Identifying research targets by **M**erging **Pa**tient And **C**linician **T**reatment information

PFIC IMPACT: February Focus Group Discussion Summary

Overview

We held our ninth PFIC IMPACT Focus Group meeting on February 20th, 2025!

- Attendees: 13 patients & parents + 4 clinicians & researchers
- Our goal for the meeting was to review our list of PC-CER targets to ensure the treatment questions and outcomes are comprehensive and organized.

Background

Project IMPACT, inspired by discussions at PFIC Network's 2022 Conference, aims to prepare the PFIC community for patient-centered Comparative Effectiveness Research (PC-CER). PC-CER compares treatments based on patient-prioritized outcomes, such as itch reduction, family quality of life, and financial burden. Comparing treatments in a systematic and patient-oriented way is key to simplifying and improving treatment decisions in the future. The first step we took in IMPACT was to develop a comprehensive list of treatment questions and outcomes to target in future PC-CER studies. Over the past year, we began compiling this list using input from patients, parents, providers, and researchers gathered through modules, focus groups, and the Treatment Experience App (TEA).

Discussion Summary

During the February focus group, participants split into three breakout groups based on PFIC PC-CER target categories: (1) Medications & Nutrition, (2) Surgeries, and (3) Diagnosis, Delivery of Care, & Other Support. Each group reviewed treatment-related questions identified previously in IMPACT in order to check whether the questions could actually be addressed in a research study as well as to identify missing questions or outcomes.

Breakout 1: Medications & Nutrition

- ***Non-IBAT & IBAT medications*.** Members shared experiences being prescribed non-IBAT medications (rifampin, ursodiol, cholestyramine) prior to IBATs, noting little to no reduction of itch, low palatability, and high burden of administration. However, many patients will still take these medications in addition to IBATs if IBATs provide incomplete itch relief.
    - Updates to PC-CER Targets:
        - Compare the effectiveness of rifampin, ursodiol, and cholestyramine in reducing itch.

        - For patients who respond well to IBATs, compare the impact of discontinuing vs. continuing non-IBAT medications on quality of life, sleep, fatigue, and medication burden.
        - For patients with partial IBAT response, compare the effectiveness of combining IBATs with rifampin, ursodiol, or cholestyramine in further reducing itch.
        - Compare growth, nutrition, sleep, and itch outcomes between PFIC patients undergoing diversion surgery alone vs. those receiving diversion surgery with IBAT therapy
- ***Other symptom management interventions.*** Members discussed sleep medications, as well as environmental and lifestyle factors affecting itch and quality of life to reveal new and specific comparators and outcomes.
    - Updates to PC-CER Targets:
        - Compare the impact of hot vs. cold temperatures on itch and quality of life in patients with and without IBATs.
        - Compare the effects of cotton, silk, and bamboo clothing on sleep, itch, and quality of life.
        - Compare the effectiveness of prescription-strength Benadryl vs. Atarax in improving sleep and quality of life.
- ***Transplant Medications.*** Members identified the need to discuss post-transplant management of pruritus with recurrent BSEP patients to identify all available treatment options. Members also discussed the significant quality-of-life impact of post-transplant diarrhea and various management options.
    - Updates to PC-CER Targets:
        - Expand the question: "*How do antidiarrheal medications (e.g., loperamide) compare to biliary diversion surgery in reducing diarrhea after liver transplant*?" by adding:
            - Imodium as a comparator
            - Quality of life as an outcome

The discussion highlighted additional meaningful outcomes to consider, including REM sleep/dreaming, bullying due to growth delays, ability to participate in activities in the heat, vitamin toxicity, medication burden (number of prescriptions, refrigeration, pill size), anxiety, and fear.

Breakout 2: Surgeries

- ***Biliary diversion.*** Members emphasized the need for a comprehensive summary of existing data on biliary diversion from studies like NAPPED to set realistic expectations and guide patients' decision-making. Leveraging existing

longitudinal datasets could potentially help answer IMPACT questions about internal vs. external biliary diversion and how outcomes differ across PFIC subtypes.

