can influence this time.

15 **Objectives.** The aim was to create a specific test for PwMS to assess the global time required  
16 to be ready to perform micturition and to assess its reliability.

17 **Methods.** The Time to be Ready to Void (TRV) was based on 2 timed steps: “mobility”  
18 stage, including standing up and walking 6 m to the toilet, and the “settled” stage, starting as  
19 soon as the individual opens the toilet door until readiness for micturition. All participants  
20 performed the TRV twice. Reliability were assessed by the intraclass correlation coefficient  
21 (ICC) and convergent validity by Spearman correlation coefficient.

22 **Results.** We included 71 PwMS (mean [SD] age 54.4 [11.7] years). Inter-rater reliability was  
23 excellent for the TRV mobility stage (ICC 0.97), settled stage (ICC 0.99) and total test (ICC  
24 0.99). Test–retest reliability was good for the mobility stage (ICC 0.88) and total test (ICC  
25 0.81) and moderate for the settled stage (ICC 0.65). Test–retest reliability assessed by a  
26 Likert-type scale was good for each stage ( $\kappa$  0.75 and 0.88). The mobility stage was  
27 correlated with the scores for the Timed Up and Go test, 10-Meter Walk Test, and Tinetti  
28 Mobility Test ( $\rho = 0.89$ ;  $\rho = 0.88$ ;  $\rho = -0.67$ , respectively;  $p < 0.0001$ ) and the settled stage with  
29 scores for the Tinetti Mobility Test, Functional Independence Measure and Nine Hold Peg  
30 test (right) ( $\rho = -0.48$ ;  $\rho = -0.36$ ;  $\rho = 0.31$ , respectively;  $p < 0.01$ ). Comprehension, acceptance  
31 and relevance were rated good by most participants (97%, 95% and 90%, respectively).

32 **Conclusion.** The TRV is a new tool to measure the global time needed to be ready to achieve  
33 micturition in PwMS. It seems useful in clinical practice for overactive bladder in addition to  
34 the classical warning time because it takes into account all the time needed to accomplish  
35 micturition (mobility, undressing, installation).

36

37 **Keywords.** multiple sclerosis; overactive bladder; urinary incontinence, urge; task  
38 performance and analysis

39

## 40 **Introduction**

41 Lower urinary tract symptoms (LUTSs) are frequent in central nervous system disorders,  
42 especially in people with multiple sclerosis (PwMS). The prevalence of LUTSs is high (32–  
43 96.8%) and increases with MS duration and severity of neurological deficiencies and  
44 disabilities[1]. Overactive bladder with urgency, frequency, and urgency urinary incontinence  
45 is the most common symptom, reported by 37% to 99% of PwMS. Overactive bladder affects

46 quality of life, and an overactive detrusor associated with detrusor sphincter dyssynergia can  
47 lead to an altered upper urinary tract (reflux, dilatation, urinary tract infection)[2–6]. In the  
48 absence of risk factors, the treatment aims to improve comfort and quality of life.  
49 Anticholinergic drugs are usually the first-line treatment, but their frequent adverse effects  
50 (constipation, xerostomia, cognitive impairment) may affect compliance and adherence[7].  
51 The risk-benefit balance of these prolonged prescriptions in PwMS should be taken into  
52 account and constantly reassessed.

53 Urinary urgency, evaluated in part by the warning time[8], only partially reflects the  
54 numerous and varied factors that can influence continence, such as the ability to anticipate  
55 and plan urination in relation to cognitive skills, patient mobility and rapid access to the toilet,  
56 autonomy or difficulty in transfer, speed of undressing, and positioning in the toilet in a  
57 correct and secure position, etc.

58 Although we can easily ask our patients about the warning time with urinary urgency (defined  
59 as the time from the first sensation of urgency to voiding or incontinence) and although  
60 specific symptom scores such as the Urinary Symptom Profile[9] or other scores can easily  
61 quantify this time, the global time required to go to the toilet and undress is much more  
62 difficult to quantify. No specific test is available. There are only global assessments of  
63 independence, focusing more on the issue of dressing than removing clothes, with a  
64 qualitative assessment [10]. However, the ratio of the warning time and the time required to  
65 go to the toilet and be ready to void probably plays a role in continence. Sensory or motor  
66 deficits of the lower limbs or balance disorders can affect walking and therefore the time to  
67 reach the toilet and to be installed in a secure position. Dexterity or balance disorders can  
68 affect the undressing phase and increase the time needed to be ready to void. Thus, in clinical  
69 practice, preventing urgent urinary incontinence in PwMS is based on increased warning time  
70 by use of anticholinergics, beta3 agonists, neuromodulation or botulinum toxin but also, and

71 sometimes principally, rehabilitation measures, assistance devices, and tailored clothes to  
72 improve the time needed to be ready to void and thus possibly improve continence.

73 The aim of the study was to create a specific test to assess the global time required to be ready  
74 to void from the moment the person with MS initiates the action of going to the toilet, which  
75 includes standing up, moving to the toilet and removing clothes and installing themselves in a  
76 right and secure position, and to assess its inter-rater and test–retest reliability.

77

## 78 **Methods**

### 79 *Study design*

80 This study was approved by the local ethics review board (RCB: 2018-A01644-51) and all  
81 participants provided written informed consent before inclusion in this observational study.

82 This study was registered on ClinicalTrials.gov (NCT04024085). Participants were recruited  
83 in a neuro-urology department during a medical appointment or a urodynamic assessment or a  
84 day hospital related to urinary disorders.

