# Psychometric Validation of the Low Luminance Questionnaire (LLQ) in X-Linked Retinitis Pigmentosa (XLRP)

**Poster PCR102**

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## Introduction

- Retinitis pigmentosa (RP) is a group of inherited diseases of the retina and occurs most commonly in isolation (non-syndromic).
- The prevalence of RP is estimated to be 1:3000, with 30% to 40% of cases inherited via an autosomal dominant route, 45% to 60% via an autosomal recessive route, and 5% to 15% as an X-linked trait.
- The condition is characterized by a progressive reduction in vision, initially manifesting as night blindness (nyctalopia), and usually becomes apparent in childhood or early adulthood, which progresses throughout the patient's lifetime.
- There is progressive peripheral visual field loss with increasingly constricted peripheral vision resulting in "tunnel vision" over time, which markedly restricts navigation/mobility and the ability to undertake activities of daily living, with associated emotional, psychological, and social impacts.
- In the advanced stage, continued retinal failure and degeneration results in central visual impairment and eventual blindness.[1]
- The assessment of PROs has become an important component in clinical trials as they provide information on the impact of a disease and its treatment from the perspective of a patient.[2]
- There is currently no licensed treatment for retinitis pigmentosa GTPase regulator X-linked retinitis pigmentosa (XLRP).

## Objective

- This study aimed to psychometrically evaluate the Low Luminance Questionnaire (LLQ)[3] in XLRP to support its suitability as a secondary endpoint to evaluate task difficulty under low luminance in clinical trials of novel therapies for XLRP patients.

## Methods

**Data Source**

- A series of Phase 1/2 studies in RPGR-associated XLRP, including Study MGT009 and Study MGT011 were used to describe the natural history and disease characteristics of the patient, assess the suitability and performance of PRO measures for potential use in clinical trials on XLRP, and identify patients who might potentially be suitable candidates for intervention.

**Description of LLQ Instrument**

- The LLQ is a 32-item disease-specific questionnaire for use in eye diseases to assess self-reported visual problems under low luminance and at night.
- The LLQ consists of 6 domains including driving (5 items), extreme lighting (8 items), mobility (6 items), emotional distress (4 items), general dim lighting (6 items), and Peripheral Vision (3 items).
- Response options include 5- and 6-point Likert Scales ranging from "no difficulty at all" or "none of the time" to "stopped doing because of your vision." Two additional response options represent non-applicable or missing data: "stopped for other reasons" and "don't do."
- The recall period is "at the present time." The time to complete the measure is approximately 5- to 10-minutes.
- The instrument is scored by domain, computed by scaling individual items from 0 to 100, and then averaging the individual items for each domain. A higher score reflects a higher functional level.[4]

**Analysis**

- Floor and ceiling effects, item fit, response categories performance, unidimensionality, internal consistency reliability, convergent, divergent, and known groups validity were assessed using baseline data from Phase 1/2 and natural history studies in XLRP (data on file).

## Results

**Item Distribution and Floor and Ceiling Effects**

- The LLQ domains have a good capacity to measure improvement and deterioration as indicated by item spread on the latent continuum on the Wright-Andrich map, except for the Driving domain (item floor effects: 35.3% - 41.2%) (Table 1).
- A ceiling effect was observed for 2 (6.25%) out of a total 32 items (Extreme Lighting domain [Items 1 and 2]). A floor effect was observed for 8 items (25%; Items 6 and 8 [Extreme Lighting domain], 24 through 28 [all Driving domain items], and 31 [Emotional Distress domain]). The following proportion of the sample (n = 34) selected the least severe answers (indicating ceiling effects) on the LLQ domains: 5.3-11.1% on Driving domain, 2.94-35.3% on Extreme Lighting domain, 5.9-14.7% on Mobility domain, 2.9-11.8% on Emotional Distress domain, 2.9-8.8% on General Dim Lighting domain, 2.9-20.6% Peripheral Vision domain. Domains Mobility, General Dim Lighting and Peripheral Vision have a good capacity to measure improvement and deterioration. Domains Driving, and to a lesser extent also the Extreme Lighting and Emotional Distress, have a good capacity to measure improvement, but rather limited capacity to measure deterioration.

