Establishing the relationship between the Worst Itch Numerical Rating Scale and EQ-5D utility in patients with primary biliary cholangitis experiencing pruritus: Pooled results from GLIMMER and the PRO validation study

PCR78

Digital poster

SCAN ME

Higher worst daily itch NRS scores, indicating more severe pruritus, have an increasingly negative impact on HRQoL in patients with PBC

Irina Proskorovsky[1], Balazs Dobi[2], Anna Halliday[3]*, Zsofia Kiss[4]

[1]PPD Evidera, Bethesda, MD, USA; [2]PPD Evidera, Budapest, Hungary; [3]GSK, London, UK; [4]GSK, Munich, Germany
*Affiliation at time of study

Background

- PBC is a chronic, progressive, immune-mediated cholestatic liver disease with debilitating symptoms, including cholestatic pruritus[1,2]
- Cholestatic pruritus affects 55–89% of patients with PBC; it has a significant negative impact on HRQoL and is associated with sleep disturbance, fatigue and cognitive impairment[1,3-6]
- Here we explore the burden of pruritus on HRQoL among patients with PBC using pooled data from the Phase 2b GLIMMER study (NCT02966834)[7] and an observational PRO validation study (GSK study 212144)[8]

Aims

- To evaluate the relationship between pruritus severity, measured by WI-NRS, and HRQoL utility outcomes, as assessed by the EQ-5D

Methods

Study population

- GLIMMER (N=147) was a Phase 2b, randomised, double-blind, multidose, placebo-controlled study evaluating the efficacy, safety and tolerability of linerixibat for pruritus in participants with PBC. The study included patients with a mean age of 55.8 years (SD=11.0)[7]
- The PRO validation study (N=141) was an observational, study collecting PRO data over 8 days from participants with pruritus and PBC[8]. Exact age of participants was not collected
- Data were pooled from both studies*

Pruritus and HRQoL assessments

- Pruritus severity was assessed twice daily using a 0–10 WI-NRS where 0 was 'no itching' and 10 was 'worst imaginable itching'[7,8]
  - Worst daily itch score was the higher of the two daily scores
- HRQoL was evaluated using the EQ-5D
  - The EQ-5D assesses dimensions of mobility, self-care, usual activities, pain/discomfort and anxiety/depression[9]
  - Utility values were derived from these responses†

Statistical methods

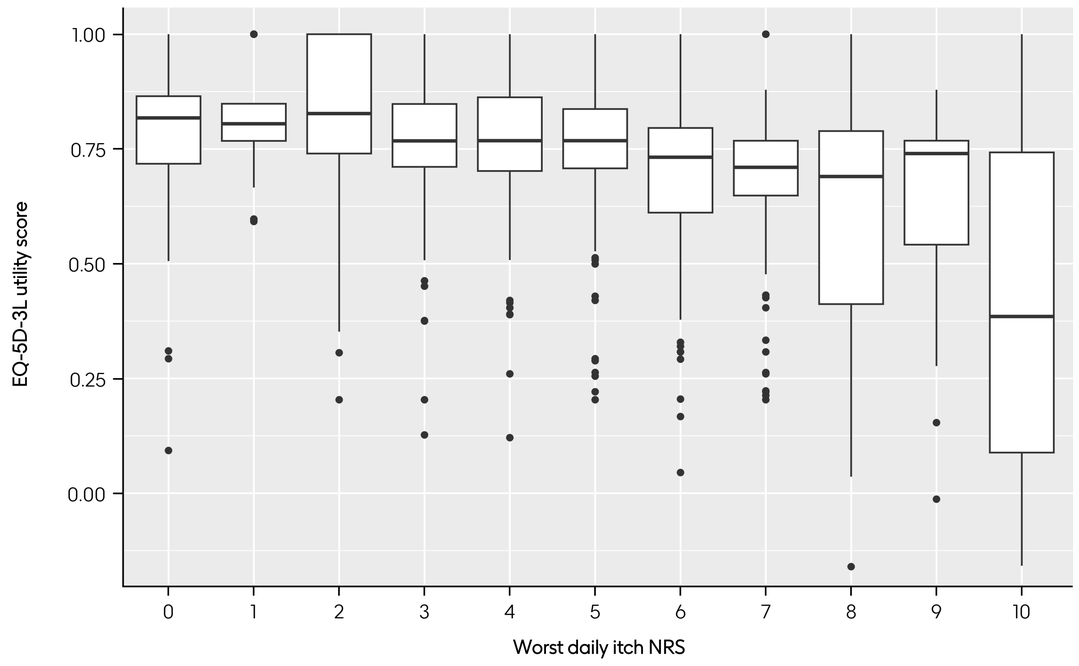
- Boxplots were used to visualise the relationship between EQ-5D utility and WI-NRS scores completed on the same day‡
- Univariate linear mixed models were fitted to explore linearity between EQ-5D utility and WI-NRS
  - Models included EQ-5D utility score as the response variable, WI-NRS as continuous covariate and a random intercept term to account for the clustering of multiple observations for each patient
  - Predictions and residuals were calculated based on the fixed effects of the fitted models and plotted against WI-NRS
- To account for potential non-linearity, a third-degree polynomial model with spline functions including WI-NRS, WI-NRS^2 and WI-NRS^3 terms was fitted
  - This multivariate mixed model was further refined using stepwise selection algorithms and 3-fold cross validation

