Pruritus in primary biliary cholangitis: the symptom that drives quality of life

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Primary biliary cholangitis (PBC) is a chronic, progressive autoimmune liver disease that, while often asymptomatic in its early stages, can manifest with debilitating symptoms. Among these, pruritus stands out as a particularly vexing and pervasive issue, profoundly affecting patient quality of life. Understanding the true burden of this symptom is important for clinicians managing PBC patients.

KEY TAKEAWAYS

- The Pivot: Patient registries are crucial for capturing the real-world impact of symptoms like pruritus in rare diseases such as PBC, moving beyond trial data.
- The Data: The PBC Ireland patient registry aims to enroll 250 patients, collecting comprehensive data on symptoms, treatments, and quality of life.
- The Action: Clinicians should actively screen for and address pruritus in PBC patients, recognising its disproportionate effect on daily functioning and overall well-being.

Primary biliary cholangitis (PBC) is a chronic, autoimmune liver disease characterised by progressive destruction of small bile ducts within the liver, leading to cholestasis and eventually cirrhosis. While ursodeoxycholic acid (UDCA) remains the cornerstone of treatment, it primarily targets biochemical markers and disease progression, often leaving debilitating symptoms like pruritus inadequately managed. This persistent, often severe itching is not merely an annoyance; it is a central driver of impaired quality of life for many patients, leading to sleep disturbances, fatigue, and psychological distress.1

The challenge in fully appreciating the impact of pruritus in PBC stems from a lack of comprehensive, real-world data. Clinical trials, by their nature, often focus on surrogate endpoints or highly selected patient populations, which may not fully capture the heterogeneous experience of patients in routine clinical practice. This gap in evidence, care, and policy has prompted initiatives like the PBC Ireland patient registry, designed to provide a national platform for understanding the disease's true burden.1

The Registry's Purpose and Design

The PBC Ireland patient registry was developed to address important evidence gaps affecting PBC patients across Ireland. This national platform aims to collect detailed, longitudinal data on disease epidemiology, clinical characteristics, treatment patterns, and patient-reported outcomes (PROs). The registry's design is comprehensive, ensuring that it captures a broad spectrum of information relevant to both clinical management and health policy.1

The registry targets an enrolment of 250 patients with a confirmed diagnosis of PBC, representing a significant proportion

of the estimated PBC population in Ireland. Patient recruitment occurs through specialist hepatology clinics across the country, ensuring a diverse representation of disease stages and treatment histories. Each participating patient provides informed consent, allowing for the collection of both retrospective and prospective data.1

Data collection involves a combination of clinical chart review and direct patient questionnaires. Clinical data includes demographics, disease duration, biochemical markers (e.g., alkaline phosphatase, bilirubin), liver histology, imaging results, and details of all PBC-specific treatments, including UDCA, obeticholic acid, and off-label therapies for symptoms. This granular clinical information allows researchers to correlate disease severity and treatment response with patient-reported experiences.1

Patient-reported outcomes are a central component of the registry, specifically designed to quantify the impact of symptoms like pruritus. Patients complete validated questionnaires covering various aspects of quality of life, fatigue, and, importantly, the severity and impact of pruritus. This direct input from patients is vital, as it often reveals burdens not fully appreciated through objective clinical measures alone. The registry uses established PRO instruments to ensure comparability with international studies.1

Capturing the Patient Experience

The emphasis on patient-reported outcomes in the PBC Ireland registry directly acknowledges that symptoms, particularly pruritus, are often the primary drivers of impaired quality of life. While biochemical normalisation is a common treatment goal, patients frequently report persistent symptoms even when liver function tests improve. This disconnect highlights the need for a more holistic assessment that includes the patient's perspective.1

Pruritus in PBC is often described as intractable and can significantly disrupt sleep, leading to profound fatigue. This fatigue, in turn, impacts daily activities, work productivity, and social engagement. The registry's detailed questionnaires aim to capture these cascading effects, providing a clearer picture of how pruritus permeates various aspects of a patient's life. Understanding how routine symptom monitoring with PROs actually improves survival is a growing area of interest in chronic disease management.

The registry also collects data on the management strategies employed for pruritus, including both pharmacological and non-pharmacological interventions. This includes the use of cholestyramine, rifampicin, naltrexone, and sertraline, as well as phototherapy or plasmapheresis in severe cases. By documenting these approaches and their perceived effectiveness from the patient's perspective, the registry can identify areas of unmet need and highlight best practices in symptom management.1

The Irish Context and Broader Implications

The development of a national registry in Ireland for a rare disease like PBC is a significant undertaking. Rare diseases often suffer from fragmented data, making it difficult to establish accurate prevalence, understand disease progression, and evaluate the effectiveness of interventions. The PBC Ireland registry aims to overcome these challenges by creating a centralised, standardised data collection platform.1

