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Patient-Reported Outcome Measures in IRDs: Informing a Consensus Statement

Todd Durham, PhD / May 28, 2025

Disclosures

- None

Outline

- **FDA Guidance on PROs**
  - Strengths and limitations of PROs
  - Why and when to use a PRO
- **Specific instruments for IRD trials**
  - NEI-VFQ
  - MRDQ
  - ViSIO-PRO
- **Develop vs. Modify?**
- **Questions to Consider for Consensus Development**

Strengths and Limitations of PROs (FDA 2022 Guidance)

Strengths

- Capture patient perspective on treatment benefit
- Assess symptoms and impacts known only to patients
- Evaluate effects on functioning in daily life

Limitations

- Challenges in content validity and development
- Measurement error and recall bias
- So many different instruments → impedes standardization
- Regulatory acceptance requires rigorous evidence of reliability, validity, and interpretability

How and Why Use a PRO? (FDA 2022 Guidance)

- PROs assess concepts of interest: symptoms, functional status, or impacts that matter to patients
- Useful in capturing treatment benefit in the absence of objective clinical measures
- Regulators (and third-party payors) encourage PROs when the patient perspective is critical in determining clinical benefit

NEI-VFQ in IRD Studies

- **Widely used despite significant problems with dimensionality - visual function vs. socio-emotional impact (Pesudovs et al. 2010)**
- **Developed for broader ocular diseases; limitations in sensitivity for IRD-specific impacts, like light-dark adaptation (Green et al. 2020)**

Sugawara et al. 2010

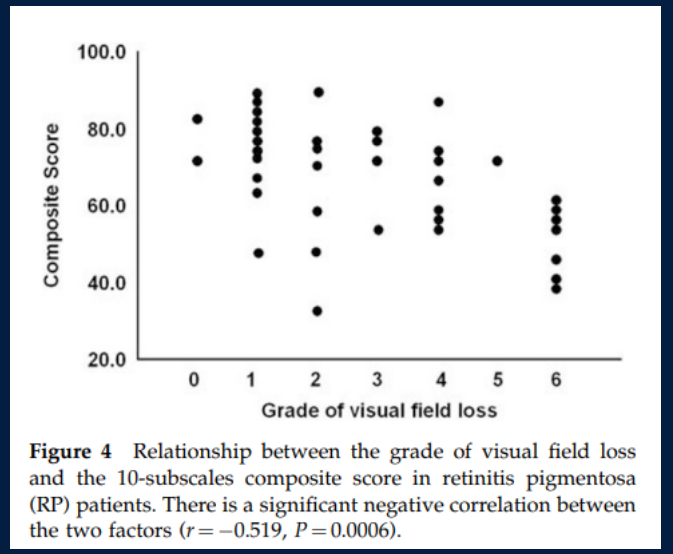


Figure 4 Relationship between the grade of visual field loss and the 10-subscales composite score in retinitis pigmentosa (RP) patients. There is a significant negative correlation between the two factors ($r = -0.519$, $P = 0.0006$).

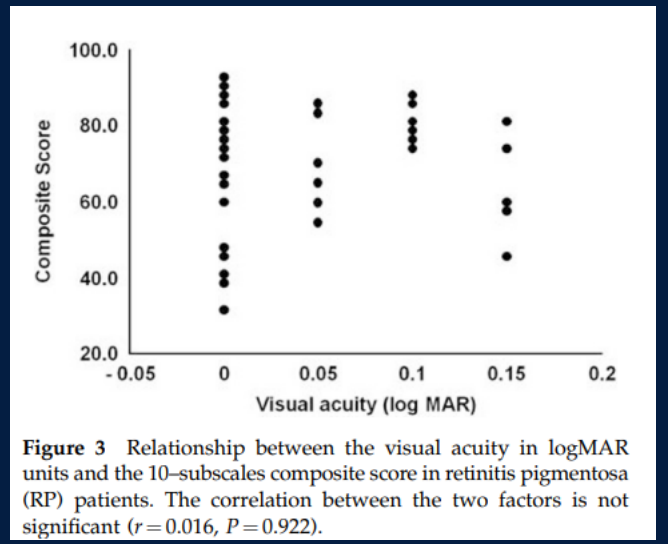


Figure 3 Relationship between the visual acuity in logMAR units and the 10–subscales composite score in retinitis pigmentosa (RP) patients. The correlation between the two factors is not significant ($r = 0.016$, $P = 0.922$).

