Poster HTA31

# Early versus Late Disease Utility Capture in Primary Lateral Sclerosis: Evaluating the EQ-5D

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## BACKGROUND

- Primary lateral sclerosis (PLS) is a progressive upper motor neuron disease characterised by motor impairment, bulbar dysfunction, fatigue, cognitive and behavioural symptoms, and broader impacts on daily functioning and wellbeing.
- The slow progression of PLS may limit the sensitivity of generic preference based measures, as clinically meaningful symptoms may not immediately translate into measureable functional impairment.
- The EuroQol 5-Dimension (EQ-5D) is widely used to derive health state utilities in economic evaluation. It assesses five domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.
- However, EQ-5D is structurally constrained by these domains and may not explicitly capture all clinically relevant aspects of PLS, particularly non-functional or less visible symptoms.
- Previous work has mapped PLS-related symptoms to EQ-5D domains to assess their structural coverage (Büsch & Kaan, 2025)[1]. However, structural mapping alone does not account for disease stage and how symptom burden may manifest differently across the course of disease.

## OBJECTIVE

To extend prior conceptual mapping by assessing how the expression of PLS-related symptoms and impacts within EQ-5D domains differs between hypothetical early and late-stage disease. To examine how these differences influence the perceived capture of disease burden.

## METHODS

### Prior conceptual mapping (structural baseline)

A previously published mapping exercise classified PLS-related constructs based on their structural represented within EQ-5D domains (Büsch & Kaan, 2025) [1]:

- Explicit representation
- No representation

This established structural domain coverage, independent of disease stage.

### Current study (stage-dependent expression framework)

Two hypothetical PLS profiles were developed:

- Early-stage disease
- Late-stage disease

These were informed by the targeted literature review (Kaan & Büsch, 2025) [2], the conceptual model (Büsch & Kaan, 2025) [3], and clinical expert input.

### Signs, symptoms and impacts included

Motor and neurological symptoms:

- Upper and lower limb impairment
- Bulbar dysfunction (dysarthria, dysphagia)
- Pseudobulbar affect
- Cognitive impairment
- Fatigue

Symptoms:

- Pain
- Depression

Impact areas:

- Activities of daily living (ADLs)
- Social participation (including work)
- Emotional impacts (distress, frustration, embarrassment, irritability)

The identified signs, symptoms and impacts were independently reviewed by two researchers and organised according to their expected relevance within the early- and late-stage disease profiles.

### Analytical approach

A domain-anchored EQ-5D framework was used to assess whether each construct is:

- Explicitly represented within EQ-5D domains
- Not represented within EQ-5D domains
- Only indirectly reflected via functional consequences (where applicable)

Importantly, analysis focused on expected expression within domains rather than empirical measurement performance.

## RESULTS

### Hypothetical patient profiles (Table 1)

**Table 1. Hypothetical early- and late-stage PLS profiles**

| | |
|---|---|
| Early-stage PLS (individual A) | Individual retains high functional independence. Upper and lower limb function is largely preserved, although mild motor smyptoms may be present. Bulbar symptoms (dysarthria and dysphargia) may be absent or subtle. The individual remains independent in self care and daily activities, with no or minimal cognitive involvement. |
| Late-stage PLS (individual B) | Individual experiences servere functional impairment with loss of independent mobility. Upper and lower limb function is substantially affected. Bulbar dysfunction (dysarthria and dysphagia) is present and functionally limiting. The individual requires asssitance with daly living and may experience cognitive impairment. |

## RESULTS, cont.

### Stage-dependent expression (Table 2)

Early-stage PLS

- Mobility and self-care largely preserved: limited domain expression
- Fatigue, cognitive and bulbar symptoms present but not reflected in EQ-5D responses
- Pain and depression may be captured if present
- Social participation impacts may not translate into “usual activities”
- Emotional impacts largely outside EQ-5D scope

Late-stage PLS

- Clear impact on mobility and self-care domains
- Increased impact on usual activities (ADLs and work)
- Pain and depression consistently captured
- Persistent lack of representation of cognitive and behavioural symptoms
- Emotional burden remains partially captured only via anxiety/depression

**Table 2. EQ-5D conceptual coverage by disease stage**

| Signs/Symptoms | “All PLS” | Early PLS | Late PLS |
|---|---|---|---|
| Upper limb | | | |
| Lower limb | | | |
| Bulbar dysfunction | | | |
| Pseudobulbar affect | | | |
| Cognitive impairment | | | |
| Depression | | | |
| Fatigue | | | |
| Pain | | | |
| Basic ADL impacts | | | |
| Social interactions/work impact | | | |
| Emotional impacts | | | |

Dark green = covered, light green = possible covered; white = not covered; ADL = activities of daily living; whether signs/symptoms or impacts are captured directly or indirectly will also depend on whether they are present and pending their severity.

### Key conceptual finding

**Across disease stages, EQ-5D capture is driven less by changes in symptom presence and more by whether symptoms translate into domain-relevant functional expression.**

### Summary of domain sensitivity

- Mobility & self-care: most sensitive to disease progression
- Usual activities: captures broader functional decline
- Pain & depression: consistently represented
- Cognitive, bulbar, fatigue, behavioural symptoms: not captured
- Emotional impacts: partially captured only

### Interpretation

This analysis demonstrates that EQ-5D is a domain-anchored instrument that strongly reflects functional impairment but incompletely captures several clinically relevant nonfunctional symptoms in PLS.

Importantly, differences between early and late-stage disease reflect not changes in instrument structure, but changes in the likelihood that disease burden becomes expressed within EQ-5D domains.

This introduces a conceptual distinction between:
(1) disease burden and
(2) and the visibility of that burden within generic preference-based instruments.

As a result, EQ-5D may differentially reflect disease burden across stages, with greater alignment in later-stage disease where functional impairment is more pronounced.

### Limitations

- Hypothetical early- and late-stage profiles not empirically validated
- Conceptual mapping based on interpretation of EQ-5D domains
- No patient-level EQ-5D data included
- Findings reflect expected domain expression, not observed measurement performance
- Limited generalisability beyond PLS and related motor neuron disorders

## CONCLUSION

EQ-5D may not fully capture important aspects of health-related quality of life in PLS, particularly in earlier disease stages where symptoms do not translate into functional domain expression.

As a result, utility estimates derived from generic preference-based measures may underrepresent treatment benefits, especially earlier in disease progression.

Alternative approaches, including disease-specific measures and vignette-based utility elicitation, may be warranted to better characterise burden and utilities in PLS.

**References:** 1. Büsch K & Kaan I. Outcome Measures Relevant for Assessing Health Related Quality of Life and Utility in Primary Lateral Sclerosis (PLS), ISPOR Europe 2025; 2. Kaan I & Büsch K. Primary Lateral Sclerosis (PLS): A Targeted Literature Review of Symptoms, Progression, and Outcomes to Inform Evidence Gaps for Rare Neurological Disorders, ISPOR Europe 2025: 3. Büsch K & Kaan I. Health-related quality of life impacts of living with Primary Lateral Sclerosis (PLS) - the development of a conceptual model, ISPOR Europe 2025. **Disclosures:** IK is an employee of Aeolian Logic Pte.Ltd; KB is an employee of KJM Büsch Consulting GmbH.



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