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Letter to the Editor

The risks of using non-specific outcome measures to capture activities of daily living in myotonic dystrophy type 2

We read with great interest the recently published study by colleagues Montagnese et al. titled "How to capture activities of daily living in myotonic dystrophy type 2?". In this study, the authors analyzed the performance of outcome measures that are specifically designed for other illnesses in a group of myotonic dystrophy type 2 (DM 2) patients [1]. It has been described in the literature how factors such as item weighting and relevance in outcome measures vary significantly between different illnesses. For this reason, we consider that the risks embedded in their conclusions are significant and worth acknowledging.

In this modern scientific era, valid and reliable outcome measures are necessary to accurately monitor the limitations in daily life activities and social participation, the progress of a disease, and its response to treatment. Ordinal scales, which provide a systemic ordering without a true numerical value, are widely used in clinical practice. However, these scales are prone to differential sensitivity, making them inapplicable for parametric statistical testing and inadequate for an accurate interpretation of clinical trial results [2,3]. Additionally, classical test theory ordinal-based metrics may include items that are not relevant to the patient's ability and may achieve a total sum score that incorrectly assumes equal weight and relevance of each item [2,4]. For health-related evaluation measurements, there are modern scientific techniques at our disposal. The Rasch analysis, for example, evaluates the probability of item completion depending on the item difficulty and the patient's ability. This process transforms these scales into linearly weighted "interval" measures and improves the quality of outcome measures and interpretation of the results of clinical trials [4,5].

Based on this concept, the R-PAct and DM1-Activ-c scales were constructed [6,7]. The R-PAct (Rasch-built Pompe-specific activity scale) was validated in a study population of 186 patients with Pompe disease in 2013 [6]. The Rasch-built DM1-Activ-c (Myotonic dystrophy type 1 activity and participation scale) was reconstructed in 2015 using 312 records of genetically confirmed DM 1 patients [7]. A fundamental fact is that myotonic dystrophies type 1 and 2 (DM 1, DM 2) are two clinically, histopathologically and genetically distinct disorders while sharing the same eponym considering their common symptoms of myotonia, muscular weakness, and muscular atrophy. DM 1 has a predominant distal weakness distribution; a congenital, juvenile, and adult form have been described, it has a higher frequency of respiratory failure, more facial weakness, a high predominance of myotonia, complaints of myalgia are rare, and it has a worse general prognosis. In contrast, DM 2 has a lower world-wide frequency, there is a predominantly proximal and axial muscular involvement, onset occurs during adulthood, respiratory involvement is rare, myotonia is less prominent, myalgia has a higher prevalence, and generally, a better prognosis is documented [8,1].

The article under discussion, aimed to evaluate the validity and performance of the aforementioned scales, R-PAct and DM1-Activ-c, among others, in a cohort of genetically confirmed DM 2 patients [1]. R-PAct was included because of the similarity between Pompe and DM 2 regarding muscle weakness distribution. They tested and compared their performance and found during the evaluation of DM1-Activ-c a higher ceiling effect in DM 2 patients in comparison to the DM 1 cohort, a maintained trend of increasing difficulty of the scale, and a moderate difference in the hierarchy of item-difficulty. No DM 2 patient scored low enough to indicate severe limitations and there was no difference observed between men and women. Additionally, there were no significant differences observed in scores over time, corroborating a slower disease progression of DM 2 and at the same time, the need for studies with a longer follow-up for a better assessment of the responsiveness in DM 2. [1]

R-PAct also had a higher ceiling effect (14.7%) that significantly differed from the results found in Late-Onset Pompe Disease patients (0.4%), the trend of increasing difficulty was maintained, and only minor changes were detected in the hierarchy of item difficulty. The low impact of myotonia in both scales was confirmed by its weak correlation coefficient, and with the use of regression analysis, they found that the major predictors of lower scores were higher age, longer disease duration, shorter 6MWT distance, and presence of myalgia. The authors concluded that DM1-Activ-c might perform slightly better than R-PAct in depicting the burden of DM 2 patients in activities of daily living (ADLs) and could be adopted for monitoring disease progression in DM 2 patients until a disease-specific patient-reported outcome measure (PROM) is available [1].

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It must be noted that this conclusion poses a risk of misinterpretation of data since it's not certain that the scales' validity can be extrapolated to another disease with different characteristics and clinical manifestations. Additionally, the use of a disease-specific scale does not guarantee that it will adequately capture the entire severity spectrum of another disorder. The increase of the ceiling effect found when evaluating the performance of DM1-Activ-c (11.6% in DM 2 vs. 7.6% in DM 1) which was attributed by the authors to a milder impairment of ADLs in DM 2, could also be explained by a possible ineffectiveness of the items to capture the most severe presentations of DM 2.

In the Rasch-built overall disability scale for immune-mediated peripheral neuropathies described in 2011 by van Nes et al., Multifocal motor neuropathy (MMN) patients were initially included assuming a pathophysiological overlap but a significantly different behaviour in functional response to tasks was observed in comparison with the cohort of patients diagnosed with Guillain-Barré Syndrome (GBS), Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) and immunoglobulin M monoclonal gammopathy of undetermined significance associated polyneuropathy (MGUSP) [4]. For MMN patients, fine motor upper limb items were considered much more difficult to accomplish than mobility items (e.g., walking, standing, and running). This supports the argument that for different illnesses, item selection and item difficulty are not always comparable. This observation led to the eventual exclusion of MMN patients from the study, but also to the later construction of an MMN-specific scale in 2015 [9].

Therefore, it is of uttermost importance to develop validated disease-specific measurement instruments to arrive to correct conclusions and avoid misinterpretations. It's uncertain that we can safely use one scale validated for one disease to measure limitations in patients with another disorder, as items that are relevant for patients with a proximal myopathy do not necessarily apply to patients suffering from another disease with similar muscle weakness distribution, or to patients with a predominant distal muscle involvement [10]. A substantial cohort of patients could be assembled using available multicenter DM 2 databases in addition to the existing DM 2 data gathered by Montagnese et al. to develop a validated DM2-specific scale that can overcome these limitations. This new scale could initially include the same items that are found in DM1-Activ-c, but a different weighting and relevance of the items are to be expected.

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Tatiana Hamadeh*
David S.H. Bovenkerk
Catharina G. Faber
Department of Neurology,
Maastricht University Medical Center,
P.O. Box 5800, Maastricht, the Netherlands

Ingemar S.J. Merkies
Department of Neurology,
Maastricht University Medical Center,
P.O. Box 5800, Maastricht, the Netherlands
Department of Neurology, Curacao Medical Center, J.H.J. Hamelbergweg z/n, Willemstad, Curaçao

*Corresponding author.
E-mail address: t.hamadeh@maastrichtuniversity.nl
(T. Hamadeh)