

The Voice of the Patient: Primary Sclerosing Cholangitis (PSC)

Report of an Externally-Led Patient-Focused Drug Development Meeting

Hosted by PSC Partners Seeking a Cure

Public Meeting: October 23, 2020

Report Date: April 11, 2022





The Voice of the Patient Report

Primary Sclerosing Cholangitis

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This report has been prepared by PSC Partners Seeking a Cure (PSC Partners) as a summary of the input shared by patients living with primary sclerosing cholangitis (PSC) and their caregivers during an externally-led Patient-Focused Drug Development (PFDD) meeting hosted by PSC Partners on October 23, 2020. This report presents perspectives shared by the individuals who participated in the meeting and/or associated patient engagement activities. Participant input has been summarized by the authors to faithfully represent the comments and themes that emerged. This report does not represent any consensus among participants or the broader population of those living with PSC and does not include all possible perspectives.

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Disclosures

The individuals listed above have nothing to disclose. The convening of this meeting by PSC Partners Seeking a Cure was supported solely by generous donations from the PSC Partners community of patients, families, caregivers, and friends.

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ACKNOWLEDGEMENTS

PSC Partners Seeking a Cure is sincerely grateful to the PSC patients and caregivers who opened their hearts and courageously shared their very personal, and often painful stories of living with PSC. We appreciate the willingness of the speakers, panelists, and attendees to be open and honest about how PSC has impacted their lives. We are also truly grateful to the supportive and tight-knit PSC community, whose generous donations funded the production of this externally-led PFDD meeting. Sincere thanks to William Lewallen of FDA, for his guidance throughout the meeting planning process, and to Ruby Mehta, MD, of FDA, for her opening remarks on behalf of the FDA Patient-Focused Drug Development Program. PSC Partners is also very grateful to Christopher Bowlus, MD, and Jorge Bezerra, MD, for sharing their clinical expertise and providing the opening remarks about PSC disease and treatments that set the stage for the discussions. Special thanks to Veronica Miller, PhD, and Mary Vyas, President of PSC Partners Seeking a Cure Canada, for moderating and facilitating this PFDD meeting, and to John, Kyle, and Eric at Dudley Digital Works for producing a seamless virtual meeting. Thank you, Joanne Hatchett, for your sleepless nights and incredible attention to detail. Thank you to team members, Mary Vyas, Rachel Gomel, Meegan Carey, and Jen Chavez. And to Joanne Grieme, Katherine Schultz, and Raquel Valerio.

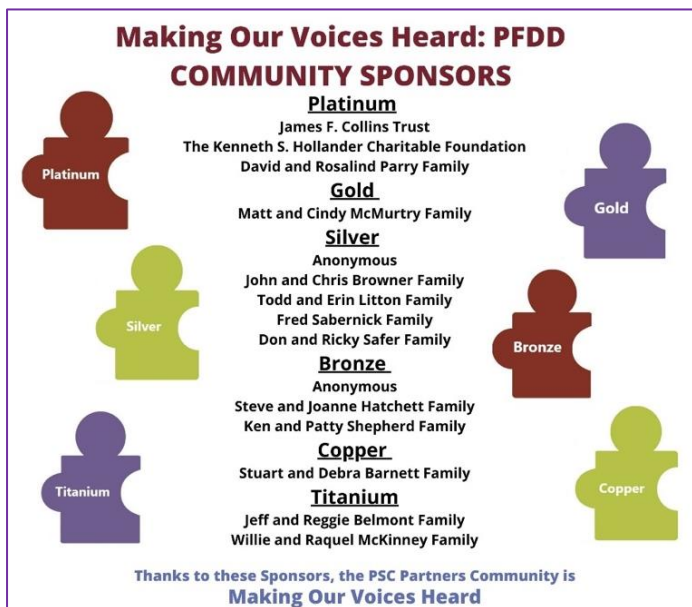
Finally, a heartfelt thank you to everyone who participated virtually in this PFDD meeting, including staff from FDA, academic and industry researchers, health care providers, rare disease advocates, and especially the PSC community of patients, families, caregivers, and friends who are the core of the program.

“Together in The Fight, Whatever It Takes!”

Ricky Safer

Founder and CEO

PSC Partners Seeking a Cure



ABOUT PSC PARTNERS SEEKING A CURE



PSC Partners Seeking a Cure – Ricky’s Story

Ricky Safer was a self-described “health, nutrition, and exercise fanatic” before she was diagnosed with PSC in March of 2004. Her “unpredictable and unrelenting journey with PSC” began in the emergency room where she was told she was having a cholangitis attack. She felt “utter fear” upon learning that PSC was rare, progressive, incurable, and potentially fatal, and that the only treatment was a liver transplant after which PSC might still reoccur. Forced to re-envision and redefine her life, she found that reliable information and support for PSC patients was woefully inadequate. With the help of her family and several other PSC patients, Safer founded PSC Partners Seeking a Cure and organized its first PSC conference in 2005. In 2015, an affiliate organization, PSC Partners Seeking a Cure Canada, was established by several parents of PSC patients.

The mission of PSC Partners Seeking a Cure is to drive research to identify treatments and a cure for PSC, while providing education and support for those impacted by this rare disease. “Every day I am made more aware of the complex and idiopathic disease that I am afflicted with,” Safer said. This externally-led PFDD meeting is the culmination of years of developing special programs and national and international collaborations, and has allowed PSC patients to share the burdens and challenges they face every day, and to provide input on the critical unmet need for treatments and, ultimately, a cure for PSC.

PSC Partners Seeking a Cure is a 501(c)(3) nonprofit organization.

For more information visit pscpartners.org.



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EXECUTIVE SUMMARY



Primary sclerosing cholangitis (PSC) is a rare, progressive liver disease that is estimated to affect around 30,000 children and adults in the United States. Chronic inflammation and fibrosis of the bile ducts of the liver can block the flow of bile, leading to liver damage. Patients with end-stage liver disease or multiple infections of the bile ducts (cholangitis) often require liver transplantation. PSC has also been associated with an increased risk of developing life-threatening cholangiocarcinoma (cancer of the bile ducts), colon cancer, and gallbladder cancer. There is still much that is unknown about the origins and mechanisms of PSC. It appears that PSC is immune-mediated and is associated with both genetic and environmental factors, and there is a strong association between PSC and inflammatory bowel disease (IBD). There are currently no treatments for PSC that have been proven to slow the progression or alter the course of the disease. The only treatment known to improve survival for PSC patients is liver transplantation, but PSC can recur in about 25% of transplanted livers.

On October 23, 2020, PSC Partners Seeking a Cure hosted an interactive virtual public meeting giving patients and caregivers a unique opportunity to share how PSC has impacted their lives. They shared their first-hand experiences with existing treatments and their unique perspectives on the unmet treatment needs of PSC patients. The meeting was developed in conjunction with the U.S. Food and Drug Administration (FDA) as an externally-led Patient-Focused Drug Development (PFDD) meeting, to complement FDA's PFDD initiative. The patient input collected at the meeting and reported here will have a lasting impact on the lives of PSC patients as it will inform the development and regulatory review of new drugs for this rare disease.

KEY MESSAGES FROM THE PSC PARTNERS' EXTERNALLY-LED PFDD MEETING

The Symptoms and Daily Impact of PSC that Matter Most to Patients

- **PSC Symptoms That Most Impact Patients' Lives**
 - **Fatigue** – extreme, different from being tired, not remedied by sleep
 - **Pruritus** – unrelenting, uncontrollable itch; often painful, interrupts sleep and slows down or prevents all routine activities
 - **Pain** – chronic, often does not improve with medication, impacts daily life, (abdominal, liver, joint, generalized)
 - **Impaired cognitive function** – “brain fog,” loss of identity, memory gaps, inability to function independently

- **Mental and emotional health issues** – anxiety, depression, post-traumatic stress disorder (PTSD); significant concern for children and young adults with PSC; emotions can intensify physical symptoms
- **Other symptoms of concern** – insomnia, varices/bleeding varices (enlarged or swollen veins in the esophagus [the tube connecting the throat to the stomach]), loss of appetite/weight loss, nausea/vomiting, as well as the consequences of osteopenia/osteoporosis (bone loss)
- **Impact of PSC Clinical Symptoms on Quality of Life**
 - **Unpredictability of PSC disease and the loss of opportunity** – “missing out on life,” not being able to attend school, participate in activities and social events, continue a career, maintain a relationship, start a family; the loss of one’s childhood
 - **Uncertainty about the future** - fears of needing a transplant, of not being able to get a transplant, of developing cholangiocarcinoma, of recurrent PSC after transplant, of loss of independence; balancing fear and hope while facing a lack of effective treatments
 - **Stress on relationships** – partners, families, friends, school/work, support systems
 - **Lack of public understanding of PSC** – the challenges of living with a disease that is often invisible, the social stigma associated with visible PSC symptoms; social stigma and bullying can be particular problems for children and adolescents with PSC
 - **Accessing care** – concerns about the MELD scoring system for transplant prioritization, obtaining insurance coverage as a high-risk patient, extensive travel or relocation in pursuit of quality PSC care, transplant, or clinical trial participation

Priority Unmet Needs:

- **Much remains unknown about the root causes and disease pathogenesis of PSC.** A better understanding is needed of the clinical course of PSC, and the impact of pediatric PSC on growth and development. The true epidemiology of the disease is also not yet fully understood, due in part to the history of PSC not having an ICD-10 code until recently.
- **Patients urgently need effective treatments for the symptoms of PSC.** The extent, severity, and impact of the symptoms of PSC are still not well-characterized. There are no proven therapies to improve how PSC patients feel and function. Participants vividly described the significant impacts of pruritus, fatigue, and pain, in particular, on their ability to function on a daily basis and on their overall quality of life. Some turn to off-label use of existing medications (e.g., ursodiol, vancomycin) and further studies are needed on the role of these drugs in symptom and/or disease management.
- **Transplant is not a cure.** Liver transplantation is a high-risk procedure with the potential for serious complications and recurrence of PSC. A true medical cure for PSC is needed.
- **More effective screening for early detection of cholangiocarcinoma is needed.** Current tools for hepatobiliary cancer surveillance are of low sensitivity and do not identify disease in the early stages when intervention could increase survival.

- **Patients urgently need effective treatments for PSC.** No treatment has been proven to increase survival of PSC patients. Treatments are needed that slow PSC disease progression, delay the need for transplant, and prevent post-transplant recurrence of PSC.
- **Earlier and more efficient diagnosis of PSC is needed.** For many, the journey to diagnosis can be long and complicated. Patients also want less invasive methods for risk prediction and prognosis. There is a need to raise awareness of PSC symptoms among providers in general, and to educate providers who treat patients with IBD about the relationship between PSC and IBD.

Taking the Next Steps Together:

- ***PSC Patients are ready and willing to participate in the search for treatments and a cure.*** PSC patients are interested in participating in clinical trials and are eager for education and information about the trial process, the safety of the investigational product, and the benefits of trial participation. To better meet patient needs, the patient perspective should be incorporated in the very early stages of clinical trial protocol development, and patients should be respected as an integral part of the clinical trial process. PSC patients can also play an important role in advancing PSC clinical trials by, for example, contributing to efforts to develop a PSC-specific patient-reported outcome tool and surrogate markers of clinical endpoints.
- ***PSC Partners is ready to help facilitate and expedite research in partnership with industry.*** PSC Partners can help with study recruitment through the PSC Partners Patient Registry and can help to identify potential barriers to recruitment and retention. PSC Partners can help educate patients about the trial process, foster trust between patients and researchers, and disseminate clinical trial information via social media platforms and other venues. PSC Partners is also actively studying ways of facilitating development of a robust, regulatory-grade natural history database to support clinical trials.
- **Considerations for PSC clinical trials:**
 - Embrace telehealth services to expand the reach of PSC clinical trials and reduce the burden of participation. The COVID-19 pandemic has revealed the power and potential of telehealth services. PSC Partners encourages clinical researchers to leverage telemedicine, home health visits, electronic informed consent, home drug delivery, and home-based surveys to engage more PSC patients in clinical trials.
 - Reconsider the need for liver biopsies in clinical trials. The increased sensitivity of imaging technologies can hopefully reduce the need for invasive, risky, and often inconclusive liver biopsy procedures.
 - Identify validated surrogate endpoints for PSC clinical trials (and recognize that normalized serum alkaline phosphatase levels do not necessarily correlate with improved quality of life).
 - Develop clinical endpoints that focus on treatment outcomes of importance to patients and on patient survival. Create validated, PSC-specific, patient-reported outcome measures for clinical trials, and include patient involvement in all stages of the tool development process.

- Design trials with expanded inclusion criteria. Many patients are willing, but ineligible to participate in a PSC clinical trial (e.g., because they are taking ursodiol).
- Consider creative approaches to collecting pediatric clinical trial data (e.g., including teenage PSC patients in adult clinical trials, incorporating a pediatric pharmacokinetics/pharmacodynamics (PK/PD) sub-study into adult studies).

The full-length *Voice of the Patient* meeting report, recorded webcast, and full set of comments submitted live and during the open comment period for this externally-led PFDD meeting are available on the PSC Partners Seeking a Cure website at <https://pscpartners.org/about/the-disease/pfdd-meeting.html>. Note that this report does not represent any consensus among participants or the broader population of those living with PSC and does not include all possible perspectives.



THE BETRAYAL IS WITHIN ME

A Poem by a PSC Patient

How do you escape

How do you win

When the battle

is fought within

Battle lines were drawn

Without my being aware

With the intention to destroy

To take without care

(This is a portion of the poem.)



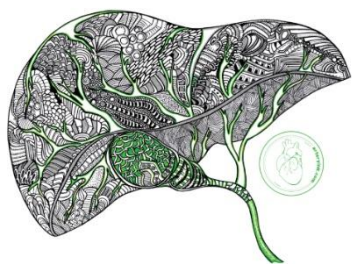
INTRODUCTION



On October 23, 2020, PSC Partners Seeking a Cure hosted a public meeting giving patients and caregivers a unique opportunity to share how primary sclerosing cholangitis (PSC) has impacted their lives. They shared their first-hand experiences with existing treatments and their unique perspectives on the unmet treatment needs of PSC patients. The meeting was developed in conjunction with the U.S. Food and Drug Administration (FDA) as an

externally-led Patient-Focused Drug Development (PFDD) meeting, to complement FDA's PFDD initiative. The patient input collected at the meeting and reported here will have a lasting impact on the lives of PSC patients as it will inform the development and regulatory review of new drugs for this rare disease.

OVERVIEW OF PRIMARY SCLEROSING CHOLANGITIS (PSC)



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A brief overview of PSC was provided by Christopher Bowlus, MD, the Lena Valente Professor and Chief of the Division of Gastroenterology and Hepatology at the University of California, Davis, co-chair of the Scientific/Medical Advisory Committee for PSC Partners, and Scientific Advisor to the PSC Partners Patient Registry.¹

PSC is a rare, progressive liver disease that is currently estimated to affect around 30,000 people in the United States alone. PSC is characterized by inflammation and fibrosis of the bile ducts within and outside the liver, blocking the flow of bile and leading to liver damage. There is a strong association between PSC and inflammatory bowel disease (IBD), and more than 75 percent of patients with PSC also have IBD, most often ulcerative colitis, although some have Crohn's disease. PSC affects all ages, including children and older adults. The median age at diagnosis is 40 years, and there is a male predominance, which Bowlus noted "is quite unusual for an autoimmune condition." The true epidemiology of the disease is not fully understood because, up until late 2018, PSC was grouped with other types of cholangitis diseases for the purposes of diagnosis and billing. PSC now has a specific ICD-10-CM code (K83.01), which will enable better monitoring of the incidence and prevalence of PSC cases. There is still much that is unknown about the origins and mechanisms of PSC. It appears that PSC is an immune-mediated, chronic inflammatory disease. Both genetic and environmental factors can increase an individual's susceptibility to developing PSC, and it is likely that abnormalities in the gut-liver axis play

¹ For a more detailed overview see Karlsen TH, Folseraas T, Thorburn D, Vesterhus M. 2017. Primary sclerosing cholangitis-a comprehensive review. *Journal of Hepatology* 67(6):1298-1323.

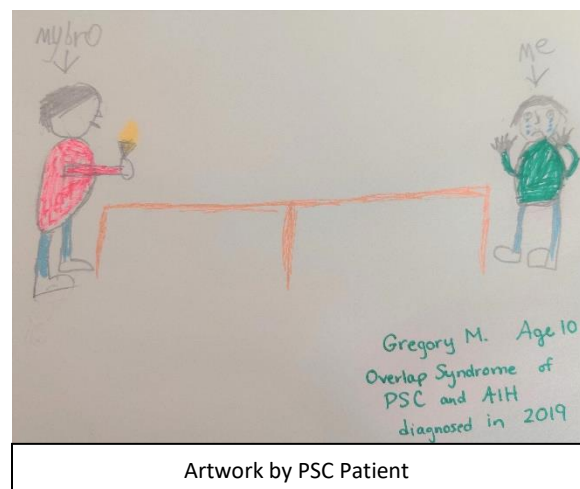
a role. It has been suggested that alterations in the gut microbiome trigger an immune response in the gut, and that altered intestinal permeability allows inflammatory cells of the intestine to migrate to the liver. This leads to injury of the epithelial cells that line the bile ducts (the cholangiocytes), and recruitment of more inflammatory cells (including macrophages, neutrophils, and T cells). This can result in more chronic inflammation and scarring in the bile duct, and recruitment of cells that promote fibrosis (such as hepatic stellate cells and portal myofibroblasts). The characteristic segmental fibrosis of the bile ducts in patients with PSC can be seen using magnetic resonance cholangiography (imaging of the bile duct). The resulting obstruction of the flow of bile can lead to liver damage, including advanced fibrosis, cirrhosis, and liver failure necessitating liver transplantation. Infections of the bile duct (cholangitis) can also occur and may hasten the need for liver transplantation. PSC has also been associated with an increased risk of developing several cancers, including cholangiocarcinoma (cancer of the bile ducts), and colon cancer. Interestingly, although PSC is rare, it accounts for approximately 4% of all liver transplants performed in the U.S., suggesting that there is a disproportionate disease burden from PSC relative to other chronic liver diseases.

PSC is classified into three main types. Large duct PSC is the most common and occurs with or without concurrent IBD. Cholangiogram reveals segmental strictures (narrowing of bile ducts), and secondary causes of these strictures are absent. Small duct PSC appears normal on cholangiogram, but typical sclerosing cholangitis histology is apparent on liver biopsy. The third type is an overlapping syndrome in which patients present with features of both PSC and autoimmune hepatitis (AIH). PSC/AIH overlap syndrome is not well-defined, and there is no consensus on diagnostic criteria or treatment. Diagnosis can be challenging, and assessment can include blood tests for liver function, imaging of the liver, and liver biopsy.

PSC IN CHILDREN AND ADOLESCENTS

Jorge Bezerra, MD, professor of pediatrics at Cincinnati Children's Hospital Medical Center and President of the American Association for the Study of Liver Diseases (AASLD) reviewed the natural history, management, and treatment of PSC in children and adolescents.

PSC in children manifests with the same typical features of inflammation and scarring in the liver that are seen in adult PSC. Similar to adult PSC, pediatric PSC is more prevalent in males, and is influenced by genetics and environmental factors. However, disease in children might be more significantly impacted by immunological factors that might drive bile duct injury and inflammation. Further investigation is needed on the causes of PSC across age groups. Specifically, do genes and immunity play greater roles in the onset of pediatric PSC versus a greater contribution of the microbiome and environmental toxins in the onset of adult PSC?



The clinical features of PSC in children and adolescents are similar to those in adults. Symptoms can include recurring abdominal pain, fatigue, easy bruising, and itching. As in adults, PSC in children can also be asymptomatic and is often diagnosed during evaluation for IBD when abnormal serum liver enzyme levels are detected. There are several key differences between pediatric and adult PSC, Bezerra explained. Children generally have higher serum liver enzyme levels at diagnosis and are more likely to have small-duct PSC. Pediatric PSC is also more frequently associated with autoimmune markers in serum (autoantibodies), and there is a greater incidence of PSC/AIH overlap syndrome in children. Disease course varies, and some children have more rapid progression of disease.²

Presentation of a sclerosing cholangitis in early childhood is called secondary sclerosing cholangitis when it is linked to a secondary cause, including a range of inflammatory diseases such as hemophagocytic lymphohistiocytosis, hyper IgM syndrome, eosinophilic cholangitis, and others. Neonatal sclerosing cholangitis, which presents in infancy, has been associated with mutations in the gene coding for the DCDC2 protein (a signaling and structural protein in cholangiocytes).³

CURRENT TREATMENTS FOR PSC

There are currently no treatments for PSC that have been proven to slow the progression or alter the course of the disease. Reports from the last three decades suggest that the median transplant-free survival of patients with PSC ranges from under 10 years to over 20 years, with the most recent studies suggesting a median transplant-free survival of more than 20 years. At this time, the only treatment for PSC that has been shown to improve survival is liver transplantation, and PSC can recur in the new liver. There are several treatments that have been prescribed to help relieve the symptoms of PSC. One of the most extensively studied is the bile acid, ursodeoxycholic acid (UDCA), also referred to as ursodiol (or just “urso”).⁴ Thus far, a broad range of studies have not shown that ursodiol enhances survival. Investigational therapeutics for PSC are targeting suspected pathogenic mechanisms of the disease related to the integrity of the gut-liver axis, the build-up of bile acids, and the development of chronic inflammation and fibrosis.

UNMET NEEDS

Bowlus described the unmet needs for PSC in three main areas: treatment of PSC liver disease, treatment of PSC symptoms, and cancer surveillance. Bezerra then summarized the unmet needs in pediatric PSC in three areas: understanding of the clinical course of pediatric PSC disease, defining the impact of PSC on growth and development, and developing effective therapies for pediatric PSC.

² For more detail on PSC in children see: Chapman R, Fevery J, Kalloo A, et al. 2010. Diagnosis and management of primary sclerosing cholangitis. *Hepatology* 51(2):660-678; and Mieli-Vergani G, Vergani D. 2010. Unique features of primary sclerosing cholangitis in children. *Current Opinion in Gastroenterology* 26(3):265-268.

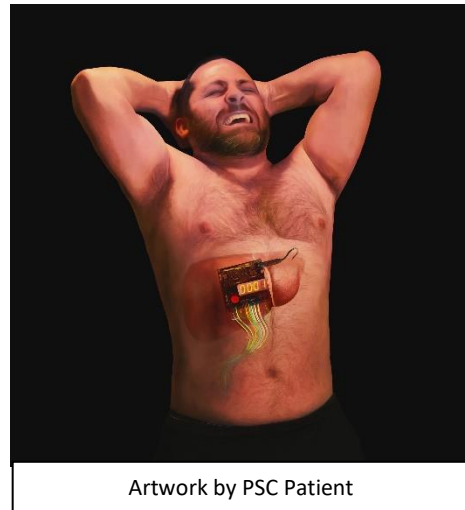
³ See Grammatikopoulos T, Sambrotta M, Strautnieks S, et al. 2016. Mutations in DCDC2 (doublecortin domain containing protein 2) in neonatal sclerosing cholangitis. *Journal of Hepatology* 65(6):1179-1187.

⁴ At this time, ursodiol is only approved by FDA for the treatment of primary biliary cirrhosis. However, it sometimes is prescribed “off-label” by physicians for patients with PSC.

General

- **Treatments for PSC Liver Disease**

Thus far, no therapy has been proven effective in increasing survival for PSC patients. Progress is hampered by a poor understanding of the pathophysiology of the disease. Further, a lack of consensus on surrogate markers of clinical endpoints impedes the design and conduct of clinical trials. At the time of the PFDD meeting, there were two drugs for PSC liver disease in phase 3 clinical studies, and several others planning to enter phase 2. Active investigation to understand the pathophysiology of PSC is ongoing, and several multicenter, prospective natural history studies are underway to identify and validate surrogate markers of clinical endpoints for use in future clinical trials.



- **Treatments for the Symptoms of PSC**

There are currently no therapies approved by FDA to treat how patients with PSC feel or function, and many patients suffer from a number of quality-of-life concerns. More than half of patients in the PSC Patient Registry report experiencing fatigue, abdominal pain, pruritus or itching, diarrhea, and sleep disturbances.⁵ The extent, severity, and impact of these symptoms are not well characterized, and understanding is hampered by a lack of validated PSC-specific patient-reported outcome (PRO) instruments. Data from the PSC Patient Registry and other cohorts suggest there are specific concerns for women with PSC who become pregnant. For example, maternal PSC appears to be associated with more frequent pre-term births and more frequent newborn admission to the neonatal intensive care unit (NICU), compared to non-PSC pregnancies. It was noted that, at the time of the PFDD meeting, a PSC-PRO instrument was undergoing validation and new PRO tools were in development.

- **Effective Cancer Surveillance**

Current tools for hepatobiliary cancer surveillance are of low sensitivity. Compared to the general population, individuals with PSC are at significantly increased risk for cholangiocarcinoma (occurring in over 1 percent of PSC patients annually), as well as gallbladder cancer, and liver cancer (hepatocellular carcinoma, known as HCC). Having PSC concurrent with IBD also increases the risk of colon cancer. More effective surveillance of hepatobiliary cancers is needed, including a better understanding of what tools are most sensitive for detecting PSC-related cancers. Bowlus noted that

⁵ See Kuo A, Gomel R, Safer R, et al. 2018. Characteristics and outcomes reported by patients with primary sclerosing cholangitis through an online registry. *Clinical Gastroenterology and Hepatology* 17(7):1372-1378.

novel molecular diagnostics and advanced imaging for use in PSC-related cancer surveillance are being investigated, and clinical practice guidelines for surveillance have been recently published.⁶

Pediatric

- **Understanding of the Clinical Course of Pediatric PSC Disease**

The natural history and clinical course of PSC disease in children and adolescents are not well understood.

There is a need for better surveillance of

complications and comorbidities in pediatric PSC patients, and more effective strategies to prevent them.

Studies are underway, such as a recent retrospective analysis which found that one-third of pediatric PSC patients also had AIH, and three-quarters also had IBD. By 10 years after diagnosis of PSC, more than one-third had portal hypertension and one-quarter had biliary complications, which significantly reduced survival in these patients.⁷

Another recent effort was the development of the Sclerosing Cholangitis Outcomes in Pediatrics (SCOPE) index, a prognostic and risk-stratification tool that uses laboratory and imaging data to predict pediatric patient outcomes.⁸ Bezerra noted that such risk stratification is very useful when designing clinical trials.



- **Defining the Impact of Pediatric PSC on Growth and Development**

Little is known about the impact of PSC disease on the growth and development of children and adolescents. There is a need for better patient-reported outcome metrics that can capture the impact of PSC on the quality of life of pediatric patients and help identify needed support systems for school, extra-curricular, and social activities. For example, important quality of life variables for children can include not only their symptoms and comorbidities, but factors such as a dislike for taking medication.⁹

- **Effective Therapies for Pediatric PSC**

There is no proven treatment for PSC disease in children or adults, and there is a lack of effective symptomatic treatments that meet the needs of pediatric PSC patients. Bezerra pointed out that the identification of new treatment targets and development of new therapeutic products require a better understanding of the causes and mechanisms of PSC. Other key needs for pediatric therapeutic development include improved non-invasive and minimally invasive diagnostic methods

⁶ See Bowlus CL, Lim JK, Lindor KD. 2019. AGA clinical practice update on surveillance for hepatobiliary cancers in patients with primary sclerosing cholangitis: Expert review. *Clinical Gastroenterology and Hepatology* 17(12):2416-2422.

⁷ See Deneau MR, El-Matary W, Valentino PL, et al. 2017. The natural history of primary sclerosing cholangitis in 781 children: A multicenter, international collaboration. *Hepatology* 66(2):518-527.

⁸ See Deneau MR, Mack C, Perito ER, et al. 2020. The Sclerosing Cholangitis Outcomes in Pediatrics (SCOPE) Index: A Prognostic Tool for Children. *Hepatology* 73(3):1074-1087.

⁹ See Trevizoli IC, Pinedo CS, Teles VO, et al. 2018. Autoimmune hepatitis in children and adolescents: Effect on quality of life. *Journal of Pediatric Gastroenterology and Nutrition* 66(6):861-865.

(e.g., imaging, serum biomarkers), pediatric patient-reported outcome measures, and participation of pediatric patients in clinical studies.

MEETING DESIGN AND DATA COLLECTION

This meeting was developed by PSC Partners to complement the work of the FDA's PFDD initiative.¹⁰ As explained by Ruby Mehta, MD, Medical Officer at the FDA Center for Drug Evaluation and Research (CDER), "Patient-focused drug development is a systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured, and meaningfully incorporated into drug development and evaluation." Patients are the experts on the symptoms that matter most to them, the impact of the disease on their daily life, their experience with currently available treatments, and their unmet treatment needs. PFDD meetings provide an important opportunity for FDA, researchers, drug developers, and other stakeholders to hear directly from patients. The voices of the patients who participated in this externally-led PFDD meeting have provided therapeutic context to inform the development and regulatory review of much-needed new treatments for PSC.

Planning for this externally-led PFDD meeting began in the spring of 2019. Sessions were designed around two key topic areas: 1) the symptoms and daily physical, emotional, and social impacts of PSC that matter most to patients, and 2) patient and caregiver perspectives on current approaches to treatment, unmet treatment needs, and priorities for drug development. To inform the development of the meeting agenda (Appendix 1), PSC Partners conducted a survey to gather data on the PSC patient experience and amplify the voice of PSC patients. The 40-question *Our Voices* survey was completed by 819 patients (or their representatives) and included 782 adult and 37 pediatric patients. Highlights from the survey are provided in boxes throughout the report and a detailed analysis of the full survey results will be described in a future publication.

The meeting was intended to be as interactive as possible and online participants were encouraged to contribute by responding to live polling questions, calling in live to comment, or submitting comments online, some of which were read live by the moderators. To supplement the input gathered at the meeting, members of the PSC community were also encouraged to submit comments to PSC Partners during an open comment period which ran from September 17 through November 6, 2020 (See appendix 4 for the full set of comments). A total of 275 comments were received during the open comment period and the PFDD meeting.¹¹

On the day of the meeting, 537 participants joined live online, including individuals living with PSC, their caregivers, and friends, as well as staff from the FDA, academic and industry, health care providers, rare

¹⁰ More information FDA's PFDD Initiative is available at <https://www.fda.gov/drugs/development-approval-process-drugs/cder-patient-focused-drug-development> (accessed March 21, 2022).

¹¹ This report summarizes the input provided by individual panelists and participants during the meeting as well as select findings from the pre-meeting survey. The report, full webcast video (including video testimonials and live polling results), and full set of comments submitted live and during the open comment period are available on the PSC Partners Seeking a Cure PFDD meeting website at <https://pscpartners.org/about/the-disease/pfdd-meeting.html>. Note that this report does not represent any consensus among participants or the broader population of those living with PSC and does not include all possible perspectives. Also note that comments presented have been subject to light copyediting as needed for clarity (e.g., spelling, punctuation) or privacy (e.g., names of patients or health care providers mentioned might have been removed).

disease advocates, and others interested in advancing the treatment and care of PSC patients. Of those, 272 identified themselves as patients (148) or caregivers participating on behalf of a patient (124). Live demographic polling suggested that the majority of patients lived the U.S. (80%), or Canada (18%). Just over half of the patients identified as female (56%), with the rest identifying as male (43%) or non-binary/non-gender conforming (1%). It was noted that this does not reflect the 2:1 male predominance of PSC. Nearly half were between 18 and 39 years of age, about one-third were aged 40 to 59 years, and about 13% were over the age of 60. The younger population of PSC patients was also represented at the meeting, with about 8% responding that the patient was under the age of 17. Although PSC affects all racial and ethnic groups, the majority of PSC patients participating or being represented were White (85%), with about 5% responding Black, and 5%, Asian.¹²

Following the introductory remarks by clinical experts on PSC (above), the meeting was organized to address the two main topic areas: the symptoms and impacts of PSC, and current and future treatments. The first topic was covered in three sessions: the impact of key symptoms on quality of life; living with advanced PSC disease in the absence of effective treatments; and the special challenges facing pediatric PSC patients. The second topic was broken into two sessions: patient experiences with managing their PSC disease and their unmet treatment needs; and incorporating the patient perspective into the clinical development of PSC treatments. Sessions included pre-recorded testimony from several PSC patients or caregivers (see Appendix 2 for transcripts); a live, moderated, virtual panel discussion; and the presentation of select results from the *Our Voices* survey. The panel discussion was augmented by live polling of online participants (see Appendix 3 for polling questions). The meeting was moderated by Veronica Miller, PhD, Executive Director of the Forum for Collaborative Research and professor at the UC Berkeley School of Public Health, and Mary Vyas, President of PSC Partners Seeking a Cure Canada, and parent of a young adult who has PSC.

TOPIC 1: PSC SYMPTOMS AND DISEASE IMPACTS



Artwork by PSC Patient

To open each of the following three sessions, individuals living with or caring for someone with PSC shared their personal stories through pre-recorded video statements. Following the presentation of their testimony, a live, moderated, virtual panel discussion was held. Online participants provided input by calling in live, submitting comments via the meeting website, and responding to live polling questions. Excerpts of live comments are interspersed throughout to help illustrate participants' experiences. (The full set of comments submitted live and during the open comment period are available on the PSC Partners PFDD meeting page).¹³

¹² The live polling results presented throughout this report are not considered scientific data but are intended to complement the input on patient disease experience obtained from the live discussions, *Our Voices* survey, and open comment period. The live demographic polling results are intended to provide a snapshot of who attended this externally-led PFDD meeting.

¹³ Available at <https://pscpartners.org/about/the-disease/pfdd-meeting.html>

LIVING WITH THE MOST SIGNIFICANT SYMPTOMS OF PSC

Patient Testimony on the PSC Symptom that Most Impacts their Life

Afsana, Tim, Jessica, Elizabeth, and Dan each described the PSC symptom that most impacts their quality of life. (Brief summaries of their statements are presented here. The full transcript of each video testimony is available in Appendix 2.)

Pain – Afsana’s Experience



What bothered Afsana most when she was diagnosed with PSC at age 16 was the impact of the disease on her social life. Over time, her emotional health also suffered, and she shared that she was bullied because she was different and received special treatment. Now 21 years of age, Afsana said, “I can confidently say that the worst symptom is the pain, and I’ve learned that pain isn’t just physical. It’s also how we feel emotionally about our lives.”

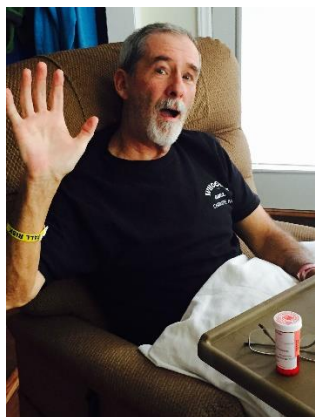
Afsana’s pain is chronic and does not improve with medication, and her overall quality of life has decreased significantly. Sleepless nights of itching and upper right quadrant pain leave her exhausted as she faces an eight-hour shift as a nursing student. “There are even days when I’m not able to stand in

“I can confidently say that the worst symptom is the pain, and I’ve learned that pain isn’t just physical. It’s also how we feel emotionally about our lives.”

the shower because I’m just too tired,” she said. The emotional toll of PSC is “completely devastating,” and Afsana said that she can’t achieve her full potential in life and reach her goals when she is too tired to get out of bed.

She described the effort she puts into “looking and acting okay and unaffected,” and her fear of losing her partner because she’s “just no fun.” The unpredictability of PSC also takes a toll, and on any given day Afsana can never be sure if she will be able to make more than one outing, prepare a well-balanced meal, clean up after, or sleep more than a few hours. Sometimes Afsana’s pain is so severe that she cannot accomplish anything, and she described isolating herself away from family and friends because, she said, “I become a mean and grumpy person.” Having PSC is “being trapped inside a brain and body that no longer work together,” she said. As her disease progresses, she is constantly reminded that pain will always be a part of her life and will prevent her from reaching her full potential. “I would never, ever wish PSC pain on anyone,” she concluded, and she emphasized the need to work together to develop symptom management approaches for PSC pain.

Pruritus – Tim’s Experience



When Tim was diagnosed with PSC in 2001, he was given just five years to live. Tim sought out a specialist at the Mayo Clinic, who gave the father of three young children and his wife hope that he could live for 10 years or more. Now, 20 years later, Tim has begun the process to receive a liver

transplant. Although his MELD score is only 17, he has severe symptoms. Tim’s most significant symptom is unrelenting itching, or pruritus, which began a year ago and has increased in severity in recent months. Tim noted that another PSC patient had described it as a “suicidal itch,” and Tim agreed. “It consumes me throughout my entire day, with itching from my scalp to the bottom of my feet and all in between. There is no spot on my body that doesn’t crave attention,” Tim said. The itch becomes almost unbearable at night when there are no distractions from the necessity to scratch. “I end up tearing up scabs previously made and leaving bloodstains on my pillows and sheets,” he said. Prescription itch medications and sleeping pills can provide temporary relief, but Tim still lies awake itching for hours. In the morning, itching slows down every part of his normal routine. “Itching hurts,” Tim emphasized. “I itch so much it feels like someone is taking sandpaper to my skin which feels inflamed and raw.” The itching on his scalp and eyelids are particularly painful, and he is concerned about damaging the silicone slings that were surgically implanted two years ago to hold his eyelids in place. His relentless itching also affects his family as they watch him suffer and can do nothing to help. “It pains them to see me have to go through this,” he said. It is also difficult for Tim to see his friends with PSC suffer. He added that many people with PSC die while waiting for a transplant or from complications after transplant. “We need help, and we need it fast,” he concluded.

The MELD Score and PELD Score

The Model for End-Stage Liver Disease (MELD) Score is a measure of the urgency of need for a liver transplant in patients with end-stage liver disease and is used to prioritize patients on the transplant waiting list. Scores range from 6 to 40. The higher the score, the more severe the liver dysfunction and the less likely the individual will survive for three months. The calculation takes into account the patient’s laboratory values for serum creatinine, total bilirubin, serum sodium, and INR (international normalized ratio, a measure of blood clotting.)

The Pediatric End-Stage Liver Disease (PELD) Score is used for children under age 12. The PELD score calculation includes albumin, bilirubin, INR, and growth failure (based on gender, height, and weight) and age at listing.

Fatigue – Jessica’s Experience



Jessica was diagnosed with PSC at age 22. “Physically, it hits me like a ton of bricks,” she said. There are days when she feels so ill and fatigued that she has to stop mid-task and go back to bed. She noted that it is difficult to explain her extreme fatigue to others because she does not look sick. Fatigue is not the same as being tired, she explained. “PSC fatigue is like having a faulty battery that you put on a charger overnight,” she said. “You never know if you’re going to get a full charge, a half a charge, or maybe a dead battery the next morning.” Jessica’s fatigue also leads to a range of other symptoms including headaches, severe nausea, and lightheadedness. As a result, she has missed numerous family functions and social events. When she does feel well enough to go, she said it takes significant

concentration to maintain focus and be able to keep up with conversations. She will often slur her words, or stop mid-sentence, unable to recall what she intended to say next. “When you have an invisible disease, people can’t see what you’re going through, and they don’t understand,” Jessica said. PSC fatigue impacts all parts of her life. “[It] prevents me from working, from spending time with my friends and my family. And it prevents people from relying on me,” she said. PSC fatigue made it nearly impossible for Jessica to visit with her ill mother, which made dealing with her mother’s death at the end of 2019 especially difficult. “This isn’t the life of the person that I want to be. It’s a life of a person that I’m forced to be,” she said. “I know that myself and others with PSC, we deserve to experience life to the fullest, but we need your help.”

“PSC fatigue is like having a faulty battery that you put on a charger overnight,” she said. “You never know if you’re going to get a full charge, a half a charge, or maybe a dead battery the next morning.”

Impaired Cognitive Function – Elizabeth’s Experience



Elizabeth, a 36-year-old pediatric nurse, has suffered with PSC since she was one and a half years old. After years of severe diarrhea, feeding intolerance, and abdominal pain, she was finally diagnosed at the age of nine. At age 13 she developed AIH, and at 14, she began to experience cognitive changes. “School became harder, my retention seemed just slightly off,” she said. Her tutors noticed that her ability to recall information from week to week was faltering. “I was no longer able to think critically like I used to. It was like living a hazy dream,” Elizabeth said. It was decided that she should leave school permanently because she could no longer keep up with her schoolwork. “I was only 15 when the

basic right of school was taken away from me due to PSC,” she said. On July 3rd, 2000, at the age of 16, Elizabeth received a liver transplant, which she described as “the gift of life” and “a miracle.” After the transplant, Elizabeth was able to complete high school and achieve her

“I can handle physical discomfort, but losing my mind, losing what makes me, me, is enough to make me crumble. The idea of losing my independence, it’s my greatest fear.”

dream of becoming a nurse. “I was given the opportunity to fully embrace life and the challenges and rewards that come with it,” she said. However, it soon became clear that there were gaps in her memory from the years prior to the transplant. “Some memories are hazy while others are completely gone,” she explained. For example, she said she barely remembers her Nana’s illness and death from cancer. At the age of 30, Elizabeth was diagnosed with recurrent PSC. “My world dropped out from beneath me,” she said. She feared what would happen to her life and her career as a nurse if her mind began to fail again. “I can handle physical discomfort,” Elizabeth said, “but losing my mind, losing what makes me, me, is enough to make me crumble. The idea of losing my independence, it’s my greatest fear.” Elizabeth asked for hope, “... hope that another child will not lose parts of their childhood due to this disease. Hope that I, and the rest of the PSC community will have the ability to live life fully and then we all will have the ability to remember the memories that we make.”

Living with Co-morbidities – Dan’s Experience



Dan, a motion graphics artist, was diagnosed with both PSC and ulcerative colitis in 2008. At that time, his ulcerative colitis symptoms were being treated with Lialda and mercaptopurine (6-MP, an immunosuppressant). He lost 30 pounds and was laid off from his job when his performance began to suffer due to his frequent bathroom breaks. Dan described experiencing stomach pain, lack of appetite,

vomiting, severe fatigue, insomnia, and emotional distress daily. He was able to work full-time again in 2010, when medication was able to keep his ulcerative colitis in remission. However, his PSC progressed to cirrhosis, and his symptoms (including severe fatigue, vomiting, lack of appetite, stomach issues, sleeplessness, and brain fog) impacted his quality of life and mental health. “Over these years, I felt like I was slowly disintegrating,” Dan said. His liver health declined significantly, and his wife divorced him because, he said, “[s]he wasn’t interested in what was in store and was tired of dealing with my chronic illness.” Dan received a living donor liver transplant in 2017, and his fatigue resolved. Within a year, he had developed rosacea and his ulcerative colitis flared, which he was able to control with prednisone and Entyvio. Unfortunately, long-term prednisone treatment resulted in skin problems and prednisone-induced diabetes. He also developed mild rejection of the transplant. He added that he has had more than 16 colonoscopies in the past 12 years due to his increased risk of colon cancer. “A liver transplant is currently the only ‘cure’ for PSC, and it was a relief when I received the liver transplant, but not all the side effects and health issues have gone away,” Dan said. He described “living in constant fear” due to the unpredictability of PSC and ulcerative colitis and the possibility of PSC recurrence, and he suffers from ongoing emotional distress and PTSD. In addition to dealing with his health issues, he has also faced challenges in dealing with the healthcare system and covering the out-of-pocket costs. “I wish there was more research done on my UC and PSC,” he said. “I don’t want to see people with this disease go bankrupt and live unfulfilling lives.”

“Over these years, I felt like I was slowly disintegrating.”

Symptoms of PSC that Matter Most to Patients – Moderated Discussion

Panelists Jerome, Tawny, Joe, and Elizabeth (who shared her testimony, above) continued the conversation on the physical symptoms of PSC that most impact their daily lives. The themes that emerged during the panel discussions and live polling were consistent with the findings of the pre-meeting *Our Voices* survey (see box on page 25).

Perspectives on the Most Problematic Symptoms of PSC



Artwork by Teen PSC Patient

Live polling respondents identified PSC fatigue and itching/pruritus as the key symptoms that most impact the PSC patient's life. Poll respondents/patients also reported being impacted by right upper quadrant/abdominal pain, anxiety and depression, insomnia, brain fog, nausea/vomiting, and bone loss/osteopenia/osteoporosis. Panelists and participants shared their personal experiences with these and other symptoms, including a range of other painful conditions, and weight loss.

- **Fatigue** – Elizabeth described vacationing with family and having to go to bed at the same time as her six- and four-year-old niece and nephew and

waking up later than them. “This is devastating,” she said. “I am missing so much of life and sleeping it away.” Yet she knows if she does not sleep enough, she will feel even worse. Joe described being tired, and yet not able to sleep.

“I am missing so much of life and sleeping it away.”

- **Itching/pruritus** – PSC itching was described by Tim in his patient testimony as “unrelenting” and “a suicidal itch” that is painful, interrupts sleep, and slows down all routine activities.
- **Pain** – Participants described a range of PSC-related painful conditions that impact their daily lives. Tawny described her arthritis as debilitating and said there are days when she has to lift her leg into the car or cannot get out of bed due to “excruciating back pain.” Elizabeth described having such severe abdominal pain as a child that “I would roll around on the floor and my parents couldn't touch me.”

- **Anxiety and Depression** – A caller, Andy, described the mental impact of the uncertainty of living with PSC, including depression, anxiety, panic attacks from “constantly wondering ... when things are going to go bad.” At its worst, PSC feels like “having a bomb inside you that always only has one second left on the clock,” he said. “[U]ntil there's at least some hope for a treatment to at least slow down progression, I don't know that that feeling, that bomb metaphor will ever really go away.” Jennifer also called in to discuss the mental health toll of PSC. Although she is generally asymptomatic, as a physician she is well aware of the inevitable outcomes of PSC, and this is very stressful. She said she has not told her young children about her PSC to avoid stressing them as well. Jerome emphasized the value of engaging with other PSC patients for support, including joining support groups for PSC patients, whether online or through PSC Partners.

PSC feels like “having a bomb inside you that always only has one second left on the clock.”

- **Brain Fog (memory problems, lack of mental clarity, poor concentration)** – Elizabeth explained that living with brain fog goes beyond not remembering words, or what she read in a book the day before, or birthdays and life events. It is a “loss of identity” and can impact the ability to live independently. Tawny described the challenge of applying for disability benefits while experiencing PSC brain fog. Her first application was denied, but after being listed for liver transplant she was able to receive benefits. An online participant commented that treatment options for hepatic encephalopathy are limited and cause constant diarrhea.

- **Weight loss** – Beverly called to share that her 34-year-old son’s most pressing problem now is



Artwork by PSC Patient

weight loss. “He is smaller than he was in high school,” she said. “I’m concerned about mentally, how he feels, being that he’s so, so skinny, and his cheeks are so sunken in.” Dan had also described significant weight loss in his testimony. Elizabeth noted that she experienced weight loss when she was diagnosed with AIH and said, “I didn’t fully realize how gaunt and how much, almost like a walking skeleton, I looked.” She had no appetite and could not force herself to eat because eating made her nausea worse. Joe described suddenly being too ill to attend

class, having at least 12 bowel movements per day and losing 20 pounds in about two weeks.

- **Dealing with Multiple, Often Concurrent Symptoms** – Many, if not most, participants described dealing with multiple symptoms to varying degrees, which was also reflected in the *Our Voices* survey. Elizabeth is particularly concerned about her ability to function and to work as a nurse if her brain fog and fatigue impact her at the same time. Tawny is dealing with brain fog, pruritus, fatigue, and painful arthritis. She shared that, “When my liver is good, my arthritis is bad, and when my liver is bad, my arthritis is good. It’s literally always something.” Catherine commented online that she experiences debilitating fatigue, bone, and muscle pain, IBD, nausea, brain fog, itching, and vitamin deficiencies, and can no longer work. “Until late stage of PSC, we do not even look sick,” she said.

