#110

Relationship Between PROMIS® 29+2 and Home-Reported Outcomes (HROs) in a Population with Severe Hypertriglyceridemia (sHTG)

Nicole Tsao, PhD; Asia Sikora Kessler, PhD; Weiying Wang, MPH; Samantha McStocker, BS; Hiba Anwar, MPH; Ainsley Belisle, MS; Sarah Villard, PhD; Amanda Healey, MPH; Montserrat Vera Llonch, MD, MPH
Ionis Pharmaceuticals, Carlsbad, CA, USA • www.ionis.com

BACKGROUND

- Severe Hypertriglyceridemia (sHTG), defined by fasting triglyceride levels above 500 mg/dL, affects 1-1.4% of the population (about 3.4 million) in the United States.[1]
- Individuals with sHTG are at greater risk for acute pancreatitis (AP) and cardiovascular events, and may experience symptoms that impact their daily lives and emotional well-being; however, evidence on the latter is sparse.[2]
- The meTriG study explores the impact of sHTG on day-to-day symptom burden and health-related quality of life (HRQoL) through self-reported symptom burden and patient reported outcome (PRO) assessments, including the PROMIS® 29+2 and PROMIS® Cognitive Function 4a.

STUDY DESIGN

- A 6-month, prospective observational study enrolled US-based adults with sHTG.
- Participants completed study activities remotely within the Folia Health® app.
- At enrollment, participants selected treatments, symptoms (HROs; i.e., participants' self-identified symptoms) and completed patient-reported outcomes that included the above PROMIS® measures. Participants were presented suggested HRO symptoms, but chose which symptoms to track.
- HROs responses were ranked on a Likert-like scale (0 "did not experience", to 5 "severe").
- Of those participants who completed both HRO and PROMIS measures for each domain, PROMIS® 29+2 domain T-scores (standardized mean=50, standard deviation [SD] =10) were calculated and their relationship to HROs was examined using Kendall correlation analyses.
- Participants were classified by triglyceride (TG) level at enrollment, 500-879 mg/dL (Cohort A) and ≥880 mg/dL (Cohort B).

RESULTS

TABLE 1: Demographic Characteristics at Enrollment

	Cohort A 500-879 mg/dL (N=113)	Cohort B 880+ mg/dL (N=53)
Age, mean (SD)	46.77 (10.98)	46.85 (9.47)
Median (Q1, Q3)	45 (40, 55)	47 (40, 55)
Gender*, n (%)		
Female	55 (49%)	30 (57%)
Male	54 (48%)	23 (43%)
Transgender	3 (3%)	0 (0%)
Education, n (%)		
Some high school	2 (2%)	2 (4%)
High school diploma	36 (32%)	14 (26%)
Trade school	10 (9%)	11 (21%)
Bachelor's degree	44 (39%)	16 (30%)
Master's degree	16 (14%)	8 (15%)
PhD or higher	4 (4%)	2 (4%)
Hispanic, Latino, or Spanish origin, n (%)		
Yes	16 (14%)	4 (8%)
No	96 (85%)	48 (91%)
Prefer not to answer	1 (2%)	1 (2%)
Race, n (%)		
Asian	10 (9%)	3 (6%)
Black or African American	8 (7%)	3 (6%)
White or Caucasian	82 (73%)	42 (79%)
Reported more than one race	7 (6%)	9 (5%)
Some other race	5 (4%)	2 (4%)
Prefer not to answer	0 (0%)	1(1%)
Body mass index‡, mean (SD)	31.76 (6.38)	32.53 (7.01)
AP Incidence		
Never experienced AP	90 (80%)	30 (57%)
Experienced AP, but not in the past year	11 (10%)	15 (28%)
Experienced AP at least once in the past year	11 (10%)	8 (15%)
TG level at enrollment, mean (SD)	612.41 (99.73)	1700.02 (889.88)
Did not answer demographic questions	1 (1%)	0 (0%)

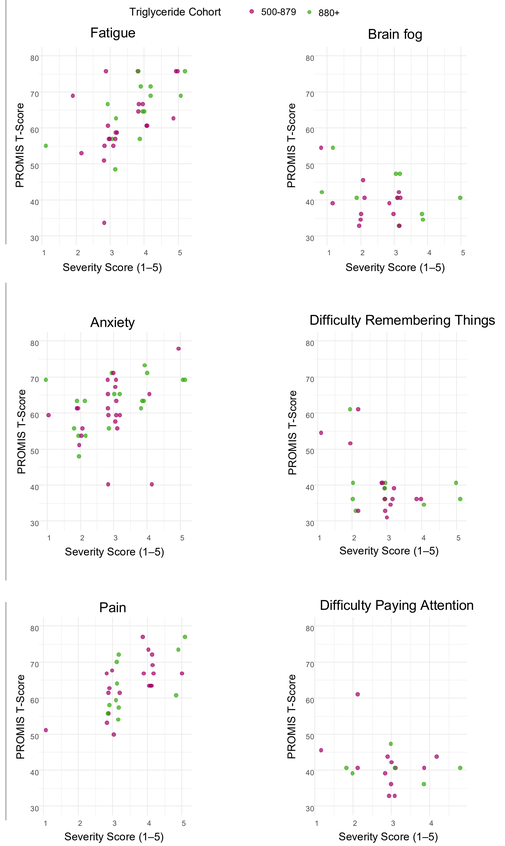
*No participant selected non-binary, some other gender, or prefer not to answer; ‡ excludes participants who did not answer body height, weight, or both questions.