### 85 *Participants*

86 Inclusion criteria were age  $\geq 18$  years with an MS diagnosis, able to walk 50 m without  
87 human help, and Expanded Disability Status Scale (EDSS) score  $< 7$ . Exclusion criteria were  
88 relapse of MS in the last 7 days and acute urinary tract infection. Participants were recruited  
89 between March 13, 2019 and May 28, 2019.

### 90 *Creation of Time to be Ready to Void (TRV) test*

91 All steps to go to the toilet were discussed and approved by expert consensus with various  
92 health professionals (7 experts in neurourology and physical medicine and rehabilitation, 3  
93 nurses with large experience in neurourology, 1 occupational therapist). The different stages

94 reported before voiding were standing up from a chair, walking to the toilet, opening the toilet  
95 door, entering the toilet, turning on the light, closing the door, getting close to the toilet,  
96 getting undressed, and sitting down if necessary.

97 The TRV was constructed based on these different steps. The patients had to stand up from a  
98 chair with armrests, walk 6 m to the toilet, open the door and turn on the light, close the door,  
99 undress and position themselves to urinate (Fig. 1). The distance of 6 m was chosen to be  
100 sufficient to evaluate the ambulation but not too great to limit the impact of possible  
101 architectural constraints during the evaluation.

102 Two major steps were defined. The “mobility” stage, starting when the examiner gives the  
103 starting signal, included standing up, walking to the toilet, and stopping when putting the  
104 hand on the door handle. The “settled” stage starts as soon as the individual has a hand on the  
105 door handle to being undressed and in the usual and secure position to void. The “interval” or  
106 “lap” function of the chronometer was used to facilitate the recording. The difficulty of each  
107 stage was assessed on a 4-point Likert scale, with 0 indicating impossible or need human help  
108 and 3 no difficulty. If the participant performed clean intermittent self-catheterization, the  
109 equipment was placed next to the toilet before the test.

110 The test was designed to be rated by a physician or paramedical staff and performed during a  
111 medical appointment. Details of clothing worn on the day of the test were noted, including the  
112 presence of buttons, a belt, pants or skirt, pantyhose, or a diaper. The use of a walking aid for  
113 the TRV was noted.

#### 114 *Procedures*

115 Medical history and descriptive data were collected. Urinary symptoms were assessed by the  
116 Urinary Symptom Profile questionnaire with 3 aspects: stress urinary incontinence (/9),  
117 overactive bladder (/21) and low stream (/9) [9]. Data for the last urodynamics were collected,

118 especially the presence of detrusor overactivity. MS severity was assessed by the EDSS,  
119 which measures impairment in 8 functional systems, and on walking ability[11]. Missing data  
120 were not replaced.

121 The test was explained to participants before they performed the TRV. Patients were asked to  
122 assess their need to void on a numerical scale between 0 and 10.

123 To assess inter-rater reliability, 2 examiners recorded the first TRV try with a digital  
124 chronometer. To assess the reliability of the TRV, a second test was attempted after at least 10  
125 min of rest, with one of the 2 examiners, checking that the need to void had not changed  
126 significantly. Reliability was evaluated the same day to limit the impact of the day's clothing.

127 To assess the convergent validity of the TRV, further tests were carried out: a 10-m walk test  
128 (10MWT)[12] at maximum speed and a Timed Up and Go (TUG) test[13] to assess the  
129 ambulation function; a bilateral Nine Hold Peg (NHP) Test for dexterity[14]; a Tinetti  
130 Mobility Test (TMT; direct quotation during the test procedure) [15] and the self-reporting  
131 questionnaire Fall Efficacy Scale International for balance evaluation[16]; the Functional  
132 Independence Measure (FIM) score[17]; and the Katz - activities of daily living index (Katz  
133 ADL)[18]. The Katz ADL was used because it includes a specific question on difficulties  
134 going to the toilet (go to the toilet, arrange clothes, clean genital area). The NHP test was not  
135 interpreted in terms of laterality in view of the two-handed nature of the tasks to be  
136 performed. The sum of the 2 NHP tests was calculated to assess the correlation with settled  
137 stage (a low score corresponding to the absence of deficit on both the right and left, a high  
138 score reflecting a two-hand deficit or a severe unilateral deficit). Convergent validity was  
139 expected between the mobility stage and the 10MWT, TUG and EDSS scores and between  
140 the settled stage and the Fall Efficacy Scale International, NHP and Katz ADL scores.

141 Divergent validity was expected between the mobility stage and the TMT score and between  
142 the settled stage and TMT and FIM scores.

### 143 *Participant perception of the TRV*

144 In a second step, PwMS were interviewed about understanding the instructions, acceptability  
145 of the test and relevance of this evaluation. These 3 parameters were assessed with a 3-point  
146 Likert scale. At the end of the instruction statement, the evaluator asked about understanding  
147 (good, moderate, poor). After the test, participants were asked about the acceptability of the  
148 test (good, moderate, poor) and its relevance in the context of MS and urinary disorders  
149 (good, moderate, poor).