Impact of PSC Symptoms on Quality of Life

Panelists and participants discussed a wide range of ways in which PSC impacts their lives. In response to live polling, more than 80% of respondents reported that their daily life was at least somewhat affected by their PSC symptoms (39%, somewhat; 31%, very much; 14%, overwhelmingly). Live polling also suggested that PSC patients’ quality of life is greatly impacted by worry about the future and the unpredictability of the disease. Functional limitations, family stress, and frequently missing school or work were also reported as concerns for PSC patients. In addition, some poll respondents indicated that others often doubt the patient’s illness because PSC symptoms are often “invisible”, and some even assume the patient’s condition is related to using drugs or alcohol.

- **The Diagnostic Journey** – When asked during live polling about the PSC patient’s journey to diagnosis, about 40% of respondents felt that the journey was “long and complicated.” About one-third responded it was “not too complicated.” Only about 20% responded the patient’s journey to diagnosis was “quick and straightforward.”

“It’s just frustrating living with an unseen and unknown disease.”

Joe said his symptoms came on suddenly, but it was at least six months before he was diagnosed with ulcerative colitis and longer before he was diagnosed with PSC. Elizabeth described her journey to diagnosis as “long and arduous.” She showed symptoms at age one and a half, but was not diagnosed until age 9, when she first had abnormal liver function blood tests. A subsequent ERCP¹⁴

indicated she already had significant liver damage, which she described as being “devastating.” A caller, Linda, raised the issue of lack of provider awareness about PSC. “I was told when I was originally diagnosed, the doctor couldn’t do anything for me until I turned yellow. When I questioned the doctor regarding ERCP, my husband told me I came across as arrogant just because I was questioning him,” she said. “It’s just frustrating living with an unseen and unknown disease.” Miller (moderator) said these comments highlight the need for better diagnostic markers so that the process of diagnosis can be less invasive, and diagnosis can be made earlier.

- **Social Impacts** – Joe said that the social impact of PSC has been especially difficult and has impacted his mental health. He has felt judged by others throughout high school, college, and now, at work. He has been called out for being late to school or work, and worries what people think when he has to rush to the restroom. In high school he was concerned that he smelled like feces, so he avoided social events.

“There’s been many times that I’ve felt left out ..., whether it’s socially, or with my family, or with my job. It never really ends.”

“There’s been many times that I’ve felt left out, whether it’s socially, or with my family, or with my job. It never really ends.” Joe added that people often do not understand the impact of PSC fatigue. “It isn’t the fact that I am not a fan of hanging out with the person, ... it’s just that I simply, physically cannot keep going sometimes,” he said. Elizabeth discussed missing most of her freshman or sophomore years of high school, and not participating in school dances, football games, or any of the usual high school activities. In addition to missing social milestones of growing up, she said she missed learning about group dynamics and how to socialize. After her transplant, she was “playing catch up academically, socially, developmentally” after having been “completely excused from life” during her formative years. “[I]t’s devastating to all of a sudden have to play catch up in the prime of your life,” Elizabeth said.

¹⁴ Endoscopic retrograde cholangiopancreatography (ERCP) is frequently used to evaluate the bile ducts. It is invasive compared to magnetic resonance cholangiopancreatography (MRCP).

- **Unpredictability and the Loss of Opportunity** – Loss of opportunity was a common theme in the testimony and panel discussions, especially with regard to young people not being able to attend school, participate in activities and social events, or start a family. Elizabeth had discussed how her school life had been taken away from her, and Joe described missing out on social interactions.

Nancy commented online that her daughter suffers from pruritus and unpredictable, intermittent, deep fatigue, and she hoped for any treatment that could better manage her symptoms so she could continue college. Kara wrote that, “PSC is an emotional and physical roller coaster” and that her 23-year-old son “nearly missed his college graduation and was released from the hospital in time to walk across the stage and receive his degree with honors.” Another caller, Jennifer, shared that both of her adult daughters have been diagnosed with PSC. One is a biomedical product engineer, and the other is in college studying to be a physician assistant. “With the diagnosis, their future becomes so unpredictable,” she said. “[W]ill they be able to have families of their own? Will they be able to find and keep a life partner who would want to carry through the burden of the disease and its destructive path?” Jerome reiterated the value of engaging with other PSC patients through support groups and offered encouragement that three women he knew with PSC had had normal pregnancies and uncomplicated deliveries.

“... their future becomes so unpredictable. ... will they be able to have families of their own? Will they be able to find and keep a life partner ...?”

- **Impact on Family and Friends** – Brett wrote in, “There are many days when I don't even have the energy to go on a simple walk with my wife and son. PSC affects everyone differently, and you don't need to have PSC to be affected by the disease.” Tawny said her parents still go to appointments with her, and her sisters are always there when she needs them. She said that even her young nieces and nephews help with her luggage when she visits because they know she doesn't feel well and is tired, and they remind her of things when she has brain fog. Marianne called in to share that her son was diagnosed with PSC and AIH ten years ago and struggled with returning to college. Over time, he learned how to handle his disease and is now working. “We've learned to enjoy just the simple things in life, just having birthdays together, and seeing each other. If he ... has fatigue, just being together with each other, we're just happy doing that,” she said. Reggie commented that their son was diagnosed with PSC 22 years ago, had a transplant nine years ago, and now has recurrent PSC. “He is very, very ill and needs another transplant. Worry is a constant companion, but so is hope.” Jerome referred participants to the PSC Partners website which has information for caregivers. The PSC Partners Annual Meeting also has workshops for caregivers.

“Worry is a constant companion, but so is hope.”

- **The Transplant Experience** – Panelists described a range of transplant experiences, always with the caveat that transplant is not a cure.

Although Elizabeth’s transplant experience was very positive, she said

“People fail to realize [that] transplant is not a cure. It’s trading one set of problems for another.”

that “people fail to realize [that] transplant is not a cure. It’s trading one set of problems for another.” She described having debilitating tremors and migraines due to post-transplant immunosuppression, which she said impacted her work as a nurse. “A transplant means you just have more time, but you still have struggles.”



Tawny described having post-transplant infections and her fear of

recurrent PSC. Jerome shared that he has few complications from surgery and no side effects from the immunosuppressive drugs. “I’m very fortunate,” he said.

The Our Voices Survey: Background and Demographics

The pre-meeting *Our Voices* survey was designed to gather data on the PSC patient experience to both inform the development of this PFDD meeting and supplement the findings. Highlights from the survey are provided in boxes throughout the report. A detailed analysis of the full survey results will be described in a future publication.

The majority of the 819 *Our Voices* survey participants responded that the PSC patient identified as female (54%). While this does not reflect the 2:1 male predominance of PSC, it does mirror the female predominance of participants in the PSC Partners’ Patient Registry and annual conferences. The majority of the patients were between 26 and 59 years of age (29% age 26-39; 38% age 40-59). PSC affects people of all ages, and the survey also included young adults (10% age 18-25 years) and children and teens (5%), as well as older adults (18% age 60 and older). Despite extensive outreach to engage the broader PSC community, the patients involved in the *Our Voices* survey were predominantly White (93%) and non-Hispanic non-Latino (86%).

The *Our Voices* Survey: Clinical Symptoms

- ***The Timing of PSC Symptoms and Diagnosis***

More than half of PSC patients surveyed reported they had symptoms before their diagnosis. About 20% said their symptoms began near the time of their diagnosis, and about 20% after their diagnosis. About 10% report they have never had PSC symptoms. Joanne Hatchett of PSC Partners observed that there is an opportunity to educate health care providers to be on alert for patient-reported symptoms of PSC, especially those providers caring for patients with ulcerative colitis and Crohn's disease.

- ***Symptom Impact on Function***

More than half of survey respondents said that, when PSC was at its worst, they suffered either major or minor impacts from at least one of the top 14 PSC symptoms (fatigue, itching, abdominal pain, liver pain under the ribs, insomnia, weakness, anxiety, loss of appetite, depression, brain fog, nausea/vomiting, joint pain, night sweats, and other general pain). During the six months prior to the survey, close to half of respondents said they experienced at least minor impact from many of these symptoms. PSC fatigue impacted more than 75% of respondents in both cases. These results demonstrate how the presence and intensity of PSC symptoms vary over time, Hatchett said, and highlight the need for improved symptom management and identification of clinical symptom endpoints for use in clinical trials.

In a follow-up question, respondents reported experiencing the impact of multiple PSC symptoms over the prior six months. Many of these symptoms have cumulative and aggregate effects which can be difficult to separate, Hatchett said, and this highlights the need for more robust symptom reporting tools.

- ***The Impacts of PSC Clinical Symptoms on Quality of Life***

PSC can be unpredictable, and more than three-quarters of the respondents to the *Our Voices* survey identified the uncertainty that comes with living with PSC as a primary concern affecting their quality of life (628/819). Other top concerns were worries about today or the future (533/819), dealing with the symptoms of PSC (417/819), loss of their ability to function independently (377/819), dealing with the lack of public understanding of PSC (167/819), the effects of having the disease on their social life (98/819), and access to supportive services (57/819).

(Survey participants were asked to select their top three current concerns about living with PSC from a list of seven possible choice. See figure in Appendix 5. Additional concerns listed by survey respondents are included in Appendix 6.)

The *Our Voices* Survey: Living with PSC

- ***Symptom Management: The Discrepancy Between Patient-Reported Symptoms and Claims Data***
The frequency of the most impactful symptoms over the prior 6 months as reported by PSC patients in the *Our Voices* survey is not reflected in the information about symptoms gleaned from a review of insurance claims data. PSC Partners engaged Komodo Health, a data-driven health care software company, to evaluate claims data from 2018-2020 for more than 25,000 PSC patients identified by ICD-10-CM diagnosis code (K83.01). This discrepancy raises questions about the extent to which PSC patients are clearly conveying the impact of their symptoms to providers, and whether providers understand the depths of the patient's suffering, and/or have effective treatments, Hatchett said.
- ***The Impact of PSC on Regular Daily Activities***
Three-quarters of *Our Voices* survey respondents said that the PSC patient was not able to do physically demanding or strenuous activities or work due to PSC symptoms. Nearly as many reported that PSC symptoms impacted the patient's social life. More than half of respondents said PSC symptoms impacted the patient's sexual interest or activity, ability to do household chores, or to manage work or school duties. More than one third felt that walking less than three blocks or driving a vehicle were also impacted by the patient's symptoms.
- ***Which was First, PSC or IBD?***
More than half of *Our Voices* survey respondents reported that the onset of PSC symptoms occurred after the patient's IBD diagnosis. About 20% said PSC symptoms appeared near the time of IBD diagnosis and 20% before diagnosis. "Over 70% of all [PSC patients] have IBD, yet the pattern is not the same for everyone," Hatchett said, and she suggested there is an opportunity to raise awareness among primary care providers and gastroenterologists who treat IBD patients about the relationship between PSC and IBD.
- ***The Impact of IBD Symptoms when PSC was at Its Worst***
More than two-thirds of respondents to the *Our Voices* survey reported that the symptoms of IBD have a major impact on how they feel and function when their PSC is at its worst. Results were comparable for both pediatric and adult patients (68% and 72%, respectively). The impact of IBD symptoms was reported as minor by 27% of pediatric patients and 21% of adults. Five percent of pediatric patients and 7% of adults reported no impact.
- ***Frequency of IBD Symptoms in the Past Six Months***
None of the pediatric respondents, and only 6% of the adult respondents reported having symptoms of IBD continuously over the past six months. The majority of pediatric respondents (69%) reported having no IBD symptoms over the past six months, and 19% reported having symptoms some of the time. Of the adult respondents, 40% reported no IBD symptoms over the past six months, and 43% reported symptoms some of the time.

LIVING WITH THE CONSEQUENCES OF ADVANCED DISEASE IN THE ABSENCE OF EFFECTIVE TREATMENTS

Patient Testimony on Living with Advanced PSC

In the second session, Kevin, Kristian, and Todd shared their personal stories of living with advanced PSC as a result of the lack of effective treatments for PSC. (Brief summaries of their statements are presented here. The full transcript of each video testimony is available in Appendix 2.)

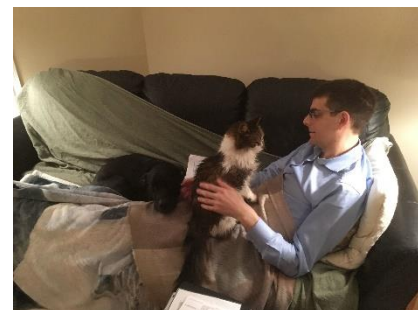
Cholangiocarcinoma – Kevin’s Story

Kevin was diagnosed at the age of 14, when a biopsy of tissue collected during gallbladder removal surgery revealed the cause of his upper abdominal pain was actually PSC. One month later, a colonoscopy revealed Kevin also had Crohn's disease. He began treatment with ursodiol, which he continued for 20 years. “In the beginning, the most difficult part of having a diagnosis of PSC was the uncertainty,” Kevin said, as he was told he would need a liver transplant “eventually.” For two decades he suffered with bouts of cholangitis which grew progressively more frequent and more severe as he entered his 30’s. Treatment consisted of pain relievers and antibiotics. In 2013, with help from his employer to cover travel expenses, Kevin began treatment at Mayo Clinic. In October of 2016, after another bout of persistent, intense pain, Kevin was diagnosed with perihilar cholangiocarcinoma which did not yet show signs of spreading. He noted that if he had “waited another few weeks, it would have most likely spread and been inoperable at that point.” Kevin and his family relocated to be near Mayo Clinic as he waited for his transplant. “One of the hardest things I've ever had to do ... was putting together a will and advanced directive with my spouse when I was only 34, 35,” he said. “Today, I'm still thankful that someone was willing to be an organ donor, and that my wait time was only seven and a half months from diagnosis to transplant.” In 2019, Kevin was diagnosed with high-grade dysplasia and early signs of colon cancer, and had a total colectomy requiring three surgeries. He said the uncertainty is still the most frustrating part of having PSC and cholangiocarcinoma. “Even with all the knowledge at the Mayo Clinic, it's still impossible to predict when or if these things are going to occur.” Kevin stressed the need for “a test and PSC protocol to identify cholangiocarcinoma earlier and find a way to slow PSC progression by slowing down scarring of the bile ducts.”

“In the beginning, the most difficult part of having a diagnosis of PSC was the uncertainty.”

Cirrhosis – Kristian’s Story

Kristian was diagnosed with PSC in 2004, but it was several years before he had symptoms, which started with jaundice in his eyes. Newly married, he and his wife moved to Ontario to be close to the Toronto Liver Center. While undergoing testing to determine the extent of his PSC, he had his first internal bleeding episode from esophageal varices and was immediately treated. “[W]e didn't even know what varices were, and here we were dealing with a life-threatening one. We were so scared,” Kristian said. He soon learned that his liver was cirrhotic, and he was placed on the liver transplant waiting list. He made



monthly, six-hour trips from Ottawa to Toronto for endoscopic variceal banding to help prevent further bleeding episodes. He was also prescribed nadolol, but said it added to the PSC fatigue and further limited his ability to be active. “PSC was now impacting our lives forever,” Kristian said. “As newlyweds, we'd have loved to start a family, travel outside of Canada, and fulfill our dreams. But because of PSC, these were no longer possible.” Jaundice, constant fatigue, and endoscopies were the “new norm,” he said. Their mental health suffered as well. Despite the efforts to control the varices, they worsened and spread, and required more complex endoscopic treatment. In 2016, Kristian had his most severe bleeding episode and said, “I'll never forget how scared I was seeing the hospital staff rushing to my assistance.”

“PSC is a terrifying chronic condition that can strike without warning and has no mercy.”

Kristian has also developed osteopenia. In 2017, he fell and broke his hip and required months of intensive physical therapy. “I'm lucky I've survived PSC, but it's only because I had a life-saving liver transplant in 2017. I am very grateful for the second chance of life,” he said. “PSC is a terrifying chronic condition that can strike without warning and has no mercy.” Kristian hoped for a cure because PSC is “a fate no one else deserves.”

Recurrent PSC Post-Transplant – Todd's Story

Todd was diagnosed with PSC at age 15. “After two years of suffering through uncontrollable itching and maddening insomnia, I received a living donor transplant from my personal hero, my brother,” Todd said. The transplant failed within days due to a clot in Todd's hepatic artery, and 12 days later he received a second transplant. Todd described “the guilt of taking my brother's liver and not being able to

“[T]he thought of having to tell my family that I'm having symptoms again is my biggest nightmare. Putting your loved ones through that kind of pain can be worse than the disease itself.”

use it.” Six years after the second transplant, PSC recurred, and he received his third transplant. Feeling well for years, Todd had gotten married and bought a house. He was expecting his first child when he came down with a fever and chills and went to bed. “I woke up days later in the ICU on a ventilator,” he said. After a month in the hospital, Todd waited two years on the transplant list for his fourth transplant. “What should have been the best years of my life were robbed from me. When my daughter was born, I could barely hold her without getting exhausted,” he said. Worried that he would die while she was too young to remember him, he wrote to her in a journal every night. “PSC is always with you,” he said. “It doesn't matter if you're post-transplant or not.”

Todd described himself as a laid-back person but said he gets a “gut-wrenching feeling that this could be it” whenever he is feeling ill. “[T]he thought of having to tell my family that I'm having symptoms again is my biggest nightmare. Putting your loved ones through that kind of pain can be worse than the disease itself.” Todd noted the emotional and physical toll of PSC and said, “I live with the constant fear that my kids will grow up without their dad ... And that is a fear that no parent should have to live with.”

Perspectives on the Consequences of the Lack of Effective Treatments – Moderated Discussion

Panelists Alison, Niall, Mónica, and Nicola shared their personal perspectives about how the lack of effective treatments for PSC has impacted their lives. There was continued discussion of liver transplantation, especially around the fears patients face, both while waiting for transplant and after

receiving a new liver. Many have dealt with bouts of cholangitis and some have developed life-threatening cholangiocarcinoma. Participants also discussed both the challenges of living with a disease that is often invisible and the stigma associated with visible PSC symptoms.

- **Living with Transplant Fears and Frustrations** – Much of the discussion focused on liver transplantation as that is often the only remaining option for patients with advanced PSC disease. Participants shared their fears of not being able to get a transplant, of the transplant procedure and recovery process, and the persistent fear of PSC recurrence after transplant. Some described the guilt they felt from receiving a donor transplant. It was again emphasized that transplant is not a cure for PSC, and that there are many potential challenges post-transplant.
 - Pre-transplant fears – Alison said, “I was so scared of getting the transplant I downplayed the symptoms for quite a while to the doctors, even though I was basically living my own personal hell on earth.” Mónica experienced a rapid decline in health after her son was born and was in need of a transplant. She described living in fear that she would not survive the procedure and how, every night while waiting for her first transplant, she would whisper in her son’s ear, “If mommy’s not here in the morning, just know that I’m working as hard as I can to get back to you.”
 - Waiting for a transplant and the MELD conundrum – A caller, Sandra, shared that her son passed away in 2013 at the age of 40 after living with PSC for 19 years. She described the frustrations of his being on and off the transplant list as his health improved and declined, and of getting to the hospital only to be told that the donor liver wasn’t suitable, or that he was second on the list. Another caller, Eric, said that “successfully getting to the stage of having a liver transplant, you’d literally almost have to die.” He had symptoms for years before he was diagnosed in 2014, and in 2015, with a MELD score of 36, he was listed as a priority for transplant. He described being excited and looking forward to “coming out the other end, extremely healthy and ready to get back to life and get back to my family.” While waiting, his MELD score dropped below 25 due to “rigorous change of my medications, diet, and exercise.” It was good news that his PSC was coming under control. However, it also meant he was moved down on the transplant list because he was now healthier than the other patients waiting for a liver transplant. Ultimately, he received a living donor transplant in 2016, and faced numerous post-transplant health challenges. “I don’t wish a transplant on anybody,” he said. Niall described himself as being “lucky enough to be sick enough to be listed for a transplant,” but added that “transplanting a liver to solve PSC is like changing the engine in your car because your battery has gone.” It is a major undertaking that does not necessarily solve the problem. Mónica shared that her recurrent PSC has been different from her pre-transplant disease and has included hospitalizations and cholangitis attacks. She is anticipating a second transplant, likely a living donor transplant, “because of the change in the MELD system and the likelihood of how sick I would have to get in order to get

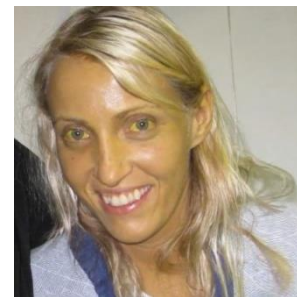
“Successfully getting to the stage of having a liver transplant, you’d literally almost have to die.”

another transplant.” Mónica said, “I know that I was very lucky, and will I be lucky again? Will I get a third chance of life? Will I get to watch my son grow up?”

- The pursuit of transplant care – Some patients uproot their lives to gain access to better care. Niall was diagnosed with PSC in 2015 and was told he had about 10 years to live. In 2017, he left the U.S. and moved back to Ireland, where he is entitled to health care, and is being treated at the Irish National Liver Transplant Program. Mónica described how waiting for a transplant impacts family, for example, where you can live (is it near a transplant center?) and where you or your spouse can work (what does the health insurance cover?).
- Living donor transplants – Nicola received a living donor transplant from her brother 11 years ago. “There’s really no ‘thank you’ you can give to someone that does that for you,” she said, and she discussed the guilt that comes with having a living donor and “putting someone through a surgery to save your life.”
- Post-transplant complications – Nicola described dealing with complications from strictures as a result of the liver transplant, as well as recurrent cholangitis infections requiring multiple drains and long-term antibiotics. Mónica also expressed concern about what symptoms she might have after her next transplant.
- **Living with an Invisible Disease** – Alison was diagnosed with ulcerative colitis at age five and PSC at 15. She received a living donor liver transplant at age 31. She was secretive about her PSC until her symptoms began to show and, as such, her friends could not understand why she avoided social situations. “PSC robbed me of the best years of my life,” she said. “I was embarrassed to wear skirts or shorts ... because my legs were literally a war zone with open wounds.” She kept her suffering to herself. “I didn’t want my family to know because they worried so much as it was. ... But when it became visible, then some of the truth did have to come out,” Alison said. An online participant, Heather, commented, “It is so interesting how you can be so sick, but not look sick. I can’t tell you how many times doctors would come into the examination room and laugh because I presented in person so much better than I looked on paper.”

"It is so interesting how you can be so sick, but not look sick."
- **Living with the Stigma of Visible PSC Symptoms** – Alison was in her 20’s when she began to develop visible symptoms of PSC, including jaundice. “I was so yellow. I had people asking me ... if I was wearing yellow contacts. It was absolutely humiliating. ... People asking me if I was wearing yellow makeup.” She experienced nosebleeds and nausea, lost weight, and her belly became distended due to ascites (fluid collection causing abdominal swelling). Her muscles would give out unexpectedly and one day, she said, “I just literally collapsed in the middle of the street.” As her symptoms became more visible, Alison said people did not want to be near her. They assumed she was contagious, or that she had been drinking. Some suggested she should “eat properly” and take better care of herself. Miller (moderator) observed that, because PSC is a liver disease, people assume that “you

"It was absolutely humiliating. ... People asking me if I was wearing yellow makeup."



have done something to your liver, and not that your liver is doing something to you ... that you absolutely have just no control over.”

- **Living with the Lack of Effective Treatments for Severe Symptoms** – Nicola said she balances her



fear with her hope for a cure. “I’m looking for a cure for the disease, or at least something that can help ... the symptoms. ... [W]e need a treatment for the itching, the varices, the fatigue, the insomnia, the pain, the infections.” She described sitting in a bathtub full of ice and scratching when her itching is at its worst, “or going out on the sidewalk and crawling my feet on the pavement, just for a few seconds of relief.” “We need something to ... ease the symptoms and let everyone get back to what their version of a normal life is.” Niall shared

that he takes a “very, very, very scalding hot shower” or puts his hands in scalding hot tap water to get some relief from his itching. In describing her PSC itching, Mónica said it is not skin itching, it is “like your blood is itchy. The bile is in your blood ... you can’t reach the itch.” Alison described how, when her legs were covered in open wounds, she would scream in the shower because the pain was unbearable.

It is, “...like your blood is itchy. The bile is in your blood ... you can’t reach the itch.”

- **Living with Unpredictability and Fear of the Unknown** – As a mother of two young boys, Nicola said the unpredictability of PSC creates stress for the family. “I never know when the next cholangitis infection is going to strike, how long I’ll be gone for. Will I need surgery? How will my husband take care of my kids?” The greatest stress, however, is the fear of post-transplant recurrent PSC. “That’s a fear that weighs on my mind daily.” After her transplant, Mónica faced a long recovery and then last year, three and a half years post-transplant, she was diagnosed with recurrent PSC. She had to leave her job at an arts high school to focus on her son and on fighting her disease, and to reduce the stress that triggers her PSC. Niall said he gets infections every three to six months. “I have no idea when this disease is going to strike.” He keeps a “go-bag” packed with his medical records and

“It is frightening to live by myself. When I get a cholangitis attack, sometimes I could be unconscious, and nobody is here to help me get to the hospital.”

medications, as well as personal items such as headphones, a charger, flip flops for the hospital, and a baseball cap because he said he becomes very sensitive to light when he is having a cholangitis attack. “I go through a period of about a week where I don’t know whether or not I should call the hospital ... am I sick enough to go in?” A participant, Serena, commented that even though she and her husband are both physicians, her husband’s recent PSC diagnosis was “terrifying and overwhelming,” and she agreed with others that “the unknowns are by far the worst part of this disease.” She emphasized the need for “treatments to slow progression, and clear diagnosis pathways for cholangiocarcinoma.” Another participant

commented that “It is frightening to live by myself. When I get a cholangitis attack, sometimes I could be unconscious, and nobody is here to help me get to the hospital.”

THE SPECIAL CHALLENGES FACING PEDIATRIC PSC PATIENTS

Patient and Caregiver Testimony on Living with Pediatric PSC

In the third session, Bek, who was diagnosed with PSC as an infant, and Alex, Richard, and Jennifer, who are parents of pediatric PSC patients, shared their personal stories of how PSC impacts children and adolescents. (Brief summaries of their statements are presented here. The full transcript of each video testimony is available in Appendix 2.)

Living with Pediatric PSC – Bek’s Experience



Bek was diagnosed with PSC before her first birthday, and with ulcerative colitis seven years later. She suffered from a range of symptoms and complications, including hepatopulmonary syndrome and bleeding varices around her ileostomy. “I was transplanted at age 13, after being officially listed for 18 months, with only a few weeks left to live,” she said. Now 22 years old, Bek said she is feeling

well, but lives a “modified life” and knows her PSC could recur. “Being diagnosed so young, I don’t have any idea what it’s like to be healthy, so it’s hard to know exactly how PSC has affected me,” she said.

Growing up with PSC, Bek said she was always smallest in her class and became more quickly fatigued than her classmates. She described being able to swallow pills by age four, and realizing she had knowledge her young peers did not, such as what a liver is. She and her family have made many sacrifices due to her health. “When you spend your childhood and teen years sick, you really have to learn to manage your expectations,” Bek said. Her health meant that her dreams of being a famous actress were shattered. Plans to instead act in commercials or be a makeup artist for movies were also crushed. She now volunteers backstage at an amateur theater company, which she said is “hard work, but doable and I love it. ... You make the best with what you’re given.” Bek is also committed to campaigning for PSC, raising awareness about the unpredictability of the disease and the need for treatments and a cure. “It’s too late for me and the damage PSC has caused my body, and we can’t bring back those that we’ve lost,” she said, “but I want to change the future for others with PSC. I want them to have hope and options in the medical realm.”

“Being diagnosed so young, I don’t have any idea what it’s like to be healthy, so it’s hard to know exactly how PSC has affected me.”

Concerns of a Parent– Alex’s Experience



Alex’s son was diagnosed with PSC the year before he started kindergarten. He had “interminable itching” and bouts of nausea and vomiting but, at first, they thought it was dry skin and a susceptibility to stomach viruses. They then worried about him having one of a range of diseases for which there are treatments, and instead they received a diagnosis of an incurable progressive disease with no available treatments. PSC impacted his ability to sleep and to play. “At his most acute suffering, he doubled over from abdominal pain at his own fourth birthday party,” Alex said. He also began suffering symptoms of ulcerative colitis. Alex described her son’s disease course thus far as uncomplicated. A recent triumph for her son was learning to swallow pills,

which Alex said means he no longer has to choke down a chalky mixture. “I’m so proud of his positive attitude,” she said, but she knows he faces a future of taking numerous pills that will not cure his PSC. Alex described her son’s excitement as he boarded the bus for the first time to go to kindergarten. An iconic moment for most parents, Alex said, “I fought a numbing, crushing sadness as I wondered whether his footsteps will lead first to his driver’s license, or to a liver transplant. I wondered how many stays in a hospital he will have to endure as his illness progresses during ... his childhood years.” His oversized backpack on his small body appeared to her as a symbol of the burden of his disease, rather than a symbol of his growing independence. She worries that her son might never be better than he is today. “As a parent, I cannot accept this. I feel like this rare disease is unfolding like a time bomb inside of my child, and I am worried about what is yet to come.” Alex said she chose to share her son’s story to emphasize the need to advance PSC research and find a cure, both “for all of those suffering today and for those like my son whose suffering lies ahead.”

“I fought a numbing, crushing sadness as I wondered whether his footsteps will lead first to his driver’s license, or to a liver transplant.”

Pediatric Transplant Journey – Richard’s Experience



Richard first noticed his son, Matthew, looked jaundiced when they were working out at the gym. It took nearly a year after that for Matthew to be diagnosed with PSC. “It was a bittersweet moment because we finally knew what the cause was, but we were devastated because it was PSC. ... [W]e knew without intervention of some sort, it meant certain death for Matthew,” Richard said. In May of 2010, when Matthew was 16 years old, his doctor told him he had six months to live

unless he could find a living liver donor. “I can still see the look of total devastation on my wife’s face,” Richard said. Matthew then received a living

“It was a bittersweet moment because we finally knew what the cause was, but we were devastated because it was PSC. ... [W]e knew without intervention of some sort, it meant certain death for Matthew.”

donor transplant of 71% of his father's liver. Richard said his wife "experienced fear, despair, and total helplessness, as both her husband and son were under the knife at the same time at two different hospitals." Richard attributes Matthew's survival of the surgery to his "inner strength and never giving up attitude." After the transplant, life was relatively "normal" as Matthew graduated high school and got his driver's license. However, two months after starting college, Matthew had an aggressive recurrence of PSC. "Matthew must have seen the look of fear and despair in my eyes," Richard said, "because one day he looked up at me and told me, 'Dad, I'm not going to die.'" Two months later, Matthew received a deceased donor transplant, and has been well thus far. He is "chasing his dreams and making the most out of each and every day. However, he lives with the uncertainty that comes along with PSC," Richard said. "He doesn't know ... whether he'll wake up tomorrow morning again fighting for his life." Richard concluded, "I would love to go to my grave knowing that there was a cure that gave Matthew a fighting chance."

Pediatric Transplant Journey – Jennifer's Experience



Jennifer's son was diagnosed with PSC and Crohn's disease at age eight, after years of failing to meet developmental milestones and suffering with nausea, vomiting, and severe pruritus that left his skin bleeding, and infected. Numerous hospitalizations and multiple ERCP procedures to place stents in his bile ducts followed. Jennifer said her son suffered with debilitating fatigue, severe insomnia, and failure to thrive. "He was literally wasting away," and received numerous courses of total parenteral nutrition (TPN). He was absent from school for more than a year and had to repeat a grade. Still, there was no relief. "And as a parent, it is the

most helpless feeling in the world to watch your

child suffer, knowing there's nothing that you can do to help," Jennifer said. At age 13, her son was listed for transplant, and they applied for and were granted MELD exception points. "We agonized over the option of a living donor. We

were torn by the thought of putting someone else's life at risk," Jennifer said. "[W]e reached the decision to proceed because it was clear our son couldn't wait much longer." In 2018, six weeks before her son's scheduled altruistic donor transplant, he was matched with a deceased donor. "The journey before and after transplant has been excruciating," Jennifer said. "My son essentially lost his childhood. He has cognitive delays because of the extensive liver damage. His transplant recovery has not gone smoothly either." In the two years since the transplant, her son has had six traumatic episodes of acute rejection. Each episode has involved "a risky liver biopsy, days in the hospital, IV and oral steroids, all with distressing side effects." His veins are scarred from numerous blood draws. "His transplant has not been the cure we had hoped for," she said. He still feels sick and takes more medication than ever before. Yet, Jennifer said, "We are hopeful that new therapies will come along that have a real impact on the symptoms of this dreadful disease. We are hopeful that patients won't have to hang their hats on a transplant that may or may not improve their quality of life. We are hopeful for a cure. We are begging for your help."

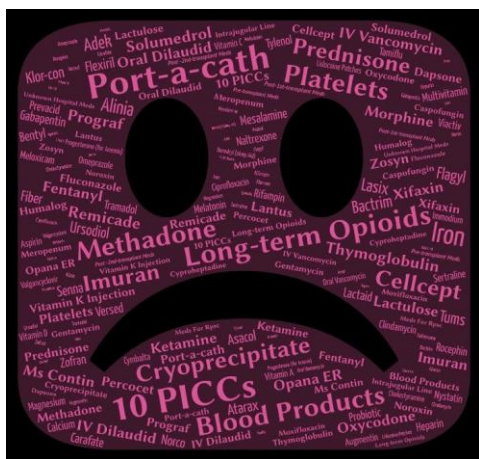
"His transplant has not been the cure we had hoped for."

The Challenges Facing Children and Adolescents with PSC – Moderated Discussion

Panelists Afsana and Chelsea, young adults who were diagnosed with PSC as children, and Willie and Richard, who are each parents of children with PSC, shared their personal perspectives on some of the unique challenges facing children and adolescents with PSC. Participants described the lengths they've gone to for symptomatic relief and access to care, and the social and mental health impacts of living with PSC as a child.

- **The Search for Symptom Relief** – Much of the conversation focused on the wide range of different approaches patients have tried for symptom relief, and the need for effective treatments and a cure. Afsana, (who shared her testimony in the first session) was diagnosed with PSC at age 16 and Crohn's disease at 17. She described her search for pruritus relief and said she has tried ursodiol, rifampin, and cholestyramine (both the pill and powder forms), which either did not help or worsened her overall health with side effects. She also tried plasmapheresis to reduce the concentration of bilirubin in her blood (a task normally done by the liver). In plasmapheresis, also called plasma exchange, blood is removed from the body, run through a machine that separates the plasma from the cellular blood components, and the cellular components are then transfused back into the patient along with

The implantation of a plasmapheresis port “was a very painful experience for me and caused a lot of PTSD.”



Artwork by PSC Patient

replacement plasma. After three months of plasmapheresis, three times a week for five hours each, Afsana decided to stop the treatment because she said the downsides outweighed the benefits. Plasmapheresis gave her a small amount of relief, she said, “around 10 to 15%.” However, the treatment required implantation of a port, which she said, “was a very painful experience for me and caused a lot of PTSD,” and she had fluid and electrolyte depletion, nausea and vomiting, dizziness and fainting, and fatigue. She had to leave school due to the extensive time commitment, and her quality of life worsened. “My friends and family did say I looked and acted like a walking zombie,” she said. Miller (moderator)

noted that plasmapheresis is a drastic measure to take “and really emphasizes the dire need to have something that would stop the symptoms.”

Live polling responses by, or on behalf of pediatric patients indicated that 47% were now taking, or had previously taken, ursodiol, and 24% reported current or prior treatment with oral vancomycin. Vyas (moderator) compared these live polling results to the findings of the *Our Voices* survey, which also indicate that patients are turning to medications that are, as yet, not approved for the treatment of PSC. Cynthia, whose daughter was diagnosed with PSC in 2012 at the age of 15, wrote in that her daughter has “lived a normal life” since starting oral vancomycin therapy eight years ago and now works as a gut microbiome researcher. Cynthia highlighted that many patients feel that vancomycin is effective for them and asked, “Why are we not focused more on understanding why it has shown efficacy in these patients?” Miller (moderator) agreed that there is heterogeneity of

response to treatment and said more knowledge is needed about why ursodiol and vancomycin work for some patients.

Sarah commented online that her daughter has difficulty swallowing large pills. Afsana agreed that it can be a struggle and said that, as a child, she would put her pill in a piece of mashed banana. “It helped me swallow it because I was pretending it wasn't there,” she said. She also used applesauce, other mashed foods, smoothies, and juice, and can now swallow pills without liquid when needed. Miller pointed out that new treatments should be developed so that they are appropriately formulated for use by children.

- **Access to PSC Care** – The challenges of finding knowledgeable PSC health care providers was also noted. Chelsea and her fiancé have now moved from Texas to Massachusetts in pursuit of better treatment for her. Her doctors in Texas were a four-hour drive from her home, “but my parents kept bringing me there because they were the only ones who knew what I had, and knew how to treat me,” she explained. Willie described their “luck” at their daughter’s primary physician recommending a PSC specialist who “just happened to be right around the corner.”

- **Never Knowing a Life without PSC** – Chelsea’s journey began with ulcerative colitis at 20 months old which was not diagnosed until age 4. She was then diagnosed with PSC at age 6 and AIH at age 9. She described the “extremely difficult” challenges of growing up with PSC, AIH, and ulcerative colitis. “I can't remember a time in my life when I was healthy. That doesn't exist for me,” she said. “I've taken tons of medications. ... I've been poked and prodded my entire life, separated from my peers, and hospitalized for various lengths of times.” Now 24 years old, she has cirrhosis and, after four years on the transplant list in three separate regions, was scheduled to receive a living donor transplant from her mother just days after the PFDD meeting. She said she has known since she was very young that she would someday need a transplant, and she described the anticipation of her transplant as “a whirlwind of emotions, kind of a roller coaster. I'm excited, but I'm also incredibly nervous for recurrent PSC.”

“I can't remember a time in my life when I was healthy. That doesn't exist for me.”

- **Loss of School and Social Interaction** – During the live polling, the most frequently identified challenges for pediatric PSC patients were physically demanding activities or sports, school or work responsibilities, and social time with family and friends. Chelsea frequently missed school because she was sick or was four hours away from home being treated. Long before the COVID-19 pandemic,

“Children don't really like what they don't understand, and I'm sure I looked funny being hooked up to an IV pole and yellow.”

she wore a mask during flu season or had to stay home if illnesses were circulating. Chelsea said she was bullied often as a child, and it was not until high school that she developed a group of close friends. “Children don't really like what they don't understand, and I'm sure I looked funny being hooked up to an IV pole and yellow.” Many thought she was contagious despite her efforts to explain her condition. Chelsea emphasized the impact of the loss of social interaction for a young child. “I felt like I was constantly the new kid in my own school district.” On the

positive side, Chelsea’s inability to go outside for recess with her IV pole meant she spent recess in the library helping to shelve books. “I fell in love with being in libraries and so now as an adult, I'm

getting my master's degree in Library and Information Science," she said. She noted that she is only able to attend part-time, but her professor and the university have been supportive.

Marnie commented that her 8-year-old son was recently diagnosed with PSC/AIH overlap syndrome. "It has impacted our life as he has not been able to attend school while on high doses of [an] immunosuppressant, and his fatigue and aches and pains have prevented him from playing sports and [participating in] activities he loves."

Julianne, age 37 and a post-transplant PSC patient, called in to discuss the importance of having the support of others in the PSC community, including PSC Partners, when fighting this disease, especially as a young person. She was diagnosed in college and said, "I had at least had the opportunity to have experiences and grow up and have a normal social life ... and get going in my adult life. PSC really robs these young people of those opportunities." Julianne serves as a mentor to the teen patients at the annual PSC Partners Seeking a Cure conferences, and said she is inspired by their strength. She added that "getting together at the conference every year is huge for them to just reach out and have somebody understand what they're going through."

- **Mental Health Impacts of Pediatric PSC** – "Growing up sick is painful for so many reasons," Chelsea said, and she highlighted some of the mental impacts of having PSC as a child. "It rips you apart inside and makes you question your own existence," she said. She felt alone and developed an eating disorder, anxiety, and depression and said she thought about killing herself. "I was just a little girl ... and I had no one to talk to about it because of the stigma surrounding it." Counselors labeled her "a worrywart," and she felt her condition was somehow her fault. She was eventually diagnosed with PTSD "from the trauma that a life with PSC causes." Chelsea said she is doing better now but still struggles and said she wants people to "understand that this disease is so debilitating. It ruins people's lives in more ways than one."

"I was just a little girl ... and I had no one to talk to about it because of the stigma surrounding it."

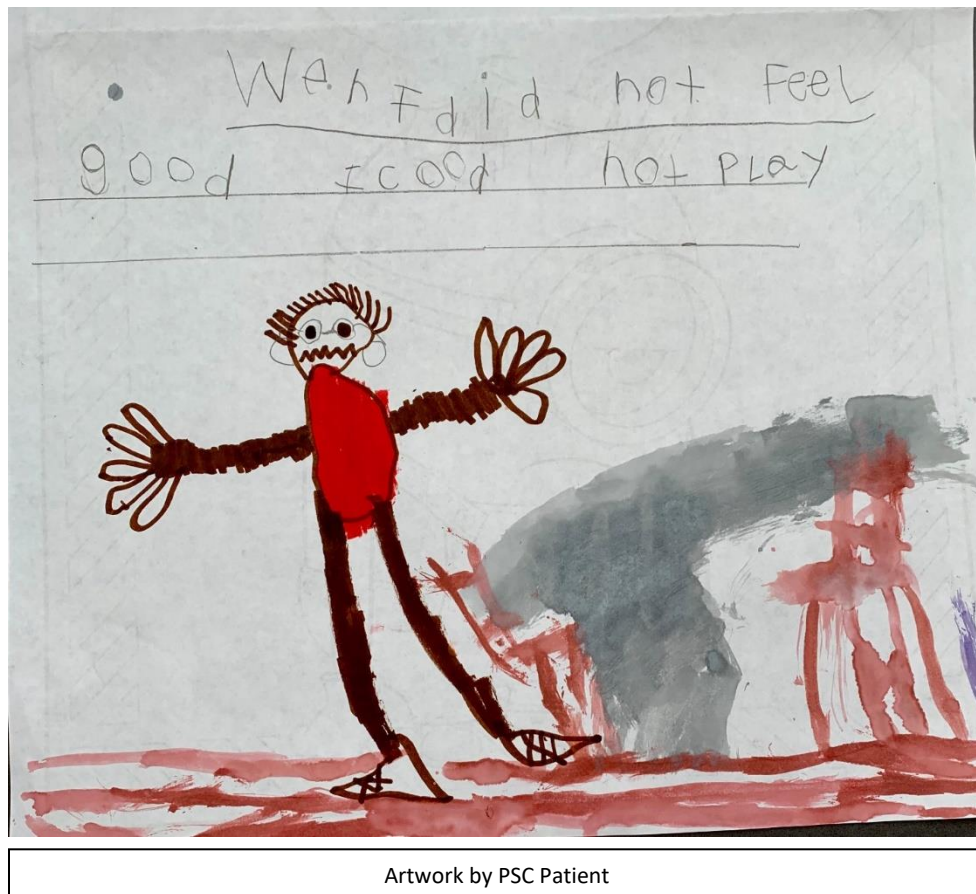
Amanda, who is 15 years old, called in to share how PSC, AIH, and IBD have affected her life. In addition to experiencing nausea and itchy skin, Amanda said her diseases also impact her mental and emotional health. "I constantly live in fear about what is to come," she said. In turn, her emotions impact her physical symptoms. "If I'm nervous or irritated, then I usually find myself itching and scratching more." Amanda emphasized the importance of funding PSC research to identify treatments and a cure.

- **Living with a Child's PSC Diagnosis** – Richard, who shared his son's story at the start of this session, described how, even a decade after Matthew's diagnosis, hearing the stories of other pediatric PSC patients "just brings all the emotions back." He said, "I'd do anything for a cure. I'd give my life. ... [T]he drive needs to continue to find cures or treatments for this so it's not a death sentence for young people with PSC, or anybody with PSC." Richard described having to live with the uncertainty of PSC as "almost like a death sentence." Yet, as difficult as it is for a parent of a PSC patient, he said, "[I] can't imagine what it's like as somebody who has PSC living with that, knowing there's no cure and no intervention that could save your life."

Willie said he remembers the day his daughter was diagnosed with PSC at age 17, and he agreed with Richard that it was “like a death sentence.” They were told there was no cure and that she was at increased risk for cancer. He described feeling hopeless. “I’m a father and there’s nothing that I can do. And I’m a scientist, and there’s nothing that I can do to tell her or reassure her that she’s

“There’s nothing that I can do to tell her or reassure her that she’s going to be okay.”

going to be okay.” He recalled the days when his daughter would say she was tired, and he thought she was being a typical teenager who just didn’t want to do something, or said she had a pain in her side and didn’t want to eat, and he thought she just didn’t like what he made for dinner. “[A]fter you hear she’s been diagnosed you just feel horrible. ... [I]t’s the day your life totally changes.” PSC takes a mental toll on families and caregivers as well. “We went through all the stages of grief and eventually came to the stage where we wanted to fight,” Willie said. His daughter received a liver transplant a year ago, and he said she recovered quickly and is doing very well. However, the fight continues, and Willie and his family hope for new treatments because they fear post-transplant recurrence.



TOPIC 2: CURRENT AND FUTURE PSC TREATMENTS

As before, each of the following two sessions opened with individuals living with or caring for someone with PSC sharing their personal stories through pre-recorded video statements. Following the presentation of the patient testimony, a live, moderated, virtual panel discussion was held. Online participants provided input by calling in live, submitting comments via the meeting website, and responding to live polling questions. Excerpts of live comments are interspersed throughout to help illustrate participants' experiences. (The full set of comments submitted live and during the open comment period are available on the PSC Partners PFDD website page).¹⁵

PATIENT PERSPECTIVES ON PSC TREATMENTS AND UNMET NEEDS

Patient Testimony on Current Approaches to Treatment of PSC and Related Conditions

In the fourth session, Kristina, Lindsay, Laura, John, and Jay shared their perspectives on the limited options for effective treatment of their PSC, and their hopes for future therapies and a cure. (Brief summaries of their statements are presented here. The full transcript of each video testimony is available in Appendix 2.)

Treatment of Pruritus – Kristina's Experience



Kristina was diagnosed with PSC and ulcerative colitis at age 17. After multiple hospitalizations, she faced the reality that her job as a public school teacher was too taxing on her health. "Battling this disease and maintaining a life worth living is a full-time job in itself," she said.

Kristina has had pancreatitis, a cholecystectomy, and 18 ERCP

procedures. She "live[s] in between the highs and the lows," as she deals with frequent biliary obstructions, cholangitis, cirrhosis, an increased risk of cancer, "and the impending doom of a liver transplant." She said, "makeup and positive attitude can hide a lot," but she is itchy, fatigued, in frequent pain, and depends on family and friends to help with housework, caring for her son, and travel to medical appointments. Her need for support increased when she developed cholestatic pruritus during a very difficult pregnancy with her son. "This debilitating itch is merciless, all consuming, and overwhelming," Kristina said. "I find myself rubbing my feet on anything, creating blisters." The itching is worse in the heat and at night, and she wakes up with broken, bleeding skin that leads to scarring. The itching interrupts her sleep, making it difficult to function the next day. Kristina has tried a range of treatments to no avail, including Vistaril (hydroxyzine), ursodiol, Welchol, Benadryl, and a multivitamin. "The non-pharmacological and alternative approaches I've tried are endless, and they create a financial hardship on my family," she said. These include "acupuncture,

"This debilitating itch is merciless, all consuming, and overwhelming."

