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Exploring the Content Validity of Patient-Reported Outcome (PRO) Measures to Capture the Patient Experience of Becker Muscular Dystrophy (BMD)

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Background & Objective

Becker Muscular Dystrophy (BMD) is a rare progressive X-linked neuromuscular disorder that causes muscle weakness, particularly in the legs and pelvic area.[1] It is considered best practice in health economics and outcomes research and required by the Food and Drug Administration (FDA), to demonstrate that patient-reported outcome (PRO) measures used in clinical trials are fit-for-purpose to assess disease symptoms and impacts that are important to patients.[2-8]
The aim of this study is to understand the lived experiences of BMD patients to inform selection of PRO measures. PRO measures for CD were chosen based on best coverage of signs and symptoms of BMD. Findings build on existing evidence from the literature to inform the development of a conceptual model.

Methods

- Participants were patients and/or caregivers of patients with a diagnosis of BMD ≥12–55 years of age, based in the US. Participants were recruited via existing patient databases, patient organizations, and partner recruitment agencies.
- Virtual semi-structured interviews were conducted and either a combined 90-minute CE/CD interview or two separate 45-minute CE and CD interviews taking place over two rounds.
- Content validity of the following PRO measures was explored through CD interviews: Brief Pain Inventory (BPI)-Short-Form item 3, Neuro-Qol - Upper Extremity and three PROMIS-57 domains: Physical Function, Fatigue and Pain Interference. Five further PROMIS-57 domains were assessed at a topline level. CD interviews included a PRO 'read aloud' exercise; framework analysis assessed PRO conceptual relevance, comprehension, and interpretation. Clinically meaningful improvement thresholds were explored qualitatively.
- CE interviews included open-ended questions to explore the patient experience of BMD. Semantic, qualitative, directed content analysis (in ATLAS.ti v9) identified concepts that were grouped into domains to develop a conceptual model.

Results

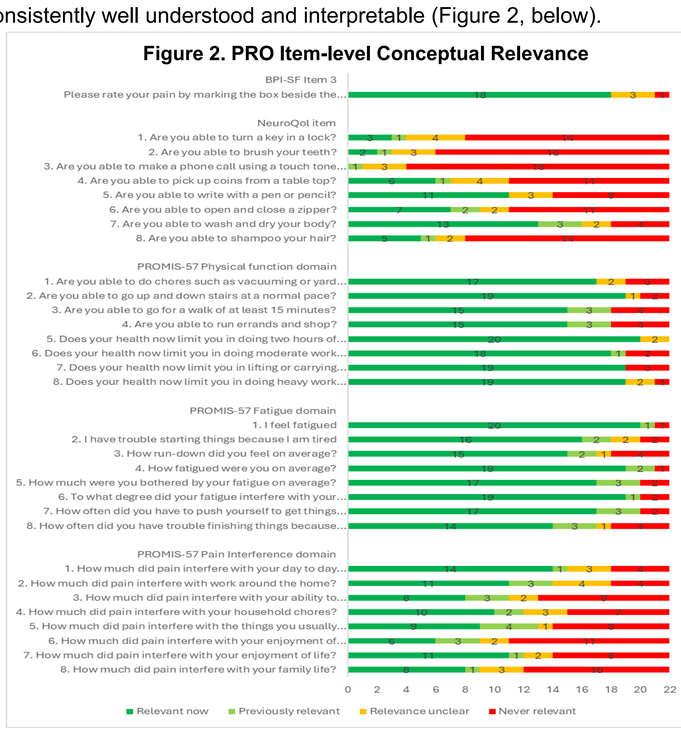
A total of 31 participants [(n=29) diagnosed with BMD or caregivers (n=2)], took part in CE interviews, with a sub sample also taking part in CD interviews (n=22).

Demographic (mean, range)	N
Age (27, 13 - 55) **BMD diagnosis age** (15.1, 1 - 46)	• 12-17 years old (n=13) • 18-55 years old (n=16)
Gender	Men (n=27/29, 93.1%)
Race	• White (n=28/29, 96.6%) • Other (n=1/29, 3.4%)
Ambulatory status • Fully ambulatory (AM1) • Required walking aids/assistance sometimes (AM2) • Required walk aids/assistance most of the time/always (AM3)	• AM1 (n=2) • AM2 (n=9) • AM3 (n=8)
Current treatment	• Physical therapy (n=13/29, 44.8%) • Not receiving (n=12/29, 41.4%)

Cognitive Debriefing: Which Measures Assess Concepts That Are Important to Patients with BMD?