### 150 *Statistical analysis*

151 Statistical analyses were performed with R for Windows (Rx64 3.4.2, R Foundation for  
152 Statistical Computing, Vienna, Austria). Descriptive data are presented as mean (SD) for  
153 continuous data and median [Q1–Q3] for ordinal data and data not normally distributed. The  
154 effect of the EDSS score on results of the TRV was measured with one-way ANOVA, by  
155 dividing patients into 3 classes (EDSS score < 4, 4–5.5, ≥ 6). Inter-rater and test–retest  
156 reliability was assessed with the intraclass correlation coefficient (ICC) for quantitative  
157 variables (absolute agreement). ICC values 0 to 0.5 were considered weak, ≥ 0.5 to 0.75  
158 moderate, ≥ 0.75 to 0.9 good, and ≥ 0.9 excellent [19]. Absolute reliability was expressed as  
159 the standard error of measurement (SEM) and was calculated as  $SD \times \sqrt{(1-ICC)}$ , where SD is  
160 the standard deviation of the calculation using all test scores from both the first and second  
161 sessions. The SEM was used to calculate the smallest real difference (SRD95%), using the  
162 equation  $SEM \times \sqrt{2} \times 1.96$ . The SRD is an estimation of the smallest real difference required  
163 to be 95% confident that an observed change in an individual score reflects a real change in



164 the underlying parameter. The SEM and SRD are presented as percentages of their respective  
165 means (SEM% and SRD%). The Bland-Altman plot provided visual interpretation, with the  
166 difference between the test and retest plotted against the mean of the 2 test sessions for each  
167 participant. For ordinal variables (difficulty assessed by the Likert scale), inter-rater reliability  
168 was assessed by percentage agreement, and test–retest reliability was assessed by the  
169 weighted kappa coefficient ( $\kappa$ ). Convergent validity with the complementary tests was  
170 assessed by the Spearman correlation coefficient.  $P < 0.05$  was considered statistically  
171 significant.

172

## 173 **Results**

### 174 *Patient characteristics*

175 We included 71 patients, with mean (SD) age 54.4 (11.7) years. The demographic  
176 characteristics of participants are in Table 1. The number of missing data in patient  
177 characteristics was less than 1%. Most patients (72%) performed the TRV without a walking  
178 device, 18% used a cane, and 10% used 2 canes or a walker. Risk of falls was considered high  
179 to very high according to the TMT ( $<24/28$ ) in 69% of participants, including 59% who  
180 performed the test without a walking aid. Concerning urinary leakage, 45% reported urinary  
181 incontinence at home and 53% during outdoor outings. All patients performed the entire  
182 procedure, so no data were missing on the test results.

183

### 184 *TRV results*

185 The mean (SD) time for the TRV mobility stage was 10.76 (6.07) sec and 19.8 (9.01) sec for  
186 the settled stage. The mean TRV scores for the mobility stage ( $p < 0.0001$ ) and difficulty for  
187 each stage differed by the EDSS score ( $p < 0.0001$  for mobility stage,  $p=0.02$  for settled stage)  
188 (Table 2).

189

190 *Inter-rater reliability*

191 Inter-rater reliability was excellent for the TRV mobility stage (ICC = 0.97), settled stage  
192 (ICC = 0.99) and total test (ICC = 0.99). Concerning difficulty assessed by the Likert scale,  
193 the inter-rater reliability was excellent for each stage (percentage of agreement at 94% and  
194 95% respectively).

195

196 *Test–retest reliability*

197 The need to void was absent or low for most participants for both tests (mean [SD] 1.8 [2.3]  
198 for the first try, 1.4 [2.2] for the second try). Eleven patients voided at the end of the first test  
199 and only 4 of them had a need to void  $\geq 5/10$  during the first test. The mean need to void did  
200 not differ between the 2 tries ( $p = 0.11$ ). Test–retest reliability was good for the mobility stage  
201 (ICC = 0.88) and total test (ICC = 0.81) and moderate for the settled stage (ICC = 0.65)  
202 (Table 3). The settled stage showed an improvement in time for 76% of patients in the second  
203 TRV try, whereas 76% of patients showed a variation of less than 1 sec over the mobility  
204 stage. All results are reported in Table 3, and Bland and Altman plots are in Figure 2.  
205 Concerning difficulty assessed by the Likert scale, the  $\kappa$  coefficient was 0.75 for the mobility  
206 stage and 0.88 for the settled stage.

207

208 *Convergent validity*

209 Scores for the 10MWT, TUG test, EDSS and TMT were correlated with the TRV mobility  
210 stage scores. Scores for the EDSS, TMT, Fall Efficacy Scale International, NHP test, FIM,  
211 and Katz ADL were correlated with settled stage scores (Table 4).

212

### 213 *Participant perception*

214 In all, 39 participants were asked about their perception of the new TRV tool. Understanding  
215 was good for most (97%) and moderate for 3%. All participants found the test acceptable  
216 (good acceptability 95%, moderate 5%). Concerning the relevance of the test, most rated it as  
217 good (90%); 7% considered the interest moderate and 3% poor.

218

### 219 **Discussion**

220 Urgency urinary incontinence is one of the major disabling urinary symptoms in PwMS. The  
221 warning time only partially reflects the possibility of continence. Here we created a specific  
222 test for PwMS to assess the global time required to be ready to perform micturition. The TRV  
223 was validated with 71 PwMS. Its inter-rater reliability was excellent for each stage and its  
224 test–retest reliability was good for the mobility stage and total test and moderate for the  
225 settled stage. The mobility stage is well correlated with walk assessment and disability, and  
226 the settled stage is correlated with balance and prehension assessment. Comprehension,  
227 acceptance and relevance were rated good by most participants.