"The non-pharmacological and alternative approaches I've tried are endless, and they create a financial hardship on my family."

¹⁵ Available at <https://pscpartners.org/about/the-disease/pfdd-meeting.html>

Bowen, humidifiers, cold showers, keeping a clean shave, icing itchy areas, oatmeal lotions, moisturizing soaps, essential oils, mineral water sprays..." She watches her diet, stays hydrated, avoids heat, purchased lightweight clothing and cooling bed sheets, and keeps the thermostat at 68 degrees. "Despite how minor the symptom of itching looks on paper, suffering from pruritus is beyond description. I feel helpless and I truly don't want it to become another all-consuming identity for me."

Management of Multiple PSC Symptoms – Lindsey's Experience



Lindsey was diagnosed with PSC at age 13. "I was blissfully unaware of the terrifying journey ahead of me," she said. By the beginning of high school, she had end-stage liver failure and progressive portal hypertension. While on a field trip, portal hypertension caused esophageal varices to rupture. "Blood had been silently leaking into my stomach all day and I could not stay awake," Lindsey said. "My friends thought it was funny, until I threw up blood in my best friend's lap. I woke up

three days later in the local hospital, after being flown by helicopter." She was diagnosed with hepatic encephalopathy (minor to severe cognitive impairment due to severe liver disease) and was prescribed lactulose. While it led to small improvements in her memory, she said, "the cost is never having a solid bowel movement again," and she stopped taking it so she could continue on the swim team and marching band. After her first liver

transplant she experienced recurrent PSC with itching, fatigue, fever and chills, and extreme abdominal pain. "For me, itching was the first sign that a transplant is a treatment, but not a cure for PSC," she said. Lindsey tried antihistamines, cholestyramine, naltrexone, and more for the itching, none of which helped (see diagram).

"The silver lining was that I took antidepressants for the itching, which didn't help the itching, but it improved my mood." She was given opioids for the extreme abdominal pain, as well as celiac plexus nerve blocks, which



impacted her ability to attend college. After her second transplant, she was again given an opioid for several weeks, after which she was placed on a six-month methadone weaning program. She described the embarrassment of having to teach her college roommates how to administer Narcan to her if needed. Now, 24 years old and three years post-second transplant, Lindsey is planning to attend graduate school. Although she looks healthy, she suffers from fevers, chills, and fatigue, and takes 31

pills each day. “PSC is no joke, and a transplant is no cure,” she said. “Someday soon, I hope to see a medication that stops or slows the progression of PSC so that we can all live our life to the fullest.”

Treatment of Acute Cholangitis – Laura’s Experience



Laura was diagnosed with PSC in 2012 and began to experience cholangitis about a year later. She described how she went to the ER twice with upper right quadrant pain, exhaustion, lack of appetite, and fever, and was sent home both times. The second time, however, she fainted while filling an antibiotic prescription on the way home and was rushed back to the hospital where they then diagnosed her with acute cholangitis and sepsis. For five years, Laura suffered frequent bouts of cholangitis and sepsis, even while taking antibiotics. “I never knew when they were going to strike,” she said. “My daughters became scared to come home from school because they worried they were going to find me on the couch again, ... or indeed, already at the hospital for a stay of several days.” As her health steadily declined, her husband took over all domestic tasks. “I could barely keep up with just basic parenting. I had to go on disability,” she said. Even with frequent and sometimes lengthy hospitalizations for cholangitis and sepsis, Laura’s MELD score was low, and she was advised by doctors that she was unlikely to ever qualify for a deceased donor transplant. “For patients like us with biliary disease, the MELD score is not an even playing field,” she said. In 2017, Laura received a living donor transplant, which she noted was complicated by the fact that her own liver “was literally oozing with infection and it was extremely difficult to extract from my body.” Laura highlighted the need for research on the impact of cholangitis and sepsis, and for the MELD system to be revised to capture the severity of PSC disease. “I can report firsthand that life with acute cholangitis and sepsis is hell for the sufferer and for those around them,” she concluded.

“For patients like us with biliary disease, the MELD score is not an even playing field.”

Management of IBD in PSC Patients – John’s Experience



John’s journey began with ulcerative colitis at age 13. As one of six children, the diagnosis presented a financial hardship for his family, and he was enrolled in a clinical trial because it would include free care. As it turned out, John was placed in the placebo group, and ultimately became sicker. His illness persisted throughout high school with “more doctor’s office visits and more meds.” This included prednisone treatment and now, at age 50, he has osteoporosis and osteopenia. “There was always worry and no cure,” he said. He also began to experience sudden and debilitating exhaustion, and looking back, he thinks this was likely the beginning of his PSC. Information was difficult to find at the time, and John said he read books, visited homeopathic healers and medical doctors, and talked to friends. He found that better diet and exercise helped his colitis somewhat. He struggled to

“I always have the fear of PSC returning.”

find affordable health insurance because he was considered a high risk. In 2003, John was diagnosed with PSC, and later, cirrhosis. About 4 years ago, after a bout of bleeding varices in his stomach, John received a living donor transplant from his brother. “I was lucky to have this option because most people don’t,” he said. Although the transplant went well, John has had reoccurring infections and hospitalizations. He takes 14 pills per day and receives IV antibiotics at home. “I always have the fear of PSC returning,” he said. Being on immunosuppressive therapy he also worries about COVID-19, as he must still go for lab testing and drive three hours for doctor visits. There is also work, and “battles with those insurance companies” to contend with. Despite the pain and the exhaustion, John finds the emotional side effects more difficult. The unpredictability of PSC places stress on families, work, and support systems. “Without a real cure for patients and their families, we can’t escape this reality,” he said.

Off-Label Use of Treatments – Jay’s Experience



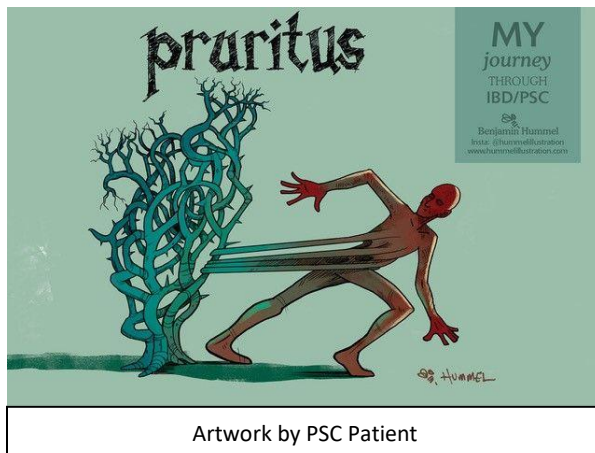
Jay’s son was diagnosed as a teenager with PSC, AIH, and ulcerative colitis. Jay described the hell of having your child diagnosed with an incurable, untreatable disease you’ve never heard of. Through his internet research, they were able to learn about the disease, connect with other patients, and share experiences. In discussing treatment approaches they learned about off-label use of existing medicines (i.e., using an FDA-approved drug for an unapproved use, one that is not

listed on the official product label). Facing a lack of options, they made the difficult decision to try ursodiol and vancomycin for their son. Jay learned that some PSC patients report feeling better and having improved lab test results while taking ursodiol. Ursodiol is not approved for the treatment of PSC, but it has been studied in PSC patients. Although ursodiol has not been shown to improve the clinical course of PSC, and there are safety concerns at high doses, Jay asked, “Have these studies taken into account how much better it makes people feel? I think that matters and it matters a lot.” Similarly, some patients, particularly pediatric patients, report feeling better and have better blood test results when taking vancomycin. “Some even report dramatic improvement with a specific brand of vancomycin,” Jay said. However, there are safety concerns about taking vancomycin long-term and there is the potential for development of vancomycin-resistant enterococci (VRE). Not every PSC patient responds to ursodiol or vancomycin, and Jay said research is needed to understand who responds and who does not. Jay noted that some doctors are reluctant or unwilling to prescribe these drugs for PSC patients. The reality for PSC patients is that they know what to expect if they do nothing, Jay said, and many are willing to try drugs off-label based on the experience of others. “Even if the disease is going to progress, feeling better matters,” Jay said. “For our son, being able to go to work, university, or to hang out with friends matters.” Jay asked FDA to work with PSC patients to help monitor the safety of long-term use of oral vancomycin, and to ensure that how the patient feels is included as an outcome when developing new drugs for PSC.

“Have these studies taken into account how much better [ursodiol] makes people feel? I think that matters and it matters a lot.”

Perspectives on Current Treatment Options for PSC – Moderated Discussion

Panelists Kerrie, Lalit, and Fred continued the conversation on current treatments and unmet needs for the management of PSC and related conditions. There was much discussion of the off-label use of



Artwork by PSC Patient

existing drugs to manage symptoms. Participants also discussed the importance of research to better understand the pathophysiology of PSC and identify medical (non-surgical) treatments and a cure. In response to live polling, pruritus and PSC fatigue were the symptoms for which participants most desired treatment. There was also some interest in treatments for abdominal or liver pain, brain fog, nausea and vomiting, and PSC insomnia. When asked about experiences with pruritus medications, half of the live polling respondents said they had never tried pruritus medications. There were no live

polling respondents who felt the medications they had tried were very effective. Although some reported moderate effects from itch medications, about one third said medications they had tried were rarely effective or ineffective. Of note, the results of the *Our Voices* survey suggest that respondents prioritize the development of treatments that improve long-term liver health, slow the progression of PSC, and reduce the risk of cholangiocarcinoma, over the development of symptomatic treatments.

- **Balancing the Benefits and Risks of Using Treatments Off-Label** – Results of live polling and the *Our Voices* survey indicate that, in the absence of approved treatments, many patients are willing to try products that are not yet proven for PSC. Participants discussed risks and benefits of off-label use of ursodiol and vancomycin, and the need for more research to understand the benefits some patients experience.

Kerrie shared her perspective as the parent of a PSC patient, an inflammatory bowel disease nurse, and the founder and president of PSC Support Australia. She described the desperation of watching her child deteriorate and living through years of “wait and see” with every new treatment. She discussed the importance of health literacy in making the decision to use a drug off-label, including taking the known safety profile of the drug into consideration. As a nurse, Kerrie has conversations with patients about the risks and the benefits of trying a treatment. As a PSC parent, she said she understands in her heart what those benefits are, and she described the need to have some medical hope before the transplant stage. Kerrie added that off-label use of drugs “can actually send us on a discovery path of finding a new treatment.” Lalit, a parent of a PSC patient and a physician, agreed with the need for treatments that can help before the transplant stage. His daughter has had two liver transplants and they have tried vancomycin and other approaches to relieve her symptoms. Jenna called in to share that she has been using vancomycin off-label for several years and said she has been “virtually pain-free, with normal labs, no complications, infections, or disease progression.” She said she has personally experienced different efficacy with different brands of vancomycin, as mentioned by Jay in his testimony. She referred participants to the work of specialists who conduct research on the efficacy of vancomycin for PSC across doses and brands.

Jenna urged FDA “to fund research on this promising, existing therapy, that saved my life and the lives of others.” Miller (moderator) noted the importance of understanding that an individual’s perception of benefit and risk is based on their own disease experience.

- **Seeking Medical Treatments and a Cure –** Although liver transplant is referred to as a “cure” for PSC, it was discussed throughout the PFDD meeting that a transplant is a high-risk procedure, is not available to everyone who could benefit, recovery can be marred by serious complications, and PSC can recur after transplant.

Lalit said “[W]e need to request and implore FDA, the pharmaceutical companies, the medical community, to please work on trying to find a medical cure.” Although PSC is a rare disease, Lalit pointed to the devastating impact the disease has on those who have it and said “[A] medical cure ... will be a tremendous benefit to the society.” Patients are trying many different treatment approaches because so much about the pathophysiology of PSC is still unknown. He called for action by the research community to study, for example, why PSC symptoms wax and wane; why some patients have recurrence after transplant and others do not; and what is the association with IBD? Lalit pointed researchers to the PSC Partners Registry, which he said can assist them in identifying potential clinical study participants (see box).¹⁶

Fred emphasized the need for medical treatments for PSC so that surgical treatments are not needed. Fred listed his numerous post-transplant complications, including cholangitis, surgical adhesions, bile blockage, leukemia, Epstein-Barr virus infection, two occurrences of

PSC Partners Patient Registry

Launched in 2014 in collaboration with the National Institutes of Health (NIH), the PSC Partners Patient Registry contains data from 1,700 PSC patients. It is annually reviewed by an Institutional Review Board (IRB), and the Registry team is HIPAA trained to protect the privacy of every Registry participant. “PSC Partners considers the registry a crucial voice of the patient,” said Registry Director Rachel Gomel. “Each patient's participation is a vote for research.”

The Registry stores surveys, including the *Our Voices* survey which was partly collected through the Registry. Surveys of Registry participants are used to capture patient-reported information to help researchers design their trials. “We've seen how involving the patient voice too late in the process has led to simple errors that [can] negatively affect trial outcome[s],” said Gomel. The Registry also assists with recruitment of patients for clinical trials.

Gomel further described that, as an infrastructure for data collection, the Registry can be adapted, as needed, to take on new functionality, such as a forthcoming portal which will provide approved researchers with access to de-identified patient data. Additionally, a new upgrade has improved features to track longitudinal data. The Registry can also serve as a database of the natural history of PSC and include patient-reported outcome tools. The goal, said Gomel, is to facilitate and expedite research and support new drug development for PSC.



¹⁶ Patients can join the PSC Partners Patient Registry online at <https://pscpartners.org/about/participate/patient-registry.html>. Note that as of February 2022, the PSC Partners Patient Registry has over 2,100 participants.

lymphoma, and, ultimately, recurrent PSC. He described it as “an immensely painful experience,” and added that being immunosuppressed, as required for transplant, “is like fighting with one hand tied behind your back.”

- **Other Unmet Patient Needs**

- PSC Disease Awareness – Francis commented online that her husband, who died in 2020 from PSC and Crohn's disease, went undiagnosed until he developed stage three cirrhosis (decompensated cirrhosis) in 2015. “Life would've been so much easier for Ed if the disease had been known more widely,” she said, “and if there had been a drug that would have given him a longer life.”
- Mental health support –Virpie wrote in to highlight the need for better psychological support for PSC patients. “In Finland we are lacking mental and psychological support,” she said. She also called for more attention to finding effective treatments and a cure.



Artwork by PSC Patients

The *Our Voices* Survey: Current and Future PSC Treatments

- ***Off-Label Use of Ursodiol and Oral Vancomycin for PSC Symptoms***

Although ursodiol and oral vancomycin are not FDA-approved for the treatment of PSC, 78% of pediatric respondents, and 53% of adult respondents to the *Our Voices* survey reported they were currently taking ursodiol. Vancomycin was being taken by 32% of pediatric respondents, and by 7% of adult respondents. Meegan Carey, Executive Director of PSC Partners, pointed out that, “although past clinical trials have conflicting efficacy results, a certain subgroup of PSC patients report that they feel and function better on urso[diol] and have decreased liver function tests.” Similarly, recent small studies of oral vancomycin have suggested usefulness in some cases. Carey highlighted that larger clinical studies are needed to better define the efficacy of these drugs and to understand who responds, in particular why pediatric patients might respond differently.

- ***Types of Medications PSC Patients are Using to Manage Symptoms***

Results of the *Our Voices* survey indicate that 20% of respondents are taking some type of medication for itch; 16% are taking medications for nausea and vomiting; 15% are taking antidepressants; 14% are taking a pain medication; and 3% are taking medication for fatigue. James McMurtry, PSC Partners board member and physician, observed that more than 50% of survey respondents indicated that itching has impacted their quality of life over the past 6 months, but only 20% reported current use of symptomatic treatments for itching. Is this disparity because the treatments are not effective, or have intolerable side effects, or perhaps both?

- ***Patient Priorities for the Development of New PSC Treatments***

Respondents to the *Our Voices* survey overwhelmingly called for the development of treatments that improve long-term liver health and slow the progression of PSC (69% adult, 83% pediatric). Both adult (19%) and pediatric (14%) PSC patients also desired new treatments to reduce the risk of cholangiocarcinoma. Despite the suffering of many PSC patients with a range of severe symptoms, treatments that reduce symptoms were less of a priority (10% adult, 3% pediatric) than those that slow the progression of PSC disease.

PATIENT PERSPECTIVE ON CLINICAL DEVELOPMENT OF PSC TREATMENTS

Testimony on Advancing Pediatric and Adult Clinical Trials

In the final session of the meeting, Lisa, the parent of a child with PSC and a pharmaceutical researcher, and Nathan, a PSC patient and a physician researcher, shared their personal and professional perspectives on advancing clinical trials for PSC treatments. (Brief summaries of their statements are presented here. The full transcript of each video testimony is available in Appendix 2.)

Advancing Pediatric PSC Clinical Trials – Lisa’s Perspective



Lisa’s son, Alex, was diagnosed with PSC and Crohn’s disease at age 11. Lisa has a doctoral degree in pharmacology and has spent much of her clinical research career in the pharmaceutical industry focused on hepatology. “Imagine my surprise ... I had no idea what PSC was,” she said. Faced with the reality that there is no cure or treatments for PSC, Lisa leveraged her professional experience, reading the literature and searching for clinical trials. She learned that Alex would likely need a liver transplant in his early 20’s and found there were no pediatric clinical trials and very few adult studies, most of which were single-center, uncontrolled studies. Nine years later, there are still no clinical

trials for pediatric PSC patients. “I understand, but I cannot accept this,” Lisa said. From her work on hepatitis C, she knew that children metabolize drugs differently from adults, and separate pharmacokinetic/pharmacodynamic (PK/PD) studies are usually required.¹⁷ Different product formulations might also be needed for children. Further, the benefit-risk profile of a product is generally defined in adults first, before pediatric studies are done.

“Unfortunately,” Lisa said, “pediatric PSC [patients] don’t have time to wait.” Lisa suggested that the minimum age for current adult PSC clinical studies be lowered to 13. “We know that many teens are the same size as adults, and they can metabolize the drug the same,” and she suggested incorporating a pediatric sub-study into adult studies to address PK/PD for participants between the ages of 13 and 18. She added that pediatric formulations might not be needed as many PSC patients have been taking medications from a very young age. Another suggestion was to establish expanded

Suggestions to advance pediatric PSC clinical trials:

- **Lower the minimum age for current adult PSC clinical studies to 13**
- **Incorporate a pediatric PK/PD sub-study into adult studies**
- **Assess whether pediatric formulations are actually needed**
- **Create expanded access programs for children under age 13 with advanced PSC disease**
- **Leverage telemedicine to enhance PSC clinical trial participation**

¹⁷ Pharmacokinetics (PK) is the study of how a drug moves through the body (i.e., what the body does to the drug). PK studies describe the exposure of the body to the drug over time, as the drug is absorbed, distributed, metabolized, and excreted by the body. Pharmacodynamics (PD) is the study of the body’s biological response to a drug (i.e., what the drug does to the body). PD studies describe the effects of a drug as it moves through the body, including how well a drug might treat a disease, as well as unintended or adverse effects of the drug.

access programs for children under the age of 13 with advanced disease, but no comorbidities, giving them the chance to possibly benefit from investigational products.¹⁸ Finally, Lisa highlighted the potential of telemedicine to facilitate both pediatric and adult PSC clinical trials. PSC is rare, and patients often do not live near a clinical center. She suggested that trial participation via telemedicine, in partnership with the local doctor, could enhance trial participation and compliance, and improve patient quality of life. “We need to think creatively and do something now to somehow bring tomorrow's medications to our children today,” she said.

Advancing Adult PSC Clinical Trials – Nathan’s Perspective



Nathan was diagnosed with PSC at age 20, two years after being diagnosed with ulcerative colitis. “Hearing the words, no cure or treatment, sucked the air out of the room. I was devastated,” he said. He had never heard of PSC and said it “sounded like a death sentence.” After seeing a hepatologist, who was unable to offer any positive guidance, Nathan sought care at a leading PSC center. “There, for the first time, I felt a sense of hope when I learned about the opportunity to participate in clinical trials.” Nathan described participating in PSC clinical trials as a “no-

brainer,” and said, “Being part of a trial felt like doing something, rather than just waiting for the natural history of my disease to take its course.” He also felt that he would be contributing to finding a treatment and a cure. Nathan was fortunate to live relatively close to a clinical center that was running PSC trials, but added that, as a busy college student, the time commitment for some studies was a drawback. For other studies, the requirement to undergo biopsy was a disincentive for him. In the ten years since his diagnosis, Nathan has moved forward despite the fear and uncertainty that comes with PSC. He is now married and a physician researcher. He described his journey of constant itching, difficulty focusing and sleeping, and recurrent episodes of cholangitis requiring hospitalizations. Three years ago, he received his first of three liver transplants. “Transplantation definitely saved my life, but at an extremely high cost,” Nathan said. His hospitalizations total more than 300 days, he has had 16 surgeries and numerous procedures, and could not work for more than two years. Like others, Nathan highlighted the need for effective

“If we can harness the lessons we're learning today, about how to deliver care virtually, we can drastically expand the number of patients who have access to clinical trials, reduce the burden of participation, and accelerate the science that will lead to life-saving and life-changing discoveries for PSC patients.”

treatments that can slow the progression of PSC and delay the need for transplant. Even if the procedure goes well, the physical toll and financial burden of a transplant can be significant. “I hope that one day PSC will no longer be on the list of common indications for transplantation,” Nathan said. “And seeing the ways in which we've been able to adapt to the reality forced upon us by COVID-19 gives me a

¹⁸ Expanded Access, also called Compassionate Use, provides a way for patients with a serious or life-threatening condition to get access to an investigational medical product that is being evaluated in a clinical trial for which the patient is not eligible to enroll, and when the patient has no other treatment options. See <https://www.fda.gov/news-events/public-health-focus/expanded-access>

lot of hope.” He described how his research team has revised their clinical trial protocols to transition completely from in-person enrollment to virtual enrollment. “If we can harness the lessons we’re learning today, about how to deliver care virtually, we can drastically expand the number of patients who have access to clinical trials, reduce the burden of participation, and accelerate the science that will lead to life-saving and life-changing discoveries for PSC patients,” Nathan said.

Perspectives on Clinical Trial Participation – Moderated Discussion

- **Participating in Clinical Trials** – Panelists Kerrie, Lalit, and Fred all encouraged PSC patients to participate in clinical trials. Fred supported participating in a clinical trial “if for no other reason than just to have that feeling in your head that I’m helping. I’m doing something to advance the cause, to make some progress. It’s better than standing still.” Kerrie agreed and added that participating in a trial gives the patient access to the clinical experts in the field of PSC research.

Live polling respondents indicated that the use of telemedicine where possible would be a key factor in making clinical trials more patient-centric. Responses across the remaining choices was comparable with participants supporting the incorporation of home health nursing visits when appropriate, home blood draw, stool or saliva sample by mail, home medication delivery, and informed consent administered online versus in the office.

Participants responding to the live polling on behalf of a pediatric patient indicated that having enough information about the trial, the safety profile of the trial drug, a recommendation from the child’s physician, and requiring no invasive procedures beyond the usual routine tests were top concerns for enrolling a child in a PSC clinical trial. Importantly, no participants responded that they would never enroll their child in a clinical trial.

Nearly all live polling participants said they would share their health data for a natural history study under the appropriate privacy conditions. Similarly, nearly all responded they would allow their deidentified natural history data to be shared beyond the original study to facilitate drug development.

- **Biopsies** – Several participants noted concerns about the requirement of many clinical trials that participants undergo biopsies. Laura called in to say that “the requirement for biopsies is hugely dissuasive for participation in trials.” She questioned the informative value of biopsies, pointing out that “PSC by nature presents in a very patchy way in the liver. And a biopsy taken from one area could show nothing and just be right beside the area that is showing something.” Liver biopsies are high-risk, invasive, unpleasant procedures that can lead to complications, Laura said, adding that she had internal bleeding and was hospitalized after a biopsy. She called upon FDA and clinical researchers to reconsider the need for biopsies and to develop other methods that could be used. Mark commented online that biopsies can be “a potential impediment to participating in future trials.” He has participated in two trials and was required to have three liver biopsies for the first, and two for the second. He asked researchers to consider whether consistent results across biopsy,

“The requirement for biopsies is hugely dissuasive for participation in trials.”

FibroScan, blood work, and magnetic resonance cholangiopancreatography (MRCP) could eliminate the need for additional biopsies.

The *Our Voices* Survey: Clinical Trial Participation

- ***Awareness of Clinical Trial Opportunities***

Nearly three-quarters of respondents to the *Our Voices* survey said they had never been approached about participating in a PSC clinical trial for an investigational medication. McMurtry acknowledged that there have not been many PSC trials, but said the results indicate the need for raising awareness about PSC clinical trials, especially among patients whose care is not affiliated with a large medical center.

- ***Current or Prior Participation in Clinical Trials***

About 12% of respondents reported current or prior participation in clinical trials, and more than 40% reported current or prior participation in non-medication studies (e.g., registries, surveys, collection of laboratory or imaging data).

- ***Patient Willingness to Participate in Clinical Trials***

A majority of respondents to the *Our Voices* survey were willing to participate in some form of clinical trial. More than half said they would be willing to participate in clinical trials of products to slow the progression of, or cure PSC (55%), or trials of new surveys or tools to assess symptoms or quality of life (55%). Forty-one percent responded they were willing to participate in a clinical trial of products for PSC symptom management. Nearly two-thirds (61%) of respondents were willing to participate in a study that might require new tests, including collection of biological samples, genetic tests, or imaging tests. Only 28% were willing to participate in a trial if it would require one or more liver biopsies. (See Appendix 7 for additional responses regarding patient motivation for participation in a clinical trial).

- ***Key Concerns About Enrolling in a Clinical Trial***

Our Voices survey respondents were asked to select their top five concerns about participating in trials from a list of 19 that were previously identified. Of greatest concern was the possibility of unknown side effects or long-term risks, followed by fears of jeopardizing their current quality of life or stability of their condition, concerns about travel time to the study center, the impact of the trial drug on their current treatment, the need for a biopsy, and whether participation might affect their opportunity for a transplant. (See figure in Appendix 8. Additional concerns listed by survey respondents are included in Appendix 9).

CONCLUDING REMARKS

PSC Partners Seeking a Cure Founder and CEO, Ricky Safer, summarized her key takeaways from this externally-led PFDD meeting.

Priority Unmet Needs:

- **Much remains unknown about the root causes and disease pathogenesis of PSC.** The extent, severity, and impact of the symptoms of PSC are still not well-characterized. A better understanding is needed of the clinical course of pediatric PSC, and the impact of PSC on growth and development. The association between PSC and IBD also needs to be elucidated.
- **Earlier and more efficient diagnosis of PSC is needed.** Patients also want less invasive methods for risk prediction and prognosis. There is a need to raise awareness among providers who treat patients with IBD about the relationship between PSC and IBD.
- **More effective screening for early detection of cholangiocarcinoma is needed.** Current tools for hepatobiliary cancer surveillance still show low sensitivity. More sensitive tools for early cholangiocarcinoma diagnosis are needed.
- **Patients urgently need effective treatments for the symptoms of PSC.** There are no proven therapies to improve how PSC patients feel and function. Participants vividly described the significant impacts of pruritus, fatigue, and pain, in particular, on their ability to function on a daily basis and on their overall quality of life.
- **Patients urgently need effective treatments for PSC.** No treatment has been proven to increase survival of PSC patients. Treatments are needed that slow PSC disease progression, delay the need for transplant, and prevent post-transplant recurrence of PSC.
- **Transplant is not a cure.** Liver transplantation is a high-risk procedure with the potential for serious complications and recurrence of PSC. A true medical cure for PSC is needed.

Taking the Next Steps Together:

- **PSC patients are ready and willing to participate in the search for treatments and a cure.** PSC patients are interested in participating in clinical trials and are eager for education and information about the trial process, the safety of the investigational product, and the benefits of trial participation. To better meet patient needs, the patient perspective should be incorporated in the very early stages of clinical trial protocol development, and patients should be respected as an integral part of the clinical trial process. PSC patients can also play an important role in advancing PSC clinical trials by, for example, contributing to efforts to develop PSC-specific patient-reported outcome measures and surrogate markers of clinical endpoints.



- ***PSC Partners is ready to help facilitate and expedite research in partnership with industry.*** PSC Partners can help with study recruitment through the PSC Partners Patient Registry and can help to identify potential barriers to recruitment and retention. PSC Partners can help educate patients about the trial process, foster trust between patients and researchers, and disseminate clinical trial information via social media platforms and other venues. PSC Partners is also actively studying ways of facilitating the development of a robust, regulatory-grade natural history database to support clinical trials.
- **Considerations for PSC clinical trials:**
 - Embrace telehealth services to expand the reach of PSC clinical trials and reduce the burden of participation. The COVID-19 pandemic has revealed the power and potential of telehealth services. PSC Partners encourages clinical researchers to leverage telemedicine, home health visits, electronic informed consent, home drug delivery, and home-based surveys to engage more PSC patients in clinical trials.
 - Reconsider the need for liver biopsies in clinical trials. The increased sensitivity of imaging technologies can hopefully reduce the need for invasive, risky, and often inconclusive liver biopsy procedures.
 - Identify validated surrogate endpoints for PSC clinical trials (and recognize that normalized serum alkaline phosphatase levels do not necessarily correlate with improved quality of life).
 - Develop clinical endpoints that focus on treatment outcomes of importance to patients and on patient survival. Develop validated, PSC-specific, patient-reported outcome measures for clinical trials.
 - Design trials with expanded inclusion criteria. Many patients are willing, but ineligible to participate in a PSC clinical trial (e.g., because they are taking ursodiol).
 - Consider creative approaches to collecting pediatric clinical trials data (e.g., including teenage PSC patients in adult clinical trials, incorporating a pediatric PK/PD sub-study into adult studies).

bile transplant donor Urso disability uncertainty
 death gluten inflammation environment jaundice
 MRCP support fecal transplant asymptomatic pain
 ultrasound nutrition early work sensation dilation
 cholangiocarcinoma depression anti-anxiety med's
 pruritis infection CCA cadaver donor diagnosed
 listed ERCP vitamin deficiency ulcerated colitis
 post-transplant hormones high-risk OB research EH
 CT genetics microbiome inhibitors caregiver PSCer
 fatigue auto-immune PSC Partners Registry Rifampin
 pain gift PIC line antibiotics immunologist hope
 Alk Phos fear liver unique fever stricture friends
 cholangitis stress biliary tract sibling stigma stent
 atrophy spouse recovery cholestasis surrender bile
 clinical trial blood test cholesterol ALT courage
 rest strength explain living donor cholestyramine
 cirrhosis symptom chronic treatment progressive
 organ donation awareness biopsy waiting FISH
 tissue risks recipient seek quality of life bilirubin
 obstruction hepatic encephalopathy enzymes scars
 sleep complications aggressive scratches bruises psc

Artwork by PSC Patient

On behalf of PSC Partners Seeking a Cure, Safer expressed her deep gratitude to the PSC patient community for sharing their voices “loudly and courageously” and providing insight into their unique PSC journeys. Together, the input from the speakers and panelists, the comments and calls from the online participants, and the responses from the 819 *Our Voices* survey participants drew attention to the key symptoms that matter most to PSC patients, raised awareness about their unmet treatment needs, and outlined their hopes and desires for future PSC clinical trials, treatments, and a cure. Safer also expressed PSC Partners’ gratitude to the staff from FDA for their participation in this externally-led PFDD meeting, for their continued support of rare disease communities, and for encouraging patients to become active stakeholders in all aspects of research.

“The burden of our unpredictable disease is overwhelming, and we hope that the FDA, pharmaceutical companies, academic researchers, and clinicians have gained a clear understanding of what it's like to live with PSC. We understand the enormous challenges that researchers face in unraveling the complexities of PSC. In addition to being a rare disease, PSC is further complicated by its heterogeneous symptoms, its erratic progression, and its unexplained association with IBD,” Safer concluded. “Our urgent need for solutions continues to increase. Patients are suffering, and we continue losing beloved community members. Industry and the FDA, we want and need your help. We are ready to work with you.”



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APPENDICES

APPENDIX 1: MEETING AGENDA



Making Our Voices Heard:

Externally-Led Patient-Focused Drug Development (PFDD) Forum

October 23, 2020, 10 AM – 4 PM ET

AGENDA

10:00 AM Welcome and Introductions

Veronica Miller, PhD, *Executive Director, Forum for Collaborative Research and Professor (Adjunct), UC Berkeley*

Mary Vyas, *President, PSC Partners Seeking a Cure, Canada*

Ricky Safer, *Founder and CEO, PSC Partners Seeking a Cure*

10:12 AM Overview and Objectives of the Patient-Focused Drug Development Program

Ruby Mehta, MD, *Medical Officer, FDA-CDER-OND-OII-Division of Hepatology and Nutrition*

10:20 AM Natural History, Clinical Management and Treatment of PSC

Christopher L. Bowlus, MD, *Lena Valente Professor and Chief, Division of Gastroenterology and Hepatology, University of California at Davis*

10:35 AM HOW DO PSC CLINICAL SYMPTOMS AFFECT MY QUALITY OF LIFE?

- **Patient Perspective on Key Clinical Symptoms – Patient Testimonials:**

Pain: Afsana

Pruritus: Tim

Fatigue: Jessica

Impaired cognitive function: Elizabeth

Living with co-morbidities: Dan

- **Overview and Relevant Results of PFDD Survey and Polling Instructions/Questions**

Joanne Hatchett, RN, MS, FNP, ACHPN, *Medical Science Liaison, PSC Partners*

- **Open Forum Q & A – Zoom Panelists**
Elizabeth, Jerome, Tawny, Joe

11:50 AM WHAT ARE THE CONSEQUENCES OF THE LACK OF EFFECTIVE TREATMENTS FOR MY PSC?

- **Patient Perspective on Advanced Disease – Patient Testimonials:**
Cholangiocarcinoma: Kevin
Cirrhosis and pre-transplant: Kristian
Post-transplant and recurrent PSC: Todd
- **Relevant Results of PFDD Survey and Polling Questions**
Joanne Hatchett, RN, MS, FNP, ACHPN, *Medical Science Liaison, PSC Partners*
- **Open Forum Q & A – Zoom Panelists**
Alison, Niall, Mónika, Nicola

12:45 PM LUNCH and view community images and artwork

1:15 PM WHAT ARE THE UNIQUE ISSUES FACING PEDIATRIC PSC PATIENTS AND THEIR CAREGIVERS?
Natural History, Clinical Management and Treatment of PSC for Pediatric and Adolescent Patients
Jorge Bezerra, MD, FAASLD, *President, American Association for the Study of Liver Diseases; Professor of Pediatrics, Cincinnati Children's Medical Center*

- **Pediatric and Adolescent Patient Perspective - Patient and Caregiver Testimonials:**
Living with PSC: Bek
Parent concerns: Alex
Living donor pediatric transplant: Richard
Pediatric transplant journey: Jennifer
- **Relevant Results of PFDD Survey and Polling Questions**
Meegan Carey, MBA, *Executive Director, PSC Partners Seeking a Cure*
- **Open Forum Q & A – Zoom Panelists**
Chelsea, Afsana, Willie, Richard

2:20 PM HOW CAN THE CURRENT TREATMENTS OF PSC BE IMPROVED AND MADE MORE TOLERABLE FOR ME?

- **Patient Perspective on PSC Treatment and Related Conditions – Patient Testimonials:**
Treatment of pruritus: Kristina
Management of other key symptoms: Lindsey
Diagnosis and treatment of acute cholangitis: Laura
Management and treatment of IBD in PSC patients: John
Use of off-label therapies: Jay

- **Relevant Results of PFDD Survey and Polling Questions**
James M. McMurtry, MD, FACS, *Board Member, PSC Partners Seeking a Cure*
- **Open Forum Q & A – Zoom Panelists**
Kerrie, Lalit, Fred, Rachel

- 3:20 PM HOW CAN THE PATIENT PERSPECTIVE BE INCORPORATED INTO THE CLINICAL DEVELOPMENT OF PSC TREATMENTS?**
- Patient Testimonials**
- **Special Considerations for Clinical Trials in Pediatric and Adolescent Patients**
Lisa Pedicone, *PhD, PSC Parent*
 - **Understanding the Patient Experience and Clinical Trials – Lessons Learned**
Nathan Baggett, *MD, PSC Post-transplant Patient*
 - **Relevant Results of PFDD Survey and Polling Questions**
James M. McMurtry, MD, FACS, *Board Member, PSC Partners Seeking a Cure*
 - **Strategies to Incorporate the Patient Voice into Clinical Drug Development**
Ricky Safer, *Founder and CEO, PSC Partners Seeking a Cure*

- 3:54 PM Summary and Wrap-Up**
Veronica Miller, PhD, *Executive Director, Forum for Collaborative Research and Professor (Adjunct), UC Berkeley*

APPENDIX 2: FULL TRANSCRIPTS OF PATIENT AND CAREGIVER PRE-RECORDED TESTIMONIES

Patient Perspectives on Key Clinical Symptoms

Afsana

When I was diagnosed with PSC at 16, the most bothersome part was its negative impact on my social life, which took a toll on my emotional health as well. Shortly after being diagnosed, I was bullied for being different and for receiving special treatment. My peers and teachers couldn't really understand the impacts of having a chronic progressive and life-threatening illness. Back then, I had no idea what I was really in for until each new symptom appeared and became unbearable. And that's when I realized that it was the beginning of a long and painful struggle I was likely going to experience for the rest of my life. Now, after five years of living with PSC, I can confidently say that the worst symptom is the pain, and I've learned that pain isn't just physical. It's also how we feel emotionally about our lives. And every day I notice myself getting sicker and sicker.

As my PSC really progressed, my quality of life also decreased significantly, and both my social and work life suffered. I'm awake at all hours of the night itching, and many days I'm so tired that after an eight-hour nursing shift, I sit alone crying and eating and resting for the first time that day. There are even days when I'm not able to stand in the shower because I'm just too tired. I also have pain in my upper right quadrant and that pain is so bad at night. I get really irritated at myself for not being able to cope with it. It feels almost like a shark biting the side of my liver radiating to my back and shoulders.

The emotional toll of this disease is completely devastating. It's knowing you have so much potential in life, but you can't reach your goals or wishes because you're just too tired to get out of bed that day. It's when your partner asks if you'd like to go out for dinner and you burst into tears in the washroom while getting ready, in fear he's going to leave you because you're just no fun. It's the effort you put towards looking and acting okay and unaffected, which is even more exhausting. It's having to walk away and set someone you love free, so they don't have to pause their life for you. And it's being trapped inside a brain and body that no longer work together. The reality of this disease is its unpredictability as we know. Maybe today I can get up and wash the dishes or make a well-balanced dinner instead of eating a bowl of cereal, or even feel like I got more than three hours of sleep.

Maybe I'll be able to have more than one outing that day. And that's something I now consider a daily win, but the worst is when the opposite happens, and I can't do anything, and when my pain is so unbearable and severe that I take it out on my loved ones. And at those times I become a mean and grumpy person to my family. And I isolate myself away from my friends. The pain, which is chronic and doesn't improve with medication for me, makes me feel trapped in this progressively diseased body and is a constant reminder that I can't reach my full potential. This pain will always be a part of my life and it will never let me forget it. And that's why it's so important we work together to find symptom management tools for PSC pain. I would never, ever wish PSC pain on anyone.

Tim

Hi, my name is Tim, and I was diagnosed with PSC in 2001. I was told back then that I had five years to live. With three young children, my wife and I searched for a specialist. We found the Mayo Clinic, and were told it would likely be 10 years, if not more, and here we are almost 20 years later. At this time, I'm beginning the transplant process, with a MELD score of only 17 and severe symptoms. My primary symptom is unrelenting itching, which was described by another PSCer as suicidal itch. I couldn't agree any more. My itching has been my greatest disability, beginning about a year ago and escalating for the last six months. It consumes me throughout my entire day with itching from my scalp to the bottom of my feet and all in between. There is no spot on my body that doesn't crave attention. It's at bedtime that it becomes almost unbearable. At night, when there are no distractions, my body unleashes an attack of itching, so significant that I end up tearing up scabs previously made and leaving bloodstains on my pillows and sheets.

I've been prescribed different itch medicine, and after some relief, eventually get back to the same severity of itching. It is absolutely miserable. Once I'm in bed, I begin to itch until I fall asleep. A sleeping pill works pretty well for a short time. In my dreams, the itching may be light or strong, and can keep me awake between two to four hours. It really sucks. Itching slows me down each morning as it interrupts every segment of my normal routine. Getting out of bed, brushing my teeth, getting dressed are all delayed due to the itching.

Itching hurts. I itch so much it feels like someone is taking sandpaper to my skin which feels inflamed and raw. The more I itch my skin the more it hurts. As I remove my clothes to go to bed, my body feels superheated like I sat in the sun too long. Itching my scalp is very painful too. My eyes can hurt from the scratching I do, which worries me as I had eyelid surgery two years ago, requiring silicone slings to hold the eyelids in place. And I don't want to tear those slings with my itching. That would mean another surgery. Itching affects my family. My brother came down from New England recently to visit me and was shocked at how unrelenting the itch was. He couldn't believe that I scratch constantly throughout the day.

My family feels badly too. They've watched this miserable itch and there's nothing they can do to help. It pains them to see me have to go through this. It pains me too to see my friends that I've met over the years at our PSC conferences go through the itching that I am. Many had to deal with other issues like ascites, hepatic encephalopathy, and bleeding varices to name a few. And many unfortunately die either waiting for a transplant or from the complications of receiving one. We need help and we need it fast. Please consider everything you can for those of us contending with this awful disease. Thank you.

Jessica

When I say the word fatigue, people often relate it to being tired. But I promise you, it is not the same thing. PSC fatigue is like having a faulty battery that you put on a charger overnight. You never know if you're going to get a full charge, a half a charge or maybe a dead battery the next morning. My name is Jessica, and when I was 22 I was diagnosed with PSC. Physically, it hits me like a ton of bricks. Have you ever felt so ill that you've had to stop what you were doing right then and there and just go straight to

bed? Well, I have days like this on a regular basis. For me, fatigue causes headaches, severe nausea, lightheadedness, just to name a few of the symptoms. Even after having nine hours of sleep, sometimes I wake up with a dead battery. Even after a nap, a simple task like emptying the dishwasher, folding my laundry, it'll send me right back to bed. PSC as a disease, and PSC fatigue as a symptom, are really hard to explain to other people because when you look at me, I don't look sick.

I have lost track of how many family functions and social events that I've missed. If I do feel well enough to go, maybe you'll see me there laughing, smiling, chatting with people. But what you don't see is the amount of concentration it takes for me just to keep up with the conversation, or when I stop in the middle of my sentences because I can't remember what I was going to say next, or when I slur my words. When you have an invisible disease, people can't see what you're going through, and they don't understand.

One of the hardest things that I've ever had to do in my entire life was put my health first, even in front of my mother's, who was dying because of Parkinson's disease. My fatigue made the six-hour trip there and back to visit impossible. And my visits never felt long enough. I can't tell you how difficult it was to leave and to see the tears rolling down her face after only being there for an hour. She passed away this December, and the loss is still incredibly difficult. Living with PSC and dealing with fatigue on a regular basis, it prevents me from working, from spending time with my friends and my family. And it prevents people from relying on me. This isn't the life of the person that I want to be. It's a life of a person that I'm forced to be. And I hope it doesn't have to be this way forever. Maybe one day, somebody might be able to figure out a way to fix my faulty battery. I know that myself and others with PSC, we deserve to experience life to the fullest, but we need your help.

Elizabeth

My name is Elizabeth, and I am 36 years old. I am a daughter, a sister, an aunt, a friend, and a pediatric nurse. I also happen to be a PSC patient, and I have been one since I was only one and a half years old. At that time, I suffered from bouts of severe diarrhea, feeding intolerance, and abdominal pain. Finally, at the age of nine, I received my diagnosis of PSC. At 13, it was autoimmune hepatitis. At 14, my life really began to change. School became harder, my retention seemed just slightly off. My health took a nosedive when I was 15. Due to missing school from being hospitalized, I had to have tutors. They noticed that recalling information from week to week began to really falter. I was no longer able to think critically like I used to. It was like living a hazy dream.

Eventually, my tutors and my parents made the decision to pull me out of school completely as I could no longer complete my schoolwork. No matter how hard I worked, my retention and working memory were lost. I was only 15 when the basic right of school was taken away from me due to PSC. At this point, my life was on hold until I could be transplanted. My miracle happened when I was 16. I received the gift of life on July 3rd, 2000. After the transplant, I made it my mission to make up for lost time. I completed high school and went on to nursing school to achieve my dream. I was given the opportunity to fully embrace life and the challenges and rewards that come with it. During this time, over many

conversations with my family, it was revealed that I have gaps in my memory from the years leading up to the transplant.

Not only are memories cloudy, some are not even there. I don't remember helping to move my sister into college. I barely remember my Nana being diagnosed with cancer and losing her battle with it. When I search my memory from this time of my life, I have memories with no clear details or just complete blanks. At the age of 30, I was re-diagnosed with PSC. My world dropped out from beneath me, and my thoughts immediately went to when the day would come again, that my life would once again be on hold. What would happen when my mind would start to go again? I am a nurse. I need to be able to think clearly and critically at all times for patient safety.

What happens when I am no longer able to support myself? Losing mental acuity and no longer being able to be a productive and contributing member of society is what haunts me the most. The idea of losing my independence, it's my greatest fear. I can handle physical discomfort, but losing my mind, losing what makes me, me, is enough to make me crumble. I am here today to ask you to give me hope, hope that another child will not lose parts of their childhood due to this disease. Hope that I, and the rest of the PSC community will have the ability to live life fully and then we all will have the ability to remember the memories that we make.

Dan

I'm Dan, and I'm a motion graphics artist living in Astoria, Queens, but I'm moving to upstate New York. In 2008, I was diagnosed with PSC and ulcerative colitis after having my gallbladder removed. I started developing ulcerative colitis symptoms that couldn't be treated with just Lialda and had to start taking an immunosuppressant drug called 6-MP. In 2009, I lost about 30 pounds. The frequent bathroom breaks at work took a toll on my job performance and I was laid off. The daily symptoms I was dealing with were frequent trips to the bathroom, stomach pain, lack of appetite, throwing up bile, severe fatigue, insomnia, and emotional distress. I spent several months in 2009 looking for work while dealing with fatigue of PSC and ulcerative colitis. In 2010, I got a full-time job again and my ulcerative colitis was in remission with medication. But the PSC symptoms of severe fatigue, cirrhosis, vomiting, lack of appetite, stomach issues, sleeplessness, and brain fog deeply affected my quality of life and my mental health.

My liver health declined so severely from 2010 to 2016 that I needed a liver transplant. And my wife asked for a divorce simultaneous to that. She wasn't interested in what was in store and was tired of dealing with my chronic illness. Over these years, I felt like I was slowly disintegrating. I was able to get a living donor transplant in 2017 and my fatigue went away. But after going off prednisone, I began developing issues with rosacea and within a year, my UC flared since I was no longer taking anything for it. I was treated with prednisone and Entyvio and I was able to get it under control, but I developed mild rejection of my liver and had to have frequent blood work. And the long-term use of prednisone made me develop skin issues and prednisone-induced diabetes. I'm 36 and since I was 24, I've had to have over 16 colonoscopies.