TABLE 2: Summary of HRO Severity Scores and PROMIS® 29+2 Domain Scores with Kendall Correlations

Self-reported HRO Symptom	Cohort A (500-879 mg/dL)						Cohort B (880 mg/dL)					
	Sample size (N)	Average (SD) PROMIS® Score	Min-Max PROMIS® Score	Average (SD) HRO severity score	τ-value	p-value	Sample size (N)	Average (SD) PROMIS® Score	Min-Max PROMIS® Score	Average (SD) HRO severity score	τ-value	p-value
PROMIS® 29+2												
Fatigue	22	61.44 (9.88)	33.7, 75.8	3.45 (0.86)	0.51	**<0.01**	14	64.93 (8.11)	48.6, 75.8	3.64 (1.01)	0.60	**<0.01**
Anxiety	22	60.27 (8.94)	40.3, 77.9	2.86 (0.83)	0.27	0.12	18	63.12 (7.18)	48, 73.3	3.06 (1.16)	0.39	**0.04**
Pain interference	19	63.87 (7.30)	49.9, 77.0	3.47 (0.84)	0.56	**<0.01**	11	63.86 (7.97)	54.1, 77.0	3.55 (0.93)	0.50	0.07
Cognitive function 4a												
Difficulty remembering things	19	37.01 (9.99)	25.0, 61.1	3.11 (0.99)	-0.54	**<0.01**	10	39.85 (7.97)	32.9, 61.1	3.1 (1.2)	-0.08	0.77
Brain fog	15	44.67 (7.47)	25.0, 54.6	2.4 (0.83)	-0.19	0.39	11	40.21 (8.03)	25.0, 54.6	2.91 (1.22)	-0.34	0.18
Difficulty paying attention	14	39.28 (9.08)	25.0, 61.1	3.00 (0.88)	-0.42	0.06	7	38.54 (6.84)	25.0, 47.3	3.14 (1.07)	0	1

PROMIS® 29+2 domains were excluded if <5 participants set an HRO baseline on the 0-5 severity scale OR if there was no appropriate corresponding HRO symptom. Values in purple indicate correlations were statistically significant.
*For cognitive function, mean PROMIS T-scores below 50 denote functional impairment, for all other measures, scores above 50 indicates severity.

FIGURE 1: Scatter Plot of Relationship between HRO Severity Scores and PROMIS® 29+2 T-scores



- Study findings demonstrated correlations between PRO and HRO scores across domains related to cognition, fatigue, pain interference, and anxiety.
- Fatigue scores showed significant, moderate to strong positive correlations across both cohorts. Both measures suggest elevated fatigue in individuals with sHTG, increasing with TG level.
- Cohort B anxiety scores showed a mild, but significant positive association, while Cohort A's scores showed a trending positive association. Both measures indicate anxiety increased with TG level.
- For Cohort A, pain interference PROMIS scores were significantly and moderately associated with HRO pain severity scores, while Cohort B showed a positive but non-significant trend.
- Cognitive function was compared to three HRO symptoms.
  - Compared with difficulty remembering things, Cohort A showed a significant, moderate negative association, while Cohort B showed no significant cohort-level association. Collapsing across both cohorts, greater difficulty remembering things was associated with greater impairment in cognitive function (i.e., lower) PROMIS sores (τ = -0.38, p = 0.01).
  - Difficulty paying attention and brain fog showed no meaningful association with cognitive function PROMIS scores.
  - Notably, cognitive function PROMIS scores are significantly below (greater than one SD) the norm in this population.
- The majority of participants (80% of Cohort A and 57% of Cohort B) reported having never experienced an AP episode.

CONCLUSIONS

- Study findings demonstrated correlations between PRO and HRO scores across domains related to cognition, fatigue, pain interference, and anxiety.
- Participants report managing considerable symptom burden across these measures, particularly cognitive function, at enrollment.
- These results revealed symptom burden among adults with sHTG beyond acute pancreatitis across multiple measures of burden.

DISCLOSURES

ASK and MVL are employees of Ionis Pharmaceuticals and own company stock; WW is an independent contractor to Ionis; SM, HA, AB, SV and AH are employees of Folia Health, which is contracted to conduct this research.

REFERENCES

1. Baass, A., Paquette, M., Lam, O., Hofer, K., Collet, J., & McClain, M. R. (2025). Prevalence, incidence, and definition of severe hypertriglyceridemia: A comprehensive review and weighted summary. *Journal of clinical lipidology*, *19*(6), 1550–1563. https://doi.org/10.1016/j.jacl.2025.08.012
2. Patel, R. S., Pasea, L., Soran, H., Downie, P., Jones, R., Hingorani, A. D., Newly, D., Denaxas, S., Hemingway, H. (2022). Elevated plasma triglyceride concentration and risk of adverse clinical outcomes in 1.5 million people: a CALIBER linked electronic health record study. Cardiovascular diabetology, 21(1), 102. https://doi.org/10.1186/s12933-022-01525-5

contact: ntsao@ionis.com