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Abstract Title: Measuring fatigue in multiple sclerosis clinical trials: why patient reported outcome measure choice is not immaterial when measuring change

Abstract Category: Clinical aspects of MS and related diseases - 13 - Patient reported outcomes

Preferred Presentation Type: Oral or poster presentation

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Introduction:
In multiple sclerosis (MS), fatigue is ubiquitous, burdensome, and frequently measured in clinical trials. MS studies have used 18 different fatigue patient-reported outcome (PRO) measures.

Objectives/Aims:
We shortlisted 6 of these 18 PRO measures (list at end*) and compared their measurement performance to determine if choice among them is immaterial.

Methods:
All 6 PRO measures were sent simultaneously to 740 people with MS. PRO measure response data were analyzed using Rasch measurement theory (RMT) methods. We examined: first, if each PRO measure was well-functioning enough according to RMT criteria; second, the degree to which PRO measures of the same fatigue component (overall, motor, cognitive) generated statistically equivalent estimates at group and individual person-levels.

Results:
The response rate was 73% (538/740). All 6 fatigue PRO measures functioned well enough to imply their suitability for clinical trials. PRO measures of the same fatigue component: were very highly correlated (error-corrected r=0.85-0.98); had >96% common variance on RMT subtest analyses; generated statistically ***equivalent*** group mean scores (t<1.3). These findings imply all PRO measures of the same fatigue component measured the same variables (albeit not identical), and that PRO measure choice for measuring change in trials is immaterial.
However, PRO measures of the same fatigue component often generated profoundly different individual person-level estimates, with statistical ***non-equivalence*** up to 40% of the time. This indicates any changes detected, and conclusions reached, are unlikely to be equivalent at the individual level. Therefore, PRO measure choice is not immaterial. Further examinations highlighted that the greater the number of items, the greater the difference between individual and group-level interpretations from different PRO measures, due to greater measurement precision.

Conclusion:
Results suggest PRO measure choice should consider both individual and group analyses. And, when selecting PRO measures, clinical trialists consider the item number as well as standard indicators (content validity, psychometric properties). Therefore, even when a group of fatigue PRO measures are high functioning and very highly correlated, the choice of measure for clinical trials is not immaterial.

* Modified Fatigue Impact Scale; NeuroQol Fatigue Scale; PROMIS Fatigue Scale; Neurological Fatigue Index MS; Fatigue Symptoms & Impact Questionnaire - Relapsing MS; Fatigue Scale for Motor & Cognitive Functions.

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Pamela Vo was an employee at Novartis during this work.

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