MSWS-32: A new patient-reported outcome (PRO) walking measure for Multiple Sclerosis (MS) clinical trials

James Close*, Tanya King*, Laurie Burke^, Jeremy Hobart*" on behalf of Plymouth's MS team
*Plymouth University Faculty of Medicine and Dentistry, "University Hospitals Plymouth; UK.
^LORA group, Royal Oak, MD, USA.

Introduction

• Advances in MS clinical trials, regulatory requirements and measurement science indicate better rating scales are needed.

• A key emphasis is measurement clarity: PROs must prove they measure clearly defined concepts in specific clinical contexts.

• "Walking" problems common & important in MS. Interpretable "walking" measurement requires concept of interest (COI) be clarified.

• MS has 3 main clinical trial contexts of use (COU) relapsing, secondary & primary progressive MS (RMS; SPMS; PPMS).

Objectives

• Develop a Walking PRO satisfying scientific & regulatory requirements for MS clinical trials in RMS, SPMS and PPMS.

• Compare the new with competing scales.

Methods (Figure 1)

1) Literature reviews:
    a) Studies conceptualising walking;
    b) Existing walking scales;

2) Conceptual framework (CF) development:
Qualitative interviews & expert input develop, refine and finalise walking conceptualisation.

3) Item content development:
Iterations of mixed qualitative & quantitative method, and cognitive debriefing generate, refine and finalise item content.

4) Measurement performance testing:
• Postal survey: data analysed WITH Classical Test and Rasch Measurement psychometric Theories (CTT, RMT);

• New PRO compared with MS Walking (MSWS-12) & NeuroQol Lower Extremity Function (NQoL-LEF) scales.

Conclusions:

Evidence supports MSWS-32 as a fit-for-purpose PRO measuring walking ability in R-, SP-, & PPMS.