228 The importance of the delay between the decision to urinate (which may follow an urgent  
229 need) and the realization of micturition depends on the occurrence of incontinence. Usually,  
230 in routine practice, a patient is asked how long he/she can delay micturition as soon as the  
231 first desire to void occurs, which defines the warning time[8]. This time reflects the  
232 possibilities of voluntary or reflex detrusor inhibition by the central nervous system control or  
233 by active contraction of the perineal muscles in the context of bladder inhibitor reflex with  
234 transient inhibition of the micturition reflex. This warning time can be improved with various  
235 treatments playing a role on the afferent pathways and/or motor efferent pathways including  
236 detrusor contraction[20,21]. Thus, anticholinergics drugs, beta3-adrenoceptor agonists,

237 botulinum toxin, tibial nerve stimulation, and sacral neuromodulation can be used to avoid  
238 urgency urinary incontinence and so improve quality of life of these patients.

239 However, this warning time does not exactly reflect the real delay needed to achieve  
240 micturition after perception of the desire to void because this time does not take in account  
241 global motor performances (sensory and motor disabilities, walking speed, difficulties in  
242 undressing and sitting in a right position, etc.). This complementary time needed to achieve  
243 micturition without incontinence is sometimes more important than the classical warning time  
244 and, obviously, not accessible to a treatment purely dedicated to overactive bladder and thus  
245 requires specific measures.

246 The TRV is the first validated tool for a quantitative assessment of the time required to go to  
247 the toilet to achieve micturition and a qualitative one on the difficulty of carrying out the  
248 different steps. It allows for evaluating the person's undressing, walking speed, and  
249 installation on the toilet, which does not exist in the available independence scales. We found  
250 excellent inter-rater reliability and good to moderate test–retest reliability, probably due to a  
251 learning effect on the second step.

252 Good correlations between the first TRV step, mobility, and the 10MWT or TUG results were  
253 expected because only a few functions are assessed during the mobility step (stand up, walk a  
254 few meters). Correlations were lower during the settled step because several functions are  
255 evaluated, and no combined test with balance, dexterity and independence exists. These lower  
256 correlations reflect the lack of assessments available for these activities of daily living and the  
257 interest of the TRV.

258 The strength of this tool is the possibility of having an objective measure of the time to go to  
259 the toilet and to be ready to achieve micturition. In PwMS, the correlation between subjective  
260 and objective measures of everyday life activities is not always good[22]. The only objective  
261 measure that could be used is the Assessment of Motor and Process Skills, but the choice of

262 the 2 daily tasks evaluated depends on the patient's priorities, requires specific training of the  
263 examiners and takes from 30 to 60 min[23]. In contrast, the TRV allows for a simple  
264 evaluation, without expensive equipment, with a short completion time. Another interest of  
265 the TRV is being able to evaluate patients in the situations most at risk of falling: transfer by  
266 standing up from a chair and sitting on the toilet if necessary, walking, and standing in a static  
267 position[24]. In PwMS, falls frequently occur inside the home[25], and when PwMS need to  
268 void, a distractive factor (the need to urinate) is potentially added to pre-existing difficulties.  
269 A link between urinary incontinence and risk of falling has been shown[26], and thus an  
270 objective evaluation of all the parameters involved is relevant.

271 The TRV allows for nuancing the need, or the failure, of anticholinergics prescribed for  
272 overactive bladder. To improve the needed time to achieve micturition and thus give time for  
273 the individual to be continent, it is sometimes not useful to choose another anticholinergic or  
274 escalate the different therapeutic strategies (anticholinergics, botulinum toxin, sacral  
275 neuromodulation) but simply to give advice for a better walking device (cane), propose  
276 adapted clothes to be quickly ready for the micturition, and prescribe physiotherapy to  
277 enhance motor and sensory possibilities. Thus, it seems important to consider the global time  
278 of the TRV but also to compare the 2 stages (mobility and settled) in order to better prescribe  
279 and adapt the specific treatments. In our study, the median EDSS score was 6, corresponding  
280 to the target population in which urinary disorders are frequent and for which the question of  
281 difficulties in accessing the toilet is relevant.

282 Some limitations of the study exist. First, the test was not performed during an urgent need to  
283 void, which could probably modify the results a little (distractibility, precipitation during the  
284 second step, etc.) but could be easier to use in everyday practice without waiting for an urgent  
285 need to void. Second, where the test is performed does not necessarily correspond to the  
286 person's home and therefore the exact conditions of daily life. Nor is it representative of the

287 outside environment, where distances are often greater and where other factors may be  
288 involved (searching for toilets, outdoor temperature, psycho-behavioral factors, etc.). The  
289 clothing worn was not standardized. The objective of the TRV is to evaluate patients with  
290 their most usual clothing and possibly advise them on ways to reduce the time required to  
291 undress or for toilet installation. If the TRV is performed during follow-up, it will be essential  
292 to take into account the clothes worn on the day of each test, which are systematically noted  
293 in the evaluation.

294 Furthermore, to assess internal consistency, some tests are validated more often in older  
295 adults than in MS, but this is the case for most balance evaluations. The test–retest reliability  
296 was moderate for the settled stage, probably due to a learning effect (76% of participants  
297 improved their time at the second try), but the primary aim is to allow for a quantitative  
298 assessment and not necessarily to compare the performance regularly. A non-timed test to  
299 teach the instructions may have improved reproducibility, as is done for the TUG test. The  
300 standard error measurement (SEM%) was above the values accepted as ensuring good  
301 reliability. However, significant variability in gait tests of 12% to 38% has been shown in  
302 several studies of individuals with MS[27,28] and reliability of other functional tests is  
303 usually good to moderate[29]. Finally, the TRV does not take into account the cognitive  
304 aspect of continence. An assessment of executive function in case of urgency incontinence  
305 could be pertinent, because the ability to anticipate and plan urination reduces the risk of  
306 incontinence. However, these precautionary voids require the physiological possibility of  
307 triggering voiding without an urgent need to void, which can be affected by detrusor-sphincter  
308 dyssynergia in PwMS.

