Initial psychometric evaluation of the Adult Symptom Severity and Impacts Scale (PKU-SSIS) using an interim data cut from the OPAL study

P029

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Background

- Phenylketonuria (PKU) is a genetic disorder affecting phenylalanine metabolism, leading to severe intellectual and neurological impairments if untreated[1]
- The 22-item PKU Symptom Severity and Impacts Scale (PKU-SSIS) was created to provide a holistic view of the impact of PKU on patients' emotional, cognitive, and physical well-being, where previous tools have largely concentrated on the implications of dietary management.[2] Content validity of the PKU-SSIS has been previously established[3]
- This study uses an interim data cut (December 2022) of OPAL, a Phase 4 multicenter observational study evaluating the real-world outcomes of pegvaliase in people with PKU, to assess the initial psychometric performance of the adult PKU-SSIS

Methods

- Adult patients with PKU (aged ≥16 years) were eligible for inclusion in OPAL if they had blood Phe levels >600 µmol/L and were either currently receiving or initiating pegvaliase at study enrollment
- Several Clinical Outcome Assessments were administered at baseline and at weeks 24, 48, and 96: the Adult PKU Symptom Severity and Impacts Scale (PKU-SSIS), PKU-Quality of Life scale (PKU-QoL), Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form (QLES-Q-SF), 5-level EQ-5D version (EQ-5D-5L), and the patient and clinician global impression scales for symptom severity and change (PGI-S/CGI-S and PGI-C/CGI-C)
- Lower PKU-SSIS scores (on a scale of 0 to 100) are indicative of lesser symptom severity and impacts
- Several aspects of psychometric validity were evaluated. Completion rates were determined by dividing the number of evaluable scores of the PKU-SSIS by the number of individuals in the sample for a given period. Baseline score distribution was reviewed for signs of ceiling or floor effects
- Internal consistency was evaluated by examining Pearson's R correlations between items across all timepoints
- Convergent validity was assessed through correlations (Pearson's R) at baseline and week 24 between PKU-SSIS responses and scores with expected relationships (see **Table 2**)

Results

- At the time of the interim data cut (December 2022), 46 participants had been enrolled. Baseline demographics are shown in **Table 1**. In this interim data cut, most patients had not reached the week 96 study end
- The number of available PKU-SSIS total scores were baseline (n=45), week 24 (n=32), week 48 (n=20), and week 96 (n=8)

Table 1. Patient sample characteristics

Characteristic	Statistic (N=46)
Mean age (years)	30.3
% Female	39%
Race	91% white
Baseline blood Phe µmol/L, mean (SD)	1033 (264)

Item completion

- Response rates were consistently high across all time points: 98% of participants had a PKU-SSIS total score at baseline and 100% at all follow-up visits, indicating strong participant engagement and reliable data collection

