Published Ahead of Print on February 12, 2021 as 10.1212/WNL.0000000000011677

Neurology®

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The Official Journal of the American Academy of Neurology

AMERICAN ACADEMY OF NEUROLOGY®

Neurology Publish Ahead of Print
DOI: 10.1212/WNL.0000000000011677

CORRECTION

Evaluation of Multiple Sclerosis Disability Outcome Measures Using Pooled Clinical Trial Data

In the Article "Evaluation of Multiple Sclerosis Disability Outcome Measures Using Pooled Clinical Trial Data" by M. Goldman et al.[1], the text contained some discrepancies within the analyses of the MSOAC data set included in the paper. The authors found that the discrepancies were present because of a coding error that produced inaccurate results in the Kaplan-Meier results. The authors regret the errors. The text below, provided by the authors, describes the corrected material:

From the Authors:

In our publication in *Neurology*,[1] we analyzed a pooled dataset comprising 12,776 clinical trial participants that had been assembled by the Multiple Sclerosis Outcome Assessments Consortium (MSOAC) to evaluate 4 performance tests as proposed components of a multidimensional test battery. We reported measurement properties; construct, convergent, and known group validity; and longitudinal performance of the Timed 25-Foot Walk (T25FW), 9-Hole Peg Test (9HPT), Low Contrast Letter Acuity (LCLA), and Symbol Digit Modalities Test (SDMT) individually and when combined into a multidimensional test battery compared to the Expanded Disability Status Scale (EDSS) and Short-Form-36 Physical Component Summary. The placebo arm data in the MSOAC database were made publicly available to support research by investigators in the MS field. Following publication of our paper, a colleague, using the publicly available placebo data from MSOAC, contacted us after finding seemingly different results than reported in our paper. To better understand the potential discrepancy in results, we returned to our analysis. Subsequently, errors in statistical program (Statistical Analysis System, SAS) coding for some of our analyses were discovered. These errors resulted in incorrect progression rates for the T25FW and 9HPT, as well as the composite measures of progression based on any 1 or any 2 measures, which included T25FW and 9HPT. In addition, while the graph of progression by LCLA was correct, in the text, we incorrectly gave results for LCLA progression (and its kappa coefficient for agreement with EDSS) using a 20% threshold, instead of the 7-point threshold stated. Herein, we report corrected results.

To compare the sensitivity to change of the performance measures with EDSS, time from baseline to 3-month confirmed worsening over 24 months was analyzed (Table 1). We previously reported that the progression rates were lower for T25FW and 9HPT compared to EDSS. In the corrected analyses, the progression rate remained somewhat lower for 9HPT compared to EDSS, while progression rates for T25FW, LCLA, and SDMT were similar to or higher than the EDSS (results for LCLA and SDMT were the same as before, as the programming error affected only T25FW and 9HPT). When the performance tests were combined into a multidimensional outcome measure, the proportion of participants with confirmed worsening on any 1 performance test was substantially greater than the proportion with confirmed worsening on EDSS. When confirmed worsening on 2 performance tests was required, sensitivity to disability progression was similar to that of EDSS. Association of the progression events defined by the performance tests was better correlated with those defined by the EDSS in the corrected analysis, though remained modest (Table 2).

Based on the previously reported analyses, we concluded that the results supported the use of the T25FW, 9HPT, LCLA, and SDMT as study outcome measures, both individually or combined into a multidimensional test battery.[1] These corrected results demonstrate better sensitivity to change for the T25FW and 9HPT than previously reported, and further support our original conclusion.

REFERENCE

[1]Goldman MD, LaRocca N, Rudick R, et al. Evaluation of Multiple Sclerosis Disability Outcome Measures Using Pooled Clinical Trial Data. Neurol 2019;93: e1921-e1931.

Table 1 Sensitivity to change of performance tests and Expand Disability Status Scale

	Kaplan-Meier estimates of the percentage (95% CI) of trial participants with 3-month confirmed disability progression over 24 months		
Performance Test	**Previously Reported**	**Corrected**	**EDSS[e,f]**
T25FW[a]	6.5	23.8 (22.8 – 24.8)	20.2 (19.2 – 21.1)
9HPT[b]	2.9	8.6 (8.0 – 9.3)	20.2 (19.2 – 21.1)
LCLA[c]	13.1	13.8 (12.7 – 14.9)	16.1 (15.1 – 17.2)
SDMT[d]	15.0[g]	15.0[g] (13.4 – 16.7)	14.5 (12.9 – 16.2)
Worsening on ≥1 performance test	Not previously reported	41.5 (38.9 – 44.1)	11.5 (9.9 – 13.3)
Worsening on ≥2 performance tests	Not previously reported	12.9 (11.2 – 14.8)	11.5 (9.9 – 13.3)

Abbreviations: 9HPT = 9-Hole Peg Test; CI = confidence interval; EDSS = Expanded Disability Status Scale; LCLA = Low-Contrast Letter Acuity; SDMT = Symbol Digit Modalities Test; T25FW = Timed 25-Foot Walk

[a] 20% threshold

[b] 20% threshold

[c] 7-point threshold: the previous paper had erroneously reported results for a 20% threshold

[d] 4-point threshold

[e] baseline score 0: 1.5-point increase, baseline score 1.0-5.5: 1-point increase, baseline score ≥6.0: 0.5-point increase

[f] The study populations available for each comparison differed, leading to differing proportions with 3-month confirmed worsening on EDSS.

[g] The previously reported result for 3-month confirmed worsening over 18 months was correct. For consistency, we report the rate over 24 months here.

Table 2 Associations of 3-month confirmed progression events defined by performance tests and by Expanded Disability Status Scale

	Cohen's κ (95% CI)	
Comparison	**Previously Reported**	**Corrected**
T25FW[a] vs EDSS[e]	0.02 (-0.00 to 0.03)	0.37 (0.35 to 0.39)
9HPT[b] vs EDSS[e]	0.00 (-0.01 to 0.01)	0.25 (0.22 to 0.27)
LCLA[c] vs EDSS[e]	0.11 (0.08 to 0.14)[f]	0.10 (0.07 to 0.13)
SDMT[d] vs EDSS[e]	-0.02 (-0.06 to 0.02)	-0.02 (-0.06 to 0.02)

Abbreviations: 9HPT = 9-Hole Peg Test; CI = confidence interval; EDSS = Expanded Disability Status Scale; LCLA = Low-Contrast Letter Acuity; SDMT = Symbol Digit Modalities Test; T25FW = Timed 25-Foot Walk

[a] 20% threshold
[b] 20% threshold
[c] 7-point threshold (results had previously been given for a 20% threshold)
[d] 4-point threshold
[e] baseline score 0: 1.5-point increase, baseline score 1.0-5.5: 1-point increase, baseline score ≥6.0: 0.5-point increase
[f] The previously reported association between progression events defined by 20% worsening on LCLA and EDSS was correct. For consistency, the association between progression events defined by 7-point worsening on LCLA and EDSS is reported here.