PRO measures, except the Neuro-Qol-Upper Extremity questionnaire, were consistently well understood and interpretable (Figure 2, below).

Figure 2. PRO Item-level Conceptual Relevance

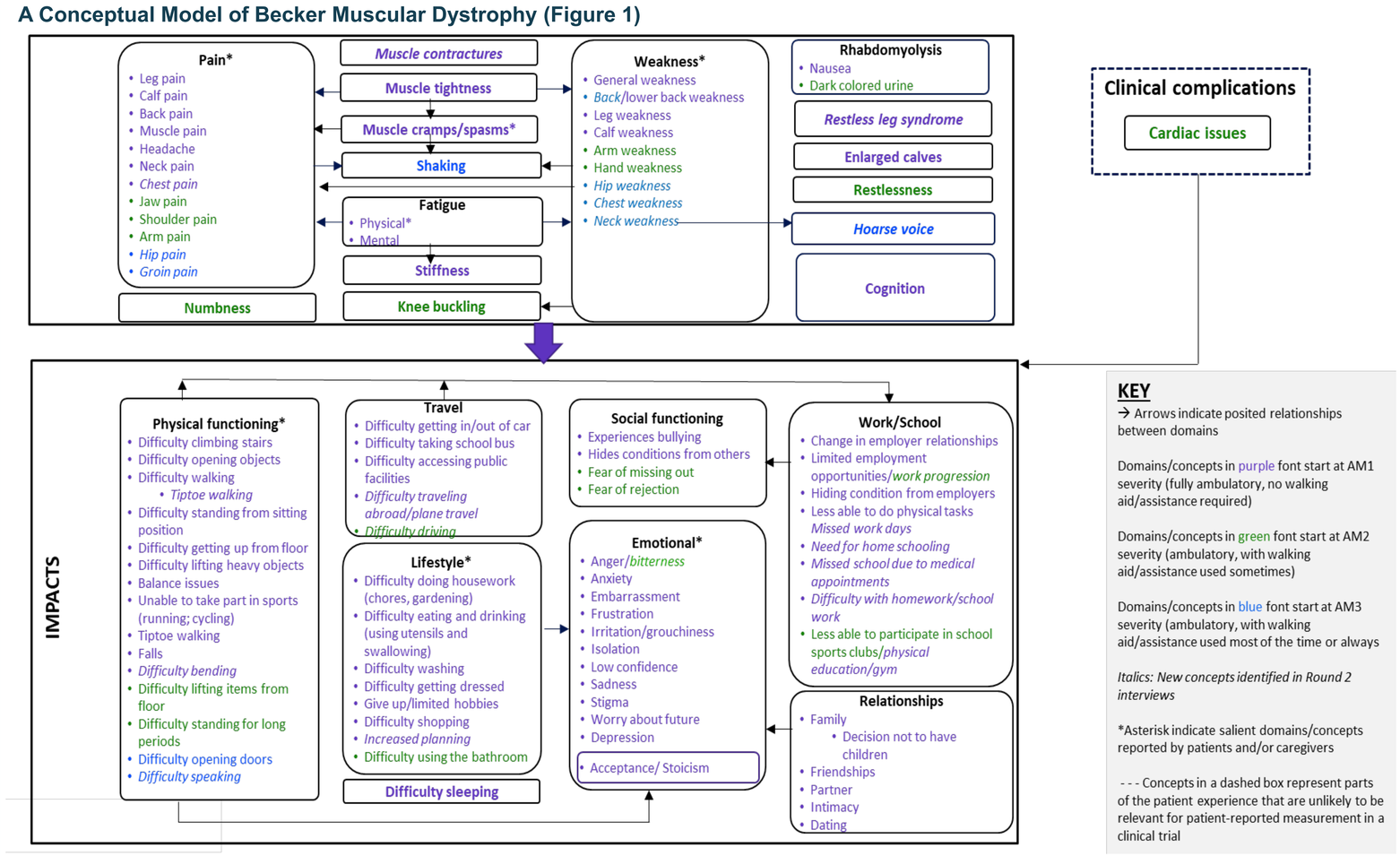


Reported Impacts &Symptoms

Impacts of BMD	% of Participants
Physical functioning	97%
Emotional wellbeing	97%
Lifestyle	84%
Work/school	77%
Social Functioning	61%
Relationships with others	58%
Sleep	45%
Travel	36%