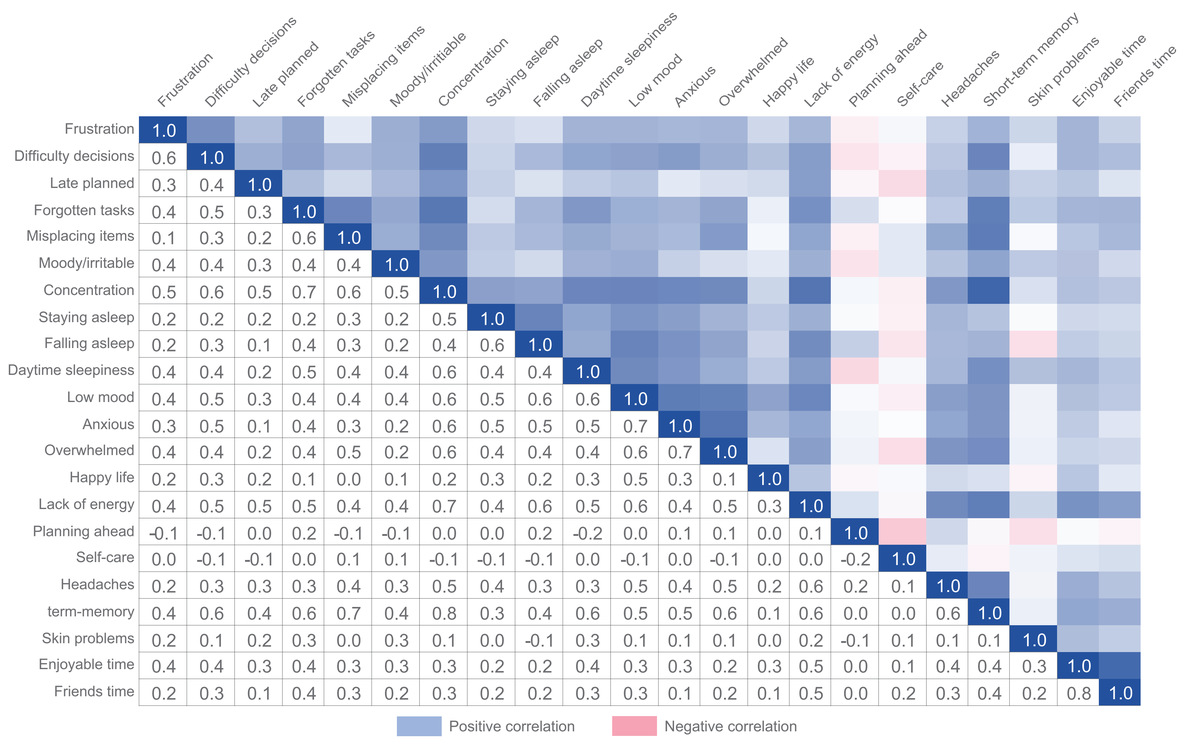
Baseline item distribution

- Item distribution was analyzed by response category, revealing a wide range of responses, with total scores ranging from 7 to 73 on the 0–100 scale, reflecting variability in symptom severity and impacts reported. This range suggests that the PKU-SSIS can distinguish varying symptom burden across individuals

Internal consistency

- Item-level correlations within the PKU-SSIS supported internal consistency, with the majority (85%) of inter-item correlations being moderate (r >0.2), and a substantial proportion (38%) considered high (r >0.5) (**Figure 1**)

Figure 1. Correlation heatmap between PKU-SSIS items



Convergent validity

- Convergent validity was supported through moderate to strong correlations between the PKU-SSIS total score and related outcome measures at baseline and week 24 (**Table 2**). Correlations were in the expected directions (except for the CGI-S at baseline), with higher symptom burden associated with lower quality of life and functioning. Sample sizes for the correlations differ due to different follow-up maturity and questionnaire completion rates

Table 2. Correlations with PKU-SSIS total score

Comparison instrument	Baseline		Week 24	
	n	R	n	R
EQ-5D VAS (Expected direction: Negative)	44	-0.32	30	-0.27
PKU-QOL overall impact (Expected direction: Positive)	42	0.51	32	0.32
QLES-Q-SF: Physical health (Expected direction: Negative)	42	-0.47	32	-0.36
QLES-Q-SF: Total score (Expected direction: Negative)	44	-0.64	32	-0.40
QLES-Q-SF: Well-being (Expected direction: Negative)	44	-0.60	32	-0.65
PGI-S (Expected direction: Negative)	45	-0.21	31	-0.47
CGI-S (Expected direction: Positive)	43	-0.13	29	0.51

Conclusions

- These findings provide initial evidence that the adult PKU-SSIS is a valid and reliable tool for assessing the symptom severity and impact of PKU on patients' lives
- A psychometric evaluation with a larger sample size is ongoing to further establish the psychometric properties of the PKU-SSIS, such as establishing a meaningful change threshold

References

1. Hillert A, et al. *Am J Hum Genet* 2020;107(2):234–250. **2.** Regnault A, et al. *Orphanet J Rare Dis* 2015;10:59.
3. Quinn J, et al. *Adv Ther* 2022;39(2):971–991.

Disclosures

This study was funded by BioMarin. Authors MK, SK, and KL are employees and shareholders of BioMarin. OS was an employee of BioMarin during the study period.

Presented at the ACMG Annual Clinical Genetics Meeting: March 18–22, 2025; Los Angeles, CA