- Updates to PC-CER Targets:
  - Compare internal vs. external biliary diversion in terms of:
    - Native liver survival
    - Itch reduction
    - Quality of life (validated survey measures)
  - Assess how these outcomes differ across PFIC subtypes and genetic mutations (e.g., BSEP truncating vs. non-truncating mutations, missense mutations).
  - Identify whether IBAT non-responders should be considered for diversion, and if so, whether prior IBAT use influences diversion outcomes.

- ***Diversion vs. Transplant.*** If a patient requires further intervention, for instance because IBAT inhibitors did not work for them, the key question becomes whether diversion or transplant provides is the more appropriate option. While itch is often the primary driver of these treatment decisions, quality of life and long-term survival are also major considerations. Members also discussed financial and emotional outcomes, recognizing that both diversion and transplant present significant challenges.
  - Updates to PC-CER Targets:
    - Compare diversion vs. transplant in terms of:
      - Itch
      - Quality of life
      - Long-term patient survival
      - Risk of cancer
      - Financial burden
      - Stress
- ***Other Considerations***
  - Members wondered whether patients who previously had diversion surgery could transition to IBAT therapy now that IBATs are available, and what best practices exist for making this switch.
  - Members considered eliminating questions related to ostomy supplies, citing the declining use of external diversion and the highly personal nature of supply preferences.
  - Itch often remains the most important factor in surgical decision-making for patients, reinforcing the need to measure itch outcomes in all comparative studies.

Breakout 3: Diagnosis, Delivery of Care, & Other Support:

- ***Reducing Time to Diagnosis.*** We explored the question: *What is the best approach to reducing the time to diagnosis for PFIC?* Genetic testing emerged as the clear answer, making a comparison of diagnostic methods unnecessary. While genetic testing therefore falls outside the scope of treatment comparison studies that we want to address with PC-CER, members shared broader concerns about the barriers to early diagnosis. These discussions highlighted key challenges that may delay diagnosis, such as high out-of-pocket costs, limited provider awareness of genetic testing, and restricted access to genetic counselors and liver specialists. Understanding these barriers is important for PFIC Network's advocacy efforts.
- ***Hormonal Influence on Itch in PFIC/BRIC Adolescents & Adults.*** Members discussed tracking hormonal patterns (e.g., ovulation, puberty) in relation to itch severity to improve understanding of itch triggers and fluctuations. This is particularly relevant for older patients, including those with BRIC, who may experience itch fluctuations in adolescence and adulthood. Linking itch patterns to menstrual cycles could also potentially help patients predict flare-ups, reducing stress and unnecessary medical tests for ruling out other causes
    - <u>Updates to PC-CER Targets:</u>
        - Do sleep quality and itch levels fluctuate in relation to the menstrual cycle in post-pubertal female PFIC patients?

Combined Discussion

Each breakout group reported key takeaways, noting that none fully covered their PC-CER target category, reinforcing the need for further discussion before finalizing priorities. The group agreed that reaching consensus on research priorities will be an ongoing, iterative process, requiring continued community input, voting, and refinement to identify the most feasible and high-impact objectives. The challenge of high treatment variability led to a discussion on creating a standardized "treatment menu" as a potential next step post-IMPACT to provide a structured framework for PC-CER in PFIC.

<u>Focus Group Wrap-Up & Next Steps</u>

- The IMPACT project team will update the list of PC-CER targets using the focus group members' feedback.
- During our last IMPACT focus group in April, we'll explore how PFIC patients and researchers can collaborate on multi-stakeholder research teams.

If you couldn't attend in February, you can still review our PC-CER research target list (visit here) and send feedback to melissa@pfic.org. Every perspective matters!

Don't miss it! Upcoming IMPACT activities…

Make sure you're subscribed to PFIC Network's mailing list to receive alerts and access links for upcoming activities:

- **Our final IMPACT module, Module 6, launches on Monday, March 24th!**
  - If you haven't taken Modules 1-5 yet, we encourage you to complete them beforehand.
- **Our last focus group will take place in April (date TBA).**
  - It will be hosted as a virtual Zoom meeting and will last 90 minutes.
- **We will conclude Project IMPACT with an in-person activity** during the Family Conference breakout on Friday, June 27, at the 2025 Cholestatic Liver Disease (CLD) Summit in Aurora, Colorado. We hope to see you there!

Please contact us anytime with feedback, questions, or concerns: melissa@pfic.org