309

310 *Perspectives*

311 In evaluating neurological patients with LUTSs, the validation of this test in other populations  
312 would be relevant. For example, in Parkinson disease, overactive bladder is frequent, and the  
313 use of anticholinergic drugs is problematic because of frequent cognitive disorders and  
314 constipation[30]. Difficulties in reaching the toilets related to walking disorders, freezing,  
315 akinesia and risk of falls probably affect continence in these patients. A TRV appropriate for  
316 patients in wheelchairs could be of interest, but in PwMS, urinary disorders are often  
317 associated with risk for upper urinary tract complications with high EDSS score, and the  
318 treatment and care issues are different. To adapt the treatment, it will be necessary to evaluate  
319 in a large cohort the role of the “warning time/TRV” ratio on indoor and outdoor continence.  
320 Individuals may be classified according to this ratio and thus therapeutics modulated  
321 according to the different categories. The TRV, combined with an assessment of LUTS  
322 (specific questionnaire, clinical evaluation, urodynamics), allows for an overview of the  
323 factors related to urinary continence and offering comprehensive management, not just  
324 focusing on the overactive bladder symptom. For the risk of falls, a multimodal and  
325 personalized management has already shown a benefit in aged patients[31] and is emerging in  
326 PwMS[32]. The identification of difficulties for continence with TRV may allow for  
327 proposing a personalized and multifactorial intervention. Thus, management may aim to  
328 improve the time needed to be ready to void, by treating harmful spasticity or suggesting a  
329 walking aid, a grab bar in the toilet for stability, or clothing adapted to the disability to  
330 facilitate undressing.

331

### 332 *Conclusion*

333 The Time to be Ready to Void (TRV) is a new tool, validated in MS, to help the practitioner  
334 measure the global time required to reach the toilet for people with overactive bladder. Inter-  
335 rater reliability was excellent and test–retest reliability good, so the test can be used in

336 everyday practice. The TRV test seems to be useful in clinical practice for people with  
337 overactive bladder because it takes in account all the time needed to accomplish micturition  
338 (time to go to the bathroom, undress, installation on the toilet) and not just the classical  
339 warning time that only assesses the importance of urgency. The contribution of TRV to the  
340 overall management of patients will be evaluated in future studies.