I have a high chance of getting colon cancer and need yearly monitoring for the rest of my life. A liver transplant is currently the only “cure” for PSC, and it was a relief when I received the liver transplant, but not all the side effects and health issues have gone away. I'm still living in constant fear with unpredictability and feeling like life is a constant battle, which has led to ongoing emotional distress and PTSD. I live in fear of recurrent PSC and ulcerative colitis. It's also hard to deal with the healthcare system. Since the transplant, I've hit my out-of-pocket max each year and everyone I've ever spoken to who also has PSC has had different experiences, but they've all dealt with pain and mental health issues due to the disease. I wish there was more research done on my UC and PSC. I don't want to see people with this disease go bankrupt and live unfulfilling lives. They're all fighters and deserve the best.

Patient Perspectives on Advanced Disease

Kevin

Hi, my name is Kevin, and I was initially diagnosed with PSC back in 1996, at the age of 14. My local doctors decided that it was most likely my gallbladder causing the symptoms, which included significant pain and discomfort in my upper abdomen area. So, they performed surgery to remove my gallbladder. Within two weeks, they narrowed it down to PSC, thanks to a biopsy collected during the surgery. They also performed a colonoscopy one month later and determined that I also had Crohn's disease. At that point, my local gastroenterologist decided to put me on ursodiol, a bile salt therapy. And I remained on that for the next 20 years.

In the beginning, the most difficult part of having a diagnosis of PSC was the uncertainty. At the time, doctors said that I would need a liver transplant eventually. I didn't know if that would be two years, five years, 10 years, but over the course of the next 20 years, I dealt with different bouts of cholangitis. Some worse, some not as bad, but they continually got worse in my upper twenties and lower thirties. And the number of bouts of cholangitis I had was increasing. The only way they treated that was with some pain relievers and antibiotics to bring down the fever.

In 2013, I began treatment at the Mayo Clinic in Rochester, Minnesota. I was supported by my employer at the time to help cover travel expenses because it was important for them for me to get to a center of excellence, to get the best care possible. In October of 2016, I was hospitalized locally. And during that timeframe, I had intense pain that would not go away. After a week-long hospitalization, I was sent up to the Mayo Clinic and within seven days I had a diagnosis of perihilar cholangiocarcinoma, which showed no signs of spreading and was most likely at stage two, thankfully. Had I waited another few weeks it would have most likely spread and been inoperable at that point.

The wait for the liver transplant was difficult. Over five months of waiting, in which case we had to relocate my family up to the Rochester area. One of the hardest things I've ever had to do during that time of waiting was putting together a will and advanced directive with my spouse when I was only 34, 35. I was called for my transplant surgery on July 5th. Today, I'm still thankful that someone was willing to be an organ donor and that my wait time was only seven and a half months from diagnosis to transplant. Things began to get back to normal in 2018. However, in 2019, after colonoscopy, they discovered that I had high-grade dysplasia and early signs of colon cancer. So, they had to do a total

colectomy requiring three surgeries for me to get back to normal. Not an uncommon diagnosis with my medical history.

As I said before, the most frustrating part of having PSC and cholangiocarcinoma is dealing with the unknowns. Will I be able to continue to work remotely or will I have to go out on leave for months on end? Can the cancer continue to grow even after the transplant? Even with all the knowledge at the Mayo Clinic, it's still impossible to predict when or if these things are going to occur. After everything I've gone through, I hope that researchers can come up with a test and PSC protocol to identify cholangiocarcinoma earlier and find a way to slow PSC progression by slowing down scarring of the bile ducts.

Kristian

Can you imagine yourself for a period of several years, when you wake up each morning, you do not feel rested despite having slept the night through? And then you need a midday nap, just to make it through to the evening. What a way to spend your late twenties and thirties, dealing with this constant fatigue because of PSC. Hello, my name is Kristian and I was diagnosed with PSC in 2004.

For several years after this diagnosis, PSC showed no symptoms. Then one day, jaundice had appeared in my eyes. This meant PSC had been causing havoc in my body. Six months after marrying, my wife and I moved to Ontario. That allowed me to be a patient of the Toronto Liver Center. There, I underwent several tests to determine the extent of PSC. While at the hospital for these tests, I had my first internal bleeding episode. After using the bathroom, I noticed blood in the toilet. I was then immediately treated for an esophageal varices bleed. And at that time, we didn't even know what varices were. And here we were dealing with a life-threatening one. We were so scared.

Confirmation then came that I needed a new liver as it was cirrhotic. I was then put through the process to be put on the liver transplant waiting list. To help reduce further bleeding episodes, my wife and I would make monthly six-hour trips from Ottawa to Toronto for endoscope procedures, which had banded my varices. I was also prescribed Nadolol, but it had reduced my ability to be active. Just what I needed when I was tired all the time. PSC was now impacting our lives forever. As newlyweds, we'd have loved to start a family, travel outside of Canada, and fulfilled our dreams. But because of PSC, these were no longer possible. The jaundice, the constant fatigue, the endoscopes. They became our new norm. Our mental health was also being impacted as we didn't know if I'd get the transplant call, or if preventative measures would work to help reduce the risk of internal bleeding, as my varices were getting worse. For they had spread into my stomach, which made treating them more difficult. The treatment then requires special glues and coils to properly secure them, as opposed to the typical bands. But despite these efforts, I had my worst bleeding episode in 2016. I'd vomited so much blood, with such force into the toilet that it sprayed the walls and the floor of the bathroom. I'll never forget how scared I was seeing the hospital staff rushing to my assistance. Regrettably, PSC did not stop with my varices. It had also weakened my bones to the point that I had osteopenia. A simple slip on the ice in 2017 then resulted in a broken hip. This was one of the most painful experiences of my life. I needed months of intense physical therapy to regain my mobility.

I'm lucky I've survived PSC, but it's only because I had a life-saving liver transplant in 2017. I am very grateful for the second chance of life. PSC is a terrifying chronic condition that can strike without warning and has no mercy. I hope a cure can be found soon as I'm well aware of its disruptive nature. A fate no one else deserves.

Todd

My name is Todd. I'm the husband to an amazing wife and the father to two beautiful children. When I was 15 years old, I was diagnosed with PSC. After two years of suffering through uncontrollable itching and maddening insomnia, I received a living donor transplant from my personal hero, my brother. Within a few days after the surgery, I developed a blood clot in my hepatic artery causing the liver to fail almost immediately. I recall very little from the 12 days in between my first two transplants. But I do remember waking up with the guilt of taking my brother's liver and not being able to use it.

The liver after my brother's lasted approximately six years before the recurrent PSC that entered its way back into my body required it to be replaced. I received my third transplant in November of 2009. Three transplants of the same organ in approximately six years. For years, I felt good. I got married. I bought my first house. I had my first baby on the way. Until one day I didn't. I came home from a business trip with fever and chills. And I remember going back to sleep on the couch. I woke up days later in the ICU on a ventilator, not knowing where I was or how I got there. I spent over a month in the hospital and nearly two years withering away on the transplant list, yet again. This time with tubes coming out of my abdomen, draining the bile and infection from my liver.

For two years, I barely lived my life. What should have been the best years of my life were robbed from me. When my daughter was born, I could barely hold her without getting exhausted. I couldn't be the hands-on dad that I always pictured myself being. I remember realizing that there was a good chance that I could croak any day and she wouldn't remember who I was. I wrote life advice for her in a journal every night because I wanted her to have words to remember me by.

PSC is always with you. It doesn't matter if you're post-transplant or not. It's always there. Every time you feel an itch or get a fever, you get this little voice in the back of your head asking, is this the PSC coming back? I'm not an anxious person. I'm probably as laid back as they get. But the thought of having to tell my family that I'm having symptoms again is my biggest nightmare. Putting your loved ones through that kind of pain can be worse than the disease itself. I've gone through four transplants because of PSC. I make light of it by telling people I'm impossible to kill. But the truth of the matter is that every time I feel under the weather, I get this gut wrenching feeling that this could be it. Years ago, I fell asleep with a fever and woke up in the ICU. Could this be the fever I go to sleep with and not wake up? That weighs on you, emotionally and physically, until it doesn't. This disease has tested me and my loved ones for years. It has caused so much unnecessary pain to so many people. I live with the constant fear that my kids will grow up without their dad because number five is the straw that breaks the camel's back. And that is a fear that no parent should have to live with.

Patient Perspectives on Pediatric PSC

Bek

Hi, I'm Bek from Melbourne, Australia, and I'm 22 years old. I was diagnosed with primary sclerosing cholangitis just before my first birthday, and with ulcerative colitis seven years later. I suffered many of the common and not so common complications of end stage liver disease, including hepatopulmonary syndrome and varices around my ileostomy that would bleed up to 400 ml at a time. I was transplanted at age 13 after being officially listed for 18 months with only a few weeks left to live. Post-transplant, I am doing quite well, but still live a modified life and with the knowledge that I may have recurrent PSC. Being diagnosed so young, I don't have any idea what it's like to be healthy, so it's hard to know exactly how PSC has affected me.

Growing up, I was always the smallest in my class by a landslide due to stunted growth. I always got fatigued a lot quicker than my peers. I could take pills by age four. I often thought something was common knowledge when it wasn't, for example, what a liver is. I've made a lot of sacrifices because of my health, and so has my family. When you spend your childhood and teen years sick, you really have to learn to manage your expectations. Dreams were shattered and then changed. I wanted to be a famous actress, but my health said no. So, then I wanted to act in commercials. Still no. Okay. Maybe I'll be a makeup artist in movies? No. Right. What about if I volunteer backstage at an amateur theater company? It's hard work, but doable, and I love it. Every single thing in my life went through that process. Nothing was planned A or B or even plan O. You make the best with what you're given.

Why do I put so much effort into campaigning for primary sclerosing cholangitis? Because we need awareness, awareness for the disease, but also for how much it varies. PSC is so unpredictable. I work hard because we need a cure. Even a treatment would be great. Did you know that there are zero treatments for PSC? We treat the symptoms, the itch, the varices, pain, fatigue, infections, and so on, but we don't treat the cause of all those problems because there isn't anything. So that's why we need to work hard to raise awareness and funds, to get treatments, and one day a cure. It's too late for me and the damage PSC has caused my body, and we can't bring back those that we've lost, but I want to change the future for others with PSC. I want them to have hope and options in the medical realm. Thanks for listening. Bye.

Alex

Last year, my son was so excited as we waited together at the bus stop for the school bus to take him to kindergarten for the very first time. He had this enormous backpack that, even on its tightest setting, overwhelmed his little five-year-old body. For other parents, it seemed like that iconic moment as each of their children climbed the bus steps for the first time into a more independent childhood towards graduation from high school. When it was my son's turn to climb the steps, I knew my worries were different. I fought a numbing crushing sadness as I wondered whether his footsteps will lead first to his driver's license or to a liver transplant. I wondered how many stays in a hospital he will have to endure as his illness progresses during this chapter of his life, his childhood years. That huge backpack that

should have been a symbol of bittersweet independence struck me as a symbol of the burden of disease that he carries.

A year before, we learned that he has PSC. For months, we knew something was really wrong and all of my worries centered around diseases for which there are treatments to explore. And yet, the final diagnosis was for a progressive disease with no treatments and no cure. My son suffered from interminable itching. We just thought he had dry skin. He suffered from nausea and bouts of vomiting, and we thought he just caught a lot of stomach bugs. At his most acute suffering, he doubled over from abdominal pain at his own fourth birthday party. At that time, he could not play or sleep restfully.

Next, he began suffering symptoms of ulcerative colitis. Still, he has had an uncomplicated course so far. Recently, my son learned to swallow pills. He was so nervous to try, but the look on his face was one of pride and pure joy when he successfully swallowed four pills that he understood absolved him from a chalky mixture that he had otherwise been dutifully choking down. I'm so proud of his positive attitude, and I'm so saddened because I understand that this represents the beginning of incalculable pills in his future that relate to management of symptoms, but don't relate to a cure for PSC.

It is hard not to wake up every day and worry that my little boy will never be better than he is today. After all, time marches on, fibrosis continues, and complications eventually will happen. As a parent, I cannot accept this. I feel like this rare disease is unfolding like a time bomb inside of my child, and I am worried about what is yet to come. I'm fiercely private about my son, and the only reason why I'm speaking with you today is because we must advance PSC research and find a cure for all of those suffering today and for those like my son whose suffering lies ahead.

Richard

Good afternoon. I've heard that losing a child is the worst possible trauma that one can experience in life, and I've come to as close as that experience as I ever wanted to be, not just once, but twice. My name is Richard, husband, father to two great kids, and most recently, a grandfather. Because of PSC, we've been on a 10-year journey that has scarred our family for life. Just speaking here today brings all those emotions just roaring back and the pain I can still vividly remember. Our journey begins with Matthew and I at the gym. As I was spotting weights for him, I looked down and I noticed his eyes were yellow and his body was jaundiced. It took the doctors almost a year to know that it was PSC. It was a bittersweet moment because we finally knew what the cause was, but we were devastated because it was PSC. You see, we knew without intervention of some sort, it meant certain death for Matthew.

Over the last 10 years, my wife, my kids, and I have experienced some of the deepest and darkest moments one could ever imagine. My worst moment was on May 12th, 2010. When Dr. Grant walked in, he looked at Matthew and he said, "Young man, you have six months to live unless you find a live donor." I can still hear his voice and I can still see the look of total devastation on my wife's face. So, 10 years ago, Matthew was 16, I donated 71% of my liver. This was the worst day in the life of my wife, as she experienced fear, despair, and total helplessness, as both her husband and son were under the knife at the same time at two different hospitals. This has left her scarred forever. We almost lost Matthew

that day. I still believe to this day that Matthew is alive because of his inner strength and never giving up attitude.

Over the next several months, Matthew's life returned to some semblance of normalcy. He graduated high school. He got his driver's license. He got accepted at university. He was loving life and enjoying it just like any normal teenager should. And then just two months after starting university, Matthew got sick again. The disease got very aggressive, and within 16 months he was sleeping 18 hours a day. I was distraught and I was in despair. I didn't believe he was going to make it. Matthew must have seen the look of fear and despair in my eyes because one day he looked up at me so, and told me, "Dad, I'm not going to die."

So just two months after that day he told me he was not going to die, Matthew got a second lease on life. He received a liver from a deceased donor. Fast forward to today, Matthew is living his life and chasing his dreams and making the most out of each and every day. However, he lives with the uncertainty that comes along with PSC. He doesn't know, as healthy as he is today, whether he'll wake up tomorrow morning again fighting for his life. I would love to go to my grave knowing that there was a cure that gave Matthew a fighting chance. I would give everything I own in my life for such a drug or a treatment. Please, we cannot let this bright light or other PSCers suffer and face death. We need to find a cure and a treatment for this nasty disease called PSC. Thank you.

Jennifer

Hi, my name is Jennifer, and I am the mom of a pediatric post-transplant PSC patient. After years of trying to figure out why my eight-year-old son was not meeting developmental milestones, constantly itching, nauseated, and vomiting frequently, he was diagnosed with PSC and Crohn's disease. Over the next seven years, he was hospitalized more times than we can count. He experienced severe pruritus, and his skin was always broken, bleeding, and infected. We literally tried every therapy under the sun to try to help his itching. He had six or seven ERCPs with stent placement in his bile ducts, no relief, never. It was awful. It was excruciating. And as a parent, it is the most helpless feeling in the world to watch your child suffer, knowing there's nothing that you can do to help.

My son also suffered from debilitating fatigue, severe insomnia, and failure to thrive. He missed a year and a half of school because his symptoms were so bad. He even had to repeat a grade. He fell asleep in class, missed school because he was too tired, and missed out on many social events because of his all-consuming fatigue. He was constantly losing weight and had to have more rounds of TPN [total parenteral nutrition] than I can count. He was literally wasting away. At 13 years old, he was listed for transplant and our family was very hopeful as we began the waiting game. Exception points were applied for and granted along the way, because the MELD system is extremely unkind to PSC patients. We agonized over the option of a living donor. We were torn by the thought of putting someone else's life at risk. It was one of the most difficult periods of our lives, but we reached the decision to proceed because it was clear our son couldn't wait much longer.

He was matched with an altruistic donor and surgery was scheduled. About six weeks before surgery, we got a call that he had been matched with a deceased donor, and he had his transplant on May 14th,

2018. The journey before and after transplant has been excruciating. My son essentially lost his childhood. He has cognitive delays because of the extensive liver damage. His transplant recovery has not gone smoothly either. He is two years post-transplant and has had six traumatic episodes of acute rejection. Each rejection episode involves a risky liver biopsy, days in the hospital, IV and oral steroids, all with distressing side effects. He has blood work so often that his veins are completely scarred up and it often takes multiple painful attempts to find a good vein.

We hoped that our lives, which were previously filled with frequent hospitalizations, procedures, and blood draws, would be more normal post-transplant. His transplant has not been the cure we had hoped for. He still feels awful much of the time. He takes more medications now than ever before, but we are hopeful. We are hopeful for the future, and we are hopeful that new therapies will come along that have a real impact on the symptoms of this dreadful disease. We are hopeful that patients won't have to hang their hats on a transplant that may or may not improve their quality of life. We are hopeful for a cure. We are begging for your help. We need you to help us find a cure.

Patient Perspectives on Current and Future Approaches to Treatment

Kristina

My name is Kristina, and I'm 29. I used to think of myself as a go-getter, but primary sclerosing cholangitis, more often than not, stops me. I was diagnosed with ulcerative colitis and PSC when I was 17. I was forced to take a leave of absence from college and ultimately pushed through. I was a passionate public school teacher for seven years, during which I was in and out of the hospital. I've now approached the reality that the job is too taxing on my health, my body, and my disease. I had to give up yet another identity that I had of myself. Battling this disease and maintaining a life worth living is a full-time job in itself. I'm hospitalized a few times a year, even the week before my wedding. Today, I've had pancreatitis, a cholecystectomy, and 18 ERCPs, most of which required anesthesia, long recovery time, and absences from work. Between the pruritus, pain, nausea, stent replacements, frequent biliary obstructions, cholangitis, cirrhosis, the heightened risk of cancer, and the impending doom of a liver transplant, I typically have to live in between the highs and the lows. While makeup and positive attitude can hide a lot, I'm itchy, fatigued, and in pain almost every day. As hardships frequently arise, I depend on my family and friends to help me clean my house, attend medical appointments, and take care of my son. My husband has even brushed my hair for me. I'm lucky to have two doctors that guide me and that I trust incredibly. My support system keeps me sane and encouraged, as this disease frequently robs me of joyous moments. My need for support grew as I developed cholestasis with extreme itching during my life-threatening pregnancy with my sweet and perfect son, but this was the first experience at what has become one of the most severe PSC symptoms, cholestatic pruritus. This debilitating itch is merciless, all consuming, and overwhelming. It's everywhere and worst of all, my feet. I don't even notice when I'm itching anymore and I find myself rubbing my feet on anything, creating blisters. The pruritus increases in intensity and severity in the heat and at night. When I wake up, I've noticed that I've broken skin and started bleeding from itching subconsciously, creating scars. The itching results in a lack of sleep, making it difficult to function the following day. As current treatments

are non-existent, not effective, and have side effects, pruritus has continued to interrupt my life and I have not found relief. I've tried Vistaril (hydroxyzine), ursodiol, Welchol, Benadryl, and a multivitamin. The non-pharmacological and alternative approaches I've tried are endless, and they create a financial hardship on my family. I've tried acupuncture, Bowen, humidifiers, cold showers, keeping a clean shave, icing itchy areas, oatmeal lotions, moisturizing soaps, essential oils, mineral water sprays, and I keep my house at 68 degrees. I monitor changes in diet, stay hydrated, avoid heat and itchy fabrics, and even purchased light or looser fitting clothing, and cooling bed sheets. I hope that my perspective can make it clear, that despite how minor the symptom of itching looks on paper, suffering from pruritus is beyond description. I feel helpless and I truly don't want it to become another all-consuming identity for me. Thank you.

Lindsey

I was 15 years old when I woke up from a three-day coma and that's when I began to realize the life and death nature of my PSC diagnosis. My name is Lindsey. I'm 24 years old, and I have already had two liver transplants because of PSC. I was diagnosed with PSC at age 13, and I was blissfully unaware of the terrifying journey ahead of me. I trusted my doctors to know everything about the disease and to give me a couple of medications to cure me.

I had no idea I would be starting high school with end stage liver failure and a progressive case of portal hypertension. Despite my illness, I signed up for all the extracurricular activities, marching band, I went on all the school field trips, and it was on one of those field trips, far from home, that my portal hypertension caused esophageal varices to rupture. Blood had been silently leaking into my stomach all day and I could not stay awake. My friends thought it was funny, until I threw up blood in my best friend's lap. I woke up three days later in the local hospital, after being flown by helicopter, and for the first time, I heard the words "hepatic encephalopathy." The medications they gave me made me feel horrible. Lactulose helps hepatic encephalopathy patients with their memory, a little bit, and the cost is never having a solid bowel movement again. The small improvements from the medicine were not worth having to miss out on swim team and marching band practice.

After my first transplant, I began to experience a typical PSC symptom that I had been lucky to not experience before, itching. For me, itching was the first sign that a transplant is a treatment, but not a cure for PSC. Some people respond well to transplant, but there are many of us for whom it just doesn't work. I had to have a second transplant for my PSC, and I'm not the only one. My recurrent PSC journey was more symptomatic than my first. I had itching, fatigue, constant fever and chills, and extreme abdominal pain. For the itching, I tried everything, but nothing seemed to work. I did antihistamines, cholestyramine, naltrexone, and more. If you name it, I probably tried it. The silver lining was that I took antidepressants for the itching, which didn't help the itching, but it improved my mood. For the extreme abdominal pain, I was on opioids for two years prior to my second transplant, and I did scheduled celiac plexus nerve blocks, which really messed up my college attendance. After my second transplant, I took Dilaudid for the first few weeks, and then after that, I saw a local pain management specialist, who put me on a six-month methadone weaning program. I remember how embarrassing it was to return to college and have to show my roommates how to use the emergency overdose Narcan medication.

I'm now three years past my second transplant. I finished college and I plan on graduate school. I appear healthy, but I still have symptoms that affect my life every day, fevers, chills, and fatigue requiring a two-hour nap most days. I take 31 pills a day, 16 of which are to treat symptoms. Knowing that there are thousands of other PSCers going through this doesn't make me feel better. It breaks my heart. PSC is no joke, and a transplant is no cure. Someday soon, I hope to see a medication that stops or slows the progression of PSC so that we can all live our life to the fullest. Thank you.

Laura

Hi. My name is Laura. I was diagnosed with PSC in May 2012, and I received a lifesaving living donor liver transplant in March 2017. Today, I'm going to talk to you about acute cholangitis and sepsis in the context of PSC, which is something that's hugely impacted my life during my PSC journey.

My experience with cholangitis began eight years ago, which was roughly a year after my PSC diagnosis. It was already hard enough being a mother of three young children diagnosed with a disease that there was no treatment or cure available. I just had to wait to get sicker in order to hopefully qualify for a liver transplant. For a few weeks before Christmas, I started to experience cholangitis symptoms, right upper quadrant pain, exhaustion, complete lack of appetite, and then I began to spike a fever just before Christmas. I went to the ER twice, and by the second time I went, I was feeling very ill, but both times, I was turned away. They tested me for a UTI and they eventually just concluded that it was just a viral phenomenon. The second time, they did send me home with an antibiotic script, just to cover their bases, but when I was at the pharmacy filling the script on the way home, I fainted for the first time in my life, and I woke up to the sound of sirens coming in the distance, an ambulance coming to get me. They took me straight to the hospital where they began IV antibiotics right away, and I was diagnosed with acute cholangitis and full-blown sepsis by that point. So, unfortunately, my cholangitis and sepsis journey had just begun from that point. From then on, until my living donor transplant five years later, cholangitis attacks and sepsis became constants in my life. I never knew when they were going to strike, and I struggled with my doctors to find a combination of oral antibiotics to keep them in check. Even taking these antibiotics, I had breakthrough cholangitis attacks all the time. These meant that I would have to go immediately to the nearest hospital and get hooked up to IV antibiotics and treated for cholangitis and sepsis. It became completely unpredictable, and my daughters became scared to come home from school because they were worried they were going to find me on the couch again, just about to go to the hospital, or indeed, already at the hospital for a stay of several days.

It became impossible to plan anything, and over the years, my health very steadily eroded because of the cholangitis and the sepsis. My husband had to take over all domestic tasks. I could barely keep up with just basic parenting, I had to go on disability, and I could just see that my health was being severely impacted, and I was going very much downhill. So, one summer, I was in the hospital with attack after attack, and I basically spent two months in the summer just hooked up to an IV basically in the hospital. So, my low MELD score at the time did not reflect how sick I was. For patients like us with biliary disease, the MELD score is not an even playing field. So I had no other choice but to go for a living donor transplant, because I was advised by my doctors that I would never qualify because of my low MELD, despite the fact that my cholangitis and sepsis made me very ill indeed, for a deceased organ transplant.

And when they did actually do my transplant, my diseased liver was literally oozing with infection and it was extremely difficult to extract from my body.

I wish the impact of cholangitis and sepsis would be considered in research, and I also wish the MELD system would be altered to take into account the severity of the disease. I ask for standardized guidelines for the frontline medical education. I can report firsthand that life with acute cholangitis and sepsis is hell for the sufferer and for those around them. Thank you.

John

My name is John. I'm a father, a husband, a small business owner, and a location scout for film and television. I have a chronic illness called ulcerative colitis and received a living donor liver transplant 13 years ago, after being diagnosed with PSC. My colitis started when I was 13. It was a tough time for me, and it wasn't easy for my parents either. I was one of six, and it was financially hard to deal with. There wasn't a lot of information out there, so we were entered into a clinical trial because my doctor's visits and care would be free. Unfortunately, I was on a placebo, so I ended up getting much sicker. Later, I was put on a large supply of prednisone. Now, at the age of 50, I have osteoporosis and osteopenia. As I got into high school, there were more problems, more doctor's office visits and more meds. There was always worry and no cure. Once I became so exhausted, I couldn't move. It hit suddenly, so I laid down at the bottom of the stairs and I now believe this was the beginning of my PSC, but I wasn't diagnosed with this until years later.

As I got older, I began to realize that, without a cure, I felt that I was out there on my own. I would seek information and advice from wherever and whomever I could find it. This was life before the internet. I would read books, go to homeopathic healers, see different medical doctors, and talk to friends. I found if I exercised and ate right, my colitis would go away for a little while. I was still taking a lot of medicine, which was bad stuff. At the time, considered high-risk, I couldn't find affordable health insurance. I would have a flare-up, go to the hospital, pretend I didn't know what was going on, get treated, be okay for a while, and then I would return when I got sick again. It's a shame that the sickest of us out there are considered high-risk and have the hardest time finding a cure.

I'd gotten used to this life and was managing, then in 2003, I was diagnosed with a rare liver disease called PSC, which went on to cause cirrhosis of my liver. After 13 long years, some varices burst into my stomach and I started to bleed. It became time. It was going to happen. I had to get a transplant. There was no other option. As luck would [have] it, my older brother was willing to donate 60% of his. I was lucky to have this option because most people don't. They get put on the list, which is long, due to the lack of healthy organs and low MELD scores. For people with PSC, the word transplant seems like a light at the end of a really long tunnel. Although mine has gone well, it hasn't been perfect. I've had reoccurring infections, week-long hospitalizations, and now I'm on IV antibiotics at home to try to deal with reoccurring infections. I still take 14 pills every day, and, in a COVID world, I'm worried about taking immune suppressing meds. I'm almost four years later from my surgery, and I always have the fear of PSC returning. The world in general right now is a really tough place. We're in the middle of a pandemic and we still have the constant need for blood work, keeping up with our meds, doctor's visits, battles

with those insurance companies, and in our jobs. My doctor is three hours away from my hometown. I can deal with the pain and the exhaustion and the way of life, but it's the emotional side effects that take the most work, the stress on the caretakers and the family, our kids, our work, our support systems, and always wondering what's going to be next and how we're going to deal with it. Without a real cure for patients and their families, we can't escape this reality.

Jay

My name is Jay, and I'm the father of a young adult who, as a teen, was diagnosed with PSC, autoimmune hepatitis, and ulcerative colitis. It's been a hell of a ride. First, we learned that our child was diagnosed with a disease that we had never heard of, and in fact, that hardly anybody had heard of. Next, we learned that there's no cure for this disease. On top of that, it turns out that there's no medicines that can be taken either. What do you do? Well, thank goodness for the internet. It was there that we learned about other people who had experience with PSC, and by meeting with them and talking to them, we learned about other approaches for treatment, including taking medicines that were not designed for use with PSC. In other words, these were off-label medicines.

Given the options, we made the decision to try these off-label medicines. It was not an easy decision to make, and I realize that different people will make different decisions based on their own situations and on the information available to them. The two medicines that I'm talking about are urso and vancomycin capsules. We've tried them both. It seems like a lot of PSC patients take urso. And what do we know? Well, that makes a lot of people feel better, it makes some people's blood numbers improve, but it hasn't been shown to improve the clinical course of the disease. We also know that it may not be safe at high doses. I know that urso is not approved specifically for PSC, but it has been studied a fair amount for use in PSC. Have these studies taken into account how much better it makes people feel? I think that matters and it matters a lot.

A similar story seems to exist for vancomycin. Like urso, many users, particularly pediatric patients, have better blood work, sometimes completely normal, and many report feeling much better. Some even report dramatic improvement with a specific brand of vancomycin, and like urso, not everybody responds. It would be great if we could learn who responds to these drugs and who doesn't. Vanco has been approved for short-term use, which I think is measured in weeks. PSCers are taking it long-term, which is measured in years, and we don't know the risks of that. One of the arguments people hear against the use of vancomycin is the risk of VRE [vancomycin-resistant enterococci], but as far as I know, there aren't any reports of VRE associated with PSC use, and the first pediatric patients began using it over two decades ago. It would be great if there was a way that we could track the use and outcomes of vanco when used for PSC. You've also heard that the brand matters, so that should be a part of what's tracked.

Some doctors are reluctant or even unwilling to prescribe these drugs. Our PSC reality, with this unrelenting progressive disease, is that we know pretty well what to expect if we do nothing. So even though patients know these drugs are not proven, many are willing to try them, especially because we hear that some PSCers feel better. Even if the disease is going to progress, feeling better matters. For

our son, being able to go to work, university, or to hang out with friends matters. When things are bad, it means weeks and weeks of not sleeping, not eating, nausea and vomiting, massive fatigue, and not being able to think clearly. My question to the FDA, is there a way you can help us monitor the safety of long-term drug use, like oral vanco? And is there a way you can help us make sure how a patient feels is accurately measured as part of any new drug development? Thank you so much for listening. I really appreciate this opportunity to convey the message.

Patient Perspective on Clinical Development of PSC Treatments

Lisa

Hi, my name is Lisa. I have a PhD in pharmacology. I have 16 years experience at Merck and Schering Plough in both regulatory affairs and clinical research. I've spent the last 14 years in hepatology. Nine years ago, my life was pretty good. I was a pharmaceutical executive and raising two young boys with my husband. Imagine my surprise when my 11-year old's labs came back with inflammation in his liver and gut. A quick trip to New York ultimately led to a colonoscopy, an upper endoscopy, a liver biopsy, and labs too numerous to count. Within four weeks, my 11-year old son, Alex, was diagnosed with Crohn's disease and PSC. Imagine my surprise. I live liver every single day and I had no idea what PSC was. No problem, let me just talk to the docs and we'll figure out how to treat this and get my son better. That's when reality hit, there are no treatments and there is no cure. Based on the literature I was reading, my son would likely need a liver transplant by the time he was 23.

My next hope was clinical research. I searched clinicaltrials.gov and looked for what would be out there for him. There were very few adult studies, and those were mainly single centers uncontrolled studies, and there was nothing for pediatrics. Nine years later, there is still nothing for pediatric PSCers. I understand, but I cannot accept this. I think back to the days when I was working in chronic hepatitis C and when parents of children with the disease would ask why the clinical trials for children were delayed. Many of the reasons that we gave focused on metabolism, children metabolize the drug differently, and a full PK/PD program would have to be done in children before we could move forward. Another was formulation. Children, many times, cannot handle the same meds that adults can, and a different formulation would have to be developed. A third was benefit-risk ratio. We would have to fully define the benefit-risk ratio in adults before we could move forward with a pediatric development plan.

Unfortunately, pediatric PSCers don't have time to wait. We cannot wait for the same program and the same stepwise program for pediatric development. We need to be creative as to how we can move this forward quicker. Some of the suggestions could be for the current adult PSC protocols that are ongoing, is to decrease the age to 13. We know that many teens are the same size as adults, and they can metabolize the drug the same. A separate sub-study within the adult program, focusing on PK/PD and slower enrollment for these children between 13 and 18, could be put together. We also know formulation would less likely be an issue. We know that these kids, they take a lot of meds, and they know how to handle it. The second would be an expanded access program for those children under the age of 13. Those children that have advanced disease have nothing else. By allowing an expanded access program, in parallel to phase three, would give them the opportunity to perhaps benefit from these

medications. And then a third, we know that COVID-19 has shown that telemedicine is a good tool. By utilizing telemedicine for PSC trials, both adult and pediatrics, would be a good thing. These PSC patients are rare and most of them do not live in the major metropolitan areas in which the research institutes are. By allowing a principal investigator to enroll a patient who lives somewhere outside of that city would allow the partnership between the local doctor and the PI to have these patients in the study and followed locally. This could improve their quality of life and probably lead to higher compliance rates. We need to think creatively and do something now to somehow bring tomorrow's medications to our children today. We need to figure out the roadblocks and find ways around these and we need to do this together. Thank you for your time.

Nathan

Hello, my name's Nathan. Today, I'd like to share with you how my experiences as a PSC patient, a three-time transplant recipient, and as a physician researcher at the University of Wisconsin gives me hope about the future of PSC. To begin, I'm going to go back to when my life with PSC began. A little over 10 years ago, I was diagnosed with PSC after living with ulcerative colitis for two years. I can't remember the exact words my doctor used when I was diagnosed, but I do remember his message. He said, one, I had a rare liver disease called primary sclerosing cholangitis. Two, there was no cure or treatment for the disease. And three, I would likely need a liver transplant one day in order to survive. Hearing the words, no cure or treatment, sucked the air out of the room. I was devastated. PSC, a disease I had never heard of, had given me, what to a 20-year old, sounded like a death sentence. Now, every PSC patient has had a different experience with their diagnosis, but I'm guessing most PSC patients can relate to a similar sense of fear and hopelessness in those first few days.

Shortly after my diagnosis, I was seen by a local hepatologist, but unfortunately, he had little to offer, so I sought care at a leading PSC center. There, for the first time, I felt a sense of hope when I learned about the opportunity to participate in clinical trials. In my mind, the uncertainty of the diagnosis made participating in a trial a no-brainer. I hoped that my participation would be a small part of finding a treatment, and ultimately a cure, for the disease. Being part of a trial felt like doing something rather than just waiting for the natural history of my disease to take its course. I was lucky, I lived close enough to a major center to be able to participate in a trial. Not all PSC patients have that opportunity. Even with the benefit of proximity, I still had to think carefully about the time commitment for some studies, because I was a busy college student. So, traveling back and forth for additional appointments, lab draws, or procedures, wasn't always realistic. Other studies that asked for patients to undergo biopsy seemed unreasonable to me because, to that point, my routine care had not yet required a biopsy.

Over the years, I learned to live with the fear and uncertainty that come with a diagnosis like PSC. I graduated from college, continued to work as a firefighter and paramedic, met and married my wife, and attended and graduated from medical school. But along the way, I faced an ever-present battle with the symptoms of PSC. I fought recurrent episodes of cholangitis that required hospitalization and antibiotics. And outside the hospital, I was constantly itchy, to the point that my scratching left my arms and legs bloody. I struggled to focus, and it was always difficult to sleep. After years of my symptoms worsening, my journey with PSC culminated three years ago, when I received a live donor liver

transplant from my cousin. Every PSC patient who has required transplantation highlights the need for better treatments to reverse the course and slow the progression of the disease. And my story is no different. Transplantation definitely saved my life, but at an extremely high cost. Since my first transplant, I've undergone two additional transplants, spent over 300 days in the hospital, endured 16 surgeries plus countless procedures, and was off work for over two years. Even for patients whose transplant goes more smoothly, the physical toll and financial burden of transplantation is evidence that PSC patients need a better option. I hope that one day PSC will no longer be on the list of common indications for transplantation. But that dream will not become a reality without an effective treatment.

So, what's next? COVID-19 has up-ended all aspects of our lives. We've learned new phrases like "social distancing", and "let's meet over zoom". And we've all figured out how to work, learn, and socialize virtually. This strange new normal has extended to my work in clinical research. Our team has spent much of the last six months revising our protocols for our clinical trial to shift from 100% in-person enrollment to 100% virtual enrollment. And seeing the ways in which we've been able to adapt to the reality forced upon us by COVID-19 gives me a lot of hope. Just this year, we've seen a 4,000% increase in routine visits for outpatient care at hospitals across the country. And if we can harness the lessons we're learning today, about how to deliver care virtually, we can drastically expand the number of patients who have access to clinical trials, reduce the burden of participation, and accelerate the science that will lead to life-saving and life-changing discoveries for PSC patients.

For me, the hardest part about living with PSC was feeling helpless. Without an effective treatment, I felt like I was just watching and waiting as my symptoms worsened, I got sicker, and my life was put on hold. But with your help, my goal is that one day, when future generations are diagnosed with PSC, their doctors will be able to deliver a different message than the one I received. Their doctors will hopefully be able to say something like, "I'm very sorry to tell you. You have a disease called primary sclerosing cholangitis. But we have an effective treatment that will help you to live a long and healthy life." Thank you.

APPENDIX 3: LIVE POLLING QUESTIONS

Demographic Polling Questions

1. Which of the following best describes your connection to PSC? Select 1.
 - A. PSC patient, 18 and over
 - B. PSC patient, under 18
 - C. PSC family, friend, or other caregiver
 - D. FDA/EMA
 - E. Pharmaceutical
 - F. Clinician/Researcher
 - G. Other
2. Where does the PSC patient live?
 - A. United States
 - B. Canada
 - C. Africa
 - D. Asia, Pacific Islands
 - E. Australia, New Zealand
 - F. Europe, UK
 - G. Mexico, Central America, South America, Caribbean Islands
 - H. Middle East
3. What is the PSC patient's age?
 - A. 17 years and under
 - B. 18 to 39 years
 - C. 40 to 59 years
 - D. 60 to 79 years
 - E. 80 and older
4. Does the PSC patient identify as:
 - A. Male
 - B. Female
 - C. Non-gender conforming/non-binary
5. How would the PSC patient describe the journey leading to their PSC diagnosis? Select 1.
 - A. Quick and straightforward
 - B. Not too complicated
 - C. Long and complicated
 - D. None of the above
6. What race best describes the PSC patient? Select up to two.
 - A. White
 - B. Black
 - C. Asian
 - D. Indigenous (Native)
 - E. Asian Pacific Islander

- F. Mixed
- G. None of the above

PSC Clinical Symptoms and Advanced Disease

1. Recently, how much have the PSC patient's symptoms affected their daily life? Select 1.
 - A. Not at all
 - B. Somewhat
 - C. Very much
 - D. Overwhelmingly
- 2) Which of the following symptoms have most impacted the PSC patient's life? Select up to 3.
 - A. PSC Fatigue
 - B. Itching/pruritus
 - C. Insomnia
 - D. Nausea and/or vomiting
 - E. Right upper quadrant/abdominal pain
 - F. Anxiety and/or depression
 - G. Brain fog
 - H. Bone Loss, Osteopenia, Osteoporosis
3. Which of the following statements have been true for the PSC patient? Select ALL that apply.
 - A. Daily function is limited
 - B. Family stress is common
 - C. Unpredictability affects life
 - D. Worry about the future
 - E. Often misses work or school
 - F. Invisible symptoms are often doubted
 - G. Drug or alcohol abuse is often assumed
 - H. None of the above

Pediatric PSC

1. Which of the following have been challenging for the pediatric PSC patient? Select ALL that apply.
 - A. Physically demanding activities or sports
 - B. Less physically demanding activities for play, fun, and exercise
 - C. School or work responsibilities
 - D. Social time with family and friends
 - E. Help with household chores
 - F. Reading, games, hobbies, and crafts
 - G. No unexpected challenges
2. What has been the pediatric PSC patient's experience with Urso and/or vancomycin? Select ALL that apply.
 - A. Taking Urso now
 - B. Tried Urso and stopped
 - C. Never taken Urso

- D. Taking vancomycin now
- E. Tried vancomycin and stopped
- F. Never tried vancomycin
- G. Taking Urso and vancomycin now
- H. Prevented from taking one or the other by cost or access

3. What might encourage you to volunteer the PSC patient for a pediatric clinical trial? Select ALL that apply.

- A. Enough information about the trial
- B. Safety profile of the trial drug
- C. Recommendation from the child's physician
- D. Option of home health care to replace most clinic visits
- E. No invasive procedures beyond the usual routine tests
- F. I am already motivated to enroll my child
- G. I would never enroll my child

Medications and PSC Treatments

1. If you have tried pruritus (itching) medications, how well did they work? Select 1.

- A. They were very effective
- B. They were moderately effective
- C. They were rarely effective
- D. They were never effective
- E. I have never tried medications for pruritus

2. Please select the two symptoms that you would most like an effective treatment for: Select up to 2.

- A. Pruritus
- B. PSC fatigue
- C. Abdominal or liver pain
- D. PSC insomnia
- E. Nausea/vomiting
- F. Brain fog

Clinical Trials

1. What would make clinical trials more patient-centric and doable? Select ALL that apply.

- A. Use of telemedicine as much as possible
- B. Home health nursing visits when appropriate
- C. Home blood draws
- D. Stool or saliva sample by mail
- E. Home medication delivery
- F. Informed consent done online versus office

2. If full privacy protections are in place, are you willing to contribute your health information to a natural history study? Select 1.

- A. Yes
- B. No

C. Maybe

3. Would you want this de-identified natural history data to be shared with screened and approved academic researchers and drug developers to accelerate drug development? Select 1.

A. Yes

B. No

APPENDIX 4: PUBLIC COMMENTS – YOUR PSC JOURNEY

The FDA encouraged public comments to enhance the patient’s voice and expand FDA knowledge of how PSC affects patients’ lives, including how they feel and function. Members of the public were asked to provide “brief comments about your PSC journey, which may be anonymously shared in the report and/or during the forum.” Comments were solicited via the PFDD meeting registration form, the PSC Partners newsletter, social media, and during the PFDD meeting. The open comment period ran from September 17, 2020 through November 6, 2020. Comments submitted before, during, and after the meeting are presented below.¹⁹

Public Comments Submitted Before the PFDD Meeting

- My son was diagnosed with PSC prior to his senior year of high school. It was devastating and completely changed the course of his college dreams and the life dreams I had for my son. Instead of going away to college as he always dreamed, he stayed local, to be near his doctors. Throughout his college years (he's now 23) he was hospitalized 15 times, yet still managed to graduate on time, with honors, with a degree in Economics. He nearly missed his college graduation as he was in the hospital the week of his commencement ceremony. Luckily, we've been blessed with an amazing team of doctors who worked diligently so he could be released from the hospital in time to walk across the stage and receive his degree. It's been an emotional and physical rollercoaster, but we remain focused on the research being done and pray daily that a cure or even an effective treatment will be found. My son is the most inspiring, positive, kind, and resilient human being I've ever known and I'm blessed to be his mother.
- I was diagnosed with PSC in 2012. The disease has progressed to cirrhosis but thankfully I am currently able to live a full life. I have a lot to be thankful for. The biggest frustration of the disease is the lack of proactive treatment and lack of knowledge about the disease. The course of treatment seems to be limited to monitoring, hope for the best, and take action when things get severe.
- My son was diagnosed at 19 years old while in college. He's a strong athlete trying to live a normal life and finish college while working toward his future. It's so discouraging that he is very itchy, has stomach aches/loss of appetite, and is just miserable at times. It's hard to have hope when there are no medications that will help. He has had to just deal with it. He has never been a depressed guy but this is wearing.
- Lack of basic understanding of disease etiology is surprising. Technological advances in data aggregation are needed to progress. This includes coordination and cooperation of international bodies across languages.
- I found out that I had PSC when I went for my annual physical. My doctor told me that my liver enzymes were elevated. I was diagnosed with PSC in 2001 and transplanted in 2013. I did not have Ulcerative Colitis or Crohns before having my transplant. I was diagnosed with IBS after transplant.
- So far no symptoms.
- Between my diagnosis and transplant I was blessed to have 24 good years while managing my PSC. If there is one thing that I would love to see help through medicine management is the ending

¹⁹ All comments were submitted by individuals. Comments do not necessarily represent the opinions of other commenters, meeting participants, or PSC Partners. Comments presented have been subject to light copyediting as needed for clarity (e.g., spelling, punctuation) or privacy (e.g., names of patients or health care providers mentioned might have been removed).

stages and its impact on daily life. Need technology breakthroughs to provide improved quality of life as PSC patients face liver killing cholangitis. How to manage the extreme fatigue, the drowsiness that can almost feel like passing out on your feet. The amount of times I would vomit all food was unbelievable. How can I help so other PSCers can face the end stage with more strength and dignity?

- Our story began 12 years ago when I took my 7th grade daughter to the dermatologist for minor acne. He prescribed daily doxycycline. Four months later she was hospitalized for massive systemic swelling. She was ultimately diagnosed with severe Ulcerative Colitis. Over the next 2 years she struggled and we thought she was going to die. She was 5 ft 5 inches and only 88 lbs. Her GI recommended a colectomy. Just before tenth grade she was diagnosed with PSC. We found a doctor and she started therapy with oral vancomycin, with no other meds. She immediately normalized. Now, 8 years later her liver and colon are both still normal. She graduated from Stanford after playing D1 sports for 4 years with a biology undergrad and microbiology master's degree.
- Diagnosed in 2011 and had a rough start, but feeling good since then. Hopeful we can find treatment options other than waiting for transplant and find an understanding of the mechanisms that are causing PSC.
- I have recently found out that another child of mine has PSC. So now my 19 and 26 year old daughters will battle this disease. We are in shock and afraid to test the other two children.
- Our 7 year old has recently been diagnosed with autoimmune sclerosing cholangitis. We have fears of what this journey will look like for him and how he will be able to live his childhood with this disease.
- I was diagnosed with Ulcerated Colitis at age 13, after several gastrointestinal doctors and having jaundice a couple times. I had an ERCP and was told I needed to find a Hepatic doctor as he believed I had PSC and would most definitely need a liver transplant. That was at about age 36. I am now 60. I have been mostly asymptomatic up until about the past 2 years where I have been experiencing some RUQ issues and gut issues. But my blood work typically looks good. I do have a blood clot in the right hepatic vein for 3 years now. On coumadin but I am switching to Eliquis. I had an INR of 6.6 this last April with black stool. Should've gone to the ER but was in the thick of covid and I live in the suburbs of Detroit, MI.
- Early diagnosis is a must. Emotional and psychological help is also crucial.
- My son was just recently in the hospital with a PSC and Crohn's flair. His GI doctors have said while not emergent it's time to start the transplant discussion. He has been referred to Thomas Jefferson Hospital in Philadelphia, PA. I will be very interested to hear what the pharmaceutical industry has to say. The cost of medication is ridiculous. No one should have to decide between bills and medications.
- After 10 years of unexplainable symptoms, I was diagnosed in 1992 when there was very little information available about PSC. What I was told was that it was rare and usually affected men over 40. I was a 28 year old woman being told this. I was then advised that by the time I was 40-50 I would require a liver transplant as there was no treatment and eventually I would have cirrhosis of the liver. At age 32 I was put on the transplant list in August and fortunately for me & my family I received the wonderful gift of a new liver in February, an 8 month wait that at the time seemed very long. Just after my liver diagnosis I was told I had IBD, either Crohns or Colitis not defined. After years of medications, and all available treatments available without surgery. I eventually had no choice but to have surgery to remove everything except my small intestines & be left with a permanent ileostomy. Today I'm 22.5 years post transplant & almost 8 years with my ostomy. I'm so thankful to my donor, medical team & family for their support. I'm also grateful as I've also had many friends who have not been as fortunate. I'm pleased that now there are so many resources available to those with PSC and that PSC Partners is working diligently to find a cure.

