

# Multiple Sclerosis Management and EDSS:

## A Great Start, But A Reason For Change Was Never So Apparent and Needed

Mark Gudesblatt<sup>1</sup>, Jared Srinivasan<sup>1</sup>, Taylor Drost<sup>1</sup>, Barbara Bumstead ANP<sup>1</sup>, Lori Fafard RN<sup>1</sup>, Kaitlyn Jaenicke<sup>1</sup>, Marijean Buhse RN ANP PhD<sup>1,2</sup>, Myassar Zarif MD<sup>1</sup>, Daniel Golan<sup>5,6</sup>, Jeffrey Wilken<sup>4,5</sup>, Cynthia Sullivan<sup>4</sup>, Timothy Fratto<sup>4</sup>, Gavin Giovannoni<sup>7</sup>

1. South Shore Neurologic Associates, Patchogue NY. 2. Dept. of Nursing Stony Brook University, Stony Brook NY. 3. Washington Neuropsychology Research Group, Fairfax, VA. 4. Department of Neurology, Georgetown University, Washington DC 5. Department of Neurology, Carmel Medical Center, Haifa, Israel. 6. Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel 7. Blizard Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London

### Objective

To explore the combined variability of functional performance in people with Multiple Sclerosis (PwMS) within groups of similar disability across important aspects of practical ability whether perceived or objective.

### Background

Since the Expanded Disability Status Scale (EDSS) was pioneered by Dr. John Kurtzke in 1967, it has been incorporated into clinical trial measurements in PwMS. When combined with reported relapse rates and MRI measurements of disease activity, EDSS has been the basis for approval of >15 Disease Modifying Therapies (DMT). Patient determined disease steps (PDDS) is strongly correlated with EDSS. No Evidence of Disease Activity (NEDA) has been proposed as the goal for optimizing DMT selection/change. Defining clinical disability status remains critical for both NEDA and treatment decisions. Use of non-linear scales to measure disability can be problematic if there is great variability of PwMS within homologous EDSS or PDDS defined disability levels. MRC manual muscle testing grading system fails to meet the Rasch model expectations in various disorders despite being the standard metric in neurology worldwide. Functional or practical patient centric ability which underlies visible disease impact reflects the combined features of cognitive function, manual dexterity, ambulation and other factors as well. If the degree of variability of these “practical abilities” exceeds 20%, this scale would no longer be “valid”.

### Methods

Retrospective review of prospective registry of PwMS that were evaluated by objective multidimensional computerized cognitive testing or digital gait analysis, and patient reported outcomes (PRO) for hand/upper extremity function and that also had simultaneous measurements of either PDDS or EDSS

### Hand Function & Tremor/Coordination PRO Overlap Across the PDDS (0-1, 2-4, >4)

Upper Extremity PRO Function	PDDS 0-1	PDDS 2-4	PDDS >4
Hand Function PRO % Variability	100%	71%	73%
Hand Function PRO % Adjacent PDDS Overlap	>50%		>50%
Hand Function PRO % Extreme PDDS Overlap	34%		
Tremor/Coordination PRO % Variability in PDDS	100%	66%	68%
Tremor Coordination PRO % Adjacent Overlap PDDS	>50%		>50%
Tremor Coordination PRO % Extreme PDDS Overlap	32%		