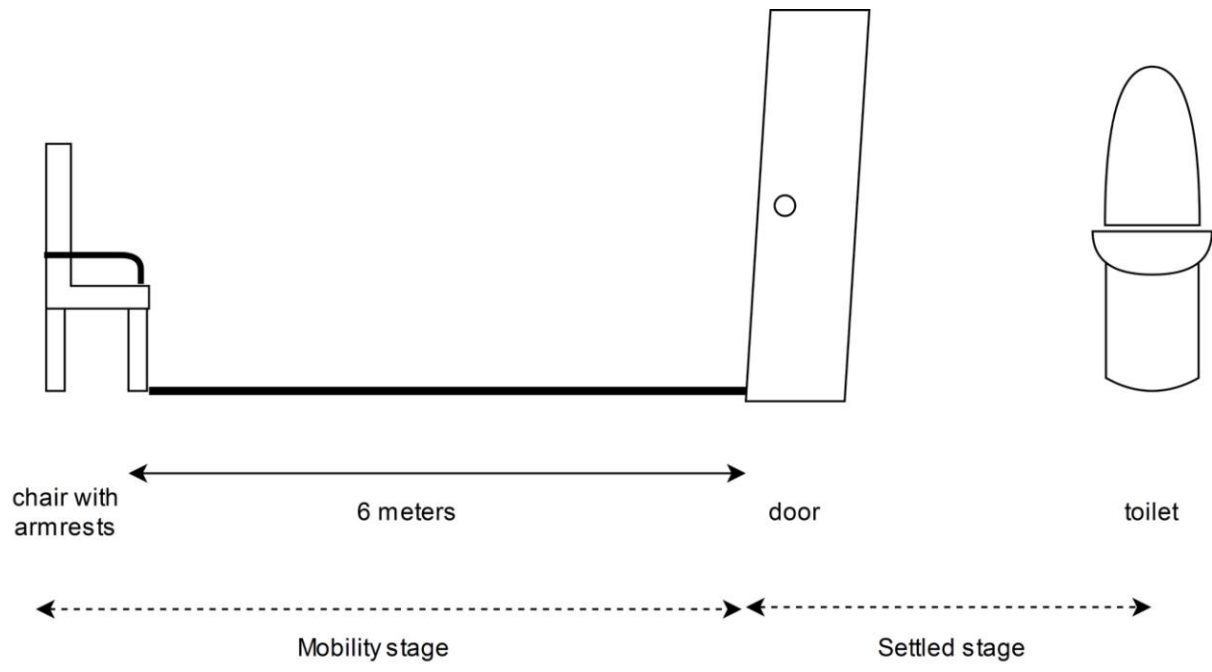
341

342



343 **Legends**

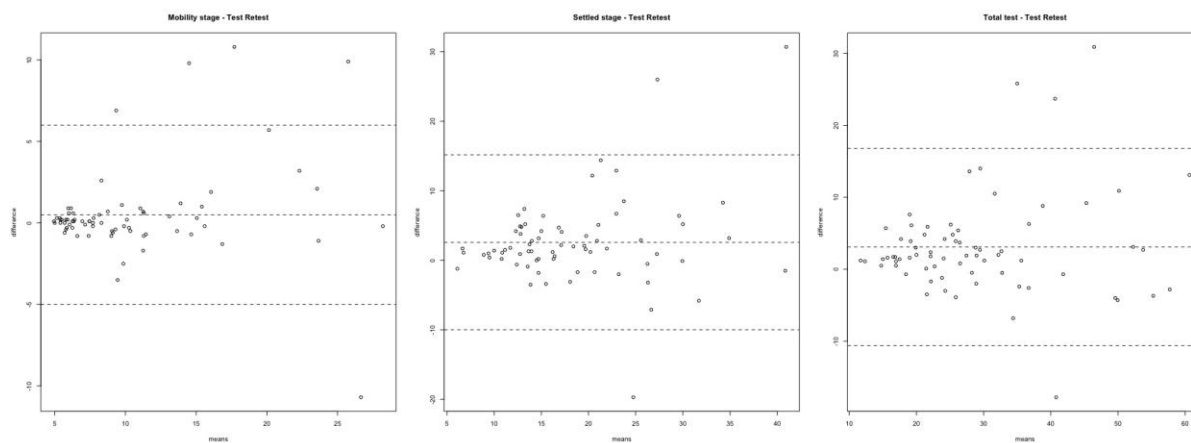
344 Figure 1. Illustration of the Time to be Ready to Void (TRV).



345

346

347 Figure 2: Bland and Altman plots showing the differences between measures from the 2 test  
348 sessions against the mean of the 2 test sessions for each participant for (A) the mobility stage,  
349 (B) settled stage, and (C) total TRV test. The line in the center of each graph represents the  
350 mean of the differences. The other 2 dashed lines indicate 95% limits of agreement (mean of  
351 the difference  $\pm 1.96$  SD of the difference between test–retest measurements).



352

353

354 **Table 1.** Initial characteristics of participants with multiple sclerosis.

355

Age, years, mean (SD)	54.4 (8.6)
Female	58 (82%)
BMI, mean (SD)	25.5 (3.5)
EDSS, median [Q1-Q3]	6 [5-6]
FIM score, mean (SD)	100.5 (11.5)
TMT, median [Q1-Q3]	20 [15-25]
Detrusor overactivity during the previous urodynamics	21 (30)
USP score, mean (SD)	361
USP stress score (/9)	1.2 (2.4)
USP OAB score (/21)	6.3 (4.7)
USP low stream score (/9)	5.8 (3.5)
Warning time, min	
≤ 5	30 (42%)
6-15	24 (34%)
> 15	17 (24%)
Micturition status	
Spontaneous void	32 (45%)
CISC	15 (21%)
Mixed	24 (34%)
Urinary incontinence	
Indoor	32 (45%)
Outdoor	38 (53%)
Clothes	
Pants/tights	68 (96%)
Skirt	5 (7%)
Belt	30 (42%)
Button	49 (69%)
Zipper	42 (59%)
Diaper	14 (20%)
Walking device during TRV	
Cane	13 (18%)
2 canes or walker	7 (10%)

363 BMI, body mass index; EDSS, Expanded Disability Status Scale; FIM, Functional Independence

364 Measure; TMT, Tinetti Mobility Test; USP, Urinary Symptom Profile; OAB, overactive bladder;

365 CISC, Clean Intermittent Self Catheterization; TRV, Time to be Ready to Void

366

367 **Table 2.** Variation in TRV test score by EDSS score.

368

EDSS score	Mobility stage				Settled stage				Total test	
	Mean (SD)	P value	Difficulty	P value*	Mean (SD)	P value	Difficulty	P value*	Mean (SD)	P value
< 4	5.81 (0.67)	<0.0001	2.75 (0.71)	< 0.0001	17.02 (7.58)	0.22	2.75 (0.71)	0.02	22.84 (7.98)	0.003
4-5.5	7.40 (2.04)		2.35 (0.81)		18.06 (10.12)		2.50 (0.76)		25.46 (10.13)	
≥ 6	13.87 (6.80)		1.53 (0.74)		21.86 (9.16)		1.94 (0.89)		35.73 (13.95)	

369

370

371 TRV, Time to be ready to Void; EDSS, Expanded Disability Status Scale; Difficulty, difficulty to  
 372 realize the stage assessed by a 4-point Likert scale: 0, impossible or need human help, and 3, no  
 373 difficulty

374 \* difference in difficulty

375

376 **Table 3.** Test–retest reliability of the TRV test.

377

	ICC [95% CI]	SEM (SEM%)	SRD95 (SRD95%)
Mobility stage	0.88 [0.79-0.95]	2.04 (19)	5.65 (54)
Settled stage	0.67 [0.50-0.84]	4.93 (27)	13.66 (74)
Total TRV	0.81 [0.69-0.92]	5.41 (19)	15.0 (52)

378 ICC, intraclass correlation coefficient; 95% CI, 95% confidence interval; SEM, standard error of  
 379 measurement; SRD95: 95% certainty representing the smallest change to be detected beyond the  
 380 measurement error; TRV, Time to be Ready to Void

381

382

383

384

385

386 **Table 4.** Internal consistency of the TRV.