- I am the PSC patient, mostly asymptomatic but I also have Crohn's and ankylosing spondylitis. I live 3 hours from my hepatologist and from someone who understands my disease. It is frustrating having to explain to my regular doctors about my disease. Also to have to tell my GI doc that yes, I need a colonoscopy every year even though I would love to skip it. There is also the frustration of family or friends who say if I wasn't taking meds for my AS maybe I wouldn't have gotten PSC. So many want to put the blame back on me as in, what did I do to get this disease. Just venting but the only ones who understand are fellow PSCers and I had never even met another PSCer until my first conference. We need a cure or at least something that is the gold standard in treating us. Thank you for doing this.
- Challenges of being isolated in the middle of the Pacific Ocean with a rare disease and no specialists in the area.
- I never realized that PSC would continue to affect my life after my transplant.
- After the diagnosis a little more than 2 years ago, my adult son has been having frequent blood tests and scans, and his medication has been adjusted accordingly. What is lacking is mental and psychological support as well as updated information about on-going research, both in Finland and internationally. Also, support and information concerning nutrition and other ways of maintaining your health (other than just taking the pills that might not even be effective) would be a welcome addition to his health care. Living in Finland, the health care people have emphasized how liver transplant surgery is very advanced in our country. What we need is more interest in finding a cure or at least more effective medicine.
- Diagnosed in 2014. 2 to 4 cholangitis events per year. Managing my disease and hoping for a cure.
- I was diagnosed with small-duct PSC in 2007. On one hand, I consider myself one of the lucky ones - I do not have UC. I've responded well to Urso-forte. It lowers my LFTs and reduces my symptoms, which have been fatigue and RUQ pain. I've been able to go on and live a full life so far. On the other hand, I can tell that the disease is still progressing. It used to be that I could go a week off of Urso before my symptoms would worsen. Now, if I miss a few doses, I experience worsening symptoms in 24-48 hours. I feel a bit like one of those characters in a cartoon who has an anvil over its head, just waiting for it to drop.
- Like many adolescents, my 13-year-old daughter had some acne. She took doxycycline to clear her skin. Eleven months later, she was hospitalized for a week. She'd never had an injury before or missed a day of school. She had always been healthy and fit, excelling in academics and sports. Diagnosed with severe ulcerative colitis, over the next two years she tried every medication that usually works for this diagnosis -- nothing helped. Her symptoms continued to get worse and were compounded by horrible side effects. One medication caused her to have pancreatitis. She couldn't breathe and woke up multiple times a night vomiting, with chest pains and bloody stools. The rest of the time she just lay in bed with cramps. We were losing hope. As a freshman in high school she was severely underweight. Her health declined by the day. As a sophomore, her blood tests showed high liver enzymes. She had a biopsy and was diagnosed with PSC. Her doctor told her that she should consider a colectomy. We found a doctor who was successfully treating children with vancomycin. We switched her care to this doctor. After a year of vancomycin, she had no symptoms. The progress in both diseases reversed and she gained 35 pounds of healthy weight. Now 8 years later she still takes oral vancomycin and has a completely normal liver and colon. We have learned that her response to the drug is dose and brand specific. Some brands and formulations did not work causing rapid (within 2 weeks of taking a different brand) increase in liver chemistries and a return of GI symptoms. Research must be done to understand the adequate dosing of vancomycin, differences in non-innovator brands of generic drug, effects of the presence of concomitant medications, essential length of treatment, and stage of disease when treatment is initiated. My

daughter's effective management of all these factors was critical to her successful and sustained response to treatment with oral vancomycin.

- I was diagnosed in January 2017. I have yet to experience any symptoms that were clearly from PSC, but I have been struggling with IBD (which is a disease with some causal entanglement). My primary concern at this point is my life expectancy. I expect medical technology to dramatically improve over the next few decades, so it's a race against the disease in my body. I really don't know who will win. I wish I felt that I had more power to help medical technology when right now I feel more like a spectator.
- I was diagnosed with PSC in August 2019 and PBC in April 2019 after having elevated LFT for 5 years. In those years prior to diagnoses, I was and still am experiencing debilitating fatigue, bone/ muscle pain, IBS, nausea, brain fog, forgetfulness (memory loss), itching, vitamin deficiencies. My sick days were becoming more and more frequent until I was deemed too sick to work. I'm a proud mom of 4 grown children and had a [career] in a growing industry of sales and finances. Until this disease has [progressed] to end stages, we do not look sick! We (PSC patients) often get overlooked and this includes the MELD Score for transplant. Please, hear our voices and let us make a difference.
- Thanks to vancomycin, these past three years of living with PSC have been virtually pain-free with normal labs and no complications, infections, or disease progression, a story quite different from many others with PSC. While my peers are preparing for liver transplant or experiencing intense abdominal symptoms, cholangitis attacks, and pruritus, I am the healthiest I have ever been. I am pleading that the FDA and drug development companies research vancomycin to understand why patients have this incredible response to particular brands. We really need support for a clinical research program to explore this and all of vancomycin's efficacy factors. Ideally, this program should include randomized trials and exploratory pilot studies, which are less expensive and quicker than full clinical trials. We patients need brevity; our lives depend on it.
- I found out about PSC Partners after my husband's passing, when looking where donations could be made in lieu of flowers. Oh, how I wished we had been availed the information, support, and encouragement. Tom died October 8, 2005 and I have been a financial supporter for 15 years in his memory and to join the fight others are in. My thanks for many who reached out to me without him - especially Ricky and Don, Joanne and Steve, and others. My heart will always be with you and him.
- PSC patient 26 years post transplant.
- My 17-year-old daughter is about 1 year into her diagnosis. We are incredibly grateful for psc.partners as we were given little information/support from docs after the initial diagnosis.
- I was diagnosed with UC in 2001 and PSC in 2002. I had no symptoms of PSC until 2008, that was the first time I experience[d] edema. It wasn't very bothersome and seemed to go away on its own. In 2015 I was dealing with some stressful things in my [life] and that same year my fatigue got a lot worse. As the years have gone on my fatigue has gotten worse, my edema is now to the point where I have to restrict and practically eliminate my salt in-take as well as take diuretics. I often get lightheaded or dizzy and I'm in early liver decompensation and it won't be long before I will most likely need a liver transplant. I have stopped working, I often need naps throughout the day to keep my energy up, and there isn't a single day that I don't have to push through nausea, headaches, feeling exhausted, generally feeling ill, and more. I'm ready for this to be over now.
- I was diagnosed with PSC in 2008, but believe that I was experiencing symptoms for three years prior. I followed the typical PSC rollercoaster for 7 years. I call it a rollercoaster because when the disease progresses to the point of needing an ERCP, it feels like you are climbing the slow, steep section of a rollercoaster track. For a few sets of ERCPs, they would preclude the big, fast drop, leaving me energetic and living life almost normally. On the way up one of these slow climbs, I had a second rare liver disease, Budd-Chiari, literally throw me off the tracks. Due to the sudden clotting in

the liver, in addition to the progressive scarring of the bile ducts, my body failed in a sudden and fast way. I'm grateful to be here today because of my liver donor and the cooperation of many medical staff at the Mayo Clinic. I have many friends that have had this terrible disease return after transplant. I believe that the only reason I have a PSC Community is because of PSC Partners Seeking a Cure. I am so grateful for the positive difference they have made on my life and the many contacts I have made while attending the annual conferences. To the Researchers, Pharmaceutical Companies, Clinicians, and FDA, you have an incredible ally in PSC Partners that is changing the lives of patients. Without PSC Partners, few of us would know another "PSC'er." We are a tiny community but we are mighty. Please give us the opportunities as patients to continue sharing our stories. Thank you for continuing your work towards better treatments and a cure. To us in the fight, it does not go unnoticed.

- It has been heartbreaking to watch my son going from being an incredibly healthy athlete to being so sick with PSC. We need research now to help us understand this disease and give hope to the PSCers. Hoping to survive the loss of a colon and then the loss of a liver is not the answer. We can do better and there are a lot of us willing to work together to help make it happen.
- My 12 year old male child was recently diagnosed with IBD. He started rapidly losing weight due to an IBD colitis flare 6 months ago; lost 20 lbs, with his weight and energy rapidly declining with fevers, right abdominal pain, nausea, vomiting, frequent loose bowels. Started on medications for indeterminate IBD after endoscopy/colonoscopy and labs in June. Put on and off antibiotics starting in June 2020 for positive colitis / cdiff, and started entocort, pentasa, prilosec in July 2020. His scopes in June concluded IBD chronic inflammation. Been admitted 2 times to a medical center pediatric unit. Once in July after a terrible bout of fevers, dehydration, bad right upper abdominal pain, nausea, vomiting. They started vanco, before admission thinking cdiff return, did CAT scan w/contrast which picked up gallbladder bile duct inflammation, with labs at that point indicated elevated liver enzymes / sludge. When admitted his pediatric team put him on IV cipro in case he had cholangitis, and continued vanco oral. All labs for infection came back negative, but still indicated sludge. ALT & AST were elevated, but going down showing improvements. His IBD inflammation is also better. They did ultrasound days after admission and being on vanco and cipro. Nothing found in ultrasound, he was responding well to antibiotic / fluids and was sent home on vanco and augmentin. He was ok for a week or so after stopping antibiotics, but then got very, very tired and his low grade fevers started to occur, then fever went up and nausea vomiting again with no appetite. At monthly follow up appointment his labs indicated liver enzymes bile sludge were back up and that indicated PSC, but UC / IBD inflammation almost normal. Dr.'s started oral vanco again, admitted him, put on IV fluids, did MRCP. The MRI/ MRCP showed his gallbladder was large and inflamed, his small bile ducts had stricturing indicating caused by inflammation - PSC and IBD was finally diagnosed as UC. No liver damage, liver in good condition. He was released days later responded to vanco IV fluids. His liver labs were better slowly going back down. Biomarkers all showed no hepatitis, other autoimmune diseases, infections. They did full workup of autoimmune diseases due to family history. Continues on vanco for 6 plus months at 250mg 4x day. He's been improving, gained 20+ lbs back since June 2020! Going down on UC meds entocort and prilosec. Still exhausted for daily life regularly, had bout of low grade fevers for a few days each week and was put on Urso 500mg 2x daily to improve bile flow in September 2020. We also switched pharmacy in mid-September and his vanco brand switched to ANI brand vanco. He's now hungry, growing, and no fevers in a few weeks now. Energy still hard for daily life but getting better. Our great GI Specialist team don't have much info on this disease. We need more research info for them please. I have hope that this past 6 months of pain, terrible health turns into remission for a long time for my son. I hope he can go without a transplant. Please help find a cure, a better outcome for life instead of transplants, high risk of cancers and complications for PSC patients with UC. I just want him to be

able to be a kid; have energy, run, play, grow into adulthood and have a future beyond PSC and UC transplants and increased risk for cancer.

- My son, now 31, has PSC and is 6 months post-living-donor-transplant. He was diagnosed with PSC in 2011, and was placed on the transplant list in 2012 with a MELD of 15. Over the years since, his health has deteriorated, and his quality of life was diminished. He could no longer work, or engage in social activities with friends. He became somewhat reclusive due to the prominent yellow color caused by jaundice. The severe jaundice caused constant itching that could not be helped with any medication. (His constant itching caused him to lose all hair on his arms and legs.) The severe fatigue was overwhelming and he spent much of the decade of his 20's sleeping. His MELD score did not, in ANY way, reflect his illness. Over the past two years he has been in the ICU three times with pneumonia and septic shock, gastrointestinal bleeds due to portal hypertension (he almost bled to death), and severe malnutrition. When the septic shock episodes happened, yes, his MELD would go up into the 30's, but because he was septic, a transplant could not be performed. During the first septic shock episode he was given a 5% chance to survive. He's a fighter and a PSC Warrior and he surprised them all and survived, and then developed a colon bleed that could not be controlled. During the time he was bleeding his hemoglobin was 4, and he was receiving constant blood transfusions (44 units in total; forty-four) until it was determined a TIPS (Transjugular Intrahepatic Portosystemic Shunt) needed to be inserted into his liver to relieve the portal hypertension to stop the bleeding. During this two-year period, he had been transported once by ambulance and once by helicopter to his transplant center due to the severe nature of his illness. At one point my son was granted MELD exception points, and was on target to receive more points, putting him higher on the list and closer to a transplant, but OPTN changed the MELD exception point rules and my son's MELD was again knocked down. The third time he was in the ICU at his transplant center, out of frustration we decided to have him transported to the Cleveland Clinic one mile away. Once at the Cleveland Clinic, the bacterial infections were controlled, his MELD went down to 19, and he was told he should find a living donor because his MELD did NOT reflect his illness. His liver had gone from fibrosis to cirrhosis (determined in December 2018) and he did not have much time left. PSC had not yet affected his kidneys keeping his MELD score lower. This disease also caused osteoporosis, kyphosis, and scoliosis as he waited on the list for 7 (seven) years. This disease is dreadful. His bilirubin was 30! THIRTY. He was severely malnourished due to malabsorption of nutrients. The months leading up to a living donor transplant he was getting monthly ERCP's and stents placed in his bile duct to try to keep the bilirubin down a bit. My son was fortunate enough to find a living donor. No one in our family was a match, and we had to reach out to the community to find a donor. Fortunately, there were many people who came forward and a match was found. Then due to some suspect CCA cells found in brushings done during my son's ERCP's, the transplant had to be postponed until a solution was found. If it were not for the innovative thinking of the transplant team at the Cleveland Clinic, my son might have had to wait even longer for a transplant, and perhaps he would not live long enough to receive it. Finally, in March of this year, my son received his living donor transplant, and was the last living donor transplant to be performed at the Cleveland Clinic when COVID-19 shut down all voluntary surgeries. We are forever grateful.
- I am a parent of a 21 year old female diagnosed at age 17. Despite being asymptomatic for the first years with perfect labs, she now has a dominant stricture in her CBD and has undergone 3 ERCPs in the last 3 months. She stayed home from college due to COVID-19 and her PSC symptoms, which continue to include pain and fatigue. She will likely have another ERCP soon. We are grateful that she is treated at a well-known medical center by wonderful physicians. Our hope is to find medical treatments to address the progression of this disease before my daughter needs a transplant.
- My journey with PSC is unusual. I was diagnosed before symptoms due to bimonthly LFT screenings with remicade infusions. After ruling out other causes of acute LFT elevations, and a biopsy showing

PSC, I was immediately started on oral vancomycin. Since my diagnosis 10 years ago, I have never been symptomatic, and two years ago tapered off vancomycin.

- After over 25 years of UC and 16 years of PSC I finally received my gift of life through a living donor transplant from my youngest sister. I am forever grateful, however life post-transplant will never be normal. There are still many obstacles to deal with post-transplant, and the fear of PSC returning and having to re-live the PSC nightmare again is always a worry. The anti-rejection drugs keep me alive but do not come without negative side effects either. I pray every day for a cure to this horrible disease.
- We have thankfully been asymptomatic since his ERCP three years ago. I try not to make him nervous by asking too many questions, but I'm on pins and needles looking for the first hint of a problem.
- I have been living with PSC for 26 years. I read and try to keep up with new knowledge and research; this is a very important piece to living with this disease. So thank you all for everything you do. God bless!!
- Wife suffering. Has been a tough journey, doctors in South Africa have been very supportive and professional. Now 16 years since diagnosis. We remain hopeful, but now feel that time is running out. Feel more can be done via biomedical engineering - implants etc.
- Hi, my daughter was diagnosed with stage 3 PSC at 19 years old. Transitioning to cirrhosis. Three years ago she started taking oral vancomycin (1000mg a day), her LFTs normalized, and a fibroscan showed normal liver 6 months later. With vanco incredibly expensive and difficult to get prescribed by doctor and covered by insurance, all us vanco users dream of vanco getting FDA approval to make this process easier, potentially saving lives of those who respond to vanco. Any insight into how to make this happen would be ideal.
- Husband is 8 years post-transplant. At 6 years, Hubs developed UC for 1st time. Bracing...
- Even being somewhat asymptomatic with PSC, according to my annual MRI, my liver is getting "stiffer" more and more each year, so I know that day will come when my liver might stop functioning well. Also knowing that I can never get life insurance is an added burden I carry.
- Mother of 34 year old male, diagnosed age 21-22. UC diagnosis at the same time, 2 liver biopsies, 2 ERCPs for 1 significant stricture each procedure, AIH recent. No UC flare ups since diagnoses (Rx Colozal). LFTs always elevated. Cholecystectomy shortly after diagnoses. Intermittent RUQ pain, major long, frequent belching.
- This journey in battling with Primary Sclerosing Cholangitis has been made more physically debilitating, emotionally difficult and financially taxing because as a rare disease it was difficult to diagnose, difficult to "convince" the medical community that my husband was ill. And even now with a diagnosis and the right health care, it's made additionally challenging as my husband suffers through the symptoms and accompanying illnesses that plague and debilitate him as we anxiously await a donor liver, something that will take years to happen. And in the meantime, he is unable to work, focus and function as fully as he once did. There are researchers and scientists who want to help develop medications for our PSC patients and we desperately need their help. It's as simple as that.
- I was transplanted at 39 years old, after suffering with hepatic encephalopathy for 2 years. I was no longer able to work, drive, care for my kids, or even wash my own hair. It was debilitating. Now I'm cirrhotic again with recurrent PSC. I'm now living alone and fear a significant loss of independence. I'm still trying to recover from PTSD from the first time. This is a traumatic disease both physically (stopped menstruating due to malnutrition and lost all my hair from physical trauma) and emotionally (depression, anxiety and PTSD all became challenges as the disease progressed).

- PSC has been a scary and emotionally challenging disease to navigate for my husband and our family. He is pre-transplant and has remained fairly stable over the past several years with the exception of recurrent pancreatitis. Hoping to meet others sharing our journey.
- My name is []. I'm an 18 year old who was diagnosed with PSC at the age of 14. I've been asymptomatic for 4 years but 5 months ago in May, I got my first cholangitis attack. This came with very terrible itching, fatigue, chills, and left side pain. Since the attack, the symptoms are not as bad as they once were but these new symptoms have yet to leave and my doctor says my disease has progressed. After that I've had many terrible symptoms prevail, such as itching, fatigue, and left side pain. I'm taking Ursodiol, Vancomycin, and Rifampin. I was taking classes at the University but moved back home after these medical issues took over my life. I'm now at home trying to fix my PSC symptoms so I can go back to living a normal life. I was once a very active, confident, and happy guy but dealing with this terrible disease has sent me into a very deep depression. My goal is to cure my PSC so I'm able to live a normal life like other college students. Since there is no cure for PSC, my morale is low and I'm looking for the light at the end of the tunnel.
- Just very recently diagnosed with PSC but suffered many apparent Cholangitis attacks in the past year. In addition to severe weight loss due to lack of appetite and fatigue, it was an extremely demoralizing time period. Even with visits to Gastroenterologists and Hepatologists very few suggestions were made as to how to exist with this disease.
- I am currently 2.5 years post transplant. I was diagnosed about a year and a half before I received my transplant, but in retrospect I can see that I likely had the disease for about 20 years. During the last few years before transplant, my quality of life became increasingly poor. I had 2 small children at home, but I could barely keep up with them. I had so many medical appointments and hospital stays, my illness became all consuming. I was an awful shade of greenish yellow for several years, and I suffered unimaginable itching and sores on my skin for 5 years. I also lost 30+ pounds, and significant muscle mass. Six weeks before I received my transplant, I almost lost my life from a severe hemorrhage due to ruptured varices. I was given 9 units of blood while the ICU team worked on stopping my bleed for hours. I was put on a ventilator and kept sedated for almost 48 hours so my body could begin to heal from the trauma. A few days later I was discharged for home, directly from the ICU because there was nothing more they could do for me. Even though I have already received my transplant, I still have concerns that I could develop recurrent PSC. I'm also worried that one of my children, or nieces, or nephews could one day have PSC too. There needs to be more research put into the development of a medication treatment option for patients with PSC. No parent should have to watch their child suffer, and no child should have to watch their parent wither away. The whole experience is quite traumatizing.
- Nearly 80% of PSC patients also have Ulcerative Colitis or Crohn's disease. I believe that by funding PSC research it could also potentially help the over three million of those in the U.S. suffering from UC and Crohn's who do not have PSC.
- Mother of 23-year-old son who is 3 years post transplant. His liver had HCV antibodies and he started replicating the virus days after transplant. After a 6 month course of Harvoni, he's HCV free and living a full life.
- Dear all, Thank you so much for the PFDD forum! My brother is a PSC patient, 54 years old with two girls, 13 and 8 years old. I'd like to receive more information about PSC patient possibilities to be part of named patient programmes in clinical trials, particularly with Nor-ursodeoxycholic acid. There is a clinical phase 3 study of Falk Pharma, Germany. Do you know something about it? Many thanks and best regards.

- PSC patient 30+ years with ulcerative colitis since age 13. I'm 60 years old now. Have mostly been asymptomatic until a couple years ago; this past year the episodes are more intense. Anxiously looking to understand how to manage them up until transplant! PSC Partners is so helpful! Thanks!
- I am the spouse/caregiver of a PSC patient who has had PSC/UC for 30+ years. Haven't had to worry much about her condition until this past year when she has been having several issues related to the condition. Feel helpless sometimes. Glad she has this support group.
- I am an adult older parent of a PSC patient who has had PSC/UC 30+ years and is beginning to progress in her disease. I believe her father passed from this disease and they didn't know it back then. He went in the hospital with gallstone problems. They pulled a stone from his bile duct and all his organs shut down. He passed 4 weeks later. I hope they get an answer to the disease soon. I hate to see my daughter suffer like this, as I also had 2 other sons pass away of different circumstances. Let's find a cure!
- I have just been involved in PSC drug development. As a result, I am interested in learning more about this pathology, patients expectations on treatment, and improvement in their quality of life, clinical endpoints and outcomes of interest for FDA.
- A 34 year-old male from Ottawa, Canada. Diagnosed with PSC in September 2020, along with ulcerative colitis earlier in the year. Many questions surrounding the onset of disease symptoms, particularly the interaction between both the inflammatory disorders, and how maintenance of IBD can benefit PSC symptom progression/severity. Looking for information on nutrition, experimental medicines, and holistic approaches to maintaining remission.
- As a friend of the family of a PSC patient, we have seen a life-long commitment to the advocacy to sustain a quality of life and life itself. Seeing this dedication has been a significant positive influence on how I view the "healthy existence" of our family members.
- Itching is persistent at this point. It is very hard to find any drug or lotion that works for me.
- I am the mother of a PSC patient, who was diagnosed with PSC in 1994. He had a 20-year marathon of living with Primary Sclerosing Cholangitis, from 1994 until his death in 2013 following a long-awaited liver transplant. He was only 40 years old when he died - - and spent his entire adult life knowing that he had a condition with no known cure. His PSC was diagnosed when he had no symptoms, donating blood showing elevated liver enzymes. Organ transplantation is one of the treatments used to treat this highly unpredictable progressive autoimmune condition, but the condition often recurs or leads to other complications. His liver status was relatively stable for a number of years, allowing him to complete his education and follow his chosen career path in music and psychology. He was married and had 3 children. He was very involved in the organization of PSC Partners Seeking a Cure and created a non-profit organization titled "More than Illness." Some symptoms he experienced when his liver function deteriorated included severe itching, jaundice, and severe fatigue. He was on and off the transplant list a couple of times, sometimes either too well or too sick to be considered for medical research studies. One of the most difficult things to deal with, for the patient and caregiver, is the unpredictability of this condition. He dealt with additional complications including severe osteoporosis, portal hypertension, increased fatigue, mild ulcerative colitis, and symptoms of progressing cirrhosis. In 2011, he was able to work about half time - - as a faculty member at a college, where he taught, practiced his career as a licensed psychologist, and conducted research. His PSC had a variable progression, and he was eventually able to be listed at 2 sites. It became his job to maintain a semblance of health, while waiting for the availability of a suitable transplant. The need for ongoing research in drug treatments is essential for all those in the huge category of autoimmune conditions such as PSC. (I myself have systemic lupus and have been maintained in a stable manner with medications for over 40 years)! PSC presents a unique challenge since it is a rare disease with a smaller number of patients, a lack of identifiable lab

markers for early diagnosis and progression of disease, and the high variability and fluctuation of both symptoms and disease process. I urge you to focus research specifically related to patient identified needs in the ongoing challenges presented for PSC patients, as well as all those with identified auto-immune diseases that have no cure. He remained optimistic throughout his illness, but at the same time was realistic and made plans for the eventuality of his death. He was passionate about raising awareness of the need for research, the need for organ donation, and especially the impact of invisible illnesses/disabilities and how they are all around us. As such, his family is committed to supporting this cause.

- I was diagnosed with AIH + PSC + UC when I was 14 years old and immediately placed on prednisone (1 year, stopped against medical advice) and later imuran (5 years, also stopped against medical advice). At the time, very little information was provided to my parents or me, other than this is the only way to bring down my ALT and AST values and prolong the health of my liver. When you are diagnosed as a child, you have little control over your choices of treatment, and my parents just did what the doctors told them, which was place me on medications with no real information on when I could stop taking these medications (which is why I had to stop them on my own without telling anyone - which I understand is probably not the best thing for a child to be doing- but it was the only way my doctors would take [me] seriously when I said I wanted to be off the immunocompromising medications). I later found out that there is no real treatment for PSC. I came to accept that, and have chosen to have my liver function monitored through routine blood work (every 3 months), versus taking immunosuppressants. While I still take cholestyramine and rifampin for my itch (although I would rather not, but I have tried everything - naltrexone, gabapentin, light therapy - short of anti-depressants), I am currently not on any treatment/ drug for PSC/ AIH. What I came to realize is that while we can reduce the inflammation in the liver with immunosuppression, this doesn't fix the "issue" (scarring of the bile ducts) nor does it treat the symptoms of PSC (itch and reoccurring cholangitis) and I would rather not live with the immediate and long term side effects of taking immunosuppressant medications. I am aware that for those who require liver transplants, immunosuppressants are life-saving, but this cannot be the only medication available to all stages of this disease.
- 28 year old male, diagnosed with UC (refractory pancolitis) at 16, leading to high-grade dysplasia at 26, and to colectomy and J pouch surgery that same year. Diagnosed with asymptomatic PSC via MRCP this year; first discovered during workup for NAFLD NYD based on elevated LFTs. Also a family physician resident in Canada.
- PSC has turned our family's lives into a rollercoaster of ups and downs every single day. My daughter has suffered with incredible fatigue, pain, nausea, and headaches almost every single day for two years. No child should have to worry or be plagued with thoughts about whether or not they will make it, or when their number will be up and they will need a liver transplant. She battles this anxiety everyday. We need to do better. We need to be able to offer these children, our loved ones, and all those patients battling PSC hope - in the form of treatment, medications, and a cure. Please!
- It's been a living hell.
- My son is 17 and was just diagnosed with PSC and Ulcerative Colitis a month ago! Obviously this has rocked his and his family's world to the core! Any support we could get from the FDA in helping with new discoveries in treatments from this disease would be helpful!
- As well as dealing with physical symptoms we deal with the equally debilitating psychological effects of living with an incurable disease which has no cure or treatment. We live with the anxiety of knowing that at any time our symptoms may escalate to a point where the only option is transplant, and then we have the worry of wondering if we will be lucky enough to receive a transplant. Post transplant we have a complicated drug regime and the anxiety of worrying if we will get rPSC

[recurrent PSC] in the new liver. We live with the anxiety of wondering if our children/grandchildren will get PSC. Once we have PSC we live with the likelihood that we will develop other autoimmune diseases. I live with other diseases, the most concerning being interstitial lung disease and osteoporosis. I attend four hospital clinics, each with consultants who treat their own specialism. No one takes an overview of my overall health. Arranging all my clinic appointments has an impact on my day to day life. It often takes a long time before we find a clinician who has expertise in PSC. I retired early because of PSC. There are cost implications concerning hospital attendance, insurance, etc. Most of us have been reliant on the Charity for accurate information about living with PSC. The supportive PSC community means that we will all have watched some of our PSC friends deteriorate and die, often at a young age, knowing that this is a fate that awaits us.

- I have really no symptoms at the moment but the uncertainty of the course of this disease is distressing and it is hard to know what to do to help since all we hear is that this disease presents itself so differently in people. It's frustrating to hear that some are able to get prescribed vanco and others are not, and no real good guidance as to when one should seek vanco from a provider who will prescribe.
- It's a hard journey. My PSC is currently asleep and I am hoping it stays that way! However, even though I am told I should not have symptoms I do. Fatigue and brain fog are my daily companions. Some days better than others. I had to stop working and use my energy to keep up with daily activities. Of note I also had a colectomy and j-pouch construction. I developed kidney problems because of losing too much fluids from my stoma prior to the j-pouch surgery. GFR is usually around 40-50. So these other factors may also play a role in my symptoms. Thankful for any contributions made to find a cure!
- I had PSC for nearly 20 years. I am currently 2 years post transplant.
- Since 2007 I've had elevated liver enzymes. I was in my late 20's and didn't really think much of it. I think back to that time now often and maybe I should've been more to active instead of reactive. I've had flares over the years, some worse than others. In 2017, I had to be hospitalized for severe abdominal pain and I also was jaundiced and felt like crap. Still couldn't figure out what was going on besides I had inflamed bile ducts. Moving forward 2019... Liver enzymes through the roof, multiple procedures and 4 liver biopsies later PSC reared its ugly head... I now have had stents placed 3 times. Extremely fatigued.... the kind that makes you want to lay in the bed all day... the kind that makes you feel like a bad mom. Abdominal pain that makes birth feel like a walk in the park and last but not least, extreme itching that feels like bugs are eating away at your insides. No cure.... why.... research trials phase 3. Will someone please come save us... we matter too.
- My brother has PSC with an overlap of AIH and ulcerative colitis who is in his twenties and it has affected our family. We are hoping that one day there will be a treatment or cure for this rare disease and remain positive for his journey with PSC with future research on the bile ducts and liver.
- I am both a physician and a patient living with PSC. I have participated in a clinical trial and hope to become an advocate for patients living with this disease, bringing my perspective as both patient and doctor.
- Our son would not be alive today without the myriad of drugs he took and is now taking, as well as his life saving liver transplant. We are so thankful for the drug research and drugs that have allowed him to almost live a normal life. My son is also grateful and is giving back by being a mentor to pre- and post-transplant patients and is volunteering for Be A Donor, as well as speaking about his disease and his journey to his transplant.
- I was not diagnosed for years. I finally found a specialist with the knowledge and training to know my symptoms pointed to a real problem. I was immediately put on Ursodiol and steroids. Within 2 years I was presenting more serious symptoms and started what I call my end journey. I escalated

quickly and ended up with a diagnosis of Cholangiocarcinoma. I successfully completed that treatment and received my transplant shortly after. I am one of the lucky ones. I live in an area with top hospitals and doctors. Once I found the first specialist he was knowledgeable enough to get me to a top liver doctor in my area.

- Besides the physical issues and symptoms like itching and fatigue, and all the MRCP's and ERCP's I've been through (which are not cheap), this disease brings a large emotional and psychological toll on a person. Depression is common, and with the physical issues makes it hard to be able to live an active life. I do feel like I'm missing out on the fun part of life, as much as I try to say "Yes" when asked to do things. Sadly, I feel like I'm one of the lucky people with this disease, based on what I know others go through.
- We have a neighbor with the disease and have followed her journey for many years.
- TWO of my daughters have recently been diagnosed with UC and PSC. I am begging anyone/everyone to help keep research moving forward so they each can begin their adult lives without having to alter their perception of the future. They have bright careers. One is a 26 year old biomedical product engineer, the other is 19 and a sophomore in college studying to be a physician assistant. With the PSC diagnosis their future becomes so unpredictable. Will they find life partners who will want to help carry their burden of this disease and it's destructive path? I'd always dreamed of them having their own wonderful children if they decided to and now I'm not sure that will get that opportunity.
- These girls need the support of the medical community, FDA and the pharmaceutical companies to find a treatment and hopefully a cure for this terrible disease.
- Just found out that I am not a good candidate for transplant due to underlying neurologic issues.
- Compensated PSC since 2014. Not caught COVID-19 (yet?). Waiting for a good vaccine so I can safely resume normal parenting time with my kids.
- The uncertainty of the disease is on my mind daily. I'll go through points of fatigue or have random pains in my upper right quadrant and never know if it's my PSC or I'm just getting old. My production at work has drastically dropped. I had to sell my house at a loss to move closer to NYC so to be closer to the best hospitals and closer to work so that I am not as fatigued from the commute. I push myself to be in shape in case I ever need a transplant. I always need to push harder than I used to in order to exercise. I fear my kids could be left without a father. Knowing that there are treatments to reverse or stop the progression of PSC would give me and my family the positivity to live our lives normally.
- With PSC it's hard to plan 10 years ahead. Will I be alive? Can/should we have another child? There's certainly pressure knowing I don't qualify for life insurance.
- My quality of life is near 0. I spend all my time managing symptoms like pain, fatigue, itching, ulcerative colitis, brain fog and going to medical appointments.
- To the PFDD members, I want people to know that I am a grateful post-transplant PSC patient. I am doing much better post-transplant, being able to enjoy life again. But the only reason I was able to get a liver transplant before I had much more severe PSC complications was that I was fortunate to have a rare blood type (B) that resulted in a shorter transplant waiting time. Even so, by the time of my transplant, I had already dealt with five years of horrible symptoms, which were getting increasingly worse (cholangitis, sepsis, late night trips to the ER, extreme itching, fatigue, multiple 3-7 day hospitalizations, 2 PICC lines, many many ERCP's, etc.) This is no way to live. There is no effective cure or treatment, which leaves patients like us in limbo for years, as life passes us by. It is a rare disease, so most people have never heard of it and cannot have empathy for what we go through. Our only hope for a better life is currently liver transplantation surgery. As a PSC patient and healthcare worker, I would like to speak out for those who are patiently still waiting. We need

to make transplantation easier for those with all of the blood types (including the common ones: O, A) so those patients do not have to spend more years suffering with low quality of life, pain, itching, GI symptoms, fatigue, jaundice, varices, ascites, encephalopathy and a multitude of other daily symptoms. Strangely, PSC is somehow being overlooked when prioritizing liver transplants. It is seen as less serious than some other liver diseases because the lab values chosen to determine risk of death focus more on renal function rather than hepatic function. The explanted livers seen by transplant surgeons at the time of transplant have repeatedly demonstrated the seriousness of the damage that PSC causes. The severity of damage often does not correlate well with the MELD scores in PSC patients, which should indicate that a different criteria should be used instead. This lack of attention to the specific characteristics of PSC is a major problem in treating PSC patients. Every patient has a different combination of symptoms but overall, there are common signs and symptoms that most patients experience as the disease worsens. This process takes many years and leaves patients unable to continue important aspects of life such as work, school, parenting, family life and social activities. When this occurs, the PSC patient can become increasingly isolated over time. The MELD score, used in every Transplant Hepatology clinic in the country, has been shown to underestimate the seriousness of PSC patient's medical condition in hundreds, if not thousands of cases, yet it is still being used as the primary determinant of liver transplant eligibility. The fact that PSC is a chronic, autoimmune condition with no causation based on life-style, alcohol usage, drug usage, etc. should help in making transplantation more available to PSC patients, but it seems to be just the opposite. PSC patients continue to be pushed lower on the list simply based on their MELD scores. They are often told they aren't sick enough which is so disheartening to a patient who has already suffered many years with severe long-term symptoms, just because their score doesn't correlate with other liver diseases. A factor that should be looked at is the disincentive to have potentially helpful medical treatments (stents, ERCP, etc) because while they could alleviate a particular symptom short-term, it then hurts the patient's priority for transplant by lowering their MELD score prolonging their wait-time. This is bad medicine. There should never be a penalty for receiving a recommended treatment. The patients are then left with no choice but to accept their lack of options and harden themselves mentally for the long haul. As the disease slowly takes away more and more aspects of everyday life (social activities, friends, ability to exercise, ability to travel, etc) the patient's lives come to revolve around doctors appointments, admissions to the hospital, blood draws and many unpleasant medical procedures. This can often lead to anxiety and depression. When this happens, family members of PSC patients are the ones who really see the overall health deterioration that is occurring. The patients themselves are simply trying to cope day-by-day, sadly adapting to increasingly worse "new normal" as the disease progresses, taking over almost every aspect of their lives. PSC patients can lose the ability to advocate for themselves. This is the main reason we need medical professionals and patient advocacy groups to represent the needs of PSC patients, so they are not forgotten in this competitive world of MELD scores and transplant criteria. Thank you for your consideration in helping PSC patients get more attention to their needs.

- Hello there. As a family member of PSC patient, I feel deeply sorry for everyone who is having the diseases. I am keen to look for a cure for all PSC patients including my father, who is consistently suffering from fevers and back pains. He did liver transplant in 2018, but unfortunately PSC recurrent. At the moment, he has just done PTC, but still he is suffering from fevers every 10-15 days.
- I was diagnosed at 20. I am now 40 and have just received my transplant 3 months ago. PSC has been debilitating, especially in the last few years. The amount of energy I was robbed of made it impossible to work, make plans, enjoy life in general. We desperately need effective treatment against this often silent disease.

- My daughter has had trouble taking Vancomycin (hates how large the capsules are).
- Due to my PSC, I now have stage IV cirrhosis and cholangiocarcinoma. Because I chose not having a transplant as my only treatment, at 59 years old I'm busy saying goodbye to friends and family. We need a cure!
- Many doctors, especially in more rural areas of the U.S., do not seem to know about PSC, and this includes rheumatologists. My beautiful mother left this Earth from this disease last year because even though she had had symptoms for years that are classically associated with PSC, there was no one doctor or specialist she saw that mentioned PSC and this was after several years of failing health and scans and a liver biopsy. Once cancer was ruled out at various stages, doctors seemed to shrug it off as is done with many autoimmune diseases, as "you'll die with it, not of it." Anything the FDA can do to educate hospitals and doctors everywhere of the lethal nature of this disease could help PSC patients catch this disease early and treat and plan accordingly.
- I have had ulcerative colitis or UC for 19 years. It has been in remission for over a decade, with only a few minor flares occurring during times of significant stress. I believe my UC went into remission thanks to the Adacolumn clinical trial I participated in at UCSF in 2005. Prior to that clinical trial I had taken almost all of the various medications that were used to treat UC, at the time. The severity of ulcerative colitis was to the point that I was going to have my colon removed but I decided to give the clinical trial a shot before going through the colon removal surgery. I began to feel better during the clinical trial and I found out at the end of the trial that I had received the actual treatment. My UC was also in remission after completion of the trial. I worry every day that the fine line I am walking with the maintenance medication, mesalamine, I am taking for UC will fall apart. Once my UC went into remission my life changed dramatically. I was active and for the most part healthy. I traveled the world for work and rarely worried about a UC incident. However in 2016 I noticed my skin was turning yellow, I had upper right quadrant pain, and I felt very ill. My primary care doctor ran a bunch of lab work but could not determine what the issue was. It was not until I went in for an appointment with my gastroenterologist that I was told I had primary sclerosing cholangitis. Three days after my diagnosis I went in for an ERCP and had a stent installed, which was removed a few months later. I have had a few ERCP's since my initial diagnosis because of upper right quadrant pain and other concerns. I also seem to experience minor cholangitis attacks every once in a while. I am still in the early stage of PSC, but the fatigue and brain fog from the disease impacts me on a daily basis. I worry daily about what my life will be like as PSC gets worse, knowing that there is no medication I can take to slow the progression of the disease and that we do not know enough about the progression of the disease. I have a stressful job and I worry every day that the disease is going to progress to the point that I am no longer able to work. I agreed to participate in another clinical trial in the hopes that it would help find a more effective treatment option for PSC. It seems that very little research has been done in regards to treatment options for PSC and I was glad to be involved. However during the initial liver biopsy to determine if I was qualified to participate in the clinical trial, I was infected with *klebsiella pneumoniae* and that led to sepsis. I ended up in the ER the morning after my liver biopsy and spent almost 30 hours in the hospital as they treated me for *klebsiella pneumoniae* and sepsis. They also found a small blood clot in the portal vein, which was not found in an MRCP that was taken less than two months prior. After I was released from the hospital, I had a difficult time communicating with the people running the trial to understand how I had gotten infected with *klebsiella pneumoniae* during the liver biopsy and whether the blood clot that was found in the portal vein occurred because of the liver biopsy. It was not until two weeks after I was released from the hospital that I spoke with the study doctor about the issues I had with the liver biopsy and that was discouraging. I am not sure why a liver biopsy was required for the clinical trial as it seems like an MRCP would have provided the details needed for the trial and put me as a patient at less risk. As I was going through the recovery from sepsis and *klebsiella*

pneumoniae I really debated whether I wanted to continue to risk my health for the clinical trial. In the end I decided I wanted to do anything I could to help everyone else who has or will have PSC and have decided to continue on with the clinical trial. My hope is that this clinical trial will be successful and we will finally have a medication that will help all PSC patients. I am also hopeful that the success of this clinical trial will lead to other medications being developed for PSC and maybe an eventual cure.

- PSC is a challenging disease and many doctors do not know how to treat this. End game is liver transplant and getting very ill before we can qualify. My daily life is very impacted and I do not have a caregiver who is close to me. I am now divorced from my former husband because he didn't really want to take care of me. I am 71 and without good support. I'm scared of how sick I will have to get before I can get a transplant, and then there are no other choices. I'm new on the transplant list and live 60 miles from my specialist and transplant team. My daughter is willing to come back from Virginia for the actual transplant and month or two afterwards to care for me. She will have to take a leave of absence and will lose income. This is very hard on me and will be on my daughter. It has required a concern about having future children, medical expenses, 6 month check ups, stress for my family due to fear.
- I have been a PSC patient for about 20 years, although I didn't get the PSC diagnosis until about 5 years ago. I have been taking ursodiol and now also on immunosuppressant and steroids. I'm symptom free and have been vegan for 1 year. Also, I'm taking milk thistle for supplements.
- My PSC journey has been unpredictable. Thank God for the support of PSC Partners.
- Clearer guidance to industry from FDA on endpoints--and ways to collaborate innovatively to find a path forward to getting therapies to patients.
- PSC has impacted every aspect of my life. The symptoms make some days impossible to function with a clear mind and full energy level. There's many days where I don't have the energy to go on a simple walk with my wife and son. New treatments and research can improve the quality of life of PSC patients, making the disease more manageable while waiting for the possibility of a cure. PSC affects everyone differently, and you don't need to have PSC to be affected by it.
- I cannot find a doctor who is knowledgeable and/or available.
- There are two primary ways PSC has impacted our lives. First, the direct impact of the disease on our daughter. She went from being valedictorian of her high school class, to struggling to finish college. The disease is so uneven that even when she starts the semester with plenty of energy and drive, small things snowball, and she has rarely been able to complete a semester. At 30, she is still living at home working a minimum wage job, which gives her access to health insurance. Which is the second impact. Her billed care is \$200,000 each and every year. The constant threat - since around the time she was diagnosed - that the ACA would be yanked out from under our feet and we would have no way to pay for her medical care. Her employer went bankrupt in February, leaving her without health insurance with less than 30 days notice. She immediately found new work, but was not eligible for health insurance for 4 months. That meant an interim period on the ACA marketplace plans and 4 out of pocket maximums in a 16-month period of time - to the tune of \$11,000 (on an income of less than \$18,000). And there is a case in front of the Supreme Court right now that threatens to wipe out even that access to care, which would be inaccessible to her but for parental financial assistance. The constant fear that care will be unavailable adds to the stress of living with a disease that often ends with death or transplant. Anything that would ease the symptoms - or level them out - so that our daughter could sustain her drive to graduate from college, at least a semester at a time, would help tremendously. The two primary symptoms are pruritis and unpredictable, intermittent fatigue.

- Went from having PBC now PSC as well. The fatigue and some pain, waiting on my new mrcp and mri abdomen, feeling a little lost.
- Chronically tired, dual diagnosis of UC (colectomy), many doctor appointments, struggle to work full time and take care of family.
- I am a 33-year-old woman with PSC. I was diagnosed at age 27. I am about to complete my Ph.D. and begin my career as a historian and museum professional. I have a lot of dreams for the next few years of my life: settling down with my partner, finding my dream job as a curator, and having a baby. However, my PSC makes all these dreams seem precarious. Will I be able to have a career? Will I be able to raise a child? How many years will I have with my family before PSC gets the better of me? These anxieties plague me every day. I NEED treatments for PSC that can improve my quality of life as my disease progresses. It would be even better if there were a treatment that protects the liver, reverses damage, or cures the disease altogether! I am an incredibly stubborn person and I will hang on as long as I can. Please give us hope that life can be better!
- My son was diagnosed "by accident" with a stomachache at age 26. Stomach was fine but the ER physician ordered lab tests including liver enzymes which surprised everyone with being "sky high" and PSC was diagnosed at follow-up doctor's visit. My son has no symptoms. Studying for his Doctorate in Philosophy, living fully. He also has IBS, managed by the FODMAP diet. He also developed an anxiety disorder and taking medication. How has it affected us? I feel like it is the elephant in the room. I feel like the clock is ticking and by the time he graduates, he may be having symptoms... I have arranged my life to be prepared to help him if needed. I helped his brother and wife buy a house in Vancouver with a suite with level access, in case the time comes in which he is very ill and needs to return home. It is psychological right now. Of interest, my father died of lung and heart issues brought on by alphasitripsy A deficiency. I carry the multiple sclerosis genome apparently. Thank you for your work. I cannot imagine the relief in learning there is more help than waiting for "a compatible cadaver liver" as it was said to us.
- I had PSC for 15 years before I was transplanted. PSC robbed me of many things such as my good health and my energy. The PSC Partners Seeking a Cure has been a gift from God. The people who I really call friends have been great at helping me along my journey with lots of advice about how to deal with the many symptoms and problems that occur on the PSC path. My dream, ultimate wish, or whatever you want to call it, is a world where PSC is cured, or controlled with medications, and I am not losing friends to this nasty disease.
- I'm 10+ years after PSC diagnosis. I now have a cirrhotic liver and see results from continuing monitoring tests relatively steady but getting a little worse, each hospital visit, each year. I've had my gall bladder removed for fear of cancer (though it wasn't cancerous, thankfully). Some form of treatment, rather than just monitoring the inevitable decline, would have been good for my body, my mind, but more importantly for my wife's peace of mind. I know I've been one of the lucky ones. Our family know PSC friends around the world who are suffering in so many ways. We know their families are suffering so much, too. When there is just nothing to really and truly effectively fight this disease, we bond as people but our spirits are palpably lifted when we hear of possible new treatments or even advances in treatment for other diseases. We all need that particular sense of hope that maybe our turn for a major medical advancement is coming around the corner.
- I have already submitted my video testimonial and artwork that will tell my story and concerns a lot better than I can write it here!
- When my daughter turned 15, she was afflicted with this disease. It put us- her parents, siblings, grandparents, aunts, uncles, cousins, and friends on a journey that has been surreal. The realization that if more people were afflicted with PSC a cure could be imminent is, in my opinion, the most

unfair and hardest thing to reconcile. I am hopeful that this meeting will help shed light and bring PSC closer to a cure/treatment.

