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.

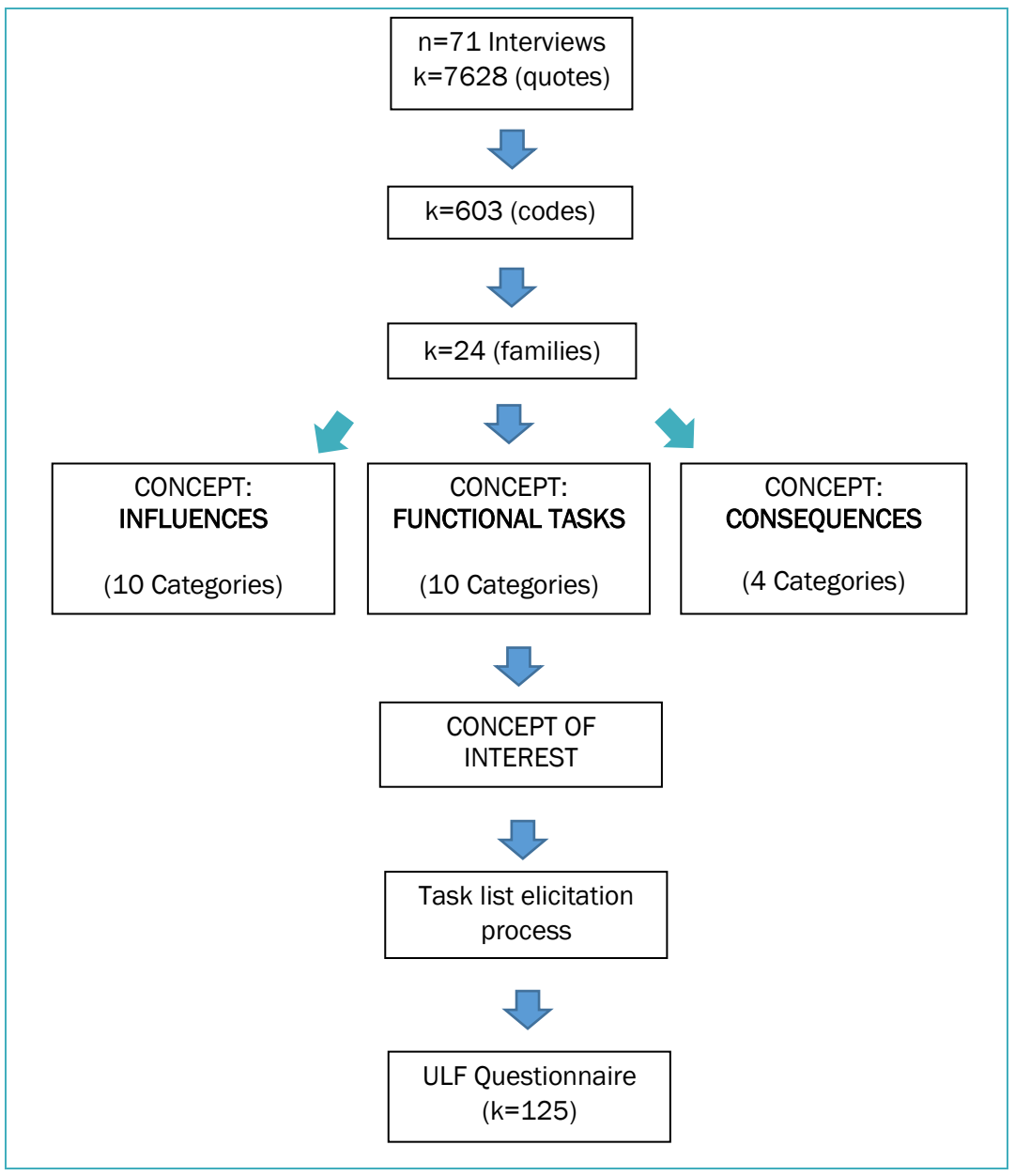
CONCLUSION

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



References

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