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# Conclusions

- Adults with primary biliary cholangitis (PBC) and moderate-to-severe pruritus experience a significant burden on health-related quality of life and impaired activity compared to those with no/mild itch
- Patient voice results highlight the unrelenting nature of itching and its negative impact on emotional/social health and productivity
- These results emphasize the need for safe and efficacious PBC treatments that can improve pruritus

# Plain Language Summary

- Patients with primary biliary cholangitis often experience itching, which can dramatically impair quality of life
- Participants with primary biliary cholangitis completed questionnaires to assess the impact of itching on their quality of life, activity, and work productivity
- A subset of participants with moderate/severe itch also answered open-ended questions via a voice response system
- Participants with primary biliary cholangitis and moderate/severe itch have reduced quality of life and activity compared to those with no/mild itch, emphasizing the need for a treatment that provides lasting relief from primary biliary cholangitis-related itching and prevents liver damage

## Introduction

- Primary biliary cholangitis (PBC) is a progressive chronic inflammatory liver disease characterized by inflammation and destruction of the bile ducts<sup>1-3</sup>
- PBC-related pruritus affects about 70% of patients<sup>4</sup>
- Pruritus can be extremely debilitating and may cause sleep, fatigue, pain, and social isolation issues<sup>5,6</sup>
- PBC treatment options, including ursodeoxycholic acid (UDCA) and obeticholic acid (OCA), have not shown clinical benefit for pruritus<sup>7,8</sup>
- Research that documents the burden associated with pruritus among the patient population with PBC is limited
- This real-world, cross-sectional, mixed-methods study assessed the impact of pruritus on patients' health-related quality of life (HRQoL), activity, and work productivity

# Objectives

 The objectives of this study were to 1) assess how patients characterize pruritus in PBC and its impact on their daily lives and quality of life; and 2) capture the patients' voices on how they describe living with PBC and associated pruritus, and its impact on their daily life/quality of life

## Methods

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#### **Study Design**

- Adults with PBC were recruited from a PBC patient advocacy group and physician panels between December 2023 and March 2024 (Figure 1)
- Inclusion criteria: PBC diagnosis, adults ≥18 years of age, currently treated with UDCA or OCA, provided informed consent, living in the USA
- Exclusion criteria: enrolled in a clinical trial for PBC treatment, unable to read/understand English, no access to a mobile device or computer, affiliated with CymaBay Therapeutics
- Enrolled participants were categorized based on the Pruritus Numerical Rating Scale (NRS) into no/mild pruritus (NMP; NRS <4) vs moderate/severe pruritus (MSP; NRS ≥4)
- Participants completed one round of multiple questionnaires (key endpoints) of validated patient-reported outcome measures
- A subset of the MSP group answered open-ended questions via voice response on how participants describe living with PBC/pruritus and the impact on their daily lives
- Differences were analyzed using regression models adjusting for age, gender, ethnicity, and treatment

### Figure 1. Study Population and Enrollment Patients recruited rough a PBC patie hrough a physic Consent not provided Not enrolled advocacy group Potential participants sent a link to screener (n = 159)(N = 90)Study completion Participants in no/mild pruritus Participants complete qualitative voice ıestionnaire (n = 21

#### **Key Endpoints**

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- Primary Biliary Cholangitis-40 (PBC-40)
- Functional Assessment of Chronic Illness Therapy

  —Fatigue Scale (FACIT-Fatigue)
- Chronic Liver Disease Questionnaire-PBC (CLDQ-PBC)
- 5-Dimension Itch Scale (5-D Itch)
- European Quality of Life 5 Dimensions 5 Level (EQ-5D-5L)
- Work Productivity and Activity Impairment Questionnaire (WPAI)

### Results

#### Table 1. Demographic Characteristics

Variable	No/Mild Pruritus Group (n = 40)	Moderate/Severe Pruritus Group (n = 50) 52.1 (12.2)	
Age, years, mean (SD)	56.7 (12.1)		
Gender, n (%)			
Female	34 (85) 40 (80)		
Male	5 (13)	10 (20)	
Nonbinary	1 (3)	0	
Ethnicity, n (%) <sup>a</sup>			
White	31 (78)	36 (72)	
Hispanic or Latino	3 (8)	8 (16)	
Black or African American	3 (8)	5 (10)	
Native American or American Indian	1 (3)	0	
Asian/Pacific Islander	0	3 (6)	
Other <sup>b</sup>	1 (3)	0	
Pruritus NRS, mean (SD)	1.3 (1.2)	6.2 (1.7)	
Cirrhosis, n (%)	7 (18)	10 (20)	