387

	Mobility stage		Settled stage	
	$\rho$	P value	$\rho$	P value
10MWT	0.88	<0.0001	-	-
TUG	0.89	<0.0001	-	-
EDSS	0.68	<0.0001	0.34	0.006
TMT	-0.67	<0.0001	-0.48	<0.0001
FES-I	-	-	0.17	0.14
NHP right	-	-	0.31	0.007
NHP left	-	-	0.32	0.007
NHP (right + left)	-	-	0.35	0.003
FIM score	-	-	-0.36	0.002
Katz-ADL	-	-	0.24	0.044

388  $\rho$ , Spearman's correlation coefficient; 10MWT, 10-meter walk test; TUG, Timed Up and Go test;

389 EDSS, Expanded Disability Status Scale; TMT, Tinetti Mobility Test; FES-I, Fall Efficacy Scale

390 International; NHP, Nine Hold Peg Test; FIM, Functional Independence Measure; Katz-ADL, Katz –

391 activities of daily living index;

392

393

394

395

396

397 **References**

- 398 [1] de Sèze M, Ruffion A, Denys P, Joseph P-A, Perrouin-Verbe B, GENULF. The  
399 neurogenic bladder in multiple sclerosis: review of the literature and proposal of management  
400 guidelines. *Mult Scler Houndmills Basingstoke Engl* 2007;13:915–28.  
401 <https://doi.org/10.1177/1352458506075651>.
- 402 [2] Giannantoni A, Scivoletto G, Di Stasi SM, Grasso MG, Vespasiani G, Castellano V.  
403 Urological dysfunctions and upper urinary tract involvement in multiple sclerosis patients.  
404 *Neurourol Urodyn* 1998;17:89–98.
- 405 [3] Onal B, Siva A, Buldu I, Demirkesen O, Cetinel B. Voiding dysfunction due to  
406 multiple sclerosis: a large scale retrospective analysis. *Int Braz J Urol Off J Braz Soc Urol*  
407 2009;35:326–33. <https://doi.org/10.1590/s1677-55382009000300009>.
- 408 [4] Krhut J, Hradílek P, Zapletalová O. Analysis of the upper urinary tract function in  
409 multiple sclerosis patients. *Acta Neurol Scand* 2008;118:115–9.  
410 <https://doi.org/10.1111/j.1600-0404.2008.00992.x>.
- 411 [5] Castel-Lacanal E, Gamé X, Clanet M, Gasq D, De Boissezon X, Guillotreau J, et al.  
412 Urinary complications and risk factors in symptomatic multiple sclerosis patients. Study of a  
413 cohort of 328 patients. *Neurourol Urodyn* 2015;34:32–6. <https://doi.org/10.1002/nau.22495>.
- 414 [6] Shakir NA, Satyanarayan A, Eastman J, Greenberg BM, Lemack GE. Assessment of  
415 Renal Deterioration and Associated Risk Factors in Patients With Multiple Sclerosis. *Urology*  
416 2019;123:76–80. <https://doi.org/10.1016/j.urology.2018.09.014>.
- 417 [7] Kessler TM, Bachmann LM, Minder C, Löhner D, Umbehr M, Schünemann HJ, et al.  
418 Adverse event assessment of antimuscarinics for treating overactive bladder: a network meta-  
419 analytic approach. *PloS One* 2011;6:e16718. <https://doi.org/10.1371/journal.pone.0016718>.
- 420 [8] Chalifoux P. Urinary continence/incontinence. Recognizing warning time: a critical  
421 step toward continence. *Geriatr Nurs N Y N* 1980;1:254–5. [https://doi.org/10.1016/s0197-4572\(80\)80041-3](https://doi.org/10.1016/s0197-4572(80)80041-3).
- 423 [9] Haab F, Richard F, Amarenco G, Coloby P, Arnould B, Benmedjahed K, et al.  
424 Comprehensive evaluation of bladder and urethral dysfunction symptoms: development and  
425 psychometric validation of the Urinary Symptom Profile (USP) questionnaire. *Urology*  
426 2008;71:646–56. <https://doi.org/10.1016/j.urology.2007.11.100>.
- 427 [10] Ottenbacher KJ, Hsu Y, Granger CV, Fiedler RC. The reliability of the functional  
428 independence measure: a quantitative review. *Arch Phys Med Rehabil* 1996;77:1226–32.
- 429 [11] Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability  
430 status scale (EDSS). *Neurology* 1983;33:1444–52.
- 431 [12] Paltamaa J, West H, Sarasoja T, Wikström J, Mälkiä E. Reliability of physical  
432 functioning measures in ambulatory subjects with MS. *Physiother Res Int J Res Clin Phys*

433 Ther 2005;10:93–109.

434 [13] Valet M, Lejeune T, Devis M, van Pesch V, El Sankari S, Stoquart G. Timed up-and-  
435 go and 2-minute walk test in patients with multiple sclerosis with mild disability: reliability,  
436 responsiveness and link with perceived fatigue. *Eur J Phys Rehabil Med* 2018.  
437 <https://doi.org/10.23736/S1973-9087.18.05366-2>.

438 [14] Erasmus LP, Sarno S, Albrecht H, Schwecht M, Pöllmann W, König N. Measurement  
439 of ataxic symptoms with a graphic tablet: standard values in controls and validity in Multiple  
440 Sclerosis patients. *J Neurosci Methods* 2001;108:25–37.

441 [15] Faber MJ, Bosscher RJ, van Wieringen PCW. Clinimetric properties of the  
442 performance-oriented mobility assessment. *Phys Ther* 2006;86:944–54.