Note: Litte variation in VA by design. You need variation to study associations ("convergent validity")

Visual field loss: 0 = normal visual field; 1 = some scattered scotomas in the midperiphery; 2 = ring scotoma; 3 = constricted visual field within the central 30 deg; 4 = constricted visual field within the central 15 deg with isolated peripheral visual islands; 5 = constricted visual field within the central 15 deg without peripheral visual islands; and 6 = constricted visual field within the central 10 deg

MRDQ in IRD Studies

- **Content generation from IRD patients; well understood by them (Lacy et al. 2021); reliable in adults and adolescents (Selvan et al. 2023)**
- **56 items in 7 domains: central vision, color vision, contrast sensitivity, scotopic function, photopic peripheral vision, mesopic peripheral vision, and photosensitivity**

Karuntu et al 2024*

	Central Vision	Color Vision	Contrast Sensitivity	Scotopic Function	Photopic Peripheral	Mesopic Peripheral	Photo-sensitivity
BCVA							
r	0.657	0.524	0.477	0.290	0.315	0.205	0.121
p-value	**<0.001**	**0.003**	0.008	0.120	0.090	0.278	0.526
LLVA							
r	0.550	0.414	0.502	0.369	0.343	0.363	0.141
p-value	**0.002**	0.023	**0.005**	0.045	0.064	0.049	0.456
Mean macular sensitivity							
r	−0.690	−0.584	−0.621	−0.551	−0.539	−0.488	−0.187
p-value	**<0.001**	**0.001**	**<0.001**	**0.002**	**0.003**	**0.007**	0.333

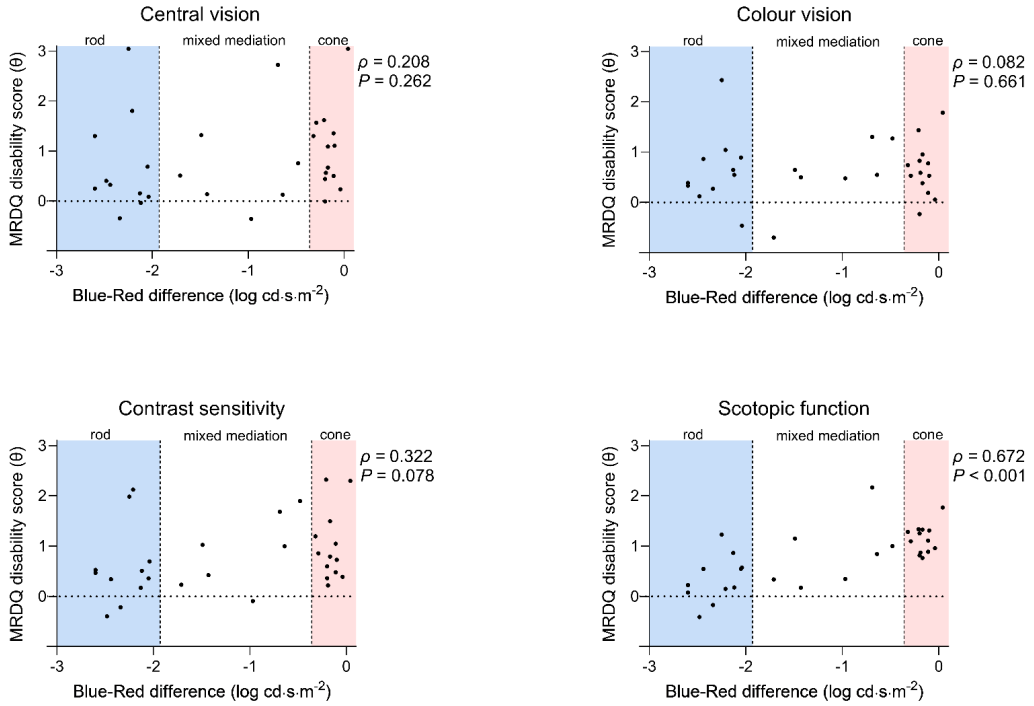
*30 adolescents and adults with RP and VA of better than LP in their better eye