**Inter-item Correlations**

- Average inter-item correlations within the specific domains ranged from 0.202 - 0.933.
- Out of a total 528 computed correlations for this measure, 207 (39%) were below ±0.30 (Figure 1). Low inter-item correlations (marked with white color) were observed particularly between items 29 - 31 and the rest of the items. The averaged inter-item correlations for items from the Driving scale, Emotional Distress scale, Peripheral Vision scale, Extreme Lighting scale, Mobility scale, and General Dim Lighting scale were: 0.842 - 0.933; 0.405 - 0.618; 0.599 - 0.752; 0.296 - 0.485; 0.202 - 0.477; 0.387-0.494, respectively.

**Reliability**

- All domains showed very high internal consistency (α = 0.777 - 0.971), and all item-total correlations were moderate to very high (0.451 - 0.971), except for item 12 from the Mobility domain ("Concerned that you might fall at night"), which had an item-total correlation of 0.248.
- Cronbach's alpha for the Mobility domain was 0.777. All but 1 item (Item 12 ["Do you worry or are you concerned that you might fall at night because of your vision?"]), contributed to Cronbach's alpha. If Item 12 had been removed, Cronbach's alpha would increase to 0.809. This result suggests an acceptable internal consistency.

**Unidimensionality**

- For the domains Mobility, Emotional Distress and General Dim Lighting the Eigenvalue for the first contrast was below 2, thus supporting the domains are unidimensional. For the Driving, Extreme Lighting and Peripheral Vision domains, the Eigenvalue for the first contrast was above 2 (thus above the threshold indicating possible multidimensionality). Velicer's minimum average partial test (Figure 2) showed strong evidence for unidimensionality for each of the 6 domains of the LLQ, except for the Peripheral Vision domain.
- For the Extreme Lighting domain, Velicer's minimum average partial was computed after excluding 2 items that had a high number of missing responses (Item 6 ["Do you get upset because you have difficulty seeing while driving in the rain at night?"] and item 8 ["Do you have difficulty seeing dark colored cars while driving at night?"]).

**Figure 1. Heatmap of Inter-item Correlations for the LLQ in XLRP**

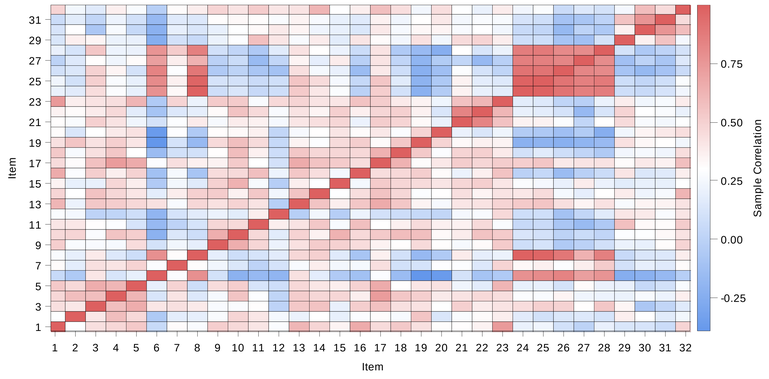
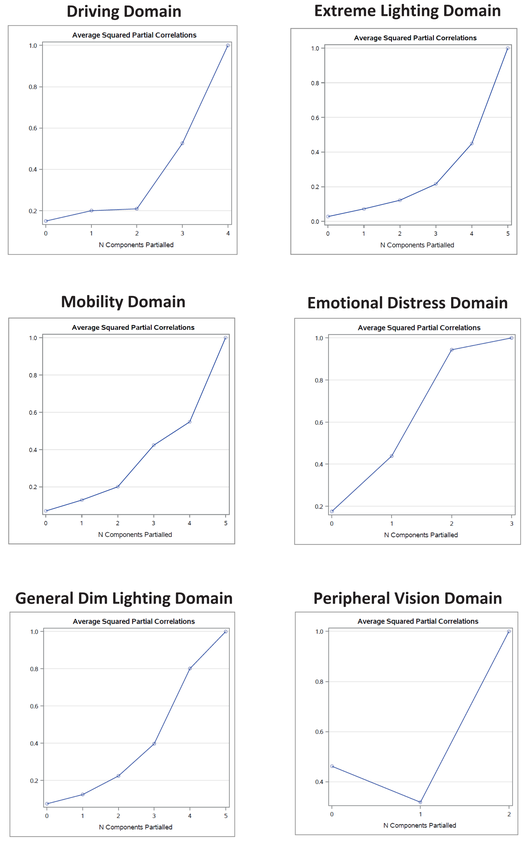



