Advancing Patient-Centered Value Assessment in Inherited Retinal Diseases: Leveraging EQ-5D-5L Vision Bolt-Ons to Support IRD-Specific PROMs

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INTRODUCTION

- Gene therapies for inherited retinal diseases (IRDs) hold promise for preserving or restoring sight, but traditional clinical measures may not fully capture their benefits.
- Patient-reported outcome measures (PROMs), especially those tailored to IRDs, bring insights into the patient-perceived effects of treatment and can complement clinical endpoints.
- However, conventional health technology assessments (HTAs) often depend on generic measures.
- Generic measures, e.g. the EQ-5D-5L, lack content validity and sensitivity in vision-related and Quality of Life (QoL) domains. This limitation can lead to under-estimation of treatment value in patients with progressive vision loss.
- IRD-specific PROMs have emerged ranging from symptom-based tools (MRDQ) to more comprehensive instruments (IRD Item Bank, ViSIO-PRO).
- These provide more patient relevant assessments but are not preference-based, therefore not directly usable in a cost-utility HTA framework.

OBJECTIVE

- To inform future research in patient-centered instrument development
- To explore how vision-specific bolt-ons to the EQ-5D-5L can bridge the gap between generic QoL measures and disease specific PROMs

METHOD

- Conduct a scoping review to examine the use of EQ-5D-5L vision bolt-ons in IRDs
- Source: Scopus database covering Web of Science, MEDLINE, EMBASE, and ScienceDirect; Key terms: EQ-5D-5L AND Vision AND Bolt-on; Search date: 16 June 2025

RESULTS

- Scoping review output: 63 records.
- None included EQ-5D-5L+vision bolt-on in IRDs, but 4 studies demonstrated its value relevant to PROM development.
- ***Content validity:*** bolt-ons capture dimensions important to patients but absent from generic measures.
- ***Construct validity:*** bolt-ons enable correlation with IRD-specific domains, supporting convergent or divergent validity.
- ***Responsiveness:*** bolt-ons increase sensitivity to meaningful change.
- ***Utility mapping:*** bolt-ons create a pathway to translate IRD PROM responses into utility values.

Summary of how the identified studies used the EQ-5D-5L vision bolt-on in ways that can inform validation of the IRD item bank or PROMs in IRDs

Use of Vision Bolt-On in selected studies	Relevance to IRD Item Bank Validation
1. Testing Psychometric Properties of 9 Bolt-Ons for the EQ-5D-5L in a General Population Sample	
▪ Added to EQ-5D-5L to examine whether it improves sensitivity & reduces ceiling effect ▪ Vision bolt-on improved known-group validity in subjects with visual impairment ▪ Structural validity showed bolt-on loaded on a different factor from the original 5 EQ-5D dimensions, confirming its unique contribution	▪ Demonstrates that vision-specific bolt-ons tap into constructs not captured by EQ-5D-5L generic domains, supporting the case for condition-specific PRO instruments ▪ Enables convergent/divergent validation of IRD items/domains by comparing scores with and without the vision bolt-on
2. Vision 'Bolt-On' Increases Responsiveness of EQ-5D: Preliminary Evidence from a Study of Cataract Surgery	
▪ Compared EQ-5D-5L with and without a vision bolt-on in pre- & post-cataract surgery patients ▪ Bolt-on increased responsiveness, measured via standardized response means (SRM) and F-statistics	▪ Supports the sensitivity of vision-specific dimensions to detect meaningful change over time ▪ Suggests that vision-specific items (e.g., IRD IB items) may capture treatment effects missed by generic tools
3. Cross-Attribute Level Effects (CALE) Modeling for EQ-5D-5L Vision Bolt-On States	
▪ Developed predictive models for utility values using EQ-5D-5L + vision bolt-on health states ▪ Found the CALE model significantly improved accuracy in utility estimation for states including the vision dimension	▪ Provides a technical foundation for mapping vision-specific responses (e.g., from IRD IB) onto preference-based utilities ▪ Suggests that modeling approaches can enhance the integration of vision-specific PROMs into economic evaluation frameworks
4. Development of 20 Bolt-On Items for EQ-5D-5L Including Visual Acuity	
▪ Visual acuity (VA) was one of the 19 newly developed bolt-ons ▪ VA bolt-on showed good divergent validity, confirming it measures a domain distinct from EQ-5D-5L's standard dimensions	▪ Highlights that VA (a core element in IRDs) can be validly represented in bolt-on items ▪ These findings can be used for cross-instrument validation, e.g., comparing IRD IB scores with EQ-5D-5L + VA bolt-on responses

- **Vision bolt-ons can reveal limitations in the standard EQ-5D-5L and justify the need for condition-specific PRO instruments**
- **Bolt-ons can serve as external comparators to test correlation with item bank domains (e.g., functioning, emotional impact)**
- **Studies show bolt-ons improve sensitivity to change, supporting the longitudinal validation of IRD-specific PROMs**

CONCLUSIONS

- Existing HTA frameworks for gene therapy in IRDs are limited because preference-based utility instruments insufficiently reflect the patient impact of visual impairment; standard trial endpoints often fail to capture meaningful functional gains in real-world settings; and long-term value (psychological, developmental, and caregiver-related outcomes), is underrepresented
- A more holistic, patient-anchored definition of value is critical to ensure innovative therapies for IRDs are fairly and appropriately evaluated
- Mapping algorithms for comprehensive IRD-specific PROMs have not yet been developed, but the Rasch-based design and conceptual coverage of health-related QoL domains suggest integration is feasible
- Joint administration of IRD-specific PROMs with the EQ-5D-5L + vision bolt-on may support more patient-centered, preference-based economic evaluations of gene therapy in IRDs

REFERENCES

Fischer MD et al. Psychometric Validation of the ViSIO-PRO and ViSIO-ObsRO in Retinitis Pigmentosa and Leber Congenital Amaurosis (2023). *Ophthalmol Ther.* 12(2):1359–86.

Lacy GD et al. The Michigan Retinal Degeneration Questionnaire: A Patient-Reported Outcome Instrument for Inherited Retinal Degenerations. *Am J Ophthalmol.* 2021;222:60–8.

Senthil MP et al. Development and Psychometric Assessment of Novel Item Banks for Hereditary Retinal Diseases. *Optom Vis Sci.* 2019;96(1):27–34.

Testing the Psychometric Properties of 9 Bolt-Ons for the EQ-5D-5L in a General Population Sample (2024) *Value in Health*, 202427 (7), pp. 943 – 954.

A vision 'bolt-on' increases the responsiveness of EQ-5D: preliminary evidence from a study of cataract surgery (2020) European Journal of Health Economics, 21 (4), pp. 501 – 511.

Cross-Attribute Level Effects Models for Modeling Modified 5-Level Version of EQ-5D Health State Values: Is Less Still More? (2023) Value in Health, 26 (6), pp. 865 - 872

Development and Testing of the Psychometric Properties of 20 Bolt-On Items for the EQ-5D-5L Across 31 Rare Diseases (2025) Value in Health, 28 (5), pp. 769 - 780

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