**Including GLIMMER data from all treatment arms and timepoints from the intent-to-treat population, and all available data from the PRO validation study, where both EQ-5D and WI-NRS were non-missing; †after mapping UK-specific EQ-5D-3L utility values ranged from −0.594 to 1, with higher scores indicating better health; ‡pooled timepoints included GLIMMER Day 1, Weeks 4 and 16, and end of treatment or study withdrawal visits, and Days 1 and 8 of the PRO validation study. For Day 1 in GLIMMER, since no itch NRS was collected in the morning, evening scores from that day were used.*

Results

- The pooled dataset included 694 observations of EQ-5D utility and WI-NRS scores from 287 patients across multiple timepoints
- The overall mean (SD) EQ-5D utility and WI-NRS scores were 0.72 (0.21) and 4.51 (2.59), respectively
- Boxplots indicated a non-linear worsening of EQ-5D utility scores with increasing WI-NRS scores (**Figure 1**)

Figure 1: **Boxplot of EQ-5D-3L utility versus WI-NRS**



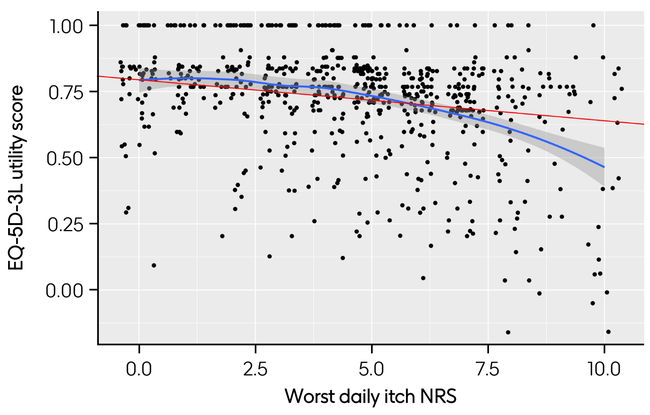
WI-NRS	0	1	2	3	4	5	6	7	8	9	10
Observations, n	56	52	57	85	83	105	90	78	46	23	19
Mean (SD) EQ-5D-3L utility score	0.782 (0.193)	0.825 (0.115)	0.793 (0.194)	0.772 (0.179)	0.762 (0.179)	0.741 (0.170)	0.682 (0.186)	0.670 (0.181)	0.593 (0.285)	0.619 (0.241)	0.420 (0.365)

Univariate linear mixed model of the relationship between EQ-5D utility scores and WI-NRS

- Residual plots indicated a non-linear worsening of EQ-5D utility scores with increasing WI-NRS scores (**Figure 2**)

Figure 2: **Univariate linear mixed model of EQ-5D-3L utility versus WI-NRS**

Smoothed utility score over time (blue curve) versus prediction from fixed effects of linear mixed model (red line)



Fixed effect*	Estimate	Standard error	P-value
(Intercept)	0.794	0.015	<0.001
WI-NRS	−0.015	0.003	<0.001

**T values are: 51.376 (Intercept); −5.921 (WI-NRS). df values are: 602.022 (Intercept); 652.651 (WI-NRS).*

Polynomial mixed models of the relationship between EQ-5D utility and WI-NRS scores

- The EQ-5D utility model including all third-degree polynomial spline functions of WI-NRS as linear predictors indicated potential overfitting, with all WI-NRS degree terms non-significant (**Table 2A**)
- Model selection was performed by multiple stepwise algorithms based on Akaike information criterion
  - The model with only WI-NRS^3 as predictor was the best-fitting model (**Table 2B**) and was selected as the base case model (WI-NRS and WI-NRS^2 were eliminated)
- The model's predictive ability was confirmed via average goodness-of-fit metrics **(Table 2B)**
  - Three-fold cross-validation confirmed that the base case model had the best performance (based on mean squared error [0.03934] and R^2 [0.10392])
  - Predictions for the best-fitting model are shown in **Figure 3**

Table 2: **Polynomial mixed models for EQ-5D-3L utility by WI-NRS**

A. Third-degree polynomial model

Predictors	Estimate	Standard error	P-value
(Intercept)	0.77479	0.02170	<0.001
WI-NRS	−0.01161	0.01783	0.515
WI-NRS^2	0.00236	0.00442	0.593
WI-NRS^3	−0.00034	0.00031	0.270

