Psychometric validation of the Mucopolysaccharidosis Health Assessment Questionnaire (MPS-HAQ) for mucopolysaccharidosis IVA

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Background

- Mucopolysaccharidosis (MPS) IVA is a rare, progressive lysosomal storage disorder characterized by multisystem clinical manifestations (skeletal, cardiorespiratory, neurological, and sensory abnormalities) that progress over time[1]
- In most cases, the clinical manifestations affect functional abilities such as mobility and self-care, which pose a burden on patients and caregivers[2]
- Elosulfase alfa enzyme replacement therapy is the recommended first-line treatment for MPS IVA[3]
- The MPS Health Assessment Questionnaire (MPS-HAQ) is a patient/caregiver-reported outcome tool originally developed for MPS I[4]; it consists of 52 items across three domains: Self-care, Mobility, and Caregiver assistance
- Although the MPS-HAQ has been used to assess functional status in MPS IVA clinical trials, its validity and reliability in this population have not yet been established

Methods

- Objective: to assess the psychometric properties of the MPS-HAQ for the MPS IVA population
- Psychometric analysis was performed on data from the elosulfase alfa phase 3 MOR-004 study (N=176) and a Managed Access Agreement (MAA) initiated in the UK following the approval of elosulfase alfa (N=39) **(Table 1)**[5,6]

Table 1. Summary of psychometric analyses

Property	Analysis dataset and timepoint	Definition	Success criterion
Item facility	MOR-004 and MAA at baseline	Floor and ceiling effects	<35% (20%, 50% also analyzed)
Inter-item correlations	MOR-004 and MAA at baseline	Inter-item correlations	|r| 0.15–0.8 range |r| 0.15–0.50 mean
Item-total correlations	MOR-004 and MAA at baseline	Item-total correlations	|r|≥0.3
Internal consistency	MOR-004 and MAA at baseline	Cronbach's alpha	≤0.7
Test-retest reliability	MOR-004 at baseline and week 12	Pearson's correlations and ICC	|r|≥0.75
Convergent and discriminant validity	MAA at baseline and week 52	Pearson's correlations	|r|≥0.5

ICC: Intraclass correlation coefficient; VAS: visual analogue scale

Results

- At a 35% threshold, ceiling effects were observed in 44% of Self-care items and 53% of Caregiver assistance items; floor effects were seen only in the Self-care domain (7%) **(Table 2)**
- Inter-item correlations were within the expected range (|r| = 0.3–0.8) across all domains, supporting domain structure **(Table 3)**
- Corrected item-total correlations were moderate to high (|r| ≥0.3) in all three MPS-HAQ domains, indicating good item discrimination
- Cronbach's alpha was >0.7 for all 3 domains, confirming good internal consistency **(Table 4)**
- Convergent/discriminant validity analyses showed conceptual similarity between MPS-HAQ and EQ-5D-5L:
  - The EQ-5D-5L Self-care domain correlated moderately/highly with all MPS-HAQ domains at baseline and 52 weeks (*P* <0.001)
  - The EQ-5D-5L Usual activities domain correlated moderately with MPS-HAQ Mobility and Caregiver assistance at baseline, and with all domains at 52 weeks (*P* <0.05)
- Test–retest reliability was excellent for all MPS-HAQ domains, with high correlations by both Pearson's r and intra-class correlation coefficient (>0.8; *P* <0.001) **(Table 5)**

Table 2. Item facility: ceiling and floor effects of the MPS-HAQ by domain

	Ceiling effect (low scores[a])				Floor effect (high scores[a])			
Domains	**Range**	**25%**	**35%**	**50%**	**Range**	**25%**	**35%**	**50%**
Self-care (27 items)	9.3–70.2%	15 (56%)	12 (44%)	6 (22%)	0–36.4%	2 (7%)	2 (7%)	0
Mobility (10 items)	11.6–34.4%	2 (20%)	0	0	5.1–26.3%	1 (10%)	0	0
Caregiver assistance (13 items)	21.5–74.8%	12 (92%)	7 (53%)	2 (15%)	0.5–29.5%	3 (23%)	0	0

[a]Items with low scores representing independence and high scores representing complete assistance

Floor and ceiling effects were considered present if >35% (or >25% / >50%) of patients achieved the worst (highest) score or best (lowest) score, respectively

Table 3. Inter-item correlations for MPS-HAQ domains

Domains	Mean	Median	Min	Max
Self-care	0.520	0.526	0.234	0.874
Mobility	0.473	0.471	0.204	0.757
Caregiver assistance	0.545	0.528	0.308	0.870

Inter-item correlations measure the extent to which scores on one item are related to scores on all other items in the scale

Table 4. Internal consistency: MPS-HAQ Cronbach's alpha for items within MPS-HAQ domains at baseline

Domains	# items in domain	Cronbach's alpha	Cronbach's alpha based on standardized items
Self-care	27	0.967	0.967
Mobility	10	0.897	0.900
Caregiver assistance	13	0.939	0.940

Correlations between scores of different items within the domains reflect the extent to which the items measure various aspects of the same characteristic

Table 5. Test-retest reliability: ICC and Pearson's correlation for MPS-HAQ domains

	Pearson's correlation	ICC (95% CI)
Self-care baseline and week 12		
Correlation	**0.895**	**0.944** (0.925–0.959)
P-value	<0.001	<0.001
Mobility baseline and week 12		
Correlation	**0.854**	**0.921** (0.808–0.890)
P-value	<0.001	<0.001
Caregiver assistance baseline and week 12		
Correlation	**0.844**	**0.915** (0.885–0.937)
P-value	<0.001	<0.001

ICC: intra-class correlation coefficient

All correlations are significant at the 0.01 level (2-tailed). **Correlations >0.5 are highlighted**

ICC and Pearson's correlations between 2 close time points of MPS-HAQ domain scores >0.75 indicate excellent reliability

Conclusions

- The MPS-HAQ displays good validity and reliability in patients with MPS IVA, supporting its use as an outcome measure to assess functional status in clinical trials and real-world studies in this population
  - Despite good overall validity and reliability, discrimination in the Self-care and Caregiver assistance domains may be limited at higher levels of functioning, which should be considered when using the tool

References

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