Signs and symptoms	% of Participants
Physical fatigue	94%
Pain	77%
Weakness	58%
Muscle cramps/spasms	39%
Mental fatigue	39%
Muscle tightness	39%
Muscle stiffness	19%
Cognition	16%
Enlarged calves	10%
Knee buckling	10%
Rhabdomyolysis associated nausea	7%

A Conceptual Model of Becker Muscular Dystrophy (Figure 1)



BMD Impacts, Signs & Symptoms

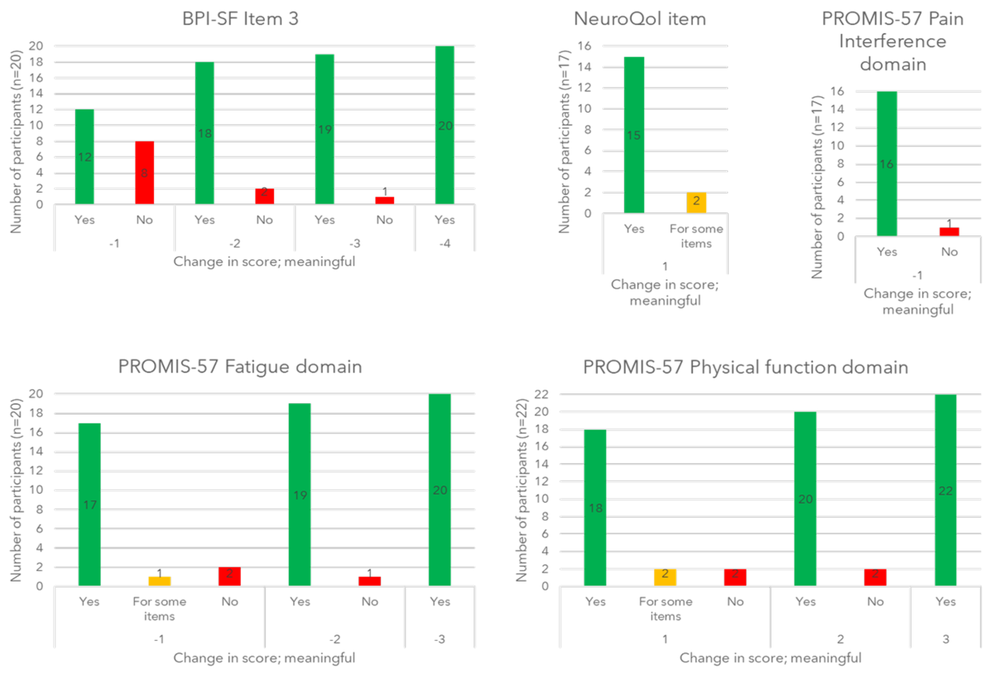
Remaining PROMIS-57 domains were understood by all participants who debriefed them.

Domain relevance (of all items) varied from 35% (n=6/17, Anxiety domain) to 89% (n=16/18, Pain Intensity domain).

Most participants considered a 1-point change in score across each PRO measure to represent meaningful improvement in their lives (Figure 3, right).

**Not all participants debriefed all PROs due to interview time constraints; PROs were not debriefed by participants who did not consider the items to be relevant.*

Figure 3. Meaningful Improvement In Score On Each PRO*



Conclusions

- The developed conceptual model incorporates novel concept elicitation interview findings and describes the adult and pediatric experience of BMD. Many symptoms and impacts were identified, highlighting the diverse experience of BMD patients.
- Conceptual mapping of PRO measures against the conceptual model suggested that the PROMIS-57 and BPI-SF collectively assess the concepts that matter most to patients, and therefore may be appropriate clinical outcome assessment measures for inclusion in BMD clinical trials.
- Cognitive debriefing interview findings suggest the Brief Pain Inventory (BPI)-Short-Form item 3, PROMIS-57 Physical Function, Fatigue and Pain Interference domains appear to be well understood and have moderate-good content validity in a pediatric and adult BMD population.

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Acknowledgements
The authors are grateful to the participants in this study.

Disclaimer
The study protocol was approved by the WCG Independent Review Board (WCG IRB; ref: (20220963)). Some authors are employees or consultants for Edgewise Therapeutics and may hold stock and/or stock options.

Presented at the 29th Annual Congress of the World Muscle Society (October 8-12, 2024) in Prague, Czech Republic.