443 [16] van Vliet R, Hoang P, Lord S, Gandevia S, Delbaere K. Falls efficacy scale-  
444 international: a cross-sectional validation in people with multiple sclerosis. *Arch Phys Med  
445 Rehabil* 2013;94:883–9. <https://doi.org/10.1016/j.apmr.2012.10.034>.

446 [17] van der Putten JJ, Hobart JC, Freeman JA, Thompson AJ. Measuring change in  
447 disability after inpatient rehabilitation: comparison of the responsiveness of the Barthel index  
448 and the Functional Independence Measure. *J Neurol Neurosurg Psychiatry* 1999;66:480–4.  
449 <https://doi.org/10.1136/jnnp.66.4.480>.

450 [18] Einarsson U, Gottberg K, Fredrikson S, von Koch L, Holmqvist LW. Activities of  
451 daily living and social activities in people with multiple sclerosis in Stockholm County. *Clin  
452 Rehabil* 2006;20:543–51. <https://doi.org/10.1191/0269215506cr953oa>.

453 [19] Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation  
454 Coefficients for Reliability Research. *J Chiropr Med* 2016;15:155–63.  
455 <https://doi.org/10.1016/j.jcm.2016.02.012>.

456 [20] Wang AC, Chen M-C, Kuo W-Y, Lin Y-H, Wang Y-C, Lo T-S. Urgency-free time  
457 interval as primary endpoint for evaluating the outcome of a randomized OAB treatment. *Int  
458 Urogynecol J Pelvic Floor Dysfunct* 2009;20:819–25. <https://doi.org/10.1007/s00192-009-0860-7>.

460 [21] Cardozo L, Dixon A. Increased warning time with darifenacin: a new concept in the  
461 management of urinary urgency. *J Urol* 2005;173:1214–8.  
462 <https://doi.org/10.1097/01.ju.0000155798.78911.57>.

463 [22] Goverover Y, Kalmar J, Gaudino-Goering E, Shawaryn M, Moore NB, Halper J, et al.  
464 The relation between subjective and objective measures of everyday life activities in persons  
465 with multiple sclerosis. *Arch Phys Med Rehabil* 2005;86:2303–8.  
466 <https://doi.org/10.1016/j.apmr.2005.05.016>.

467 [23] Doble SE, Fisk JD, Fisher AG, Ritvo PG, Murray TJ. Functional competence of  
468 community-dwelling persons with multiple sclerosis using the assessment of motor and  
469 process skills. *Arch Phys Med Rehabil* 1994;75:843–51.

- 470 [24] Matsuda PN, Shumway-Cook A, Bamer AM, Johnson SL, Amtmann D, Kraft GH.  
471 Falls in multiple sclerosis. *PM R* 2011;3:624–32; quiz 632.  
472 <https://doi.org/10.1016/j.pmrj.2011.04.015>.
- 473 [25] Gunn H, Creanor S, Haas B, Marsden J, Freeman J. Frequency, characteristics, and  
474 consequences of falls in multiple sclerosis: findings from a cohort study. *Arch Phys Med  
475 Rehabil* 2014;95:538–45. <https://doi.org/10.1016/j.apmr.2013.08.244>.
- 476 [26] Finlayson ML, Peterson EW, Cho CC. Risk factors for falling among people aged 45  
477 to 90 years with multiple sclerosis. *Arch Phys Med Rehabil* 2006;87:1274–9; quiz 1287.  
478 <https://doi.org/10.1016/j.apmr.2006.06.002>.
- 479 [27] Vaney C, Blaurock H, Gattlen B, Meisels C. Assessing mobility in multiple sclerosis  
480 using the Rivermead Mobility Index and gait speed. *Clin Rehabil* 1996;10:216–26.  
481 <https://doi.org/10.1177/026921559601000306>.
- 482 [28] Feys P, Bibby B, Romberg A, Santoyo C, Gebara B, de Noordhout BM, et al. Within-  
483 day variability on short and long walking tests in persons with multiple sclerosis. *J Neurol Sci*  
484 2014;338:183–7. <https://doi.org/10.1016/j.jns.2014.01.001>.
- 485 [29] Lamers I, Kelchtermans S, Baert I, Feys P. Upper limb assessment in multiple  
486 sclerosis: a systematic review of outcome measures and their psychometric properties. *Arch  
487 Phys Med Rehabil* 2014;95:1184–200. <https://doi.org/10.1016/j.apmr.2014.02.023>.
- 488 [30] McDonald C, Winge K, Burn DJ. Lower urinary tract symptoms in Parkinson's  
489 disease: Prevalence, aetiology and management. *Parkinsonism Relat Disord* 2017;35:8–16.  
490 <https://doi.org/10.1016/j.parkreldis.2016.10.024>.
- 491 [31] Hopewell S, Adedire O, Copsey BJ, Boniface GJ, Sherrington C, Clemson L, et al.  
492 Multifactorial and multiple component interventions for preventing falls in older people living  
493 in the community. *Cochrane Database Syst Rev* 2018;7:CD012221.  
494 <https://doi.org/10.1002/14651858.CD012221.pub2>.
- 495 [32] Martini DN, Zeeboer E, Hildebrand A, Fling BW, Hugos CL, Cameron MH.  
496 ADSTEP: Preliminary Investigation of a Multicomponent Walking Aid Program in People  
497 With Multiple Sclerosis. *Arch Phys Med Rehabil* 2018;99:2050–8.  
498 <https://doi.org/10.1016/j.apmr.2018.05.023>.

499

500