

Background

- Primary biliary cholangitis (PBC) is an autoimmune cholestatic disease affecting the liver that has debilitating impacts on individuals' health and quality of life.
- PBC is characterized by progressive destruction of the liver's bile ducts that leads to impaired bile flow (cholestasis) and accumulation of toxic bile acids (Selmi et al. 2011).
- PBC can progress to cirrhosis and eventually liver failure (Poupon 2010).
- As a rare disease, PBC prevalence is uncertain (Dahlqvist et al. 2017). However, it has been estimated between 6.7 and 940 cases per million-population (depending on age and sex) (Kumagi 2008).
- Itch (pruritus) has been one of the most common complaints amongst PBC patients (Selmi et al. 2011). Occurring in 20% to 70% of PBC patients (Selmi et al. 2011), pruritus can impact sleep and even lead to suicidal ideation (Younossi et al. 2000).

Objectives

- A cross-sectional, qualitative study involving individual, in-person qualitative interviews was conducted with PBC patients experiencing itch.
- The study objectives were:
 - To understand PBC patients' itch experience and its impact
 - To examine the content validity of three existing pruritus patient-reported outcome (PRO) measures: Itch Numeric Rating Scale (NRS); 5-D Itch Scale, and the Itch Visual Analog Scale (VAS)
 - To inform the endpoint selection for a Phase III clinical trial focusing on itch

Methods

- Institutional review board (IRB) approval was obtained in both the United States (US) and Canada.
- Participants were identified through PBC patient advocacy groups and had to have a score of ≥ 4 on the Itch NRS.
- A standardized semi-structured interview guide was used to conduct the interviews. Participants completed three PRO measures:
 - The NRS Itch is a one-item scale designed to capture patient's itching on an eleven-point scale ranging from 0 ('No itching') to 10 ('Worst possible itching') with a 24-hour recall period.
 - The 5-D Itch Scale is a brief but multidimensional questionnaire designed to be a measure of itch with five dimensions: degree, duration, direction, disability, and distribution. It has a 2-week recall period.
 - The Pruritus VAS is a 100-cm line (0 (no itching) to 100 (worst possible itching)) which participants mark to describe the severity of their pruritus. It has a 24-hour recall period.
- Participants were engaged in one-on-one, semi-structured concept elicitation and cognitive interviews conducted during a PBC patient conference (as well as at locations convenient to participants).
 - During the concept elicitation portion, participants described their PBC itch experience.
 - During the cognitive interview portion, participants completed an electronic version of the Itch NRS and 5-D Itch Scale and reviewed a paper version of the Itch VAS. Participants were then asked questions assessing their comprehension of each instrument.
- All interviews were audio-recorded, transcribed, coded, and analyzed.

Results

Participant Sample Description

- Table 1 presents demographic information on the 12 adult PBC participants with itch who were interviewed.
- Fifty-eight percent of participants (n=7) were from locations throughout the US, while 42% of participants (n=5) were from locations throughout Canada.
- All participants reported receiving medication to manage their PBC. Most participants described their PBC severity as "moderate," "moderate and severe," or "severe."

Table 1: Participant-reported Sociodemographic and Health Characteristics

Characteristics	Total Sample (N=12)
Mean age (SD)	60.3 (13)
Female gender, n (%)	11 (92%)
Racial background, n (%)*	
White	12 (100%)
Black or African American	1 (8%)
Asian	1 (8%)
American Indian or Alaska Native (US only)	1 (8%)
Number of years living with PBC since date of diagnosis	
<1	4 (33%)
1-5	2 (17%)
6-10	1 (8%)
≥ 11	5 (42%)
How often do you experience itching for PBC, n (%)	
Once a day	4 (33%)
A few times a day	6 (50%)
A few times a week	1 (8%)
Missing ¹	1 (8%)
Highest level of education, n (%)	
Some college	3 (25%)
College degree	6 (50%)
Postgraduate degree (US only)	3 (25%)
Yes, prescribed medications for treatment or management of PBC related itch?	12 (100%)

* Not mutually exclusive.
¹Participant left this answer choice blank

PBC Participant Experience with Itch

- Participants described their itch as feeling like something crawling under the skin, having an involuntary reaction to scratch, or a tingling or creepy sensation that often wasn't relieved with scratching (Table 2).

Table 2: Participant Experiences with Itch

Crawling	001-009: "It feels sort of like ants crawling around in your skin or something. It's really hard to describe and a lot of folks have trouble with describing that itch. I seem to have it on my palms the most. My palms are constantly, well, you can see..." 001-004: "I know with my ear and my arms it's like crawling like I've got to scratch because there's something on my skin. With my feet, it's almost more like not a burn but something I've got to get off my foot, like something's there." 001-010: "Like bugs crawling on you, kind of like you've got to rub it to make it quit tingling. I guess that's the best way I would describe it."
Creeping	001-003: "It seems like it just kind of creeps, it's like a creepy feeling. It tends to feel like it's a sudden itch and then you scratch it, goes away and then you have to go back to it again. It's in pretty well the same spot."

- Fifty percent of participants reported experiencing PBC-related itch a few times a day, while an additional 33% reported experiencing itching once a day.
- Table 3 provides participant quotations describing itch frequency, severity, and duration.

PBC Participant Impact from Itch

- All participants reported itch impacting their lives. The most commonly reported impacts from itch were about sleeping, daily activities, and social functioning from scratching in public or having sores on their skin (Figure 1).

