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

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Background
Pivotal and registrational trials often use patient-reported outcomes (PROs). Regulatory authorities require PROs be 'well-defined and reliable measures of specific concepts in specific clinical contexts' (1). However, a literature search (2) demonstrated that none of the 24 upper limb function (ULF) PROs examined: conceptualised ULF, clarified concepts or examined concept equivalence in different Multiple Sclerosis (MS) clinical contexts (3,4).

Objective
Develop an ULF PRO to meet regulatory requirements for trials of relapsing, secondary and primary progressive MS (RMS, SPMS, PPMS).

Method
Preliminary ULF conceptual framework was developed from literature searches of studies conceptualising ULF / impacts, concept elicitation (CE) interviews and focus groups. The measurement concept of interest (CI) was clarified and saturation examined. Concept and response category options were tested by postal survey (n=392 MSers) applying Rasch Measurement Theory (RMT) analysis. Draft PRO was tested in a subsequent survey (n=833 MSers) with RMT analysis and cognitive debriefing interviews to develop a final UL PRO.

Results
- Preliminary conceptualisation was constructed from: n=71 individual CE interviews (n=26 RMS; n=23 SPMS; n=22 PPMS), and n=5 focus groups with MSers and clinical experts.
- Measurement concept selected. Saturation examination supported content consistency in RMS, SPMS and PPMS. Preliminary survey (n=392 MSers) satisfied RMT criteria for measurement of a clinically and statistically cohesive concept supported 5-item response categories.
- Final survey (n=833 MSers) of k=125 ULF items, 56% response rate (n=465) at day 15. RMT analysis and cognitive debriefing interviews are being used to develop a final UL PRO instrument.

Conclusion
The first study seeking to: conceptualise MS impact on ULF, *de novo*; identify and define a concept for measurement; examine the concept's equivalence across RMS, SPMS, PPMS. The resulting ULF PRO is designed to meet regulatory requirements for developing an instrument for use in MS clinical trials.

References

1. Close et al. Measuring upper limb function in MS: Which existing patient reported outcomes are fit for purpose? ECTRIMS 2019 P815 (Session 2, Thursday 12 Sept).

2. Food and Drug Administration. Guidance for Industry. Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labelling Claims. 2009

3. Terwee et al. COSMIN methodology for evaluating the content validity of patient-reported outcome measures; a Delphi study. *Quality of life research*: 2018; 27(5):1159-70.

4. Food and Drug Administration. Guidance for Industry and FDA Staff: Qualification Process for Drug Development Tools. 2014