- Our son was diagnosed with PSC 22 years ago. Nine years ago he had a transplant. This summer PSC made its ugly presence known once again. Since June there have been two week long hospitalizations. He currently is experiencing the third hospitalization, so far for three weeks. He is very, very ill. He needs another transplant. Worry is a constant companion, but so is hope.
- I have a family member who has been impacted by PSC and is now starting to look at liver donations to prevent organ failure. My family has already experienced great loss due to other significant health diagnoses and it would mean a lot to my family to see treatments/drug development not have to destroy the life of another loved one or take her from us too soon.
- PSC has impacted my life by trying different medications trying to find the best treatment. It impacted my life positively by not damaging my liver more often I drank.
- PSC has been in my life for 12 years and in the forefront for the past 8. It has altered my life path in many ways from career, to family, where I have lived and when and how many children I've had (or rather not had). The decline prior to transplant was severe and scary. Now with rPSC my hope has an urgency, because I know what may be coming and that luck may not be on my side-so I need the science to be.
- PSC is reducing the quality of life of too many people in our communities. It effects artists, scientists, parents, lawmakers. It is imperative to find a cure and/or a viable treatment for this disease.
- Treatments and drug development would give my sister-in-law the chance to continue living her life as a mother to two boys, wife, mother, and all around amazing woman. It would give our family the chance to breathe easier knowing she is safe and healthy.
- My sister had PSC and then a live donor transplant from my brother so this is near and dear to my heart. Let's find a cure so other families don't have to live what we went through!
- Cholangiocarcinoma survivor/post resection 15 yrs.
- I felt that gem/cis did me a lot of harm and no good. Have to have better way of assessing benefit.
- Right now PSC is destroying my son's life.
- My sister has rPSC... her health deteriorated for years and, thankfully, she had a successful transplant. Right around her two year liver-versary she started to notice symptoms again and was diagnosed with rPSC. The worst impact has been to watch her ability to dream for herself and her family deteriorate, especially as she has had to quarantine since March in light of covid.
- I see how this impacts a close family member and how there is no solution or medicines. Something needs to be done to help manage or treat this horrible disease.
- My journey with PSC starts in the Fall of 1992 when I had a side ache. After much medical testing, I was diagnosed with PSC on December 2, 1992. The next several years of my life were spent exercising to get into shape for a liver transplant -- my eyes and skin were turning yellow and I was itching a lot, sleeping a lot due to fatigue and losing 30 pounds, which left me skin and bones. I had two small sons, aged two and five, and was thinking I would never see them grow up. On June 29, 1999, I had a liver transplant. Through daily exercise (including ice hockey two times per week) and evolving to a vegan diet, I have been able to maintain a somewhat healthy lifestyle. I still like to sleep all I can and take an hour nap every afternoon due to fatigue. I was able to have a 20-year liver transplant party last summer with 75 of my friends and supporters and even the liver doctor who did the transplant in attendance. All of my days being alive are good. Some are much better than others. I pray for a new medication or therapy that will slow down or stop the progression of PSC for myself and the 30,000+ other PSCers in the world. It is our only hope. I will soon (July 10, 2020) be 75 years old and have high hopes that I will be able to see my 2-year-old twin granddaughters graduate from high school.

- Our 8 year old son was recently diagnosed with AIH/PSC overlap. It has impacted our life as he has not been able to attend school while he has been on high doses of immunosuppressant and his fatigue and aches and pains have not allowed him to play in sport which he loves.
- Every day I fear that my son will no longer be able to have his bile ducts cleared, that his liver will fail and he will die. He was diagnosed at age 14 and 13 years later, I continue to fear for his health. It is a terrible thing and I only wish it were me and not him.
- It is all consuming and worrying that there is no cure. The thought of liver cancer is terrifying and always in your thoughts. PSC is debilitating and effects our whole family.
- We could really use help from the FDA and other agencies to find enough funding for studies across multiple medical centers to get large enough populations, as well as an indication for vancomycin as a treatment to make it easier for patients to gain access to try it from their doctors and insurers. I think it's the only treatment keeping me alive and functional today.
- I have been diagnosed with PSC since 2006, it has been a long journey. The key has been an anti inflammatory diet: fish, white meats, fresh vegetables, fruits, coconut milk, no processed sugars, no fried foods, yogurt. My body just relaxed, I have held my weight and my LFTs are normal. It has really mitigated any symptoms. Plus, mindfulness meditation each day, and exercise.
- Retired primary physician three years post transplant.
- Diagnosed with AIH in 2003, with PSC overlap several years later, my fatigue increased to the point I could no longer find/hold conventional employment. I went on disability in 2016, essentially into a government-sanctioned "poverty trap" and just now I might finally be getting subsidized housing: basically a tiny efficiency apartment with no parking. On immunosuppressant medication for years, which might have contributed to developing renal cell carcinoma with a tumor removed in 2016. The one bout (2 weeks) I had with pruritis around 2009, I was too distracted to perform my job, and no medications helped without making me too drowsy to work. PSC/AIH have drastically impacted my life and financial independence. Even with SSDI and SNAP, I can barely survive, renting just a room with no kitchen the past 9 years (which makes maintaining a proper nutritious diet difficult).
- I was diagnosed with PSC, UC, and cirrhosis at age 21. I'm now 33. Since being diagnosed with all three, and grateful for great medical care & medication early on, the PSC and UC are both in remission / asymptomatic. Though blood work does show I still have it and my liver is doing okay, this is something I'm aware of every day. I have and will continue to fight for a cure for others and myself.
- PSC turned our lives upside down. It's something that's constantly on our minds whether my husband is the hospital with a cholangitis attack, or just experiencing mild itching. The symptoms may come and go but the fear never goes away.
- PSC has been a heart rendering journey both positive and negative. We know people who have died and our daughter would have as she was in acute liver failure and was given only two months left to live. She would not be here today, if it hadn't been for her donor sister and cancelation of someone's surgery, so she got to be scheduled in before she was on her death bed. Having 2 daughters under the knife for six hours was very stressful. The transplant was successful but it is life changing. As well the disease can attack the new liver and you, always wonder if or when this might happen. Hopefully soon there will be drugs developed to treat or cure PSC, as it is a terrible disease and affects the whole family on a constant basis, as it generally is a progressive disease and does not go away.
- In 2014 I began working at a local pediatric hospital in Philadelphia. On my first day, I was introduced to one of our clinic nurses, who is running around clinic a mile a minute, with an enormous smile on her face. Little did I know that I had just met my best friend. A few months into our friendship, I have learned that she had quite a medical history. She was diagnosed as an infant

with PSC and received a liver transplant at age 15. Despite doing remarkable after her transplant, she was re-diagnosed several years ago. Our friendship over the years has grown into more family than friendship. We have vacationed together, we have worked together, and we have built lives together. We also talk about our future. We joke about where we will retire, and all of the meaningless things that will do when we are old and gray. Working in rare disease, I understand the challenges that face the patients and families of rare diseases. Throughout our friendship, I have seen what this diagnosis has done. My friend needs to sleep throughout the weekend in order to get enough stamina in order to work for others throughout the week. My heart races every time the phone rings, and I see that it's her, because I'm worried that she is in the emergency room. I annoyingly ask each month 1 to 2 days after she gets her labs to see how her numbers were. Same with her MRI. I have seen that when we planned vacations we've had to schedule rest time in order to make sure that she doesn't get too fatigued. And I comforted her when our colleague started grad school, as this is a goal that my friend knows her body won't let her achieve. But the thing that has affected me the most is our future. I don't believe you can put a price on a human life, but if I could, her value would be incalculable. I try to distract myself when I see her struggle, denying the fact that I know that she will need another transplant someday. And I even get worried those times when we talk about being old and gray, and retiring in Alaska, when I know the road that will lead us there is not very forgiving to my friend. I am attending this panel with the FDA for her. I am attending out of frustration and confusion as to why this has taken so long. I am attending because I am desperate. I am attending because those living with the every day challenges of PSC deserve better. I am attending so that she no longer has to sacrifice life goals due to her illness. I am attending for our future vacations. I am attending for our retirement plan. Much of this may sound very selfish, and it is. But I can assure you if you had someone in your life like her, you would be fighting too.

- I was diagnosed with PSC and UC in 2020. I am married with three young children (10-5). The thought of continually getting sicker and not being able to enjoy life with my family as we once did is in itself a disease for my wife and I. The uncertainty of the future of living with two incurable and progressive diseases is a new phenomenon for us. Any promise of a cure or at least some treatment would be in and of itself be a boost to our mental and physical healths.
- My niece is a PSC patient and her health has had long term impacts on her parents and sister: emotionally, time commitment and financially. Having a child who is chronically ill, you always worry, not only about how they feel each day but about their future--quality of life and will it be a reasonably long/normal life span. My niece deals daily with feeling not up to par because of the illness and the meds she takes for her illness. She has occasional admits to the hospital due to her lab results and has had a couple of surgeries which may or may not be related to her PSC. If a cure or improved treatment for PSC were to be found maybe my niece and certainly other people could live with much fewer medical complications, therefore fuller lives.
- I've had multiple stents put in and taken out, biopsies, turned yellow, been on the verge of the transplant list and then come back but today I woke up, took my pills, saw the sunrise, kissed my sleeping wife and dog goodbye and got to go to work. Without the work of the people that might see my words here, and the ones that came before you, I would be dead and the world would continue on without me. Many thanks to the wonderful doctors/nurses and other health professionals as well as those advocating, raising funds and supporting people like me. It can be daunting to know that you live with something everyday that will kill you if left unchecked and still may kill you even if you are diligent. As much as it weighs on me personally I know that it is frequently on the minds of those around me that I love and that part hurts infinitely more. I am lucky. I am able to manage my disease. You will never hear me complain to anyone but since you're asking it's frustrating to go around the endless carousel of blood test, medication, appointments,

refills, forms, insurance, diets, etc. I am fortunate that I have access to top notch care given my location and familial support, etc. but my heart goes out to those dealing with the same thing as me that don't happen live 20 mins from a world class hepatology clinic and work with doctors that are willing to go above and beyond during what must be their personal time in order to help and have people surrounding them that will take notes at appointments and help keep them on the right track. My eternal gratitude to those that are working on ending, mitigating or supporting the fight against this disease and ones like it.

- I was diagnosed with PSC at the age of 24. It was traumatic to hear at such a vibrant part of my life. I was determined not to let it define me and it for the most part hasn't. At 29, doctors determined it was time for transplant but as my MELD score was a 7, I had no hope of receiving a deceased donor liver. I was fortunate that I had been warned early on that this could be the case and that I should start searching for a live donor. My brother matched and a little over a year ago, he donated 67% of his liver to me. The recovery has been as smooth as possible but still isn't easy. The anti-rejection medications have their own difficulties and the fear of recurrent PSC is very much there, especially as I had my transplant so young. I'm hopeful researchers will develop drugs to cure or mitigate the disease so that I don't have to have another transplant in the future.

- I was going through some old writings and came across information from August 2011 where my daughter gave her description of PSC symptoms.

"Hi, all! I've had quite a few people write to me recently asking me for help in describing the way something feels to friends, a doctor, etc. So, I thought maybe it'd make a good topic heading. If you all have any suggestions, will you just jump on in so we can get a good list going for those who need help explaining exactly what we go through? I personally believe we need to invent new words for fatigue and itchy and achy and the like since they don't begin to describe what we go through, but since we can't, guess this'll be the next best thing! :) Here are some suggestions: RUQ (Right Upper Quadrant) pain: Sort of like a prickly brick lodged under your rib cage. Like a heavy water balloon under the rib cage. Itching: As if someone dropped itching powder on you and combined it with a severe case of poison oak. Under the skin itching as if red ants are living inside your skin and setting fires. Aching: Like a severe flu on steroids. Where every part of you hurts and aches, including your fingers, arms, legs, just lifting them up or moving your arms to pick up a glass, turn a page, etc. causes pain/discomfort. Feels like your body weighs 700 pounds. Feels like you're put together by rubber bands that are stretched way too tight. Feels like your body is about to crack or snap it's pulled so tight (like a guitar string that's ready to snap). Fatigue: Pervasive, mental, physical, emotional. Too tired to turn on the tv or read, can't focus on conversations or remember, understand what is being said. Repeat same things over and over. Misuse words (like asking for a sandwich so you can call someone back---okay, yes that was me. I asked my dad to hand me a sandwich so I could call a friend back...and didn't even realize what I'd said wrong!) Feel like you could sleep for weeks but you aren't getting any rest. Never wake up feeling refreshed. Exhausted whether you sleep 26 hours or 26 minutes. Feel like a zombie. Feel like you're not human or in your own body. Stare into space for hours without comprehending you're doing so."

Public Comments Submitted During the PFDD Meeting

- We have witnessed our friend suffer with the symptom of fatigue, as well as others throughout the 10 years we have known her. We have also seen it get progressively more severe. We truly wish for a medicine that can help her and many other people live a more normal life, as we know her quality

of life could be so much more than it is now. It broke my heart to watch her testimonial and those of others. Please listen and seriously consider creating drugs that will help.

- Thank you all - your stories were so informative, touching, and from the heart. It has helped me to understand the disease.
- Excellent, honest presentations by PSCers addressing the many challenges they face with a wide variety of symptoms, treatments or lack thereof, surgical complications, and the need for more research and patient involvement in that research. I'm hopeful the FDA took note of this enthusiastic and well intentioned Partners Seeking a Cure team. Thank you!
- Hello, I am adding one last comment. For me, the biggest fear about the disease is developing cholangiocarcinoma, and it is an area that research towards finding solutions would be so appreciated. I had a CCA scare 6 months ago, and I am now being monitored as I have an area that is high risk for turning to cancer. Once someone receives a CCA diagnosis, it feels like it is the end of the road for options. You become ineligible for a deceased donor liver transplant, and you suddenly need to go to a highly specialized hospital because not all have a CCA protocol. I was told by my doctor that he would send me to Mayo should I have come back positive. Being diagnosed with CCA should not become an "end of the road" situation, and any research or development on detecting it or treating it would be so meaningful to our lives.
- I am a PSC patient. I would just like to comment that PSC research is so important to the lives of us patients and our loved ones. Our lives would dramatically improve if we could find ways to slow progress of the disease, or even cure it. Or, if the difficult symptoms I fear (I have yet to experience them), and many others feel every day, could be managed. For me, I am already cirrhotic and it is just a question of when I will start to decline. I am deeply fearful of how I will handle working, having a family, and simply living life when all of the symptoms arrive. I often wish for a world where a doctor could tell me "you will experience itching, but this medicine has few side effects and can reduce it almost completely." Or that our fatigue could improve and we could have the energy to participate in life again.
- Excellent forum. How many trials are now in progress for new medications?
- Thank you to EVERYONE that made this possible!!!
- Well done. I appreciate all the effort that went into this workshop. And appreciate all the support and information for my daughter. And for me the caregiver. Thank you.
- I have enjoyed sharing my life journey with my PSC family. Together we will find a cure for PSC. Thank you PSC partners. Much Love
- Well done! Thank you everyone for your powerful stories and information.
- Thank you for putting this forum together - awesome work! <3 Not sure how I can help in the future, but would love to be involved somehow.
- Excellent conference! Thanks for your work on this.
- While I realize oral vanco does not work for everyone, when it does work, it is truly a lifesaving miracle. PLEASE work towards approving it for PSC so those that can thrive on it, are able to continue to get it prescribed, and more importantly, covered by insurance. My daughter's doctor told her she would have to drop out of college and move to a place with a better chance of getting a liver in time, and once we found another doctor that would prescribe vanco, six months later her fibroscan showed a normal liver, all labs normal. Now, with a new job with bad insurance, she faces not being able to afford her life saving medication. PLEASE HELP vanco get FDA approval. Thank you for your time and help resolving this matter.
- Hi, I'm 26 years old and I've been living with PSC since 2017. I'd like to share my experience using the off-label drug vancomycin and share my plea for the FDA to fund research on this promising existing therapy that saved my life and the lives of many others. These past three years I've been

virtually pain-free with normal labs and no complications, infections, or disease progression. While my peers are preparing for liver transplant or experiencing intense abdominal symptoms, cholangitis attacks, and pruritus, I am the healthiest I have ever been. Unfortunately, vancomycin is often discounted because of its many nuances. My physician at a major medical center has identified at least five factors that affect efficacy, including brand and dose. Two capsule brands return elevated liver enzymes to normal, halt fibrosis, and eliminate the need for transplant, while five oral brands have no effect. In 2018, my pharmacy accidentally ordered me one of those five brands. Swallowing those brown pills was detrimental to my health because it started the year-long flare that put me in the hospital, and forced me to drop out of postgraduate school. So I am pleading that the FDA and drug development companies research vancomycin through a clinical research program to explore all of its efficacy factors. Ideally, this program should include randomized trials and exploratory pilot studies, which are less expensive and quicker than full clinical trials. We patients need brevity—our lives depend on it. I believe we owe it to the PSC community to fully explore vancomycin and potentially save thousands of people just like me. I want to make this a reality and I'm happy to connect with you to discuss further details. Thank you.

- While I'd love to participate in clinical trials, I've been told I likely won't be able to because I've also been diagnosed with fatty liver. Even though my hepatologist feels the fatty liver is having very little impact on my labs or my condition, it's a question mark that could corrupt the trial results.
- I would really appreciate help from the FDA to coordinate and fund large NIH or other federally backed PSC studies across multiple medical centers, and to get an official PSC indication for vancomycin to improve accessibility and insurance approval for the drug. I was diagnosed at 27, and I almost died from acute liver failure with an ALP of 2480 at the worst, but I recovered and have been more or less normal with extremely slow fibrosis progression for the last 9 years up to age 34 because of vancomycin. I don't want any other patients to die because of a lack of access to a treatment that seems to work about 80% of the time if you have the right brand and right dose.
- Fred's comments about the effects of immunosuppression brought to mind my daughter's experience after her second transplant. Between the fifth and sixth months post-transplant, she had a cascade of infections: C-diff, CMV, influenza (despite being vaccinated), norovirus, and a new EBV infection with a very high viral load. More than 2 1/2 years later, her EBV level is still elevated and she has received CTs and MRIs every 3-6 months to surveil for PTLD (post-transplant proliferative disorder).
- The enrollment of PSCers in the registry is very helpful to the Community of PSC Partners Seeking a Cure for our hopes of having a treatment in the near future.
- With all the transplant being performed I would think there would be less complications after surgery. Will there ever be a data base where doctors all over the world can cross reference like genetic code? There are too many issues that arrive after transplantation. There are too many minor surgeries. Mother of a PSC angel.
- Hi, I'm just trying to decide if I want to join a clinical trial and probably won't as I feel the liver biopsy is too invasive.
- Thank you PSC Partners & to all the patients who have shared their stories today. We're as motivated as ever to continue our research in PSC. Although our center was only founded about a year ago, we have come to see what an incredible community is present with PSC Partners - we see the same on the research side! We have many projects coming up to address the unmet need of PSC patients.
- Autoimmune diseases are a major target for clinical research but are mainly focused on the more prevalent autoimmune diseases such as IBD, rheumatoid arthritis, and psoriasis. Being a rare disease, PSC is NEVER considered in early stage development, so our plea to drug development

companies is to consider PSC earlier in development based on the fact that, unlike the other autoimmune diseases, we have no existing treatments and the impact on quality of life is substantial for those of us fighting this disease.

- My daughter was diagnosed with PSC and ulcerative colitis at age 13. Her doctor mentioned that vanco was being used as a treatment for early-stage PSC, but he did not prescribe it for her because her disease was already advanced when diagnosed. A year later, she was listed for transplant, and 10 months after that she received her FIRST transplant. She was in 10th grade. 26 months later, a liver biopsy revealed that my daughter had recurrent PSC. She was a high school senior who had just been offered a scholarship to her top-choice college. Her doctor immediately put her on vanco, ordering the brand and dose recommended by the medical center doctor who pioneered this treatment. But the vanco was hard to get. We had to jump through many hoops with our insurance company to get it covered, since it wasn't an FDA-approved treatment for PSC. I wish I could say that vanco was a miracle cure for my daughter's PSC. It was not, though many others have used it with great success. While she was in college, her health declined dramatically, and she needed a SECOND transplant just before her senior year. However, vanco saved her colon. Her UC had become severe following her first transplant. Steroids and a biologic brought little relief but many side effects, and discussions about a colectomy had begun. However, to our surprise, the vanco prescribed for her recurrent PSC ended her UC misery, and her colon normalized. Twice since then, her doctor took her off vanco and twice her UC flared back up. Nearly seven years later, she still takes vanco. PSC patients have been using vanco off-label for 25 years. As a PSCer's mom, I urge you to accelerate the research and regulatory processes that could lead to FDA approval of vanco therapy for both PSC and IBD, so that patients who need it have this option. My main points - while vanco works for PSC in many people, it doesn't for all and we need to explore other treatments; and - vanco DOES work for IBD for some people and should be studied/hopefully approved for IBD associated with PSC.
- Thank you all for the comments. There were some regarding Vancomycin usage. Oral Vancomycin is study being conducted at Mayo Clinic and is enrolling in MN, FL, AZ. Randomized, double-blind, placebo-controlled. More info and contact info can be found at clinicaltrials.gov.
- For trials of new medication for PSC, many patients are dissuaded from participating when there is a requirement for biopsies. The usefulness of biopsies is questionable in trials as PSC develops in a patchy manner in livers, and this highly invasive and risky procedure gives many pause.
- We will never forget finding our daughter napping because of the sheer exhaustion. She looked like death door and someone who was seeking refuge. We wondered how this could possibly be good for her.
- I still take URSO and decline quickly without it. I also took Rifampin for pruritus which made my life more livable up to my transplant. These off-label drugs can help make our lives much more manageable. This has to be respected.
- My lovely daughter with PSC was treated with an anti-depressant for her itch as well. It is well known that anti-depressants have a black box warning about adolescents and young adults under the age of 25 can experience suicidal thinking and attempt. Well, my daughter had to be taken off the anti-depressant because she experienced suicidal thinking from the drug! Anti-depressants are meant to treat depression as the category indicates and using it for PSC itch is a double whammy to an already death sentence diagnosis in young people. As such, a patient focused drug treatment for PSC for young people is desperately needed to avoid at risk-behaviour during an already challenging developmental stage of adolescence.
- Because of my chronic acute cholangitis and sepsis, I had a doctor tell me once "That isn't reflected in the MELD scoring system. You'll be dead before you ever qualify for a deceased donor."

- I am the mother of a PSC young adult. My son was diagnosed in 2015 when he was a junior in college. He was able to finish college; however, his disease progressed rapidly with the jaundice, abdominal pain, ascites and intolerable itching. He was fortunate to receive a liver transplant in March 2018. He was able to get a job in his field after the transplant; however, he was diagnosed with repeat PSC in spring 2020. He doesn't talk about the disruption that this disease has had in his life - and keeps plugging along. As a parent, it is very hard to watch him lose weight again and wondering what lies in his future. My wish is that therapies that have been shown to be effective in some patients become widely available (i.e., vancomycin) so that all PSC patients can access them without professional or financial barriers.
- Re: the question about the difficulty with pill size...Oral vanco solution is available for pediatric patients so that they do not need to swallow a pill.
- Thank you to all of the presenters and panelists for sharing their struggles and stories of hope. I especially relate to Chelsea's story of the mental health effects of PSC and associated diseases. Our son was diagnosed at 13. He is currently a junior in college and despite some ups and downs, physically he is managing fairly well. However, like many others, his mental health has been significantly impacted. It is difficult to find hope without a proven treatment.
- I completely agree with a telephone caller! The teens are amazing! I've mentored them as well and they are such an inspiration!
- As I've walked alongside my sister over the last 10+ years as her PSC progressed... she got a transplant... and then now as she deals with recurrent PSC, it's been heartbreaking that there is not much she can do for the symptoms or to manage the disease. More is needed - for the benefit of those with PSC and for the millions those resilient people impact. Thank you for this event and allowing so many voices to be heard!
- PSC can easily hide eating disorders. It's so insidious, especially for young women. I had so many people tell me I looked great as I shed weight because my body was shutting down and I was dying. I've had to do so much healing after transplant around this issue. Thank you for bringing this up.
- Is there any future for research on designer drugs for PSC as in other diseases?
- Thank you for taking the time to hear our stories. My son was diagnosed with PSC just over a year ago. He's 10 years old. With the resources available to us in Chicago, we were fortunate that his diagnosis only took a few months.
- As with many other speakers today, the biggest challenge about his diagnosis is the unknown for his future. What will his quality of life be like? Will he pass this to his children? Will he be healthy enough to have children? Is he going to need a transplant? And probably the most terrifying - will he be mentally strong enough to face the challenges thrown at him? At 10 years old, he's currently in therapy to hopefully provide him with the tools to never go to a dark place. After his diagnosis, I made the decision to "Not wait for someday" and began planning all of the things I wanted him to experience while he feels well enough to do them. COVID has hindered many of those, but we take the opportunity to treasure the small moments together. However, COVID also allowed me to participate in this meeting today and for that, I'm grateful. I also don't want to wait for someday to find a treatment - I'm asking for that now. For a year, I've prayed that the science progresses faster than the disease. Please help make that a reality for him and all of the other children like him. Thank you.
- My daughter was diagnosed with PSC in 2012 at age 15. She has taken vancomycin therapy now for over 8 years and has a completely normal colon and liver. She has lived a normal life since starting oral vanco, graduated undergrad and graduate school with a degree focused in gut microbiology, and is now a gut microbiome researcher. Vanco has shown efficacy in numerous patients

worldwide-- if a number of variables that impact this therapy are managed properly. Why are we not focused more on understanding why it has shown efficacy in these patients?

- The symptoms are terrible, but what keeps me awake at night is the likelihood of losing my husband to this terrible disease. Hearing the news of the passing of James Redford from complications of PSC and CCA drives home this fear. Like Mr. Redford, my 35 year old husband has had two liver transplants, and is in the beginning stages of recurrent PSC. We need a cure... we need a way to stop fibrosis and disease progression.
- Thank you for fighting for all of us.
- Excellent talk by Dr Bezerra. Thanks.
- Risk factors between gallbladder removal and PSC, and does it exacerbate IBD, or help cause IBD and accelerate PSC? Two and a half years ago I was diagnosed with PSC after gallbladder removal and ERCP.
- Any correlation with celiac disease? Both my adult kids have celiac; one with pic [PSC?].
- Have Crohn's, PSC, and cirrhosis on amgevita injection dose increased six weeks ago. I have very bad joint pain now every day. Is this common with PSC or is it Crohn's?
- Looking forward to hearing parents speak.
- My sister-in-law just spoke on a panel with fellow transplant recipients. I cried during the whole time. I don't know if medical professionals have any idea what it takes to keep going with this disease. The insidious symptoms, the stigma, the constant uncertainty, the loss of life trajectories. I know it is rare, but the wreckage PSC causes in people's lives is wildly disproportionate. Mónica shouldn't have to be so heroic. She is a brilliantly talented woman who lights up every room she's in. She shouldn't have to live her life as a prisoner to this disease. I'm begging anyone who has influence over policy, research dollars, anyone in a position to put more energy towards curing this disease to do it. It's so under-researched, and it's robbing incredible people of their lives. It doesn't have to be this way.
- Hoping for a bio marker for PSC and AIH (autoimmune hepatitis).
- Not only can recurrent PSC cause the need for a second transplant, but, sadly, blood clots and strictures can put one back on the waiting list - even years after the first transplant - much like what happened to the earlier panelist. It's sad that transplant is the only option for some.
- The 12 months before my transplant, I spent 6 out of 12 months in the hospital but my MELD was low 20's. I missed 4 years of my children's lives due to the level of illness and hepatic encephalopathy. As someone mentioned earlier, I have foggy and missing memories. However, my memory loss extends to prior to illness. I now have recurrent PSC and am cirrhotic. Even though I am very closely followed it was not discovered until I was cirrhotic. I have small duct PSC. I now am finally back to work after a 6 year fight back. I have worked in mental health again for the past 2 years and am fearful of when it will hit me so hard I have to stop again. The first time I had regular and small duct.
- I was a "groomsmaid" at my brother's wedding, but the itching was so bad that I needed to leave the reception to return to my hotel room, take my entire formal suit off, scratch every inch of my body, put the suit back on, and finally return to the celebration.
- I just want to point out how messed up it is that we, as PSC patients, have to hope to be SICK ENOUGH to get on the transplant list. Or how backwards it is that being sick enough to make it on the transplant list, or make it to the top of the list is considered to be "lucky". After listening to the testimonials so far and hearing everything PSC patients go through and the symptoms we have... how is it possible that we aren't consider to be "sick enough"? This just isn't right.
- We had to buy red sheets because our bedsheets were covered with blood from my itching and open wounds on my body. "Suicidal itching" is an apt description.

- Parent of two adult PSCers.
- I struggled with acute cholangitis / sepsis for five years prior to transplant. I started carrying a thermometer with me everywhere, and if my fever got over 100F I would have to drop everything and go to the hospital. It made life very difficult for my husband and three daughters.
- My 21 year old daughter was diagnosed with Crohn's and PSC at age 17. She has been asymptomatic with her PSC until this summer when she was diagnosed with a dominant stricture in her common bile duct. Three ERCP's later she still has narrowing, and suffers from stabbing right upper quadrant and back pain, and daily diarrhea. As a senior in college she's taking her classes virtually from home which allows her to take naps several times a day and be close to her hepatologist, and the endoscopist who surely will be performing another ERCP. My daughter is otherwise healthy, has normal lab values, but has a dominant stricture from PSC. We have talked a lot about symptoms, but I'd like to see the pharmaceutical companies work with physicians and researchers to reverse or stop the disease progression! Thank you!
- Wanted to thank and give hugs to Kevin, Kristian and Steven, for their testimonials!
- Hello, My doctor has not prescribed any medication specifically for PSC. I take Humira and a steroid for my IBD. The hope was if the inflammation went down in my colon then the PSC would go into remission. Is that a solid plan for treatment? Other patients are on drugs like Urso and I have never been on those drugs.
- I am three and a half years post Living Donor Liver Transplant from PSC. Although I'm now healthy, Todd's heartfelt words on the constant worry hit home. The specter of recurrent PSC rears its head every time I feel an itch or begin to feel slightly "off". So many of my friends have been diagnosed with recurrent PSC... the stress of PSC has never truly left me, and unless there are more effective treatments and / or a cure, I don't believe it ever will.
- Kevin mentioned the challenge of writing a living will. <https://prepareforyourcare.org/en/welcome> The Conversation, by Angelo E. Volandes, M.D. addresses living will and end of life challenges. A palliative care resource: <https://getpalliativecare.org/>
- My husband was diagnosed with PSC just this past year. We are both physicians - despite our knowledge and training, the PSC diagnosis is terrifying and overwhelming. He was initially diagnosed with Ulcerative colitis, and has already had a colectomy. We thought that was the end of our ordeal, and then we got this PSC diagnosis. The unknowns are by far the worst part of this - we have no idea how quickly his disease is progressing or will progress. When will he need a liver? How quickly will it move? If he gets a transplant will he be okay? And let's not forget about the horrifying thoughts of cholangiocarcinoma - which is often caught too late and takes too many young lives. We need treatments, options to slow down progression and clear diagnosis pathways for cholangiocarcinoma.
- As a caregiver, watching my son suffering from this horrible disease in the last three years is a nightmare I do not wish upon anybody. Listening to the patients sharing their symptoms and struggles, I have tears rolling down my cheeks. I want to give them a big hug. Thank them for such a wonderful speech representing the community. Also thank you the organizers and the panel!
- Hi again, as we all are seeking a cure I would be interested of the current drug studies. For example HighTide is currently preparing a phase 2 study on HTD1801. What are the first outcomes of the phase 1 study? What about cilofexor? In a 12-week, randomized, placebo-controlled study, cilofexor was well tolerated and led to significant improvements in liver biochemistries and markers of cholestasis in patients with PSC. What can the doctors in this panel discussion tell us about these drugs?
- Just in response to the comment about coming across as arrogant... When you go to a hospital and the nurses have to Google your liver disease, you learn pretty quick that you need to be your own

advocate, do your own research, and you learn not to trust medical professionals so readily. It's a scary thing to have to go to Emergency, or a doctor and know that you will likely have to explain your disease to them and probably also have to explain the treatment they will need to give you. If we, as patients, don't question the treatments or decisions others are making about our lives... it could mean we might not see tomorrow.

- I was a caregiver, and the most important thing I learned from my son was: 1) He kept a journal of his years of PSC and Crohn's disease. I can only encourage all PSCers to be their own voice in a disease that's old, but still a puzzle to the doctors. 2) Continue to share your story because it can help someone else on that same journey as you.
- I was diagnosed in 2017, and during that first year I had over 16 hospitalizations. I could not make it more than 4 weeks without a cholangitis infection. Even worse, was how PSC affects my other chronic conditions. As a Type 1 diabetic, my blood sugars are unstable due to the chronic pain, infections and fatigue caused by PSC. I would love an effective treatment and cure for PSC so I can control my other chronic conditions as well.
- With so many PSCers so tired, has there ever been research at the overlap of PSC with nonplastic (Non anemia's, sickle cell disease, Beta-Thalassemia's, G6PD shortage, spherocytosis etc. Are these potential factors really excluded? They don't come out with the standard tests. The genetic overlap in disease-making genes with ischemia, hypoxia, and PSC is 97%.
- Hello, I am from Barcelona, 40 years old, and currently on the transplant list. I would like to share another limitation that I have faced due to PSC beside the shared experiences in this forum. It is related to my career projection. I am an industrial engineer and unfortunately, I have to decline options for better job positions due to several crises and cholangitis in the last years, beside the symptoms limitations which increase with the time.
- We are PSCers' parents. It is extremely important for the caregivers to have a support system also. There are too many unknown things that develop whether pre- or post-transplant. This is a road you don't want to walk alone.
- What are your recommendations or thoughts in helping hepatologists consider FDA (off label medications) or non-FDA products (supplements) in assisting PSC symptoms? Especially when they don't even want to consider this route?
- Hi everybody, I want to thank you for this terrific online-forum on that terrible disease and for the opportunity to take part, to listen and learn and to submit comments. I am a PSC-Patient, first diagnosed with PSC in 1986 at the age of 20 years. I suffered 3 liver transplants due to recurrence of PSC in 2006, 2015 and 2019. Although the last transplant occurred just last year, unfortunately a PSC-recurrence has already been diagnosed in June 2020 again. I know most of the pains and symptoms that have been described so far today and I wish all the best for their lives. Despite all the impairment and restrictions in practical life I still try to take part in my friends and family-, work- and practical life and to still try to function as a part-time lawyer for copyright and IP in the music and film business. When I sometimes wonder if being alive is worth the pain, I mostly come to the conclusion to still be happy to live and to raise my minor daughters. So I wish you all energy, courage and enough strength to handle dark thoughts and depression I am sure we all know too well. Always be aware that there are others who love and need you. All the best to everybody here and thank you again for this phenomenal forum to make PSC voices heard.
- The thing that scares me the most about this disease, more than death even, is that I won't die but will live for 30 more years, but will spend that time expecting to die anytime, and will end up a miserable old man talking about all the time I wasted.

- It's so interesting how you can be so sick, but not look sick. I can't tell you how many times doctors would come into the examine room and laugh because I presented in person so much better than I looked on paper!
- Commenting on the uncertainty of PSC as part of my story happened last year when I was waiting to pick my wife up from work. All a sudden I started feeling heavy contraction-like symptoms in my upper right quadrant that came as fast as they went. This went on for a little bit, and my wife had to leave work early because of this pain, so we could travel to Cleveland to the emergency room. I had no fevers just pain. This just shows one instance where your life seems to be going ok but within an hour you are in the emergency room with one of the worst pain you've ever felt.
- While I am mostly asymptomatic, I do experience brain fog and fatigue but I look ok. My husband doesn't understand the brain fog and gets frustrated with me. I have tried to explain to him but he doesn't get it. Anything to help the brain fog would be wonderful.
- The difficulty and sadness associated with future uncertainty has increased as I have gotten older. I was diagnosed at 16, at the same time as receiving my UC diagnosis (UC is what brought me to the doctors, not PSC). In 2015 I was confirmed to be cirrhotic. My husband and I want to start a family, but in the past 2 years between UC flares and liver complications, we still have not received approval by doctors to go forward. There is tremendous pressure to have a child before my PSC/cirrhosis worsens since I am still healthy on that front, but a CCA cancer scare and desire to retest in 6 months, as well as UC flares, has prevented us from trying for about 1.5 years. The thought that such a big life decision will be decided by my illness is difficult to accept. I am lucky that I still have the chance. Having treatments that slow disease progress (or cure it!) would be so helpful and could help future patients better plan for their future.
- Treatment for pruritus is very limited. I was itching for years, and tried everything from light therapy to various medications (gabapentin, naltrexone), as I was trying to avoid rifampin because of its contraindication with my birth control. I had to get a non-hormonal IUD so that I could start the rifampin, which was less of a choice than I would have liked. Although the rifampin is working and controlling my itch, I am not too comfortable being on an antibiotic for the foreseeable future.
- Being a Naturalized Citizen, with family, friends and acquaintances in Europe (Italy), are doctors, scientists in the U.S. and Canada, working and collaborating, sharing information with European colleagues? Are patients in other parts of the world on the same medications? Thank you. I am the Grandmother of a six year old boy, with PSC.
- I was diagnosed back in 2013 via routine bloodwork for my annual physical and UC. I have since been "asymptomatic." At least I believe. I do certainly have the brain fog and feel like I need to push myself more to conduct physical activity. I do not like to blame this disease for these things but am not sure if it is simply exhaustion of being a father of three with a busy career, or natural aging, or is it PSC? It's pretty frustrating and feel like 44 years old is too young for memory loss. Thank you to the FDA for listening to us.
- I can completely identify with the ticking bomb analogy.
- These stories all are familiar to my husband's experience. He received a living donor liver transplant from his brother at age 46 after suffering from UC since childhood and PSC for 13 years. He is kind, hard working, creative, funny, adventurous - and a dad of a 13 year old girl - who needs him very much. We are grateful for the transplant - but he suffers from recurrent infections of indeterminate causes since his transplant - every 2, 4, 8 weeks. They hit him out of the blue, knock him out - with fever, nausea, vomiting. So far oral antibiotics work - but living with the uncertainty of wondering when it will be identified as rPSC [recurrent PSC] or bile duct cancer - or when the antibiotics don't work, and he faces painful death from sepsis. Our family - my husband, daughter, and I - all live with the specter of this bomb going off at any time that a caller described. We don't want to scare people

and we continually try to appreciate each day we have - but terror and the spectre of disaster are constantly with all of us - and it is traumatic.

- My son was diagnosed almost three years ago. A lot of what everyone is talking about he goes through. He was just diagnosed with bipolar but I'm wondering if it's more just the anxiety of dealing with PSC and Crohns. He also has Asperger's so it's hard to get him to talk about what he is dealing with, then he ends up in the hospital because he hasn't told me he is feeling sick. What is the name of the 2 drugs that are in phase 3 trials? The one or two drugs that are in phase 2 trials?
- My daughter was diagnosed with PSC in 2012 at age 15. She has taken vancomycin therapy now for over 8 years and has a completely normal colon and liver, lived a normal life, graduated undergrad and graduate school with a degree focused in gut microbiology, and is now a gut microbiome researcher. Vanco has shown efficacy in patients worldwide if a number of variables that impact this therapy are managed properly. Why are we not focused more on understanding why it has shown efficacy in these patients?
- Yes! The itching, fatigue and brain fog are real! It's so nice to hear of others who truly know how you feel!
- I'm a 27 year old Family Medicine resident from Canada diagnosed with PSC this year after 8 years of severe ulcerative pancolitis, resulting in a colectomy in 2017 after developing high grade dysplasia. I know the FDA has pushed in recent years to focus on patient-related outcomes, but I'd urge for an equivalent push to encourage development of drugs with a disease modifying ability. Ideally to prevent the fibrosis that develops with chronic inflammation. This would ideally target those like myself in the early stages of disease and prevent progression. Thank you for holding this event!
- Throughout my journey with PSC I suffered from brain fog. After my transplant it seems to be getting worse. I have been told it is a side effect of the Tacrolimus that I must take to survive. I am heartened to know I am not the only one with this issue. I really would like to see more done in this area to help us. I am in danger of not being able to work as I cannot effectively communicate anymore.
- Are there patients that have had more issues with UC versus their PSC?
- My diagnosis happened as a result of blood test results while being treated for UC. It was flagged then but not ever mentioned before.
- While I was able to work up until transplant, I would often experience severe fatigue and brain fog. The best way I can describe it, somedays I would go to work early in the morning, and several hours later, it's like my brain would finally arrive to participate. It did not matter how much sleep I would get, I rarely felt rested in the morning. I also hid itching under my desk and away from coworkers. There were times that I was in tears at night due to relentless itching.
- Is the insomnia secondary to pruritus or an independent factor?
- Thanks Afsana, Tim, Jessica, Elizabeth and Dan! Hugs to all for your strong testimonials!
- Thank you to everyone for sharing their stories and experiences!
- I am very sad to hear people talk about their PSC symptoms. These symptoms dominate my daily life but it is worse to hear that other people are suffering too.
- No question here. Just a note of thanks. Thank you to all of the patients who continue to share their voice for all those with PSC. Your bravery is inspiring for us all.
- Excellent summarization of this very complex disease Dr Bowlus. Will we be discussing the two drugs in Phase 3 trials? Thanks.
- Well said Ricky! I remember the day of my diagnosis vividly and your personal story so captured the start of this important forum!
- My first drug trial involved three liver biopsies. My current drug trial involves one biopsy at the beginning and one more at the end in 2021. Biopsies may be a potential impediment to participating

in future trials. In a perfect world, I would like to use the last biopsy in my current drug trial to be used to start the next, within a reasonable time, realizing serious collaboration would be required between different trial sponsors. Or, consider the correlation between all my diagnostic tests showing consistent results between biopsy, fibro-scan, blood work, and MRCP, eliminating the need for additional biopsies.

- Amazing and heart touching introduction by Ricky. Thanks.
- My husband passed away on August 16, 2020 from PSC-Crohn's. He battled this disease undiagnosed until he presented with Stage 3 cirrhosis in 2015. By that time he was not a candidate for a liver transplant. He was aware of Crohn's and had been treated for that disorder for a number of years. Life would have been so much easier for him a) if the disease had been known more widely, b) if there had been a drug that would have given him longer life. Thank you.
- In 2014 I began working at a local pediatric hospital in Philadelphia. On my first day, I was introduced to one of our clinic nurses, who was running around clinic a mile a minute, with an enormous smile on her face. Little did I know that I had just met my best friend. A few months into our friendship, I have learned that she had quite a medical history. She was diagnosed as an infant with PSC and received a liver transplant at age 15. Despite doing remarkable after her transplant, she was re-diagnosed several years ago. Our friendship over the years has grown into more family than friendship. We have vacationed together, we have worked together, and we have built lives together. We also talk about our future. We joke about where we will retire, and all of the meaningless things that will do when we're old and gray. Working in rare disease, I understand the challenges that face the patients and families of rare diseases. Throughout my friendship with her, I have seen what this diagnosis has done. My friend needs to sleep throughout the weekend in order to get enough stamina in order to work for others throughout the week. My heart races every time the phone rings, and I see that it's her, because I'm worried that she's in the emergency room. I annoyingly ask each month 1 to 2 days after she gets her labs to see how her numbers were. Same with her MRI. I have seen that when we planned vacations we've had to schedule and rest time in order to make sure that she doesn't get too fatigued. And I comforted her when our colleague started grad school, as this is a goal that she knows her body won't let her achieve. But the thing that has affected me the most is our future. I don't believe you can put a price on a human life, but if I could, her value would be incalculable. I try to distract myself when I see her struggle, denying the fact that I know that she'll need another transplant someday. And I even get worried those times when we talk about being old and gray, and retiring in Alaska, when I know the road that will lead us there is not very forgiving to my friend. I am attending this panel with the FDA for her. I am attending out of frustration and confusion as to why this has taken so long. I am attending because I am desperate. I am attending because those living with the every day challenges of PSC deserve better. I am attending so that she no longer has to sacrifice life goals due to her illness. I am attending for our future vacations. I am attending for our retirement plan. Much of this may sound very selfish, and it is. But I can assure you if you had someone in your life like her, you'd be fighting too.
- I recently had a liver biopsy for a clinical trial. I am in the early stage of PSC and for the most part was healthy going into the liver biopsy. I was infected with *klebsiella pneumoniae* during the liver biopsy, which led to sepsis. I ended up in the ER 24 hours after the liver biopsy procedure and spent 30 hours in the hospital being treated for the infection. While I was in the hospital they also found a blood clot in my portal vein that was not there in an MRCP that had been taken less than two months prior, so I assume it developed from the liver biopsy. I never heard from anyone involved in the clinical trial while I was in the hospital even though I kept telling the ER doctors treating me that I was part of a clinical trial. It took me almost a week to recover from the liver biopsy issues, during which time I could not work. I did not hear from anyone running the clinical trial during that time to

see how I was doing or ask if I had any concerns about what had happened. I proactively tried reaching out myself because I had been put on a blood thinner for the blood clot, but was given no direction on how long to take it. I was able to get in contact with the nurse for the doctor running the trial, via the hospitals My Health app, but did not get to speak to the doctor running the trial until two weeks after I had been released from the hospital to discuss my concerns. That entire time I was not sure if I needed to be concerned about the blood clot in my portal vein and if there were going to be any long term effects from being infected with *klebsiella pneumoniae* during the liver biopsy. The blood thinner I had been given for the blood clot was not even listed on my release notes from the hospital, so I had no clue how long I was supposed to be taking it and what impact it might have to my overall health. I am happy to participate in any clinical trial that will help find a treatment or cure for PSC, but it seems like patients need to be treated better and communication improved. There are dangers to liver biopsies and in this case I do not understand why an MRCP would have been sufficient to get the data needed for the trial. Liver biopsies are very invasive and put clinical trial participants at risk, when they potentially need not be.

- To see your first grandchild grow up as a lovely, gentle, caring little boy, and at the age of 4 to be diagnosed with PSC is terrifying. To see my son and daughter-in-law struggle with having a little boy with this condition rocks my world and slowly kills me mentally. Prayers and science must come together to find a cure. Our grandson is now 6 and to see him taking meds is an unbearable sight. Knowing and hoping that doctors are working hard for him and many like him, gives us hope when we look into his deep, beautiful, hopeful and happy eyes. Please help.
- Living with PSC is so frustrating as few doctors are familiar with it. I was told when I was initially diagnosed that the doctor couldn't do anything for me until I turned yellow. So thankful for PSCPartners, or I would still be in the dark. Through their conferences and FaceBook pages I have been able to educate myself and find a specialist even though I have to drive to another state. When I questioned a doctor regarding a ERCP, my husband told me I came across arrogant, just because I was questioning him. It's just frustrating living with an unseen and unknown disease.
- Here to listen to the patients, caregivers and clinicians for PSC.
- We have lost too many people along the years to PSC; a cure has to be found. Living with symptoms of itching, fatigue, etc. are not understood, and believed by many that we can change the way we are, but that just isn't so. New medications could help so much to improve quality of life for PSCers.
- What can be done to make medications more affordable?