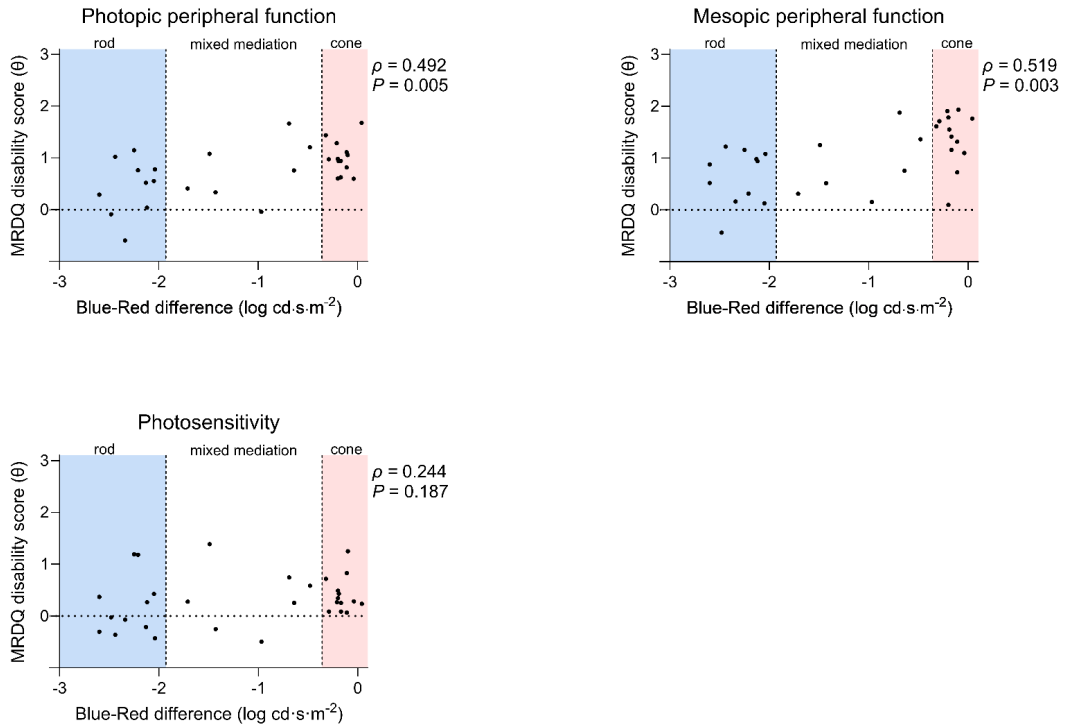
MRDQ Association with FST Blue-Red

(Karuntu et al. 2025*)

FST blue-red differences are positively correlated with disability scores in the scotopic, mesopic and photopic peripheral domains.

Full-field stimulus test (Blue-Red difference)





*31 adolescents and adults with RP and VA of better than LP in their better eye

ViSIO-PRO in IRD Studies

- **Developed for RP and LCA via patient/caregiver interviews and social listening (Kay et al., 2021; Audo et al., 2023); strong content validity: grounded in qualitative research; reliable; psychometrically validated for RP/LCA in multiple countries**
- **Items specified lighting conditions and familiarity of environment (Audo et al. 2023)**
- **44 items in 4 domains: visual function symptoms, vision-dependent daily activities, mobility, and distal HRQoL**

Fischer et al 2023*

Total scores are correlated with patient global impression and age.

	Group	N	Mean (SD)	P-value
PGI-S				
	None	6	1.14 (0.60)	<0.001
	Mild/Mod.	39	1.86 (0.71)	
	Severe/Very Severe	38	3.17 (0.73)	
Age	12-17 years	18	1.61 (0.62)	<0.001
	18-35 years	25	1.95 (0.70)	
	36-60 years	28	3.06 (0.82)	
	61+ years	12	3.03 (1.17)	

*83 adults and adolescents with RP; VA worse than 20/60 in the worse eye

Strategic Considerations for Developing or Modifying a PRO

Develop a New PRO When:

- No existing instrument (or part of an instrument) covers the concept of interest
- Target population is underrepresented
- Existing tools lack validity, reliability, or patient relevance

Modify an Existing PRO

- Core structure is sound but missing IRD-specific domains
- Requires tailoring for language, cultural adaptation, or age group
- Supplementing with new modules or integrating with digital health tech

Regulatory Considerations

- Content validity must be established or re-established
- Measurement properties (reliability, responsiveness)
- Is it important to patients?
- How will it be used as an endpoint?

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Thinking About a Consensus

1. How to define a valuable set of instruments, considering variety of therapeutic approaches / MOAs?
2. What kind of reporting standards to ensure the community continues to learn through experience?
3. How to future-proof the instruments, considering the pace of technology?
4. When might we rely on caregiver reports? Is the patient the most reliable reporter of his or her functional status?
5. What role could PROs play in demonstrating the potential relevance of surrogate endpoints?

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Thank You

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