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

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## BACKGROUND

Pivotal & registrational trials often use patient-reported outcomes (PROs).

Regulatory authorities require PROs to be 'well-defined & reliable measures of well-defined concepts in specific clinical contexts' (1).

None of 24 ULF PROs we examined: conceptualised ULF, clarified concepts & examined concept equivalence in different MS clinical contexts (2,3,4).

## OBJECTIVE

Develop a ULF PRO meeting regulatory requirements for trials of relapsing, secondary progressive and primary progressive MS (RMS, SPMS, PPMS).

## METHOD

*Stage 1: Develop preliminary ULF conceptual framework*
  Literature search for studies conceptualising ULF / impacts;
  MSers concept elicitation (CE) 1-2-1 interviews & focus groups;
  Clinical expert focus groups.

*Stage 2a: Select and clarify measurement concept of interest*
  Consideration of domains in the context of treatment goals;
  Revised analysis in relation to concept of interest (CI);
  Examine saturation across MS clinical context.

*Stage 2b: Test concept and response category options*
  Postal survey of example items with response categories;
  Rasch Measurement Theory (RMT) analysis.

*Stage 3: Draft and test instrument*
  Postal survey of draft PRO with cognitive debriefing interviews;
  Rasch Measurement Theory (RMT) analysis.

## RESULTS

No studies conceptualising ULF were identified (2).

Preliminary conceptualisation (Fig 1) constructed from: n=71, 1-2-1, CE interviews (Table 1); n=5 focus groups with MSers & therapists;

Concept for measurement selected. Saturation examination supports content consistency in RMS, SPMS and PPMS;
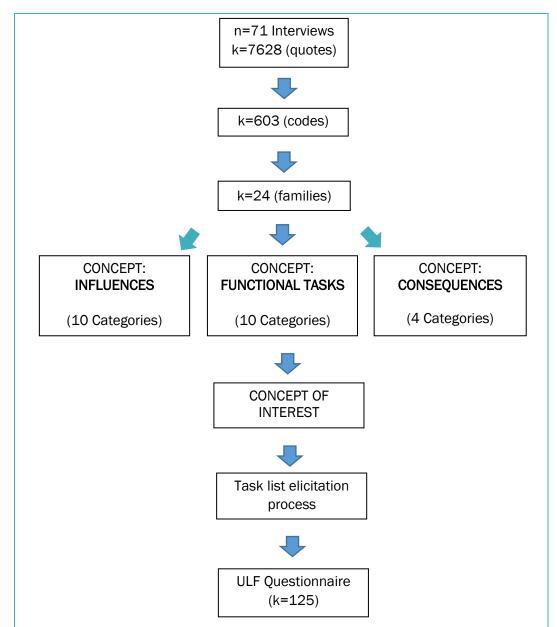
Preliminary survey of k=101 ULF items in n=392 MSers, satisfied RMT criteria (targeting, item performance, person measurement) for measurement of a clinically and statistically cohesive concept supported 5 item response categories.

A preliminary ULF PRO is being field tested in n=833 MSers, with return rate of n=465 (56%) by day 15. RMT analysis will be applied, followed by cognitive debriefing interviews to develop a final UL PRO instrument.

## CONCLUSION

This is the first study seeking to: conceptualise MS impact on ULF, *de novo*; identify & 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.

## Table 1: Concept elicitation interview sample demographics

| Variable | RMS | SPMS | PPMS | Total |
|---|---|---|---|---|
| n | 26 | 23 | 22 | 71 |
| Percent female | 81% | 61% | 45% | 63% |
| *Age:* Mean (SD); | 49.9 (11.2) | 56.7 (8) | 58.2 (10) | 54.7 (10.4) |
| Range: | 23-68 | 42-70 | 30-75 | 23-75 |
| EDSS: Mean (SD); | 4.9 (2.1) | 6.4 (1.5) | 6.5 (1.1) | 5.9 (1.8) |
| Range: | 1-7 | 1-8 | 3-8 | 1-8 |
| 9-HPT time: Mean (SD): | 36 (31.7) | 55 (48.6) | 66.9 (49.32) | 51.7 (44.7) |
| Range: | 21-180 | 22.3-206.5 | 24.4-175.7 | 21-206.5 |

## Figure 1: Code evolution from quote to concept



Figure 1: Code evolution from quote to concept

## References

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