• The sample included 40 NMP and 50 MSP participants (**Table 1**)

 Participants were mostly female; demographic characteristics were generally balanced between the NMP and MSP groups

### Results

Table 2. Unadjusted Mean Scores for HRQoL and Work Productivity Scales Among Individuals With Moderate/Severe Pruritus and No/Mild Pruritus

Outcome, Mean	Score Ranges	Range Description	No/Mild Pruritus Group (n = 40)	Moderate/Severe Pruritus Group (n = 50)
PBC-40 domain scores				
Symptoms	7–35		17.9	20.9
Itch (n = 33) <sup>a</sup>	3–15		5.6	8.9
Fatigue	11–55	Higher scores	30.2	37.4
Cognitive	6–30	represent lower QoL	14.8	19.1
Emotional	3–15		9.2	10.4
Social	10–50		29.3	35.6
FACIT-Fatigue score				
Total	0–52	Higher scores represent less fatigue	32.2	23.9
CLDQ-PBC score				
Total	1–7	Higher scores represent better health	4.9	3.9
5-D Itch score				
Total	5–25	Higher scores represent lower QoL	9.7	14.4
EQ-5D-5L score				
EQ-5D index	-0.573 to 1.000	Higher scores represent	0.78	0.63
EQ-VAS	1–100	higher QoL	64.4	60.8
WPAI scores				
% activity impairment due to PBC	0–100		36.3	56.6
% work time missed due to PBCb	0–100	Higher scores represent	5.8	9.8
% impairment while working due to PBCb	0–100	greater impairment	32.4	46.5
% overall work impairment due to PBCb	0–100		35.2	49.7

Based on the unadjusted mean scores for HRQoL measures, participants in the MSP group had worse QoL scores than in the NMP group, as measured by the PBC-40, FACIT-Fatigue, CLDQ-PBC, 5-D Itch, and EQ-5D scales (Table 2)

• Among employed participants, unadjusted WPAI scores were impaired to a greater extent in the MSP group compared with the NMP group

#### Table 3. Linear Regression Models of the Association Between MSP With HRQoL and Work Productivity Among Participants With PBC<sup>a</sup>

Coefficient

Outcome	Score Ranges	Range Description	(MSP vs NMP Group) <sup>b</sup>	95% CI, <i>P-</i> Value
PBC-40 domain scores				
Symptoms	7–35		2.26	(0.55, 3.97), .011
Itch	3–15	Higher scores represent lower QoL	4.18	(2.91, 5.45), <.001
Fatigue	11–55		7.24	(3.63, 10.85), <.001
Cognitive	6–30		3.53	(1.43, 5.63), .001
Emotional	3–15		0.72	(-0.46, 1.90), .239
Social	10–50		4.18	(0.67, 7.69), .022
FACIT-Fatigue score				
Total	0–52	Higher scores represent less fatigue	-8.26	(-12.85, -3.67), <.001
CLDQ-PBC score				
Total	1–7	Higher scores represent better health	-0.87	(-1.38, -0.36), <.001
5-D Itch score				
Total	5–25	Higher scores represent lower QoL	4.87	(3.56, 6.18), <.001
EQ-5D-5L score				
EQ-5D index	-0.573 to 1.000	Higher scores represent	-0.14	(-0.24, -0.04), .005
EQ-VAS	1–100	higher QoL	-3.58	(-11.01, 3.85), .348
WPAI scores <sup>c</sup>				
% activity impairment due to PBC	0–100		0.20	(0.08, 0.32), <.001
% work time missed due to PBC <sup>d</sup>	0–100	Higher scores represent	0.04	(-0.06, 0.14), .349
% impairment while working due to PBCd	0–100	greater impairment	0.17	(-0.03, 0.37), .236
% overall work impairment due to PBCd	0–100		0.13	(-0.07, 0.33), .204