Public Comments Submitted After the PFDD Meeting

- Thank you again for the chance to join you and your community last month for your groundbreaking PFDD meeting.
- My child has PSC. He is a 12 year old male. He is so tired everyday; he sleeps most of the day. He is on 21 pills per day. He was just diagnosed with PSC and UC. Our life is 100% different. Each day he is so tired he can't think and struggles with school. This is all increasing his anxiety because he also has had severe anxiety since he was a toddler, always had stomach issues but is also diagnosed with selective mutism, ADHD. There needs to be more help for PSC patients, especially pediatric patients. My poor child is so exhausted from lack of iron and vitamins he needs to function. The doctors didn't have much information to provide me, and I've researched on my own. Please, even a treatment to somehow help patient[s] absorb nutrients better, or even research on what foods or nutrition guides would help pediatric patients live their lives instead of sleeping so much. We pay so much money for medication and hospital bills.

- I'm originally from Rochester, NY area now living in Florida. My late husband died from PSC complications in 2015 at age 65. He was diagnosed at age 46, was followed every 6 months by a GI and was relatively healthy until age 64 when his bili was elevated on routine lab work. One thing led to another: stent placement, sepsis, hospitalization, stent placement with resultant gastric perforation, emergency surgery and near death, 2 months in acute care, home, more stenting every 8 weeks, SLOW recovery, stent removal to "see how he'd do without stents," decline in condition after 6 weeks, me getting him set up to go to Cleveland Clinic for a Living Donor Transplant (younger daughter offered for a year to donate), me driving him 270 miles to the Cleveland Clinic in a terrible rainstorm at 2am, him admitted to MICU, then to Pre-Transplant floor for workup, his daughter backing out on the Living Donor 2 weeks after getting to the Cleveland Clinic, him deteriorating further, trying to hang on until he could get listed, him suffering from increasing Hepatic Encephalopathy, another admission to MICU, and liver failure. After discussion with his doctors and confirming what I already knew, I called family and my brother set it up so I could have my husband transported back home so he could die at home. I got him home (via ambulance with 2 paramedics) and he died 2 days later. The doctors at the Cleveland Clinic were wonderful but his Hepatologist in Rochester left my husband in the lurch. He said, "I can't do any more for you. You need a transplant." He never referred him to a transplant doctor or even mentioned that was an option until it was way too late. He never even called me back to extend his sympathies after I called his office to inform him of my husband's death. I think educating PSC patients and their caregivers to available options is vital to helping people make decisions that will benefit their health. My husband could've been transplanted long before he died had his doctor made appropriate referrals.
- I was diagnosed with PSC at 25, and within a year I had the energy of someone 85. It took off [in] my 20's even though I have had the fortune of having a transplant at 29, five years ago, it will almost certainly shorten my life. Living with PSC is incredibly difficult, the fatigue is awful, the itching is unbearable, the weight loss is atrocious, it's a very hard burden to bear. The transplant is not a cure, you trade one set of problems for another. I work at [a lab] where we help bring drugs [drugs?] to market every year. I know it's incredibly difficult it needs to happen, we need good treatments and a cure.
- It amazes even me how bad the fatigue can be. There are times I'm too exhausted to even plan things I'd like to do, too exhausted to make a phone call etc., because my brain is too exhausted to work properly.
- I am a male 43 year old, diagnosed with ulcerative colitis and PSC since about 3 years. 3 Years on Mesalazine + ursodeoxycholic acid... Without markable results. Spring 2020 Coloscopy - bowel inflammation. Talked to get imuran, I refused to take it, and wanted better vedulizomab. They refused first to give it to me. Then my blood tests results showed that I even cannot get imuran, so I got vedulizomab, first time in August. Until now 4 times, in 2 weeks again.... UC a bit better, but my liver tests went crazy, so they gave me prednisone first 15mg a day for 2 weeks, now I take 10mg a day since 2 weeks. I tried to talk to the doctor to try the vancomycin, but he refused and he even did not look to any of the material I sent him... He meant - If You want to try vancomycin, please look for someone who prescribes it to You. If You find someone and You try it, let me know if it did work, but I will whether prescribe nor recommend nor indicate that. Please I have now some questions: I am getting vedulizomab, to try to get my UC under control. But probably without influence to PSC (which I understand as another important subject for me). Vancomycin (if correct understood), could help me get the UC under control AND by PSC the liver tests (and later then MRCP results) maybe making better or even also as good as in the beginning of the disease. But, if the vancomycin would not help, then there is a risk, the vedulizomab would not help any more, so there is a risk, that I will have problem with UC again AND PSC, but if I try vancomycin, I can get help for UC AND PSC, but if I stay now on vedulizomab only (without vancomycin), I will by luck get my UC under

control (but without influence to PSC at all?). What would You recommend please??? I seem to be the only person in CZ who is interested about more possibilities and looks for informations outside of Czech republic too. Thank You VERY VERY much.

- On May 18th, 2017, my then healthy 16-year-old son [] had acute pancreatitis which landed him in the emergency room for the first time. The doctors at the children's hospital could not figure out the cause and said it was idiopathic. When [he] was released 10 days later, we were so relieved that he recovered. Little did we know that was just the beginning of our ordeal which quickly turned our life upside down. Within a couple of months, he had 5 more episodes of recurrent pancreatitis, followed by cholangitis. He lost 25 kg in a year. That was his last year of high school while his friends were busy preparing for college. [He] spent a lot of time in the hospital, including once in the ICU. He had his gallbladder and appendix removed, had a stent put in, later taken out due to infection. He was diagnosed with PSC following a liver biopsy and many other tests. We as parents were traumatized by the frequent emergency room visits, and devastated by the life threatening nature of the disease, not to mention the fact that there is no cure. When he started college in a different city, we sold our house and moved with him. Even if we managed to be physically there for him, it pains us to watch his health deteriorate in front of our eyes. We never felt so helpless. Within a year since diagnosis, his liver deteriorated from fibrosis to cirrhosis, and he was listed for transplant. In the meantime, we were told it is almost impossible for him to get a liver from a deceased donor due to the low MELD score and his O blood type. My husband and I were both tested. We are now searching anxiously for a living liver donor, hoping a stranger would be so kind to come forward. It is a huge sacrifice we ask people to make for his sake. It would be a tremendous debt we don't know how to ever repay. Yet we have to do this and we pray for it to happen, as it is clear to us – He needs a new liver and he needs it soon. My heart goes to all PSCers and their families. I know exactly how much they are suffering. Please put a stop to this. We need a cure.
- Thank you for listening to my voice and my reality. I am reeling as a mom who has two daughters recently diagnosed with PSC. I need your help with research and attention so my daughters can begin their adult lives without having to alter their perception of the future. For now, they have bright careers. One is a 26 year old biomedical product engineer, the other is 19 years old, and a sophomore in college studying to be a Physician Assistant. With the PSC diagnosis their future becomes so unpredictable without your attention and help. Will they be able to continue living a good life? I am in shock these are my healthy, athletic, vibrant, fun, sweet girls. My fears that circle through my head nightly are whether they will be able to have families of their own? Will they be able to find and keep life partners who will want to help carry their burden (physically and mentally) of this disease and its destructive path? I have so many fears. These girls, me, my husband, their sister, their brother, and many others need the attention and support from all of you listening... the FDA, pharmaceutical companies, the medical community, and researchers, to find treatments, and hopefully a cure. Please help. Love, me
- I suffer from PSC, and lately I have been having uncontrollable itching on the legs and arms. It has affected my quality of life. Is there any treatment out there that can help relieve the itching? Currently, I am taking hydroxyzine to assist in the relief. Thanks!
- I was diagnosed with PSC about 11 years ago. I went into liver failure 3 years ago and had to have a tips procedure to remove toxins from the liver. Unfortunately, the toxin levels were higher than expected, got into the blood stream, and caused brain damage, hepatic [Segers] and severe memory loss. Luckily, I was able to have a transplant about 10 months later. My life is still affected due to anti-rejection medicine that lowers my immune system. Obviously my family has been affected by this. Before the transplant I had to have home health care when I wasn't in the hospital because I couldn't take care of myself.

- I am a two time liver recipient due to PSC. Since I have been taking Prograf since 2008 my kidneys are starting to fail and I worry about possibly having to receive a kidney transplant in the years to come. I would like to hope to be able to take an alternate form of medication to preserve my kidneys.
- I was diagnosed with PSC in 2006, but it wasn't until late 2019 that I started to be severely impacted by the symptoms. My bilirubin was rising exponentially and the scratches and scabs on my arms and legs was all the evidence one needed to see this. The itching was incessant. I would rub my feet on the rugs, only to develop burns and peeling skin. I would bury my feet in sand and rocks, scraping them for minutes on end because the pain was a relief from the itching. I would walk barefoot in the snow, or taking extremely hot showers just to have a different sensation. It hurt to wear clothes. I couldn't stop, no matter how hard I tried. I experimented with six different medications and nothing helps: cholestyramine, cbd, naltrexone, zoloft, benadryl, and gabapentin. My bilirubin rose to a 40. I didn't even know it could get that high. I was so yellow I was starting to turn green. I didn't even look like myself anymore. There needs to be more research to cure PSC, or at the very least slow down the progression of this horrible, terrible disease. There needs to be a better medication that can quell the unbelievable, incessant itch that goes down to your very core. There needs to be some sort of relief. Although I eventually was diagnosed with cholangiocarcinoma (CCA), I suffered for months with itching and jaundice. I went through procedures monthly- some worked and some didn't. I had ascites for what seemed like my whole life at the time. I could barely walk toward the end. Then, I received a transplant. I am doing well now but every time I get a tiny itch, I am afraid the PSC has come back already. I've endured enough. We need a cure.
- My daughter was diagnosed with PSC/ ulcerative colitis at age 15. Her symptoms began at age 11 after taking doxycycline for acne that affected her gut. She had severe pancolitis and was recommended by her local GI to consider a colectomy. Through my research I connected with 2 doctors and learned about vancomycin as a possible treatment of PSC/UC. She immediately responded. Today, her only treatment is 1000 mg BID of vancomycin, and she remains healthy with completely normal liver functions, a normal MRCP and MRE, and a normal colon. Vancomycin reversed all indications of both conditions and saved her life. She graduated from Stanford last June with a BS in biology and has just finished her Master's degree at Stanford in (gut) microbiology. She was even healthy enough to be a four-year D1 athlete at Stanford. Here is her story recently published by Stanford University:
https://gostanford.com/feature/indomitablespirit?utm_source=fb-organic&utm_medium=commpost_2019-05-09_1A2B4C&utm_campaign=lacrosse_otherpd_feature Over these 8 years we have learned that the efficacy of this treatment is dependent on dose and brand of vancomycin. These variables are detailed in a case report that I submitted 2 weeks ago with doctors from Mayo Clinic, Stanford, Miami, and Yale. My daughter's life was given back to her with vancomycin. I truly hope that the FDA decides to fund studies to better understand and define the factors that have resulted in a sustained clinical and therapeutic response in many PSC patients.
- As a mother of an 18 year old boy that was diagnosed in September of this year, our life for the last year has been nothing but the struggle and suffering on behalf of my son and us as a family. Watching him being sick with nausea, loose stools, fatigue, and fever off and on, and not being able to help him as a parent is the worst nightmare that no parent should face. So please, please, help us find a cure or control the symptoms and help so many young kids suffering. Way too young for this. Thank you so much.
- My son was diagnosed with early PSC in June 2019. He also has ulcerative colitis. His liver enzymes were elevated to 8x the upper limits of normal until he started oral ANI brand generic Vancomycin. 1500 mg per day taken in 3 divided doses of 500 mg each dose. His liver enzymes have remained

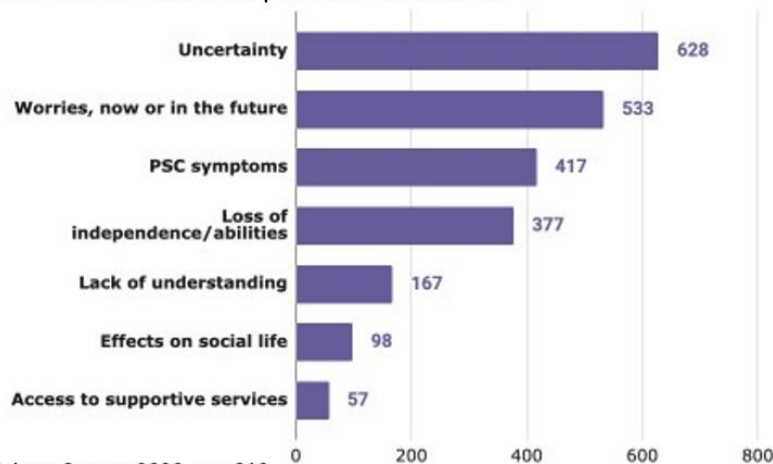
normal to date and he had improvement in his MRCP liver scan. Also his colon was completely normal on his colonoscopy. Please consider the data showing vancomycin helps many PSC patients and is standard in pediatric patients. It's a better alternative than waiting for a liver transplant and is allowing him to feel great and finish medical school where he is doing GI research.

- I am an RN and my husband is a physician. We are both involved in research and very frustrated oral Vancomycin is not being routinely prescribed. Urso is routinely prescribed for PSC off label and has not had the same beneficial effects as oral Vancomycin.

APPENDIX 5: OUR VOICES SURVEY - CURRENT CONCERNS OF PEOPLE LIVING WITH PSC

Concerns about Living with PSC

What are your current concerns about living with PSC?
Choose your THREE most important concerns.



Source: Our Voices Survey 2020, n = 819

APPENDIX 6: OUR VOICES SURVEY - ADDITIONAL CONCERNS OF PEOPLE LIVING WITH PSC

Survey respondents were asked to list additional concerns about living with PSC that were not included in the question presented in appendix 5.²⁰

- I recently divorced rather than live with someone who was not a nurturing compassionate person. He told me of a few occasions he is attracted to younger, healthier women, he can't help it. I initiated the divorce. He is very self centered.
- Medical insurance (ACA) must NOT be repealed!!
- Being able to live a productive life, being more independent, not feeling so emotional regarding my future.
- Financial worries - if unable to work and health insurance coverage, LTD (long-term disability) was denied.
- The wait time to get a transplant, as PSC doesn't always play the MELD score game. Seems like it may never happen until too sick to recover fully from transplant.
- Managing my type 2 diabetes, my ostomy (41 years), my strength and mental capabilities, ability to drive and my eyesight and hearing.
- Not qualifying for transplant because of age, etc.
- Other diseases due to the PSC.
- Life expectancy.
- Ability to conceive or sustain a healthy pregnancy.
- Leaving a spouse and family when I feel great and am active.
- Not being able to be a full and equal parent to my young child.
- As the primary caregiver in my family, if I get ill, who will help?
- Dying young.
- I would have checked ALL [the] boxes if I could.
- Unpredictable political/administrative decisions that affect the medical community and funding for cure and treatment research.
- What kind of government nursing support can I get if I have no one that can help me through the stages of PSC if I get a transplant or cancer?
- Fear that disability qualifications will kick me off of status as disabled then not be able to get back when things are worse again.
- Living by myself, so when I get a cholangitis attack sometimes I could be unconscious and nobody there to help me get to hospital. This is because my blood pressure would be really low.
- How hard it is with constant, incurable pain to get real acknowledgment and treatment because the pain is so debilitating I can't get out of bed, or take care of myself.
- Not different than above, but more than three of the above are my current, major concerns.
- Difficulty planning financially for an uncertain future.
- Losing my ability to reason.
- Not knowing the symptoms that would be indicators for if my PSC is getting worse. I didn't know anxiety, pain under the ribs, or loss of appetite were symptoms.

²⁰ All comments were submitted by individuals. Comments do not necessarily represent the opinions of other commenters, meeting participants, or PSC Partners. Comments presented have been subject to light copyediting as needed for clarity (e.g., spelling, punctuation) or privacy (e.g., names of patients or health care providers mentioned might have been removed).

- Having a baby.
- I am unable to get life insurance because of my diagnosis of PSC and ulcerative colitis, which puts my family in major financial risk.
- I have a working diagnosis without any symptoms or confirmation.
- Stress on family.
- Financial stress from being unable to work and potentially moving to obtain a liver.
- Lack of knowledge among medical professionals.
- Fear of the pain and trauma of near death.
- I had a LDLT [living donor liver transplant] 8 months ago. No current concerns, but uncertainty was the biggest.
- Recurrence of the disease and living well with a transplant (I received a transplant two years ago).
- Recurrence of PSC post transplant would be very heartbreaking.
- Not being able to actively pursue a career in which I studied for.
- Concerns about the future, predictability of the condition is so varied and makes it difficult to plan for your life and future. Concerns over no real cure, feels like waiting for the inevitable liver transplant which carries its own challenges and worries.
- I would have also selected lack of understanding. My biggest concern is residual HE [hepatic encephalopathy] and dealing with that post transplant, and needing to get financial assistance because I'm unable to work. Also an increase in anxiety and depression post transplant because I'm unable to work and my concern for the future.
- When/if I will be able to/should take one or more COVID-19 vaccines.
- Medical bills, prescription bills, insurance premiums, independence, and number 1 worry (fear) professionals not up to date on treatments, management of disease controversial, and no one willing to be "the orchestra leader" in the specialties.
- Occurrence of rPSC [recurrent PSC] post-transplant.
- Uncertainty and what it means for my children.
- Reoccurrence, needing a second transplant.
- Feeling like a doctor treats you more like a guinea pig than a patient.
- Recurring PSC.
- I have had my liver transplant 6 months ago, so I do [not] know what to answer in the questions so far.
- Having children, being healthy enough to have a family.
- I could check them all.
- How to manage care for elderly parents, impact on my caregiver.
- Having children.
- Guilt of wanting relationships, and children knowing I may or may not get to see them grow, and leaving my partner to do it alone.
- Worried about possibility of needing a second liver transplant.
- My brother who was otherwise healthy died because he only obtained a transplant AFTER bile duct cancer occurred. Earlier intervention could have saved his life (i.e., preventative transplant).
- Traveling, taking care of children.
- My fear is that once I go off my parent's insurance plan my vancomycin will no longer be covered. I also worry that one day the Vanco will stop working.

- Work until retirement age.
- My children will inherit the disease. Also, trying to explain to my little children about my disease.
- I had liver transplant recently, so I choose answers I would choose if I did not have new liver.
- Intractable itching.
- I have enter[ed] the end-stage of PSC and am facing many end-of life-decisions. Do I want a transplant, even if we have to move to another state? Should [I] choose hospice because transplants don't always provide a good quality of life. My doctor referred me to a transplant center so I can be evaluated and get answers. This stage of PSC is very complicated and emotional.
- Randomness of symptoms and nothing other than pain killers and nausea suppressant to resolve symptoms and hope I don't get an infection requiring hospitalization and IV antibiotics. ERCP availability when needed. [I] have waited in a hospital for 5 days for an ERCP after passing a stone.
- Different treatments for different geographical areas. Availability of medication depending on country. Dying, not having a patient advocate when I am unable to speak for myself.
- Received my transplanted liver 7 years ago.
- Organs now going to Northern States from the Southern states because of a new law dated February 2020. The people in the north should become donors. I don't feel this [is] fair. A lot of people can die because of this law. If you are a donor, you should have access to an organ before those that aren't donors. People may think I am mean for that comment, but I have been a donor since I started driving 43 years ago.
- Being unsure if emotional and physiological symptoms are caused by PSC or a product of the mind always on alert regarding PSC.
- Concerns that I will not be able to get a transplant because of severe chemical sensitivity. Concerns that I could not maintain immunosuppressants to keep from rejecting liver.
- Post transplant, no PSC symptoms.
- I have no concerns at this time. My PSC was cured by my transplant 22 years ago.
- Living alone with the disease and living in a state that would not let me choose to end my life if I got terminally ill.
- The fact that it might affect my kids. My two oldest boys are now about the age at which I was diagnosed.
- Not addressed in this survey so far, are the difficulties and additional concerns that come with post-transplant care (i.e., finding transplant centers that understand PSC and recurrent PSC; finding an appropriate amount of immunosuppression that balances you between rejection and cholangitis infections).
- Not knowing what the best strategy is for me (e.g., is it possible diet may affect disease progression, even though my doctor doesn't think so and there haven't been any scientific studies yet).
- Affordability of medications before and particularly after transplant. Receiving a transplant may be only available if I have the money to pay for the pharmaceuticals. [Thus], having access to a lot of money is a life or death issue.
- Negligent medical care.
- Finding a hepatologist that I can trust and who will agree to work with me as a patient on Vancomycin.
- I worry most about my parents and how they will cope when my health gets worse. They already are so worried, when I have a symptomatic period - I don't know how they will handle the time before a

transplant, when my health will be at its worst. Additionally, I worry about my ability to finish my academic studies. Third, I worry about a decreased mental ability due to hepatic encephalitis [encephalopathy] or after having a transplant. I wouldn't be able to work in my future job or the way I want to.

- 2010 liver transplant ended my ride with PSC. No recurrence of PSC [or] of HCC because of transplant.
- Concerned that there is no definitive knowledge about the CAUSE of PSC.
- Accessing comprehensive healthcare.
- Being diagnosed with cancer.
- I am afraid of getting recurrent PSC and of symptoms of the medication, such as osteoporosis and skin cancer. Also, afraid of bowel cancer due to Crohn's disease.
- No medication/drug to lessen or cure besides transplant. Stress - both physical and mental of the constant medical tests.
- I have no concerns.
- Fear of developing a relationship with a significant other [with] such a debilitating chronic disease. Prior to transplant I worried my husband would leave, just not be able to handle it all. Lack of quality of life.
- Likelihood of child developing PSC.
- How it affects having a family. Limits on having children and caring for the one I do have.
- I have had a live transplant from my son and now I have rPSC so I am [concerned] about the progression of the disease this time round.
- I'm concerned particularly about COVID-19 and my PSC. I have a severely low immune system from my PSC, and I was studying to be a teacher. Now I don't know what I'm going to study and what I'm going to become and do for my career now. I have to completely change my life plan because of it and on top of that I'm terrified I'm going to get deathly sick with COVID because other people don't feel it's necessary to wear a mask. I can't leave my house because of it.
- The impact on my family.
- Ability to have and raise children; ethics of having children; ability to have a fulfilling career.
- All the rest of the concerns... 3 was not enough.
- Impact on my relationships. Worried my boyfriend will leave me.
- I am frightened that I will die and not be able to care for my son.
- Too sick to work and yet too healthy to rely on disability, and disability doesn't pay enough to support my family, so it's literally damned if I do and damned if I don't work situation... if I work I have ridiculous high insurance and can't afford for the whole family and lose Medicaid... if I don't work I get Medicaid but disability takes forever to kick in and isn't enough to support the family and if wife works it takes away from that and Medicaid loss... you literally can't win or get ahead and forget about buying a house or keeping a good job because of [the] amount of sick mornings and bad days, hospital appointments and procedures. Literally can't get ahead or have a life worth a sh__.
- Concern over ability to care for my children or placing a burden on them of dealing with health concerns of their parent.
- Social Security Disability Insurance (which I secured on my first application 11 years after my PSC diagnosis, when fatigue had intensified), along with most social welfare programs (e.g., SNAP,

without which I could not make ends meet) seems overweighted against applicant fraud, and less of a help to people like me who would PREFER TO WORK, but are unable to obtain/hold conventional employment. I believe there are many less physical jobs that I could still do well, but what employer would be willing to hire someone in their late 50s (as when I applied for SSDI, having resisted for several years, and then only on the strong advice of my therapist), who now and then would need to lie down for 30 minutes? This leaves self-employment as the only option... but with the current system, who would dare start down that road (needing to report 40 hrs. of work per month whether or not any income was generated), and risk losing their benefits? (I was once unjustly dropped from SNAP years ago, and know how it can take months to reinstate benefits... there were also other "close calls" due to clerical ineptitude at the DTA). The whole system is counterproductive, rewarding passivity and penalizing initiative. It feels like a part time job just maintaining documentation and reporting current with SSDI, SNAP, Medicare/Medicaid, and Lifeline (Safelink) telephone. I wish the time and energy (and worry/stress) I spend on these activities could instead be channeled to earning my own living, and relieving taxpayers of the burden... as long as I am healthy enough to do so.

- Not being able to make decisions for myself, not getting the care I need.
- Please note that I have already had a liver transplant. I am aware that PSC can reoccur.
- Concerned about being too old for a transplant (76) and the prospect of the horrible death caused by liver failure.
- I am post transplant. I worry that should the PSC destroy my new liver, I may be too old to receive a new one. I have worked hard to be healthy again.
- Concern about having cancer and she had cancer after 2 years of PSC.
- I believe all of the concerns listed in question 24 are applicable to my situation however I only selected the top three as instructed.
- Not getting transplanted soon enough and then getting sicker with issues like varices, ascites, or HE.
- Guilt and anxiety surrounding the certain need for a living donor.
- Loss of work or ability to continue current work.
- Earning enough money to pay for medications and hospital care. Worry about death.
- I'm terrified of dying young and leaving my son behind.
- My grandmother has PBC. I have PSC. What chance does my son have of getting PSC?
- My current doctor isn't doing everything he should be doing for me. Not running the right tests, not explaining the disease and how a lot of my problems seem to be associated with PSC. How there are chances of me getting cancer. Not doing anything for treatment. How can I find a better doctor with the proper training?
- Worry local doctors won't take me seriously as my hepatologist is out of state if I have health issues.
- Trapped in a low MELD score unable to get a transplant before getting deathly ill!
- Cost of medications as I am retired.
- Speed of progression of PSC.
- Concerns of not being able to live the life I wanted too, or shorter life expectancy.
- I had a transplant recently and am optimistic now.
- Have had a transplant without recurrent PSC so no concerns with that now.
- Genetic components of PSC and my children's health.

- Identifying treatments, studies, and funding, are not taken seriously because the disease is not very common.
- I'm also concerned about my work, I need to work 100% and I don't know if I will be able to in the future. Another concern is about my little children. It is not fair to have a sick mother who works the whole day and, once at home, she is too tired to do any other activity related to them.
- I had a liver transplant. I think most of the fatigue I experience now is because of my medication regime.
- Fear of early death. Actually, I feel well, symptoms (mostly severe fatigue) may be more related to terrible sleep habits rather than PSC.
- A bit confused by the wording of some of the questions since I've had PSC twice and had two liver transplants, but have been disease-free for 11 years. Should I be taking this survey at all?
- Really no current concerns, only about the possibility of a return of the PSC following my transplant.
- Really no concerns after years post-transplant. In 70s now if liver failed may exclude me from transplant. No worries or concerns. Just checked 3 because you asked.
- Death or being too sick to get a transplant even if on transplant list.
- Overwhelming uncertainty on disease progression and lack of professional knowledge in region I reside.
- My husband and I had started to discuss having a baby right around the time of diagnosis. I am very concerned about being able to have a successful pregnancy, but also feel that I do not have the time to wait until my condition worsens enough to need a transplant. On top of that, doctors have been giving me conflicting information.
- Cholangiocarcinoma IF and when it happens it Will be too late. AND the need to have contact with hospital etc = that my child will see herself as a sick person and therefore limited her own life.
- I had PSC earlier. Then I had transplant. Again after 5 years of transplant I face PSC and UC.
- Reoccurring PSC, kidney problems due to anti-rejection medications, cancer.
- Fear that after a transplant other diseases appear like latent tumors. Fear that PSC will come back after a transplant.
- My biggest worry is if I can't get a transplant and die before my children become adults. They are so little and need a mom.
- I am a VA 100% disabled Veteran. If I find a live donor, will the VA pay for the testing and the transplant surgery for my donor? Or do I need to start saving money to pay for the donor myself? I have absolutely free health care through Veterans Affairs.
- How it will impact my family?
- Leaving my wife alone...
- How the pandemic is impacting movement on clinical trials and the possibility of a cure. Getting the support I need while there is so much focus on Covid. Sharing news with other peers and their response. I don't want people to think of me as different or weak.
- Unsure of progression of disease. Unsure if disease is being managed proactive.
- The uncertainty surrounding the ability to get a liver transplant when needed.
- No knowledge of PSC in my country.
- I have no definitive answer on my daughter's health and life expectancy as I'm told it's not common in children.

APPENDIX 7: OUR VOICES SURVEY - MOTIVATION FOR CLINICAL TRIAL PARTICIPATION

Survey respondents were asked what would motivate them to participate in a clinical trial.²¹

- Not sure.
- A very high potential rx [treatment]/intervention.
- If I had no other options for my condition.
- Really not sure. Would need more info.
- If the drug being studied was promising for slowing down PSC progression and wouldn't worsen my current condition.
- Possibility of longer survival as I have been on transplant list for 2 years and MELD score is in the way of transplant. Very sick but not reflecting in MELD.
- Nothing.
- Better understanding of the risks involved.
- Positive results from early trials to show PSC is controlled or slowed.
- Cure.
- No new medications.
- Possibility of helping others.
- Avoid transplant.
- Nothing at this time - my young family is my priority.
- A complete explanation of the goals being sought regarding the trial.
- Depends on the trial.
- Chance of helping find a treatment/cure.
- Helping to find a cure.
- Improvement of health and less symptoms.
- To help find a cure.
- Good research team, useful purpose of the research with good odds.
- At this point I don't know.
- To find the drug to slow the progression of PSC.
- If it would have a chance of improving current symptoms; if it was non-invasive.
- I don't want to take any added risks by participating in a clinical trial.
- To discover Cure for PSC.
- Search for a true treatment and/or cure.
- Slow progression before my liver is too damaged.
- Easier access to stud[y] location.
- I am very interested in participating.
- Not sure. I've never been in one.
- Phase 3 clinical trial.
- Not sure at this point.
- If the trial looked very promising and would not compromise my health further.

²¹ All comments were submitted by individuals. Comments do not necessarily represent the opinions of other commenters, meeting participants, or PSC Partners. Comments presented have been subject to light copyediting as needed for clarity (e.g., spelling, punctuation) or privacy (e.g., names of patients or health care providers mentioned might have been removed).

- If I am a good candidate for a trial, and it's strongly based in science, I'm doing it.
- I am open to participating in clinical trials.
- A true promising drug.
- Lower risk (at least phase 3) chance at slowing or stopping progression.
- Help myself and others.
- Location and time.
- To help the future of PSC patients.
- Help my small group of fellow PSCers and potential future PSCers.
- Not much. Already had a liver transplant 30 years ago.
- Expenses paid, additional rewards for participating.
- If I was near death with no other option.
- If no side effects.
- A cure.
- A stipend.
- To find a cure.
- Support from my Hep [hepatologist].
- Knowing it helps get closer to a cure.
- Time to research more. Right now UC, anxiety and depression are [my] focus.
- Doctor recommendation.
- Helping to be part of the cause to find a cure!
- If I could be assured it would not affect the other diseases or medication I take.
- Convenience.
- To assist in finding a cure.
- More understanding of the disease, hope for the future.
- If it fit into my schedule easily.
- Relief.
- Safety and better health.
- Promising research.
- It depends. Either desperation or truly wanting to help others both come to mind. I participated in a trial studying pancreatitis and ERCP procedures. It was very easy and there was no risk.
- If I have this disease, I might as well make the best use of it.
- Contributing to finding a cure.
- Later stages of a trial.
- Nothing. I don't want to be a guinea pig, not trusting staff & medicine.
- Lessening medications, reduce risk of rPSC [recurrent PSC] for everyone.
- A guarantee it wouldn't affect my symptoms, progression of the disease or quality of life negatively. The amount of time I would need to attend appointments would be minimal.
- Improving quality of life for future patients.
- My symptoms.
- The successes of the people doing the study.
- Approval of my doctors.
- To help find a cure.
- A cure for my cirrhosis.

- There are people in worse condition than I am and a cure/treatment needs to be found.
- Positive facts quickly and a personal, professional doctor, willing to study the benefit, if any, to someone my age.
- In Dutch!
- If I ran out of options in my treatment.
- Safety and payment.
- Possibility of finding a cure.
- Very promising, or fits easily in with my life.
- Access to liver specialist and frequent testing.
- If I was more sick. If I need a transplant. If I had cancer.
- Feeling that I was making a contribution to the fight against PSC.
- If I thought it will not impact my health or ability to work.
- Only if it is a possible cure.
- Does not damage liver further.
- Knowing it is for a cure versus a treatment.
- Hope for a cure.
- Knowing I would actually be taking a drug not placebo.
- Want to participate but have not qualified for 2 trials.
- My doctors.
- Recurring PSC.
- I'm already motivated to participate.
- I can't participate in trials [which are] medicine-based, because [of] my allergies to medicine.
- I don't want others to suffer like I have.
- To help find a cure!
- Compensation.
- If it was paid participation, like compensation for putting what health I do have on the line for those coming behind me.
- Helping people in the future.
- New drug developments to curb symptoms or cure the disease.
- Want to help people.
- Suggestion by my Transplant Surgeon.
- Helping others in the future.
- The ability to be a part of finding a cure.
- Helping to find a cure.
- Advanced treatment/possible cure for PSC.
- Hope for a cure.
- Finding a cure or stop the progression of PSC.
- Knowing my risk would be very low... and money.
- A cure.
- If there have been tests on animals that show positive results and proven safe on humans.
- If symptoms were unbearable or [the] outcome started to change, I would accept the risk of a trial.
- Chance of positive outcome.
- The idea of being closer to a cure!

- What motivates me is to know that I might be helping to find a possible cure, or a way to reduce the symptoms.
- Helping to find a cure.
- If it was something that couldn't possibly have direct effects on my health (blood draw, saliva, biopsy, etc., but not a medication).
- Interest in a cure!
- Understanding PSC better.
- Cure!!!
- That it was being done by a well-prepared and well-known researcher.
- A chance for a cure.
- My greatest fear is that one of my children or grandchildren will develop PSC, so if I can somehow prevent that by participating in a trial(s), I certainly will.
- Finding a cure.
- A cure.
- Hope to find a cure.
- Results.
- Potential for cure.
- A convenient location.
- Unsure.
- Knowing whether or not I receive a placebo.
- Local labs, virtual visits, making it easy for the patient with fewer disruptions to life and schedule.
- Currently nothing.
- To help others.
- Find a cure.
- I am very cautious with trials, as I don't want to jeopardize my current, so far, uncomplicated, health.
- Because I have such a rare case, I would be interested if it were the right trial.
- Possible access to treatment, and contribute to the PSC community.
- Must believe in the study. I'm taking a risk to help others.
- Confidence in the trial team and support from physicians.
- No possibility of placebo.
- Chances to help the next generation.
- Money.
- Helping others.
- Helping find a cure or treatment.
- A promising treatment, better understanding of PSC.
- For the good of myself and others with PSC.
- A cure.
- To help find treatments!
- More access to understanding what trials exist.
- Positive outcome and financial stability so it won't hurt us financially.
- Trial for medication that would help my type of symptoms, or for a drug that is considered a potential game-changer.

- If it would improve my quality of life.
- If it was in my city and safe.
- I'm not sure.
- Chance of decreased PSC symptoms.
- Not sure currently other than hope for a PSC cure.
- Finding answers for myself, but also lots of other people.
- If my hepatologist recommended it.
- I am motivated and asked if I could, but [was] told no due to kidney function level.
- Positive long-term results.
- Certainty of no risk.
- A cure.
- Cure for the disease.
- Advancement of the PSC disease and really sick with no other options.
- If I knew it was safe.
- Optimistic outlook.
- A treatment with a very hopeful effect.
- Being able to have all care locally.
- Hope.
- For the greater good of helping myself and other patients.
- Not sure.
- The ability to advance science for the greater good.
- To help in finding new or investigational medications focused on slowing progression or curing PSC.
- Would be happy to do it for others.
- Having evaluations that were non-invasive other than blood work and knowing the drug was safe long-term.
- Being part of the process to eventually having a cure or a treatment.
- Low risk.
- Hope for a cure.
- Would love to participate.
- If my transplant team recommends it.
- Promising phase 1 or phase 2 results.
- Help find effective treatment.
- Promising preliminary results.
- Promising meds [medications].
- Money, or access to PSC liver support for young adults.
- If I didn't once have CCA [cholangiocarcinoma], I would do it.
- A promising intervention!
- Ease of participation.
- If a study was very promising on reducing symptoms, especially itching.
- Finances.
- Access.
- Ability to continue after trial.
- To help future patients.

- Improvement of symptoms, slowing progression.
- Disease progression.
- Availability.
- The chance to help other people with this disease.
- Chance/hope for improvement for me and for others.
- Not having to go off vancomycin. My symptoms would return almost immediately.
- Chance to help develop treatments for PSC.
- Possible improvement for my health and helping move PSC research forward.
- I understand that PSC require[s] long-term study/trials, it's still quite rare illness, so it's not easy to get a proper group to validate results of trials.
- Help find a cure.
- Being able to help find a cure for PSC.
- Knowing I could be helping research for a cure move forward.
- Cure, reversal of disease.
- Finding a cure for PSC.
- The possibility of a cure.
- No side effects and something that has shown very good results so far.
- The drug had already gone through safety trial.
- Helping myself and others.
- Hope for some progress.
- A hope that there will be a cure/better ways to manage to symptoms. Not just for myself but for other patients.
- Potential PSC treatment.
- Aid in finding a cure for PSC.
- Compensation for time.
- Having access to background information and being able to speak with study collaborators regarding concerns.
- Move the field forward and improve quality of life for people. Hope for a cure or good treatment.
- Help myself and others.
- Don't require motivation, keen to help.
- Knowing that others could benefit from the research.
- The opportunity to help find a cure for a PSC.
- Hope.
- I'm up for any trial. I want to find a cure more than anything else in this life.
- I am willing to participate!
- Finding a cure to slow progression to stay asymptomatic.
- Hope for a working medication or better understanding of the disease.
- Improve my current situation.
- My health and desire to have a good long life with my husband and kids.
- If my GI/hepatologist would suggest it.
- See progress on PSC front.
- Feasibility; clinical potential; science.
- Desire to help others.

- To help myself and others.
- The potential to help find a cure for others, including my niece.
- Give something to community, help to find the cure.
- Access to transportation.
- I am very motivated to join a clinical trial but cannot at the moment due to trying to start a family.
- A drug with a known safety profile. Having faith in the pharma that is running the trial.
- A chance to change my health for the better, I have been in a trial for UC... I am usually up for an opportunity.
- If my transplant team thinks it's a good idea that I participate.
- Contribute to advancing knowledge about PSC.
- A real chance to help advance treatment options for PSC.
- Improved quality of life.
- Search for a cure.
- If I develop symptoms.
- A chance to help PSC researchers and be a viable candidate for the study.
- I could manage the expectations within my daily routine and it wouldn't appear to affect my current level of disease stability.
- Maybe helping to find a cure.
- That it would be safe and beneficial.
- High impact potential of the trial medication.
- If traveling a long distance, help with lodging or transportation if needed.
- Helping others.
- If I was in an emergency situation where participating in a trial could provide access to treatment that could help my prognosis.
- To help find a cure.
- If it has good prospects as a cure or improvement of the disease vs "a shot in the dark".
- Knowing that the benefits outweigh the risks. Having my local hepatologist and transplant coordinator consent to me being in a clinical trial.
- If I got recurrent PSC, I would participate in a trial with the hopes of helping the clinical trial team have a big enough sample size to make their research reliable, especially if there were high hopes for finding a treatment.
- Providing more data for researchers as this is such a rare disease.
- If I believed the treatment had a good chance of having a positive effect on my long term health, and low risk.
- The expected reward needs to outweigh the expected risk.
- Already motivated.
- I would consider joining a clinical trial that only involved taking the brand of the current PSC medication I'm on (Vancomycin). For example, a clinical trial testing various doses and/or length of time taking Vancomycin. The reason I'd consider this is because I wouldn't have to stop taking Vancomycin because it's provided me incredible results thus far.
- Better treatment options for future and current PSC patients, myself included. Better understanding of the disease: how it comes to be and its mechanisms. Earlier detection of PSC patients.
- Being involved as active participant in moving research forward.

- Money to cover costs of time / transport.
- Knowing what I was letting myself into.
- Monetary incentive. Access to a promising drug. Access to a promising drug that could help with both PSC and Crohn's.
- If a study showed promise in treating symptoms or curing PSC.
- If it was nearby and didn't interfere with my work schedule.
- The hope of finding a cure.
- It would depend on the developing of symptoms and also on the potential toxicity of the medication being tested.
- To potentially improve understanding of the illness to help others in the future.
- To be able to extend the life of my liver.
- A high expectation of a positive result.
- To find a cure.
- Compensation for additional trips to site. Only a few trips a year.
- Hope for cure.
- Not too invasive and shows benefits.
- I don't have any PSC symptoms since my transplant. Don't know the value.
- To find new ways to control the advancement of PSC.
- My doctor getting my study results/ records/ results of testing. Receiving generalized study results. Paid travel, meals, etc.
- Good rapport with the clinical trial team - information and communication.
- Finding a cure.
- Patient-led information. My hospital/consultant taking lead in trial.
- If I knew it wasn't going to affect my current and future ability to parent my child.
- Finding a cure for myself and helping others.
- To help people with disease.
- Known side effects.
- Finding a cure, so people do not have to live with PSC as I have for many years.
- The drug shows promising results in early phase of the clinical trial.
- Appropriate fit for me into a diagnostic category.
- Hope for myself and others.
- I don't have really any symptoms, but have only been diagnosed for less than a year and I want to help find a cure.
- If my quality of life deteriorated. Right now my PSC is pretty manageable.
- I am waiting to retire soon to participate in the Vanco trial.
- If I had rPSC [recurrent PSC] and there was a drug being tested for its ability to slow or stop progression.
- If it was easy for me to participate and I understood the type of medication I was given.
- The knowledge that it may help myself and others.
- Phase 3 study that seems promising; minimal side effects or disruption to IBD treatment; payment for my time.
- If current treatment stopped working.
- Keeping on site visits fewer. Being able to do testing, blood draws, etc., more local.

- Research to show that clinical trial might be a potential cure.
- Financial stipend.
- Finding a cure.
- If the drug would STOP THE ITCHING!!!!
- The concept that my participation can [possibly] help so many other people living with PSC.
- Potential to find a new treatment for PSC that could improve mine and others conditions.
- Finding a cure.
- A cure.
- I would love to participate in any trial, particularly one where I receive medication to prolong my life. I think is so unfair and selfish that I have never had an episode where I had esophageal varices other than my initial first and only occurrence in ----. Some of us have a very good reason to live!
- Wanting to help find treatments and/or a cure.
- Compensation.
- Explaining the study well... especially for transplant patients like me.
- Understanding goal of trial, mechanisms of action, side effects.
- If it involves a cure for PSC.
- Improvement of condition.
- Chance of getting an effective treatment.
- To cure PSC.
- If my doctors encouraged me and felt it would not in any way be detrimental to my health.
- Easy (close and not time consuming).
- If it already showed positive results.
- I really don't know. I would have to take it on a case by case basis.
- Death.
- One to relieve fatigue.
- Improvement of fatigue/stamina and/or eliminating susceptibility of cholangitis attacks.
- Minimally invasive and time consuming, gift for participating at the end of throughout each check point, doing the surveys from home on my phone in bed, minimal drug side effects, promise to reduce symptoms.
- A phase three trial with positive results. Since I do not currently experience any symptoms, I would be looking for a solution that was nearing completion.
- If PSC recurs.
- Help to find a treatment or cure for the disease.
- The possibility of slowing or stopping disease progression, helping to identify treatments that would help others.
- The knowledge that it could bring new meds.
- Previous trial experience.
- Knowing that the study is being conducted by a trusted medical center and backed by sound research.
- Finding a cure.
- I am pretty interested in participating now.
- Not sure.
- Having the study results sent to me unprompted.

- Options running out. Helping others in the future.
- Possibility of a cure.
- Better quality of life.
- Promise of longer life.
- Trusting the trial team and understanding the potential beneficial outcomes of the study.
- Being directly asked - like this survey.
- The drug is known to be safe and effective and has proven to improve other conditions. I would be more likely to participate if I knew that I could continue taking the drug if it improved my PSC.
- Right now, I rule myself out due to transplant evaluation and hopeful listing.
- To help future PSC patients.
- A high chance of favorable outcome and an improved quality of life.
- Being informed of clinical trial results at the end of the study. Access to more information about where to find clinical trials.
- Helping to find a cure.
- Possible PSC treatment or cure.
- I'll do it.
- Helping others who maybe have a chance to cure the disease.
- A guarantee that it won't make my condition worse.
- An optimistic trial.
- Benefits of outcome from participating.
- To find out what the cause of PSC is.
- I had a transplant and rPSC. Usually not a candidate.
- Reimbursement of fuel costs to travel and hotels if required. Also for procedures to be paid for.
- Getting a transplant sooner!
- To help everyone with PSC.
- If I get told that it would be a high chance of curing PSC or making my symptoms go away.
- The possibility of increasing knowledge about PSC.
- Wanting to help find a cure for PSC, alleviation for symptoms, or reduced risk of worse complications like cholangiocarcinoma.
- The possibility of finding a cure for PSC.
- The chance to help docs learn more about the disease.
- Helping to find cure/treatment/answers for myself and for relatives and anyone else with PSC.
- That I would be informed of everything ... including all the risks and that if complications arose, I would receive immediate interventions and follow up care.
- Helping work towards a cure.
- A hopeful treatment. Preferably non-invasive but not a deal breaker.
- Reduce my current pains and to improve long term liver status.
- To find a cure!!!
- Knowing it'll help other patients in the future.
- Not much now.
- If my condition became less stable, I would be more motivated to participate.
- Finding a cure.
- Money.

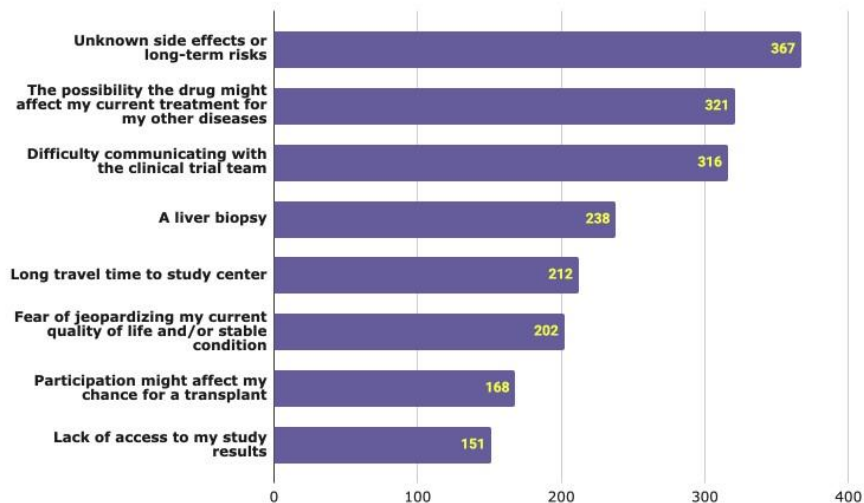
- Guarantees of some kind.
- Slow or cure PSC.
- Already asked but told no.
- Finding a cure.
- Helping others who may have the disease.
- A cure for PSC.
- Unsure.
- The fact that it may help find a cure for PSC.
- No risk to me and help to others in the future.
- Beneficial to myself and others.
- Knowing that I would be getting the trial drug.
- Since I have only recently been diagnosed, being fully educated is key. Knowing what the doctor thinks about it and how my family feels. Maybe one day for now I'm learning all I can about what I have.
- If I knew it might improve my health/life or the lives of others with these diseases, if I were compensated for my time (away from earning a living, or with family, etc.)
- Finding a cure for the PSC.
- To help me control or stop PSC.
- Already in a study.
- Willing to consider any trial which has a better or comparable risk-benefit profile to my current successes with vancomycin.
- Being able to participate from my home - no travel to clinics out of my state.
- Knowing very specifically the goals of the trial, AND knowing whether I was receiving the trial med or a placebo.
- If I could ensure that PSC would never return now that I have had a transplant.
- Helping the researchers to find a cure for this disease.
- Best case scenario: open label, slow progression of PSC and liver fibrosis.
- Help others.
- Close proximity to where I live. Short drive time and testing time.
- Feeling desperate, which is not something I feel right now.
- All questions asked and answered.
- The hope of a cure to prevent PSC developing in others.
- Knowledge of how being healthy and Crohn's under control and having a transplant that is doing excellent can help.
- Knowing that I am contributing to progress towards making life easier for PSCers.
- Improved quality of life; wanting to help others; fear of rPSC.
- Novel mechanism of action.
- The possibility of finding a cure or a medication helpful for myself and others.
- Finding a better solution for the management of PSC.
- Progression management.
- Better quality of life.
- Possibly being a part of something that could help ALL PSC patients. My own health.
- Compensation.