Results

Figure 1: Participant Descriptions of Itch Impacts

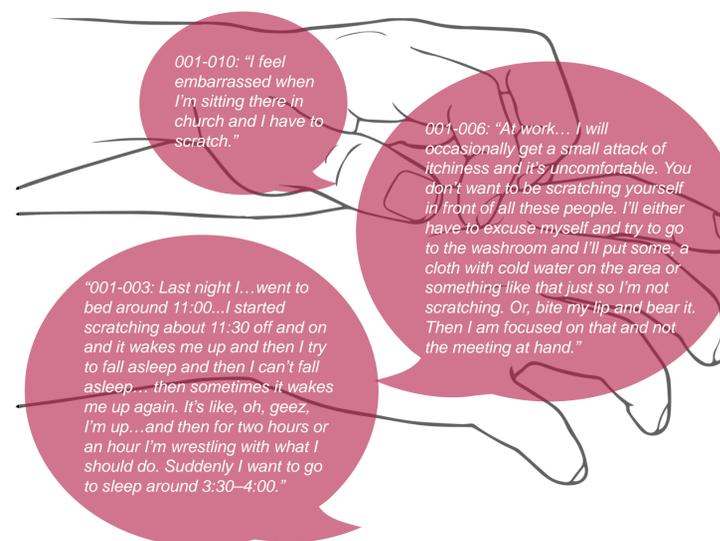


Table 3: Participant Responses Describing Itch Frequency, Severity, and Duration

Itch Frequency	001-014: "Every night, in the middle of the night, and—like it starts like in the evening and it's just continuous. And then it seems...when [it]...gets to be morning, it lets up some, but I still have itching." 001-010: "I'm so used to it, but it's a daily thing. I'd say at least 40 times a day I'm scratching something, usually my head."
Itch Severity	001-005: "Oh, it's an extreme itch. I'm a very heavy sleeper but the itch can wake me up during the night.... It seems like it's internal because you can scratch and scratch but the itch isn't relievable. I break out in sores... on my arms and sores on my legs, and bleeding of course, but the itch is extreme."
Itch Duration	001-002: "All the time, it just varies. Sometimes, like right now it's not terrible but I still will feel the need to itch some"

PBC Participant Experience Completing Itch PROs

Itch NRS

- Most participants (92%) demonstrated a clear understanding of the NRS instructions.
- All participants reported that the NRS question was easy to answer. Most participants (82%) responded that the 0 to 10 response scale was appropriate.
- For the remaining participants, at least a 3-point reduction (17%), a 1- to 2-point reduction (17%), a half-point reduction (8%), or any level of reduction (8%) on the scale would reflect a meaningful change.
- Half of the participants (50%) described a meaningful change in itch on the NRS as at least a 4- to 5-point reduction on the scale with a decrease in their itch intensity to "almost symptom-free" or "almost no itch," or an improvement in their quality of life (Table 4).

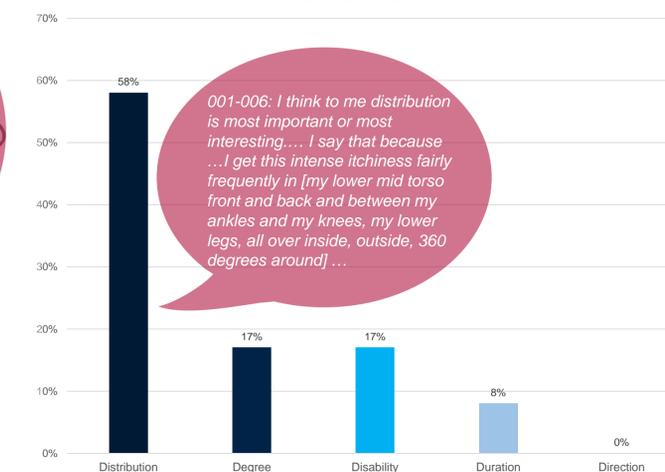
Table 4: PBC Participant Evaluation of Meaningful Change

Meaningful Change of NRS	INTERVIEWER: So, if you're at that five and above stage for itch going into the clinical trial, what would be your expectation if the treatment worked, what number would you then be? 001-005: "I mean even if...I was at number ten, if [a treatment] brought me down to number five, I'd be feeling good about it. The real solution would be getting down to number one."
Meaningful Change of VAS	INTERVIEWER: If you were given treatment for your itch at the present 60, on this scale what would be a meaningful change for you? 001-006: Sure. I think, again, very similarly would be 30 or less would make the change, maybe on this one 35 [laughter] I guess. Yeah, certainly in that range or lower makes it a meaningful change.

5-D Itch

- Figure 2 outlines the 5-D Itch dimension most important to PBC patients.

Figure 2: PBC Patient Evaluation of Most Important 5-D Itch Dimensions



Itch VAS

- When completing the Itch VAS, 67% of participants understood that they had to mark a line or an X to indicate the severity/rating/experience of worst possible itch in the past 24 hours.
- Participants reported a meaningful change on the VAS ranging from a 5- to 55-point (average 30-point) reduction.

Conclusions

- This study identified itch as an important symptom for PBC patients with multiple impacts.
- Study results were used to inform the selection of PROs for a Phase III clinical trial.
- Participants considered the Itch NRS, 5-D Itch, and Itch VAS relevant instruments for assessing itch.
- Participants found that the following would reflect a meaningful change in treatment effectiveness: a 3- to 5-point reduction in the Itch NRS score (>66.7%) and a 5- to 55-point (average 30-point) reduction in the itch VAS (100%).

References

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