Conceptually & empirically better than MSWS-12 & NQoL-LEF

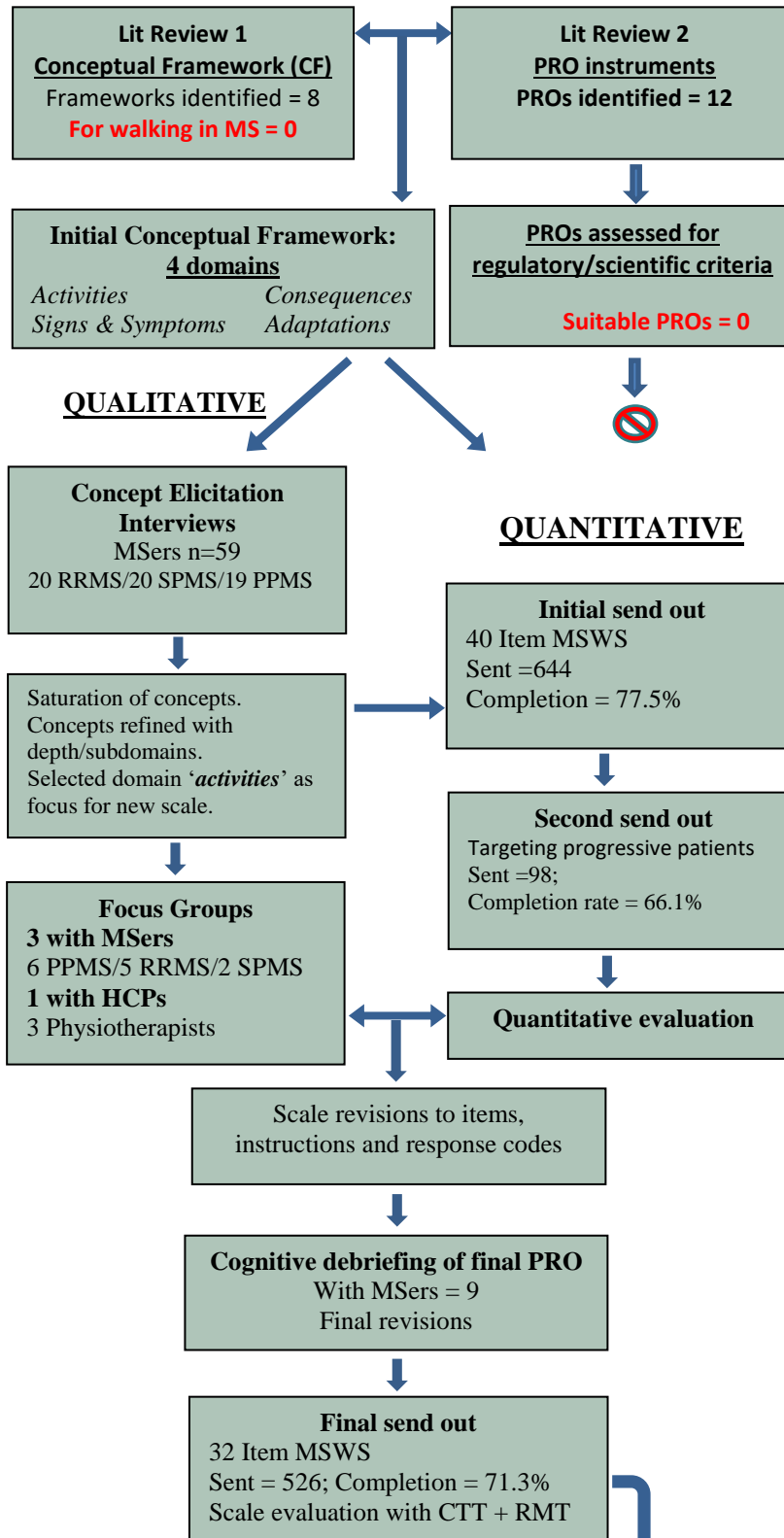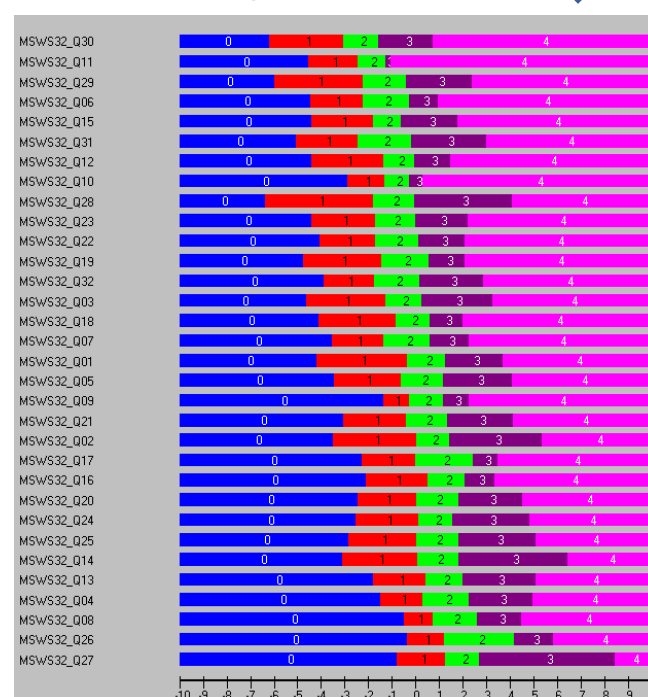Figure 1: Scale development process

Figure 2: RMT Threshold Map

Results-1: Literature reviews

a) n=1673 publications reviewed: no walking ability conceptual frameworks (CF) for MS identified.

b) n=9025 publications reviewed: 12 existing measures identified, none met regulatory and scientific guidelines.

Findings used to inform initial CF and item set.

Results-2: Conceptual Framework

• 4-domain conceptualisation derived from MSer 1-2-1 interviews (20 RMS, 20 SPMS, 19 PPMS) & 2 therapist focus groups [FG].

• *Activities people do specific to walking* domain chosen for scale development as proximal concept for trials in all 3 MS COU.

Results-3: Item content

• Saturation analyses demonstrated concept content consistency for RMS, SPMS & PPMS.

• Postal survey data analyses (n=664; n=98; k=40 item PRO) informed thinking.

• FGs (n=13 MSers in 3 FGs; n=3 therapists in 1 FG) refined items further.

• Quant- and Qual-itative results finalise 32-item PRO.

• Cognitive debriefing interviews (n=9 in 3 FG) finalised items and wording.

Results-4: Evaluation PRO Performance

• Data from n=526 MSers;

• Classical Test Theory (CTT):
    • Low item-level missing data.
    • Low floor (0.8%) & ceiling (8%) effect.
    • Principal components analysis (PCA) supports one score from the 32 items.
    • Reliability high: Cronbach's α=0.99.

• Rasch Measurement Theory (RMT): (figure 2)
    • *Targeting*: good for item performance and person measurement evaluation;
    • *Items*: thresholds ordered; continuum clear; fit good; no scoring bias; no differential functioning (DIF);
    • *Persons*: fit good; separation high; error low.

• Performance comparison
    • Superior to MSWS-12 & NQoL-LEF