- If a long-term, far-reaching study was conducted focused on new medicines or clinical treatments to alleviate PSC symptoms or slow disease progression, I would be highly motivated to participate.
- Lower risk with trial drug; low risk my PSC would advance; prolong liver functionality.
- Great potential for success in study.
- Chance to cure PSC. Financial incentive.
- Hope of a cure or effective treatment.
- Finding a cure and helping others.
- See hope again.
- Help to discover a cure or stabilizing treatments.
- Hope to live a long, good and health.
- Travel pay if travel and time off work is required.
- A more human touch (a video, a webinar, a conference vs a web page or a printout) explanation from the research team about why they need participants. It's hard to gauge whether this is just a nice to have or a critical thing. Also, when a human being talks to you about what the positive outcome might be, I would be much more likely to participate.
- I would participate in a clinical trial if there was a high chance of benefits for myself and others and a relatively small chance of serious side effects.
- A real chance at being able to participate and raise my child into adulthood.
- If it helps find a cure or treatment.
- Hope.
- Anything to help people feel better.
- Making it as easy as possible to participate in.
- If nothing else worked for me.
- Help finding new treatments/cure.
- Hope.
- To improve the quality of life for me and for others.
- Clear communication of goals and purpose with experts in the field and supported by a reputable organization that is focused on a cure.
- Access to promising therapy.
- That I could learn things during the process. That I would know that I was helping myself and others. That I was treated very well and welcomed into the process like a partner.
- Information. If my disease showed obvious progression (stable atm [at the moment]).
- Certainty knowing it would not detrimentally hurt my current remission.
- To help find out "why" or cause of this disease.

APPENDIX 8: OUR VOICES SURVEY - KEY CONCERNS THAT PREVENT PATIENT PARTICIPATION IN CLINICAL TRIALS

Ranked Patient-Reported Concerns

Which patient-reported concerns might prevent you from joining a clinical trial? Select your TOP FIVE (out of 19 options)



Source: OurVoices Survey 2020. n = 819

APPENDIX 9: OUR VOICES SURVEY - ADDITIONAL THOUGHTS/CONCERNS ABOUT CLINICAL TRIAL PARTICIPATION

Survey respondents were asked to share any additional thoughts or concerns they have about participating in clinical trials that were not included in the question presented in Appendix 8.²²

- Now that I have been diagnosed with cirrhosis, I don't think I qualify for them.
- We need many more!
- The unknown, worse symptoms.
- Fear of getting sicker.
- Fear of the unknown.
- With expectancy life of 3 more years, prefer to focus on known drugs to maintain reasonable life experiences.
- Totally supportive, just would like to know risks involved to minimize any exacerbated progression of PSC.
- Not available locally at my health care provider.
- Being able to do trial in my local area.
- Not being able to get pregnant.
- Experience shows that one is well looked after during drug trials.
- Wish there were clinical trials occurring in Canada.
- Reputable company.
- I'm a big fan.
- Because I don't live in a major city, I feel my chances for participating in a clinical trial are slim to none.
- I also have RA and some days pain from that.
- Jeopardizing current stable condition.
- My body is so weird reacting to medication now, it's crazy.
- Always be happy to be in the control group with the medications and vitamins I am now taking.
- With PSC being so volatile and individual, it's hard to know what may set it off. I am reluctant to participate in a trial that may aggravate my PSC.
- If I was to participate, I really have to look over the risks involved and if it would affect my current way of living.
- We live in the Philippines which is very far from the United States.
- Scared.
- Amount of travel.
- I've been told by a hepatologist that studies always exclude patients with PSC-AIH overlap, which is very frustrating.
- Probably would not be eligible due to other comorbidities, and age.
- I would like to see more clinical trials being conducted from a well known (recognized) University.
- I think they are a way to help the medical profession and others with this disease.

²² All comments were submitted by individuals. Comments do not necessarily represent the opinions of other commenters, meeting participants, or PSC Partners. Comments presented have been subject to light copyediting as needed for clarity (e.g., spelling, punctuation) or privacy (e.g., names of patients or health care providers mentioned might have been removed).

- My first liver biopsy, done years ago, was a very painful experience. A more recent biopsy was much less painful. But it was not successful in collecting a sample. I even participated in a liver biopsy sample taking trial without success (my cirrhotic liver seems hard to sample). I have (should say "we" as all decisions are made equally with my wife) declined to participate in one trial because it involved 3 (or perhaps more?) biopsies.
- Side effects.
- Having to disrupt my education and long term professional goals.
- I would be very excited to be included in a clinical trial.
- Sometimes the eligibility criteria can be too narrow. For example, I am concerned when I get cirrhosis I will not be eligible.
- Last resort only approach.
- If they made the patient stop current therapy (i.e. oral vancomycin).
- I feel like being early decompensated is not worth messing around with clinical trials because of procedures and even a slim chance it might negatively affect my current quality of life.
- I'm in the UK. USA is leading in research and trials. I feel the support isn't as great compared to the USA.
- I don't do well with strangers or the unknown.
- Domicile - I'm in Canada vs US, etc. So regional or geographic constraints.
- Safety.
- I am supposed to be involved in a clinical trial but COVID-19 may be hampering the study.
- Need to work to support my family. Cannot participate in any trial that may impact my ability to work or reduce my overall health.
- Worry it might affect my transplant.
- I currently take vanco and live my life normally. I would be scared to go off of it and then have it not work upon going on it again.
- Effect of drugs on other current physical conditions.
- I hope more clinical trials become available to help treat/cure this disease.
- Post-transplant so may not qualify for many trials.
- I live in Australia. No clinical trials here yet. One was supposed to start last November, but I don't think it has begun.
- Not sure if I would do a trial study.
- My age (78) excludes me from most studies.
- All the ones listed above are concerns (I could only select 5).
- My husband died 11 months ago. Got pancreaticobiliary cancer.
- I have been deemed ineligible due to my other health issues.
- Would gladly participate if asked.
- I would really like for someone to study the effect of vancomycin on the gut microbiome and correlate with response. We need to understand why certain patients respond and others do not.
- They should make them as easy as possible on the patient. Give feedback on the study results to participants.
- I have never been asked to participate in a clinical trial. Side effects of medications is of concern to me.

- I had great results in a small clinical study that had no placebos. My liver function bloods went down by half. My fatigue improved and no cholangitis for 5 years. But the study was small and the drug maker didn't want to spend more money on PSC. The results remain confidential so I only know that it helped me for five years. I'm glad PSC Partners is working on research funding for orphan diseases.
- I took part in a clinical trial and have not been able to get ANY information about the trial.
- Chances of it being back fired and getting worse.
- Ability to participate from Canada.
- When a treatment is deemed potentially helpful, and is shown to have positive effect during the trial, patients within the trial should be offered the choice to continue on the treatment. This disease is progressive, so any treatment with positive effect should be continued!
- Feel inaccessible.
- Test results not shared with me.
- If you're as transparent as possible then it's all I ask.
- I also live with hypertension, fibromyalgia, and joint pain.
- Being on the placebo and worsening my disease.
- I work alongside my MDs who follow me for my UC/PSC post-surgery. I trust them at all times and would need their consent to agree to join a trial that involves medications/procedures.
- My experience is that one is very well taken care of whilst on clinical trials.
- As an educator I believe in research and the scientific method!
- Since diagnosed in 2012 I've been nearly 100% asymptomatic. My test results have been very stable, and no changes are evident. I'm not sure my current condition would be beneficial in a study or trial.
- The experience has been very good.
- Biggest worry I would have is it affecting my current health baseline (currently PSC is under control after second liver transplant).
- Though I have some arteriosclerosis (up to 50%), I'm otherwise healthy and active. Had a heart attack while on a clinical trial. Told that the trial showed no cardio ill effects, but my cardiologist does not otherwise have a clear cause for heart problem. Not sure if trial contributed or not.
- Getting more participants.
- Mostly I am afraid of long term side effects and destabilizing my current condition, where my PSC symptoms are under control.
- I live in Canada. Most of these studies would be in the USA or possibly Europe. How would the logistics work to submit samples and be tested via MRI, CT, etc., and do the follow-up (by Zoom?)
- I think clinical trials are important for getting new medications on the market. I know there are many concerns that would hold my peers back from participating (invasive procedures, time off of work, travel).
- In general, I'd be happy to be participating in more.
- I would like to see researchers partner with patients in co-designed clinical trials.
- Getting more information from my specialist.
- I would feel good about possibly helping find a cure for future generations.
- I may consider participating in a larger trial once a smaller trial with same drug proves successful.
- I've had a transplant so I don't know which trials would be suitable. Need more information.
- For people that access healthcare regularly and rely heavily on medical professionals, added engagement in those environments can be draining.

- At an advanced age, there would not be time to evaluate the results before transplant.
- Was considering one but they wanted me to come there a lot of times and I have a job.
- I would like to see if the anti-rejection good be designed so that there are not as many side effects that make so that other drugs would not be needed. Thank You.
- Making myself sicker.
- Disruptions to work and life, unknowns, the risk that it makes me worse or creates new problems, prefer not to be on any medication.
- Whether they are focused on post-transplant patients, and the exclusion of this group may affect how results can help those with rPSC.
- If it lessens my quality of life.
- I have comorbid diagnoses which require a variety of treatment methods - I have a Kock Pouch after my J Pouch failed (created during a total colectomy). I have pouchitis, Hashimoto thyroid, I had a full hysterectomy with bilateral salpingo-oophorectomy at 31 because of polycystic ovarian syndrome/ endometriosis/ thickening uterine lining. I have lung damage from prolonged exposure to formalin/formaldehyde. I have psoriasis. All these autoimmune issues could alter my efficacy as an appropriate trial candidate. My PSC progressed rapidly, from diagnosis at 30 to transplant listed at 37. Understanding the reason/ contributing factors to my progression is something I'd love to see studied and understand.
- I want to do it, but I have two small children. Do I take a risk with my life when they depend upon me? I just don't know.
- Too often the study centers are far away from my home. I cannot afford to travel frequently to the center.
- My principal concern is cholangiocarcinoma. I'm not interested in studies aimed at intermediate markers. UDCA for example is aimed at an intermediate marker (reduces ALT/AST), but does NOT reduce or delay risk of cholangiocarcinoma or all-cause mortality. So I don't take UDCA. Most trials won't accept me because I have had colon cancer and total colectomy, recurrent pouchitis and also kidney disease, arthritis leading to joint replacement, recurrent blood clots (I'm on an anticoagulant medication apixaban) and I'm sometimes on an antidepressant (Wellbutrin) when things are bad.
- I'm interested in lifestyle choices that help improve overall health and help manage symptoms and progression.
- I would love to participate in any trial, particularly one where I receive medication to prolong my life. I think [it] is so unfair and selfish that I have never had an episode where I had esophageal varices other than my initial first and only occurrence in ----. Some of us have a very good reason to live!
- COVID-19.
- As a woman in her childbearing years, I would love for a trial that I wouldn't have to stop trying to get pregnant for two years to complete this.
- Not eligible for many due to normal ALP.
- I was asked to participate in a study years ago... I was happy to oblige, until the REAM of paperwork was put in my hands, asking for several signatures. I finally had to ask if I could take it home to read; they said yes (how could ANYBODY sign such a ponderous stack within 10 minutes in an examination room?). Once I read it carefully, it was clear that basically anybody the study team felt needed access to my data would be granted it... with that access then trickling down to other removed

parties, getting their access only from the previous party, not the original study team. This loss of control of my medical data was the killer. How stupid.

- I cannot drive so it is hard for me to get to doctors and clinical trials.
- I have had this disease a very long time and I do not know if I have the energy or mindset to complete a clinical trial.
- Too many have too much paperwork.
- Concern that more harm than good will be done.
- I've heard I don't live close enough to any study sites.
- None, have been on 2 for IBD.
- I don't think that most doctors understand how difficult it is to live with PSC. Trials are not focused on quality of life.
- Lack of understanding of the impacts the medicine/trial could have on my quality of life. A succinct and dumbed down (for non-medically trained individuals) brochure or document that depicts the intent, potential outcomes, and potential risks of the study. Often times the study documents provided are too complex for me to bother with performing research in order to understand its contents. In large part, I am unaware of the specific expectations of participants (multiple times I have been asked to participate in the study and when signing the documentation, I have to ask the researcher if I get disqualified for having taken antibiotics recently and usually that disqualifies me and is wasteful of each party's time and energy) and the expected outcomes for studies I have participated in.
- I participated in one already. I find no objections as long as the center is close enough to home.
- I live in Canada so there haven't been any opportunities to participate. Don't seem to be any trials taking place here.
- Would need to be flexible to my family, as this disease already dictates so much.
- I think clinical trials are essential and a wonderful way to get closer to a cure or treatment.
- It does seem unfair that the participants are in the dark after the trial has ended.
- I usually can't do them because I have overlap-autoimmune hepatitis and PSC.
- I would need a good explanation as to what the anticipated outcome would be as well as the risks.
- I am on the fence and would really need to consider the opportunity if chosen. This is all still new to me and I am still coming to terms with the condition.
- Fear of being taken off my current meds. Fear of exacerbation of PSC or other irreversible organ damage or loss of physical function, i.e., neuropathy, etc.
- As I get older, I'm less likely to take this type of risk.
- I am symptom free right now so don't want to jeopardize that and also access to good medical care if something goes wrong.
- Time involved to participate in a clinical trial.
- I wouldn't know where to go looking for participation in them.
- I have worked on many projects related to finding funding for PSC trials, there are mountains of paperwork and pointless political and bureaucratic objections to overcome in getting funding, and releasing results. None of the major universities want to work on trials without millions of dollars to pay for research overhead. So despite claims to the contrary it's close to impossible to kick off a trial in the first place.
- Are there any Clinical Trials based in Canada?

- I would only participate in a phase 3 clinical trial because I think it's safer.
- Necessary in the development of new meds.
- I am on medications that are helping me now and don't want to upset that.
- Would my gastroenterologist approve?
- I feel more doctors should encourage PSC patients to seek participation in clinical trials. In my experience thus far, doctors have ZERO recommendations for symptom management.
- I'm doing well post-transplant 23 years and don't want to jeopardize my health. Would have welcomed this over 30 years ago when barely anything was known about this disease. Took 10 years for diagnosis. Keep up the great work trying to find a cure.
- I have no symptoms and actually feel great. Hoping to stay cancer free or if not that it is a CCA in a specific spot so I can get a transplant (living donor or other).
- I honestly would have no regrets doing trials.
- Taking a trial medication when condition is stable is a concern.
- I am glad that they are going on and very hopeful that there will be a cure and medications soon. I am worried that they are being stopped or slowed down by the pandemic. What can we do to keep the focus on PSC and other rare diseases?
- That they might worsen my condition. That they might result in unexpected negative consequences down the track.
- Too scared to try experimental meds after the pain and procedures at diagnosis. Now I'm in remission and scared to do anything to jeopardize it.
- Not interested in taking any medicine trials.

APPENDIX 10: OUR VOICES SURVEY - ADDITIONAL REFLECTIONS ABOUT LIVING WITH PSC

Survey respondents were asked if there was anything else they would like to share with the FDA, drug developers, or researchers.²³

- Am curious about what came first: my intestinal symptoms (1964) or PSC liver conditions (2016)? Did the 1979 ostomy delay the PSC conditions (2016)?
- Better communication.
- Considering pregnancy in younger aged women diagnosed with PSC. A lot of unknown information on pregnancy and PSC, and medications used to treat it.
- Diagnosed Diabetes Type 1 at the same time as UC and PSC.
- Don't give up!
- Exception points should be granted to those with PSC with regards to liver transplants, above those who are obtaining livers as a result of alcoholism. Non-alcoholic PSC patients have done nothing to bring this disease upon themselves.
- Find a cure. I have a terminal illness and that is always in the back of my mind no matter how well I feel.
- Fund more research for liver and bile duct diseases. We also need Vancomycin to be considered as a PSC medication. Because it is often used off-label for those with PSC and UC, it is not accepted by many health insurance agencies. It needs to be tested and approved by FDA for use by PSC patients.
- Give us a full copy of the protocol and lots of info about the rx [prescription].
- Help is needed for people with PSC, no viable treatment available now in lieu of liver transplant.
- Hepatic Encephalopathy is so scary and dangerous and not known about. It would be great if there was another medication that would help get the toxins out of the body without the severe side effects of diarrhea constantly. Also, the itching that occurs with PSC is debilitating and so severe and life altering and leaves lifelong scars and makes you feel like you're going insane. I feel that it is one of the symptoms that needs to be addressed immediately. It literally feels like you are allergic to your blood, and you have ants under your skin.
- I also have chronic kidney disease Stage 3, high blood pressure, and congenital anemia.
- I also suffer from severe migraines and take meds for them. Amovig, Naratriptan, Naproxen, Zofran.
- I also was diagnosed with Mesenteric Panniculitis - Gastroenterologist feels my Crohn's, PSC and the MP are all related to the same genetic disposition that prompts the autoimmune response likely responsible for all 3.
- I am scared. It is not a fear that goes away over time, but one that rests beneath the surface. Please keep working towards an accessible treatment.
- I know this is a rare disease that doesn't impact a large portion of the population. But for the portion it does effect, we would love to have more information on what's going on with our bodies. I have heard people compare this disease to a ticking time bomb. It's scary and anything I can do to help with testing I am all for it.
- I know we are a small subset, but please find a way to include those with overlaps or comorbidities.
- I think being close to the doctors conducting these trials would be a big thing for me.

²³ All comments were submitted by individuals. Comments do not necessarily represent the opinions of other commenters, meeting participants, or PSC Partners. Comments presented have been subject to light copyediting as needed for clarity (e.g., spelling, punctuation) or privacy (e.g., names of patients or health care providers mentioned might have been removed).

- I think losartan = heart medication that I am taking, and drinking a cup of coffee is helping me.
- I was only 21 when diagnosed with this horrible disease and have been struggling for 3 years. I'm 24 now, have a desire to marry someday, and have lots of kids. Now, I'm not sure if this will be possible. I have so many problems (jaundice, sleeping, fatigue, pruritus all over my body, low energy). It's difficult to have a social life. Now with liver cirrhosis, I'm sure I'll need a transplant in the next 10 years. Let's find a cure or better drug treatment to "clean out" these bile ducts. If there was more research and money put towards seeking a cure, I can be confident that my future children will not inherit this disease and go through similar problems. I want to be able to see my children grow up, experience my grandchildren, and live a long life! Please issue funding to support PSC and AIH. This sucks!
- I would like to make sure that Canada is included in this research?
- I would like to see a new way to receive transplants that are ruled by MELD score.
- I would love to find an easier way to be diagnosed. It takes several months or longer to determine if it is PSC.
- I would really want a cure for my son's PSC. He's only 18 years old. As a mother it breaks my heart to see him suffer from all the pain brought about by PSC. I want him to enjoy life, achieve his dreams, and fulfill his purpose.
- If not a cure, there is a need for PSC treatments.
- Interested in homeopathic remedies.
- It would be nice if medication was more affordable.
- Keep up the good fight.
- Listen to the research that is out there by the MDs. See the results. Utilize this to their benefits (drug developers), researchers.
- More attention on PSC and a cure would be amazing.
- More needs to be done regarding studying the effects of exercise in PSC.
- More studies on vancomycin.
- Need more medicine choices!
- Need more treatments. Need more interest and study on Vancomycin, and why it works. Need more research on gut biology.
- No, but maybe a clarification on the answers about the symptoms at its worst time. These were pains below the sternum lasting 1-3 hours (with raised liver blood values afterwards), so not really chronic symptoms. During those 'attacks' I could not do much else than lay curled down, so very disabling, but besides the attacks, life was mostly fine.
- NOR URSO - where are we with the trials?
- One PSC clinical trial I was to be involved in has been postponed due to COVID-19. A negative impact but understandable. I hope this pandemic will have some positive impacts on PSC research through drug trial acceleration, or international cooperation, or whatever lessons and best practices can be learned.
- Please do not back down on pursuing treatment for PSC.
- Please do what's in the best interest for the patient instead of making millions for pharmaceutical companies.
- Please help find a cure.
- Please help us.

- Please help with this horrible disease.
- Please put everything you can into research/trials into finding a cure, or slowing down the progression of the disease.
- Please run studies on essential oils. They really help!
- PSC has such a small sample size of patients overall, I wish there were more that accepted international participants. Better sharing of information across borders for our shared outcomes.
- PSC is a debilitating disease.
- Secondary symptoms of PSC like itching, fatigue, etc. are significant detriments to quality of life. Itching does not go away with topical treatment. While I hope the main focus of drug development is curing or significantly inhibiting PSC progression, it would also be nice to see an increased emphasis on management of symptoms - specific medications designed for PSC symptoms versus having to use off-label products, or products developed for similar situations, but that do not work well with PSC (i.e., many of the itching meds).
- Status of current PSC clinical trials... (particularly Nor-Urso).
- Stop overcharging for medications that other countries have cheaper access to.
- The diagnosis of PSC liver disease is devastating. It changes your life. You experience chronic fatigue, and you live in constant fear of the unknown, or that you will take a turn for the worst. The prospect of maybe needing a liver transplant is terrifying. Having no treatment for my disease is very sad and gives you little hope for the future. I have chronic anxiety worrying about my condition and whether I will be around for my family in the future.
- The importance of highlighting that the disease affects people of all genders and ages, and is not simply a "disease of older men."
- There is so little known about PSC in medical circles as well as the general public. It is a very frustrating disease because there is literally no way to predict the course of it daily, weekly, monthly, yearly. The level of uncertainty for PSC patients and caregivers is very challenging. We need as much help from the FDA, researchers, and the medical community as possible.
- There needs to be more public awareness. I had never heard of this disease until I was diagnosed. Sadly, even most of my doctors other than my gastroenterologist knows very little about this disease. It is very discouraging when we as patients are told, "we just don't know much about it." Therefore, much needs to be done in research and drug development. I support that wholeheartedly as well as public awareness.
- There should be a way to make ursodiol more cost effective for PSC patients. It has improved my symptoms but due to the fact that it's not recognized as a PSC medication it is very expensive. I pay out of pocket \$600 for a 90 day supply.
- This disease is horrific. Please spend some more time and resources to help get some type of treatment.
- This is a challenging disease and it seems to present in several different ways. Gut health is important and needs more research and investigation as to how it relates to PSC.
- This is a disease that DOES affect children and can be devastating to families as they work through diagnosis. The complications that long term inflammation can create are horrific to contemplate for anyone and particularly when looking at a young child. There is great momentum, and research has come leaps and bounds over the last decade. This is a huge gap in treatment for a wide spectrum of patients, is often an invisible disease (until end stages when it is not). Transplant is viewed as a treatment but creates a host of other problems and is an ineffective treatment for many who have

recurrent PSC. MELD scores on the way to transplant also do not effectively manage the sickest PSC patients to transplant effectively. With the research underway we need support from all angles to find the cure and reverse / pause liver fibrosis for PSC patients so they can retain their original liver.

- This is a very difficult disease to live with. Most people don't understand the everyday challenges we have and that our diet, life style, etc didn't bring this on.
- Too many trials focus on how we "feel" about symptoms and not enough on actually researching the disease.
- We (patient and family) need options for this terrible disease. There are not many options, and it seems like the opportunities for liver transplant are becoming less and less as other diseases (NASH, alcohol-induced liver disease) grow in numbers. Patients with PSC may feel much worse than their MELD scores indicate. This disease affects such a wide age range - children to adults. It's not like this is a disease of the elderly. It's very scary to learn in your 20s that you may only have 10 years ahead of you or be facing a liver transplant (if you're lucky). Additionally, I think as soon as a diagnosis such as PSC is made, patients should be immediately plugged into other services such as counseling, etc. My husband and father to my two young girls (infant and 18 months) attempted suicide because of this disease and the stress it brings to his life. I also wish that our country would explore doing an "opt out" program for organ donation rather than an "opt in" program so more organs would be available to PSC patients.
- We may be a small community overall, but we are eager and willing to do what's necessary to find treatments and a cure for this disease. As a post-transplant patient, there is little that has not already been done to my body from an invasive perspective, and I am willing to do what it takes to be part of the solution.
- We need a cure!
- We need a medication now that will stop this awful disease.
- We need more people to sign up to be organ donors. Access to meds/treatment should be a right and not determined by health insurance.
- We need something more effective to help with the itching. I make myself bleed multiple times a day from scratching, and scratching makes it worse. Help us, help me.
- What do I know, I'm not a doctor. There are some things that will never have a cure and this might be it. Finding a treatment would be very helpful. Quality of life is huge.
- Would like a better drug to control pruritus and for liver pain.
- Would like to see orphan drug designations and expanded indication for current drugs on the market.
- Would want to hear potential reasons why I got PSC. My UC/pancolitis was severe at diagnosis, and once that was under control I haven't had a flare since (20 years). I had an infected cyst and was on heavy antibiotics 6 months prior to UC symptoms starting. This all seems related. Would be interested in hearing "patterns" among patients.
- You can be our guardian angels!!!
- This is a rare but expensive disease. The treatment, a liver transplant, along with the required follow up care/medications can be cost prohibitive. We need a drug to slow or stop the progression as to avoid needing a transplant.
- Please remember that this horrible condition is not alcohol related, and there is not something we did to cause it. I've never touched a drop of alcohol in my life, have never tried any type of drug not given to me by a doctor, and I've never smoked anything. I have an amazing wife with whom I have

three amazing children, I've been a middle school teacher for over 20 years, I eat very healthily, and I exercise regularly (ran marathons for 12 years), yet there is nothing I can do to stop this awful disease from killing me early. And though we've done nothing to bring on this disease, those who drink themselves to liver disease often have higher priority for liver transplants. We're penalized for making healthier choices.

- I feel strongly that there may be a distinct disease subtype of PSC patients who respond to oral vancomycin. These patients must be identified. In addition, brand of vancomycin has been shown to affect response. I have had a return of my GI symptoms and liver chemistry elevations in response to brand change on 3 occasions. I renormalize after returning to the effective brand. So, dose, disease stage, phenotype, brand, age all must be correlated with response to better understand why this drug works for some patients. I believe that a dysbiotic microbiome holds the key for at least a certain subgroup of PSC patients.
- Fatigue and abdominal pain is underestimated by all, in regard to the negative effect to the PSCers quality of life.
- Make sure there is no chance of contamination of instruments/scopes etc., that are being used, which could harm the patients who participate.
- Antihistamine may be helping.
- Please find a cure for PSC. Better treatments for the horrible itching, anxiety, and the unknown that this disease does to me.
- I participated in a trial and I have not been able to receive any information about the trial, the results, or my results since the trial ended. But the hospital and the company have been unavailable. My blood work was very disturbed by the trial. For example my gamma GT went from normal to 1600 during the trial. I am angry and frustrated. I have repeatedly tried to contact the hospital.
- I have been also recently diagnosed with Bilateral Vestibular Loss. The consultant concluded that my immune system had damaged my vestibular apparatus as a result of having autoimmune disease.
- Medication for itching needs an upgrade. Cholestyramine is difficult to take daily and rifampin induced amenorrhea, which is not practical long term especially in young adult women. There needs to be a focused effort on the symptoms of PSC given that currently there is no treatment or medical cure. Seems like there isn't even a good enough solution to the symptoms other than gravol, buscopan, and tylenol when a stone decides to get stuck in the bile ducts.
- Yes, please continue the work you are doing! Please look into the gut biodome [biome], and probiotic/specific foods that can reduce inflammation. Vancomycin has potential, but there are lots of anecdotal information that different brands work differently. Please study this further. Please look further into transplantation and what can be done pre-transplant to improve acceptance. Nutrition studies would also be helpful to improve health pre-transplant. Lastly, dialysis-type treatment that can be done while awaiting transplant. Research into improving organ transplant rates.
- Thank you for considering research options. There are many people out there whose lives will be dramatically changed for the better if a cure or more effective treatments are developed.
- If we can find cures and vaccines so quickly for other illnesses, you should be able to for PSC as well. It seems like money talks and that's sad.
- The thing about PSC is that until you are very, very ill, nobody can tell you are sick. Explaining it to people is tiresome. Because it is a rare disease, and because symptoms develop slowly, it is an invisible illness to others. The symptoms are mostly intensely personal unless you develop jaundice,

ascites, or encephalopathy. With PSC, it's not the mountain ahead that wears you out, it's the stone in your shoe. It's the fatigue, the itching, the sleeplessness, the encephalopathy, the pain, the diarrhea, the existential dread. I was so very lucky to have an excellent medical team both pre- and post-transplant less than 2 miles from my home. I was so lucky that I had a healthy, xx year old son willing to donate part of his liver who was a perfect match. I have a very supportive group of friends and family members. I have a devoted and loving husband. I have no other autoimmune diseases. I have excellent health insurance. And still, this disease almost killed me. Every joy was diminished, every sorrow was amplified. By the time of my transplant I was exhausted, fragile, and complacent. I am so grateful for the chance to live a full, happy life again. I ache for those who are not as fortunate.

- I just wish there were more I could do.
- Good luck.
- Any focus on pediatric treatments are in dire need from companies. The long term damage from PSC in small bodies is unknown.
- Why did my generic form of ursodeoxycholic acid triple in price a few years ago? I now purchase a year's supply of Ursobilane in Spain when I am travel there --@25c/pill versus 98c/pill in the USA.
- Good luck and hurry up!
- The unmet needs for our patient community are great. It would be a dream if there would be a drug to slow progression of PSC.
- I had my colon removed in November of 2019, not sure how that affects my participation in surveys.
- Loosen up privacy laws regarding medical data. Should have anonymous national and international data banks. Stop siloing information!
- A multiple choice answer in a survey doesn't adequately explain the impact this disease has on our lives. It affects us every single day, from wondering when you're going to die, when things are going to take a turn for the worse, to writing about whether or not you'll be able to hang out and have fun with your kids/family or if you'll spend the day in bed with heating pads and whatever pain meds you can find.
- Concern regarding progression and cancer is scary.
- Keep doing your research, get the funding.
- Flagyl kept my cholangitis in check after transplant. I had chronic diarrhea for over a year before my local gastroenterologist prescribed it. I was cured within two weeks. The diarrhea would return every 3 months and the flagyl cured it. This continued for 7 years with slightly longer times between episodes as my prograft dosage was reduced from 5 to 1 mg/day and then transitioned to 2 mg/day rapamune. Bottom line is that high levels of immunosuppression aggravated my cholangitis.
- I wish there would be more trials on vanco for adults.
- Please understand that pruritus is not just a simple itch. It is debilitating and cannot be controlled by any medications that currently exist.
- HELP.
- Sharing information between companies to perform a meta-analysis of all previous drug trials to see if some drugs may be helpful.
- Finding a treatment for PSC would vastly improve my quality of life, if only by giving me hope that there is something out there to counteract the impacts of this debilitating disease. I am 29 years old and I find myself unable to plan for my future because I don't know how my disease will progress

and when I will become unstable and dependent on others while I wait for a transplant. It is a fear I've had since I was 20 years old.

- Help with quality of life.
- If a good potential treatment is developed, please fast track it through the process, since my fear is I will be too far progressed to where a new drug won't help, or I won't qualify to receive it.
- Thank you for agreeing to meet with PSC Partners and its members. This PSC disease can be a silent disease like other liver diseases. It only reveals itself after it already has taken a heavy toll on the liver. Other liver diseases (HCV, HBV, PBC) have had advances in their treatments (thank goodness for that though) but PSC has had no significant treatment advances.
- It's frustrating not having a standard of care for PSC.
- Many questions asked about my "PSC symptoms"—because I can't tell which symptoms are from PSC versus other causes, I answered these as though it had asked about my "symptoms."
- Medication prices are astronomical and burdensome for people with PSC. Disability payments are eaten up by the cost of medication. The fear of access to healthcare is enormous if one wants to try to work. It is a matter of life and death to have fully protecting coverage and pharmaceutical access. Currently, we are left with no solid help to count on. Everything is up in the air and constantly changing in regard to health care and pharmaceutical access. There is no peace of mind for someone with PSC in the USA due to this fundamental lack of protection. We are left dangling on our own hoping to find a way to survive. It is a very cruel system as it stands. Those with a rare disease are condemned due to a lack of care and therefore resources from the government. We are punished for being sick - it is shameful to run a country like this.
- FMT [fecal microbial transplantation] and Vancomycin should be part of the Standard of Care for PSC.
- Vancomycin saved my life: It stopped the inflammation from spreading throughout my liver, it lowered my liver enzymes to a normal level, and helps keep my ulcerative colitis in remission. Vancomycin has also saved many others. It's heartbreaking that there are hardly any clinical trials, research studies, or funding to learn more about why the ANI Pharmaceuticals brand of Vancomycin has such a powerful impact on patients' lives. My plea to you is that you explore ANI Vancomycin as a possible PSC therapy. My dream is that, one day, Vancomycin will be an FDA-approved and normalized treatment for PSC. Thank you.
- I am willing to participate in research/ clinical studies but it seems like there aren't any? (minimal) in Calgary, Alberta.
- Been good after having my common bile duct opened.
- History or [of] disease and end of PSC, no recurrence.
- Please find a cure for IBD, AIH, and PSC. We need more available treatments and a cure for these diseases. We also need less invasive measures to study the liver than a biopsy.
- Go to the PSC Support Facebook page for information from afflicted.
- Why would you not have listed Vancomycin as a medication for UC? My son went through every other medication with no relief. Vancomycin allowed him to live a normal life. More than anything, doctors treating these diseases need to communicate. Being the mother of a PSC/UC patient has been the most painful experience of my life and the lack of communication with one another, sharing information and overall progress in the medical field is profoundly disappointing and stunning. This incidence of PSC is much higher than is reported. This is just another indicator of how much is not known about this disease. My son is one of three boys in a two mile radius that have

PSC. There are only 2000 children in their entire high school and three of them had PSC. Your data is not accurate!

- When can I stop immunosuppressants?
- Please realize that although as a whole we may not be a large group, each one of us has a life and family who consider us their world.
- The fact that transplant is a treatment not a cure. Better ways to screen for rPSC [recurrent PSC] for small duct.
- Diet needs to be investigated as a cure. What we put into our bodies affects everything. I believe a vegan diet can either cure, or drastically reduce symptoms and improve quality of life.
- Patients for whom there are no therapies/cures are enthusiastic about trials which may offer hope. Older patients [are] eager to participate if it may lead to benefits for younger patients.
- There are groups like future parents, pregnant women and post-transplant patients who are not included in trials and therefore risk-benefit discussions always have more uncertainty because they are based on less evidence.
- I would ask that they consider spreading more awareness of the disease as well as any alarm bells associated with it. If I hadn't had cancer, I would've never found out I had PSC. All I knew was that sometimes my liver enzymes were high and there were indications of a generalized inflammatory response in my body (those bloodwork results happened intermittently throughout the last 20 years of my life, but doctors assured me it was nothing). When the doctors saw that my liver enzymes didn't normalize after chemo, they began asking questions -- that was way after I had my gallbladder removed at the beginning of my treatment even though there were no signs of a gallbladder stone. It was a real struggle to convince my medical team that the gallbladder had to come out, but they were very glad they did once they realized that while there were no stones, there was a powdery substance and the gallbladder itself was so diseased that one of the surgeons questioned how I could live like that. They assumed it was in bad shape because of chemo, but after the PSC diagnosis, it's pretty clear that chemo wasn't the main culprit (thought it probably didn't help, haha). I lucked out, I have no symptoms and the disease seems mostly dormant, but I have other relatives with the same gallbladder issues (no stones, just a powder, had to have it removed, feel so much better now) and have been nagging them to get screened (so far, no luck). I know it's a relatively rare condition, but early detection seems to really make a difference and I know how lucky I am that I caught it before any of the symptoms had a chance to manifest themselves. Now I'm leaning towards veganism and a low inflammation diet to help my liver cope with stress (also helps with IBD), so I at least have a chance at avoiding complications and a transplant in the future. I can still go through this with my quality of life relatively intact. I've heard horror stories from people who have PSC to a more advanced degree, and I wish they had the same luck I did.
- Any researchers tried natural medicine, i.e., herbs, etc., to help PSC?
- To people outside the medical community, Cancer is the big word. That buzzword is familiar, the life and death stakes are understood instantly. Lay people understand things like chemo and radiation. Having PSC is not the same. We begin a course of treatment which right now varies based on region and access to trials for new therapies. There are no true experts because PSC looks different every time. There are no guarantees that this antibiotic/ wonder drug/ transplanted organ will stop this onslaught. It isn't a cause many rally around. Some of us (myself included) get told we don't look that sick. I don't [have] jaundice. But my bilirubin results in monthly blood work are high. I have to explain every time I see a new doctor or nurse why I am not currently supplementing my diet with

certain vitamins - they make me worse. I have fought to be understood when I say that laying on my side is painful and it's an unmoving rock slab between my lungs and what's left of my small intestine. I've cried trying to be heard when physicians say, "all your problems are your thyroid." I have traumatized my husband as he found me unresponsive on a couch from hepatic encephalopathy. It's not Cancer, I am chipperly reminded. The implication is that it could be worse. No. The answer to that is no. If I had cancer, I'd have tools to fight, I'd have the understanding of friends every time I say I'm having a hard time. My own body is trying to kill me. I can't stop it, I have trials and theories to mitigate it instead of a plan that's proven to cure this, and I have no timeline. I am fighting every single day for my liver and my life. Cancer is awful. I wish it on no one. I've carried 2 parents through it, and both are now gone. I am not saying Cancer is easy - I'm saying it's an easier cause to understand. I need the help of researchers, drug developers. I need some allies in this fight who can find causes of it, discover the aggravating factors which accelerate progression, clarify the mitigating factors so the pharmaceutical companies can narrow drug research and development. We are a chorus of "save us" with voices of children all the way through to late adulthood. We are the patients ready to do everything required to survive. We are aware that our lifetime may not be the one where cure goes from hope to real. But we stand as one voice, asking you. Help us? You may not cure PSC and that's okay. But we need allies in every capacity to advocate research. The easing of suffering for those who bloody and scar their bodies from itching. The support for therapies which slow down progression. There are myriad ways to improve the experience of we the patients. This is not Cancer. Please understand that every PSC patient you meet, each unique case, is still a person who is asking for help. We are still here. Please, see us. Know that we are grateful for every advance in medication. We are still here. And we need you.

- I am a healthy person right now other than my UC (which is under control) and fortunately no PSC symptoms, just found out by blood tests for UC. I want to stay as healthy as I can, for as long as I can, and hope that a cure can be made a priority for people with this disease.
- Please do more research on, and expand the role of, vancomycin in the treatment of PSC.
- The treatment options are so limited to symptom control and even those are not used by some providers. More teaching of providers is needed.
- Please be sure to consider women and women's health when developing drugs and treatments. Do not default to the male body as the standard patient.
- My symptoms have swallowed my identity and taken away activities I enjoy. Now they threaten to ruin my romantic partnership. I am most interested in enjoying the same quality of life I had prior to my symptoms for however long I have left to live.
- I believe there should be greater recognition by drug developers (and disability insurers) of CLUSTERS of problems that go along with PSC. For some of us, it is not as simple as ulcerative colitis leading to PSC, and the combination not being severe enough to justify long term disability. I have also had colon cancer, total colectomy, recurrent pouchitis for which I take Visbiome probiotics and/or Cipro during flare-ups, recurrent blood clots for which I take apixaban as an anti-coagulant, kidney disease leading to acute kidney injury and several hospitalizations when electrolytes get severely out of whack, arthritis of multiple joints leading to joint replacement, celiac disease for which I'm on a gluten-free diet, pain for which I take CBD as a treatment I find helpful with minimal side effects, and depression for which I take Wellbutrin as an anti-depressant when things get bad. I sometimes think there is an autoimmune gremlin at work ripping apart my body from the inside. After a successful lawsuit against my disability insurer, my finances are no longer a source of anxiety.

I have a strong background in life sciences, stay on top of the research (medical journals, PSC Partners conference material (THANKS for putting this online!) not the misinformation in the press) and do all the suggested evidence-based things to manage my symptoms pretty well. Through trial and error and various hospitalizations I have developed a very complex program of fixes and contingency plans to keep me from going in the ditch (again). I have a supportive wife and kids, live in a great city, and to an outsider, I would appear to be living a pretty normal life. My principal concern going forward is accelerated mortality due to cholangiocarcinoma. My secondary concern is managing risks attached to living donor liver transplant in combination with anti-rejection drugs (which would be expected to severely limit future travel... there's more of the world to see before my time is up and international travel is a major "positive quest" and motivational goal for me!) Symptom management beyond what I'm already doing is not really a concern until I get significantly worse. If researchers could aim at any one thing, my suggestion would be to find the auto-immune gremlin that is the root cause underlying my entire CLUSTER of problems. Aim upstream at the root cause, not downstream at symptom management.

- Just diagnosed.
- I participated in the clinical trials for Prograf.
- It would be great if there was a medication to combat the itching with PSC.
- I wonder if there is a specific gene that is triggered. Will the drug trigger more problems?
- Please note that we do not all have the same disease as far as how it presents, order, severity, or rate of progression, so different aspects will be of more or less importance to each of us.
- I've had this disease for 23 years and there hasn't been a single FDA-approved advancement in slowing/treating/curing this awful disease. I essentially take the same drugs now that I did when first diagnosed. It seems to me drug companies would benefit in developing something that improves quality of life as they can sell it for the long haul of the dreaded disease. Curing it would be best.
- 1. Because [of] the MELD system required by UNOS, I was at the point of death before my score was high enough to compete for a liver. My dire condition also resulted in my hospitalization post-transplant to be extra long. 2. Just before my health went into rapid decline, ERCP revealed my bile ducts were completely blocked. Pruritus was terrible. I received an external hepatic drain. Though inconvenient, it resulted in my pruritus going away during my final decline before transplantation.
- PSC is considered rare but still affects many people and deserves robust research to find treatments and cure.
- Please help us find a cure! I came close to dying while waiting for a transplant. Now I worry the disease will return and attack the new liver.
- Any hope is better than the internet searches for this disease.
- As a physician-patient, I'd prefer more focus be placed on objectively meaningful outcome measures (biopsy/MRCP changes) vs symptom control.
- Find a cure!
- There is very little help available for understanding and managing pain. Drugs currently available are not all that helpful.
- Lack of information about what is working and what is not.
- None at this moment, however, I would like to have the opportunity to revisit this question at a later time (or multiple times) to add additional thoughts as it is a guarantee more information could be added that is not of mind at this moment.

- Currently, my life is controlled by my severe itching, muscle and body wasting, lack of appetite and edema. The itching is the worst thing I've ever experienced. If you can't help us get exception points for this horrendous side effect, I would hope that you would heavily focus on eliminating this hell.
- Please identify vancomycin as a medication for PSC. Please reduce the cost of vancomycin.
- Please continue to work with insurance companies to make drugs accessible. Doctors should have the power to be able to prescribe what they feel is best for their patient and should not be forced into prescribing a medication because insurance covers it. I currently am navigating this as I work through biologics to treat my Crohn's ileocolitis. The order of certain drugs ingested, while new drugs are coming out all the time, can make a difference for how those newer drugs work. Please continue studying the newer drugs and do not give too much power to one drug company to tie the hands of our capable doctors.
- PSC is a horrible and debilitating disease. It is increasing in frequency especially among women and children. We are desperate for a cure or at the very least a treatment that slows the progression and obviates the need of one or more multiple liver transplants.
- Lower the cost of these drugs!
 - Ursodiol - \$119/month
 - Rifaximin- 1,200/month
- Please keep working on this!! It is so important!!
- If a patient is willing to help out in a study, why don't the researchers offer some help with the cost of the drug for the participants after the study is successful?
- Please remember we all have loved ones who care about us.
- Thank you for working to find a cure for us!
- Since there is no cure for PSC, I would like to see a study of the long-term psychological effects of living with this knowledge and the effect it has on the psyche. I feel that not enough emphasis is put on this. PSC patients should be given exception points on MELD scores when they are listed for transplant to even the score. I would like to know why 1/2 of the MELD score is kidney function and PSC patients usually do not have poor kidneys until they are very sick with overall organ failure. Why can't this be part of an argument for exception points! We are beyond the meds to slow down this disease. We are now in a holding pattern in need of a transplant but in "MELD score Purgatory." Unacceptable!
- We need an opt-out system.
- To live with a disease that is slowly killing me is often crippling to think about. My son is 5 and I often think about not being around to take care of him. Every year that passes I get an MRI and see my organs getting more enlarged and stressed, it's hard to deal with. I work out every day, cut alcohol completely and eat a healthy diet and it makes no difference. It's a defeating feeling to know you can't do anything to help yourself.
- An immediate family member of mine and a close friend of mine have PSC, which feels like too many people for such a rare disease.
- I'm living in Denmark. I presume all research, etc., is going on in the USA?
- Please make these drugs affordable to the general public. People shouldn't have to die over a lack of access to a lifesaving drug.
- More information about this disease out to the masses so that more people understand and know what to do about it.
- Please help us.

- We need more research to find a cure.
- Side effects.
- Long term effects of Prograf (post-transplant drugs) and preventing reoccurrence.
- Wrap up the Rx [prescription] solutions in order to save lives.
- Please make it easier to define clear criteria and endpoints for successful trials, and easier to put new things up for trials without so many political headaches. It is hard enough to get enough patients nationally to sign up for a trial without all of the bureaucratic difficulties involved in the project itself. Consider some of the rare disease reforms adopted in the last few years by the European Medicines Agency which have made it easier to work on this in the EU market.
- I really wish that more physicians understood the disease, even though it's a rare one.
- My symptoms and findings (beading and strictures) started after undergoing a complex laparoscopic cholecystectomy. Gallbladder was plastered onto the bile duct (no discernible cystic duct). Underwent ERCP 10 days later for retained stones. I was fine for 7 months, and then had the episode of cholangitis, 3 years ago. No episodes since.
- Marijuana (smoked) saved my life from the horrible, debilitating symptoms of pruritus in 2007-2009. It was the only thing that worked since all other medications required metabolization in the gut--and mine was not working. At the time, no one had heard of using cannabis. Not sure about currently. But I probably would have killed myself if not for relief provided by marijuana.
- Focus on a cure and fund meaningful research. Just because the incidences are rare in our population does not mean that they are less traumatic than any other disease. One patient is significant if it were your loved one.
- Please find a cure for PSC! Please help with the itching.
- Need more emphasis on rare liver diseases.
- Do not hesitate to let patients "take risks" with their PSC prognosis. To date, in Canada, there are not many solutions to allow patients access to alternative medicines/treatments. As I stated before, there is simply a "wait and see" approach to disease management.
- I would love for research to be done on using essential oils to help with cirrhosis of the liver. I had a positive experience using frankincense - it completely opened a blockage that my doctors thought was cancer... in a week.
- Thank you for all the work you do!
- My son was almost perfectly healthy prior to doing allergy autoimmune therapy. He also never took any medication prior to the therapy, but was put on meds during therapy to keep asthma and allergies under control. Six months into therapy, symptoms of colitis started to appear. Our theory is there may be a connection with UC and PSC and allergy autoimmune therapy with meds.
- Research on ways of living (food, sports, stress, etc.) would be interesting, and not only new drugs.