**Table 1. Summary of Psychometric Results of the LLQ at Baseline**

| Parameter | Threshold for Acceptability | LLQ | | | | | |
|---|---|---|---|---|---|---|---|
| | | 5-item Driving | 8-item Extreme Lighting | 6-item Mobility | 4-item Emotional Distress | 6-item General Dim Lighting | 3-item Peripheral Vision |
| Complete data | -- | 100% | 100% | 100% | 100% | 100% | 100% |
| Proportion of sample with ceiling effects at baseline | ≤ 25% of sample | 0 - 11% | 3 - 35.3% | 0 - 14.7% | 0 - 11.8% | 0 - 8.8% | 0 - 20.6 |
| | % of items | 0% | 25% | 0% | 0% | 0% | 0% |
| Proportion of sample with floor effects at baseline | ≤ 25% of sample | 66.7 - 73.7% | 0 - 77.8% | 0 - 11.8% | 0 - 29.4% | 0 - 17.7% | 11.8 - 23.5% |
| | % of items | 100% | 25% | 0% | 25% | 0% | 0% |
| Average inter-item correlations within scale | ≥ 0.40 and ≤ 0.90 | 0.842 - 0.933 | 0.296 - 0.485 | 0.202 - 0.477 | 0.405 - 0.618 | 0.387 - 0.494 | 0.599 - 0.752 |
| Item-total correlations | ≥0.40 | 0.842 - 0.971 | 0.451 - 0.680 | 0.478 - 0.722 | 562 - 0. 835 | 0.597 - 0.798 | 0.728 - 0.867 |
| Cronbach's alpha | ≥ 0.7 | 0.971 | 0.795 | 0.777 | 0.815 | 0.858 | 0.875 |
| Convergent validity: EQ-5D as reference | n/a | \|0.157 - 0.303\| | \|0.174 -0.609\| | \|0.288 - 0.533\| | \|0.006 -0.465\| | \|0.215 -0.635\| | \|0.157 -0.504\| |
| Convergent validity: Clinical assessment as reference | \|≥ 0.30\| | \|0- 0.604\| | \|0.329 -0.785\| | \|0.097 - 0.719\| | \|0.074 - 0.456\| | \|0.047 - 0.717\| | \|0.054 - 0.742\| |
| Known groups validity | ≥ 0.20 SES | 0.042 - 1.169 | 0.532 - 2.196 | 0.361 - 1.08 | 0.702 - 0.040 | 0.085 - 1.247 | 0.589 - 1.191 |
| | *P* < 0.05 | 0.113 - 0.896 | 0.001 - 0.242 | 0.015 - 0.500 | 0.367 - 1.000 | 0.023 - 1.00 | 0.006 - 0.475 |

EQ-5D = EuroQol 5 Dimensions; LLQ = Low Luminance Questionnaire

**Figure 2. Velicer's Minimum Average Partial Test LLQ Domains**




## Conclusions

- The LLQ was evaluated to understand the psychometric parameters in an XLRP population.
- Most domains demonstrated a good measurement properties to capture both improvement and deterioration of the condition, with all domains showing high internal consistency and well-performing response categories.
- Velicer's minimum average partial test showed strong evidence for unidimensionality for most domains.
- These findings support the LLQ as a valid, self-reported measure of task difficulty under low luminance/at night in XLRP patients.

## References

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## Disclosures

This study was funded by Janssen. PB, EA, JX, and SR are employed by Janssen. EP, LF, SH are consultants of Clinical Outcomes Solutions, a health outcomes research company commissioned by Janssen to conduct the research reported in this paper. MM was a chief investigator in the clinical trial sponsored by Janssen reported in this poster.

## Acknowledgements

Editorial support provided by the Medical Communications department at Clinical Outcomes Solutions, Chicago, US and to Sam Rousell, MS (Clinical Outcomes Solutions, Folkestone, UK) for programming assistance.

Presented at the International Society for Pharmacoeconomics and Outcomes Research 2024, Atlanta, GA, US, 5-8 May 2024.