Measuring Upper Limb Function (ULF) in MS Clinical Trials: Definition, Conceptualisation, Measurement.

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Background
Pivotal & registrational trials often use PRO measures;

Regulatory authorities require PROs be “well-defined & reliable measures of well defined concepts in specific clinical contexts”.

None of 24 ULF PROs examined conceptualised ULF, clarified measurement concepts & examined concept equivalence in different MS clinical contexts (Close ECTRIMS2019).

Objective
To develop a ULF PRO meeting regulatory requirements as suitable for MS clinical trials of people relapsing, secondary progressive and primary progressive MS (RMS, SPMS, PPMS).

Method
Developed preliminary ULF conceptual framework:
- Literature search for studies conceptualising ULF/impacts;
- MSers concept elicitation (CE) interviews & focus groups;
- Focus groups with clinical experts.

Select and clarify measurement concept of interest
- Consideration of domains in the context of treatment goals;
- Revised analysis in relation to concept of interest
- Examination of saturation across MS clinical context

Test concept and response category options
- Postal survey of test items with response categories;
- Rasch Measurement Theory (RMT) analysis.

Results
No studies have conceptualised ULF (Close ECTRIMS2019).

Preliminary conceptual framework (Fig 1) constructed from CE interviews (Table 1), n=4 MSe & n=2 therapist focus groups;

Concept for measurement selected. Saturation examination supports content consistency in RMS SPMS PPMS;

Preliminary survey of k=101 ULF items in n=392 MSers, satisfied RMT criteria (targeting, item performance, person measurement) for measurement and supported 5 item response categories.

Conclusion
This first study seeking to conceptualise MS’s UL impact, identify & define a concept for measurement, examine the content validity of this concept across different MS clinical contexts.

A preliminary instrument is being field tested in n=800 MSers.

Figure 1: Conceptualisation process

Table 1
Concept elicitation interview sample demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>RMS</th>
<th>SPMS</th>
<th>PPMS</th>
<th>Total</th>
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<tbody>
<tr>
<td>n</td>
<td>26</td>
<td>23</td>
<td>22</td>
<td>71</td>
</tr>
<tr>
<td>Percent female</td>
<td>81%</td>
<td>61%</td>
<td>45%</td>
<td>62%</td>
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<tr>
<td>Age: Mean (SD); range</td>
<td>49.92 (11.22); 23-68</td>
<td>56.74 (7.97); 42-70</td>
<td>58.23 (10.04); 30-75</td>
<td>54.70 (10.44); 23-75</td>
</tr>
<tr>
<td>EDSS: Mean (SD); range</td>
<td>4.9 (2.14); 1-7</td>
<td>6.4 (1.52); 1-8</td>
<td>6.5 (1.10); 3-8</td>
<td>5.9 (1.81); 1-8</td>
</tr>
<tr>
<td>9 Hole-peg test time:</td>
<td>35.99 (31.69)</td>
<td>55.03 (48.62)</td>
<td>66.88 (53.17)</td>
<td>51.73 (49.32)</td>
</tr>
<tr>
<td>Mean (SD); range</td>
<td>21-179.9</td>
<td>22.3-206.5</td>
<td>24.4-175.7</td>
<td>21-206.5</td>
</tr>
</tbody>
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