<sup>a</sup>Adjusting for age, gender, ethnicity, and UDCA and OCA treatment. <sup>b</sup>As an example, a regression coefficient of 2.26 indicates that being in the MSP group is associated with an increase in the PBC-40 index symptom score of 2.26 points (scores range from 7 to 35, with higher scores indicating worse QoL). WPAI scores were analyzed as fractions, so 0.20 represents 20%. WPAI scores (except for the Activity Impairment score) were only calculated for participants who indicated being currently employed (NMP, n = 21; MSP, n = 17). 5-D Itch, 5-Dimensions Itch; CLDQ, Chronic Liver Disease Questionnaire EQ-5D, European Quality of Life 5 Dimensions; EQ-5D-5L, European Quality of Life 5 Dimensions 5 Levels; EQ-VAS, European Quality of Life Visual Analog Scale; FACIT-Fatigue, Functiona Assessment of Chronic Illness Therapy-Fatigue; HRQoL, health-related quality of life; MSP, moderate/severe pruritus; NMP, no/mild pruritus; OCA, obeticholic acid; PBC, primary biliary cholangitis; PBC-40, Primary Biliary Cholangitis—40; QoL, quality of life; UDCA, ursodeoxycholic acid; WPAI, Work Productivity and Activity Impairment Questionnaire.

- Compared with the NMP group, and after controlling for confounders (including age, gender, ethnicity, and UDCA and OCA treatment), the MSP group had statistically significantly worse PBC-40 mean scores in Symptoms, Itch, Fatigue, Cognitive, and Social (all P < .05) but not Emotional (P = .239) domains (**Table 3**)
- The MSP group had worse scores on the FACIT-Fatigue (P < .001) and 5-D Itch (P < .001) scales, and lower CLDQ-PBC total (P < .001) and EQ-5D Index (P = .005) scores
- The MSP group reported statistically significantly greater WPAI activity impairment compared with the NMP group (P < .001)
- The MSP group reported statistically lower work status compared with the NMP group (42% vs 53%; data not shown) Among employed participants, the MSP group reported a greater probability of impairment while working and overall work impairment due to PBC
- Differences in these scores were not significant, possibly because less than half of participants were employed

# **Patient Voice Quotes**

#### **Unrelenting Itching**

Most participants described their pruritus as consistently intense

"The itch that you get from PBC versus a bug bite or poison ivy, you can't satisfy the itch. Scratching it doesn't satisfy it. It comes from the inside out, and you can dig and dig and dig and it just doesn't get satisfied. I have had to teach myself that I need to ignore it the best I can...It's an inside-out [itch] that you can dig and dig, and you can dig yourself to bleed, and it just isn't satisfied."

#### **Social and Emotional Impacts**

Itch can lead participants to self-isolate, avoiding social activities or choosing to stay home

"The itching is so embarrassing because the aftereffects of itching, it looks like sores or bruises. You itch until your skin is raw. So, physically, it doesn't look attractive. Emotionally, it gets you down because of what your body looks like... When you itch so bad, you want to excuse yourself, not being around them [other people]."

Around half of participants believe others are judging them when they are scratching an itch

"It does get in the way, and it does make you want to just hide away from anybody that's able to witness that." It's not any fun, and it's quite debilitating, and it just makes you feel isolated in a sense."

Several participants feel embarrassed itching in front of others

#### **Productivity Impacts**

- A handful of participants reported that itch impacts their work by distracting them and making it "hard to focus" or accomplish tasks
- Night-time itch may compound this by keeping them awake, leaving them tired the next day
- In severe instances, itch forces them to leave work or use paid time off to stay home

"It's hard to sleep...And then...I'm itching while at work, which makes it very hard to focus, it's very distracting, and very hard to get anything done. So, I'm less productive."

# **Study Limitations**

- The key limitations of this study include the potential for self-selection bias, which may have resulted in a sample that is not representative of the general PBC population
- Disease stage was not adjusted for, and its influence on HRQoL may be unaccounted for
- Additionally, recall bias may have affected the accuracy of the self-reported data, and social desirability bias could have influenced participants' responses
- Generalizability to the broader PBC population may also be limited due to the small sample size

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