### Results

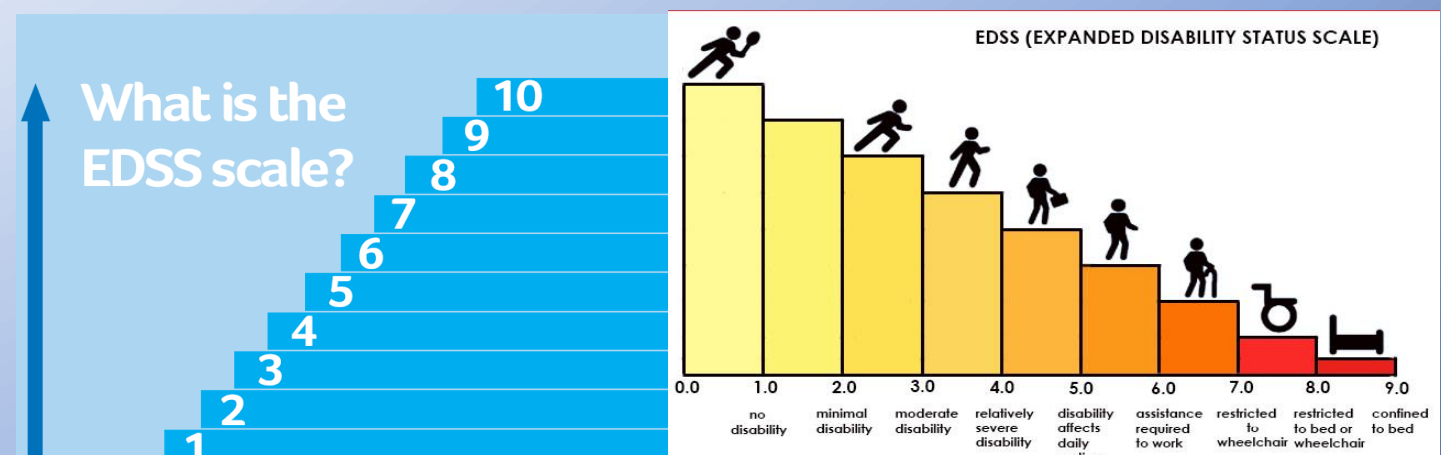
- Cognition:** Cohort 258 PwMS; Gender: 73% female; Age: 46+/-10 years, completed multidomain computerized cognitive testing and EDSS
- Ambulation:** Cohort 254 PwMS; Gender 72% female; age 46+/-10 years, completed digital gait with mean normalized velocity of preferred walking speed.
- Manual Dexterity:** Cohort 783 PwMS; Gender 74% female; Age 49+/-11 years completed NARCOMS PRO for both hand function and tremor.

### Gait Velocity Variability and Overlap Across the EDSS

Mean Gait Velocity Objective Measure	EDSS 0-2.5	EDSS 3-4.5	EDSS 5-6.5	EDSS >7
% Variation Mean Normalized Velocity (MNV)	24%	34%	53%	Not Applicable
Adjacent EDSS Overlap % MNV	29%		25%	
Any EDSS Overlap % MNV	36%			

### Cognitive Domain Scores Overlap Across the EDSS (0-2.5, 3-4.5, 5-6.5, >7)

Cognitive Domain Objective Measure	Adjacent EDSS Group % Overlap	Extreme EDSS % Overlap
Global Cognitive Summary Score	65%	42%
Memory	65%	65%
Executive Function	65%	35%
Attention	60%	38%
Information Processing Speed	58%	43%
Visual Spatial	66%	63%
Verbal Function	70%	66%
Motor Skills	55%	32%
# Cognitive Domains Impaired >1SD (Total Cognitive Impairment)	72%	38%



### Conclusion

While the EDSS greatly advanced the treatment of MS, the degree of variability of disease impact within and across disability groups warrants immediate abandonment of this measure of care. While the McDonald Criteria for the diagnosis of MS has undergone multiple revisions, the scale to define the disability impact from MS has not been revised. Defining and measuring disease impact should be replaced both in clinical trials and routine care with the use of objective patient centric multidimensional quantitative validated examiner independent measures of disease impact to identify critical impact earlier than just relying on the visible impact so as to allow improve treatment selection, monitoring for progression and need for treatment change or other intervention. This approach could enhance the shared decision making process and ultimately reduce accumulative disability and economic burden of ineffectively treated disease. The time spent for routine care visits for information to make effective decisions does not provide sufficient objective information to balance out the lifetime of disability that people affected by MS might have to live with.