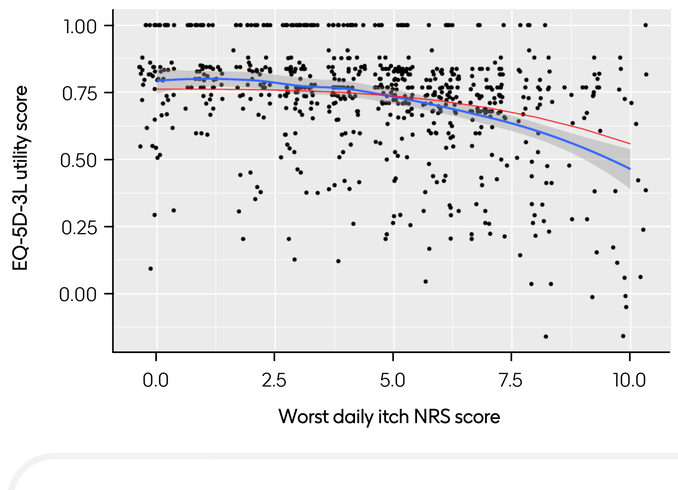
B. Reduced best-fitting model: fixed effects*

Fixed effect	Estimate	Standard error	P-value
(Intercept)	0.76168	0.01151	<0.001
WI-NRS^3	−0.00020	0.00003	<0.001

**T values are: 66.187 (Intercept); −6.636 (WI-NRS). df values are: 385.603 (Intercept); 656.407 (WI-NRS).*

Figure 3: **Polynomial mixed model of EQ-5D-3L utility versus WI-NRS**

Smoothed utility score over time (blue curve) versus prediction from fixed effects of the base case model (red curve)



Study limitations

- GLIMMER used EQ-5D-5L (5 level scale) and the PRO validation study used EQ-5D-3L (3 level scale); to ensure compatibility across the studies, UK-specific EQ-5D-3L utility index scores were derived by 5L to 3L crosswalk algorithm[10] in the GLIMMER study[7] and 3L value set in the PRO validation study[8]
- Exact age of patients enrolled in the PRO validation study was not known and therefore age couldn't be included in the regression models. Thus, to estimate EQ-5D-3L UK utility for the cost utility analyses using this mapping, additional age adjustment is recommended

Conclusions

- The relationship between EQ-5D utility and WI-NRS was not linear, based on the pooled data from the GLIMMER and PRO validation studies
- The relationship highlighted that higher WI-NRS scores, indicating more severe pruritus, have an increasingly negative impact on HRQoL
- A third-degree polynomial model proved to be the best-fitting model to describe the relationship between EQ-5D utility and WI-NRS

Abbreviations

df, degrees of freedom; HRQoL, health-related quality of life; PBC, primary biliary cholangitis; PRO, patient-reported outcome; SD, standard deviation; WI-NRS, Worst Itch Numerical Rating Scale

References

1. Mayo MJ, et al. *Dig Dis Sci.* 2023;35704252
2. Lindor KD, et al. *Hepatology.* 2019;69(1):394–419
3. Gungabissoon U, et al. *BMJ Open Gastroenterol.* 2024;11:e001287
4. Hegade VS, et al. *Clin Gastroenterol Hepatol.* 2019;17(7):1379–87.e3
5. de Veer RC, et al. *Hepatol Res.* 2023;53(5):401–8
6. Lindor KD, et al. *Gastroenterology.* 1994;106(5):1284–90
7. Levy C, et al. *Clin Gastroenterol Hepatol.* 2023;21:1902–12
8. Currie BM, et al. ISPOR Europe 2024; Abstract PCR123
9. EuroQol Research Foundation. EQ-5D-5L User Guide. https://euroqol.org/publications/user-guides (Accessed 27 August 2025)
10. Hernández Alava M, et al. *Pharmacoeconomics.* 2023;41:199–207

Acknowledgements

Editorial support (in the form of writing assistance, under the direction and guidance of the authors, collating and incorporating authors' comments for each draft, assembling tables and figures, grammatical editing and referencing) was provided by Gillian Wallace, MSc, of Fishawack Indicia Ltd, UK, part of Avalere Health, and was funded by GSK.

Disclosures

These studies were funded by GSK (study 201000 and 212144). **IP** and **BD** are employees of Evidera, which received funding from GSK to carry out this study. **AH** was previously employed by GSK and holds financial equities in GSK and Novartis. **ZK** is an employee of GSK and holds financial equities in GSK.

Presenting author: Irina Proskorovsky, Irina Proskorovsky@thermofisher.com