The registry's protocol, published in Therapeutic Advances in Rare Diseases, details the methodology for data governance, ethical oversight, and data security. This robust framework ensures that patient confidentiality is maintained while enabling valuable research. The registry adheres to national and international data protection regulations, including GDPR, which is important for sensitive health data.1

The insights gained from the Irish registry will not only inform national healthcare policy but also contribute to the broader international understanding of PBC. By standardising data collection, the registry facilitates future collaborations with other national and international PBC cohorts, allowing for larger-scale analyses and the identification of global trends. This is particularly important for rare diseases, where individual country cohorts may be too small to draw definitive conclusions.1

One of the key benefits of such a registry is its ability to identify disparities in care or access to treatment. If certain regions or patient demographics exhibit poorer outcomes or less effective symptom management, the registry data can highlight these issues, prompting targeted interventions. For instance, if patients in rural areas report higher rates of severe pruritus due to limited access to specialist care, this information can drive policy changes to improve equity.1

Limitations and Future Directions

The open-label, observational nature of a patient registry is an obvious caveat. Unlike randomised controlled trials, registries cannot establish causality between treatments and outcomes. They are designed to describe real-world patterns and generate hypotheses, not to prove efficacy. But, for rare diseases, observational data from registries often provides the only feasible way to gather comprehensive information on disease natural history and treatment effectiveness in diverse populations.1

Another limitation inherent in any registry is the potential for selection bias. Patients who agree to participate may differ from those who do not, potentially skewing the demographic or clinical profile of the cohort. The registry protocol outlines efforts to minimise this by recruiting from multiple specialist centres across Ireland, but complete elimination of bias is impossible in an observational setting.1

The reliance on patient-reported outcomes, while important for capturing subjective experiences, also introduces variability. Patient perception of symptom severity can be influenced by numerous factors, including mood, coping mechanisms, and cultural background. While validated questionnaires help standardise these assessments, they do not eliminate individual differences in reporting. Still, the direct patient voice is indispensable for understanding the true impact of a symptom like pruritus.

The registry's initial enrolment target of 250 patients, while substantial for a rare disease in Ireland, may not be powered to detect subtle differences in outcomes for very rare subgroups or specific treatment regimens. Larger international collaborations will be necessary to achieve such statistical power. But, this initial dataset provides a robust foundation for future, more targeted research questions. The registry also serves as a model for other rare disease communities looking to establish similar platforms, highlighting the importance of a structured approach to data collection and governance, much like efforts to understand how inflammation drives sickle cell disease pathophysiology.

Future directions for the PBC Ireland registry include expanding the scope of data collection to include genetic information, biobanking of samples, and integrating with other national health datasets. Such integration could provide even richer insights into disease pathogenesis, risk factors, and long-term outcomes. The platform could also serve as a recruitment hub for future interventional studies, streamlining the process of identifying eligible patients for clinical trials. The Sherlock's Diseases of the Liver and Biliary System textbook remains the definitive reference for understanding the complexities of hepatobiliary diseases like PBC.

The PBC Ireland patient registry represents a significant step forward in addressing the unmet needs of patients living with this chronic condition. By systematically collecting data on symptoms like pruritus, it aims to improve

understanding, refine clinical practice, and advocate for better patient care. The registry's success will be measured not just by the volume of data collected, but by its ability to translate that data into tangible improvements in the lives of PBC patients.

CLINICAL IMPLICATIONS

The PBC Ireland patient registry highlights a key point for clinicians: pruritus in primary biliary cholangitis is not a secondary concern. It is a primary driver of patient suffering and significantly degrades quality of life, often independently of biochemical markers. Relying solely on liver function tests to gauge patient well-being misses the profound impact of this symptom.

GPs and specialists alike must actively screen for pruritus, using validated tools if possible, and not dismiss patient complaints as mere discomfort. Effective management of pruritus can dramatically improve a patient's daily functioning, sleep, and mental health, even if it does not alter the underlying disease progression. This holistic approach is essential for comprehensive PBC care.

The registry's focus on real-world data highlights the limitations of relying exclusively on highly controlled clinical trials for rare diseases. Registries provide the granular detail needed to understand the heterogeneous patient experience and identify gaps in current treatment paradigms. This data is invaluable for informing guideline development and advocating for better resource allocation.

For pharmaceutical companies, the registry data will illuminate the true burden of symptoms like pruritus, potentially guiding the development of novel therapies specifically targeting these debilitating aspects of PBC. A drug that effectively alleviates pruritus, even without significantly altering liver biochemistry, would represent a substantial improvement in patient care and market opportunity.

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REFERENCES

1. 1. Nesbitt G, Curley A. The PBC Ireland patient registry: study protocol for a national platform on primary biliary cholangitis. Ther Adv Rare Dis. 2026;7:1-10. doi:10.1177/263300402641783366

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