

Voice of the Patient report

Externally-Led Patient-Focused Drug Development (EL-PFDD) Meeting for ARPKD Patients and their Families

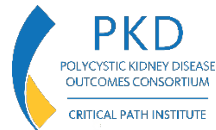
Meeting held virtually on August 29, 2023, 10 a.m. – 3 p.m. EST

Report date: January 26, 2024

Meeting Organizers



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Autosomal Recessive Polycystic Kidney Disease (ARPKD) Voice of the Patient Report

The Polycystic Kidney Disease Foundation’s (PKDF) mission is to fund research, advocate for patients, and build a community for all impacted by polycystic kidney disease (PKD). This *Voice of the Patient* report was prepared on behalf of PKDF as a summary of the input shared by families and caregivers living with Autosomal Recessive Polycystic Kidney Disease (ARPKD) during an Externally-Led Patient Focused Drug Development (EL-PFDD) meeting, conducted virtually on August 29, 2023.

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Consulting Partners include Larry Bauer, RN, MA, and James Valentine, Esq. and from Hyman, Phelps & McNamara, P.C.

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James Valentine, Esq. and Larry Bauer, RN, MA are employed by Hyman, Phelps & McNamara, P.C., a law firm that represents patient advocacy organizations and companies that are developing therapeutics and technologies to advance health. The PKD Foundation contracted with Chrystal Palaty, PhD from Metaphase Health Research Consulting Inc. for assistance in writing this report.

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Thank you to our speakers, Dr. Kirtida Mistry from the FDA, Dr. Erum Hartung from the Children’s Hospital of Philadelphia, and Dr. Max Liebau from the University Hospital of Cologne. Your eloquent presentations created a strong foundation for the rest of the day.

Thank you to all of the PKD Foundation staff, supporters, and advocates who have given countless hours to ensure a successful EL-PFDD meeting, including Susan Bushnell, Elise Hoover, Nicole Harr, and the PKD Parents Community. Thank you to Wendy Vanasco and Sorin Fedeles from the PKD Outcomes Consortium at the Critical Path Institute, as well as members of the ARPKD/CHF Alliance for assistance with meeting planning.

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Thank you to the researchers working in labs and clinics all around the world, striving towards a better understanding of basic and translational ARPKD science. With your help we are moving closer to additional future clinical trials. Thank you to all the representatives from advocacy organizations, pharma companies, federal agencies, and research centers from across the world for attending our meeting.

Finally, an enormous thank you to all the members of our ARPKD community of patients, parents, caregivers, and families who attended our meeting and shared their personal stories and lived experiences with ARPKD. This meeting could not have been as impactful without each and every one of you. We are grateful to have this opportunity to ensure that patient and family perspectives are considered in the drug development and regulatory processes.

Our hope is that this meeting will encourage future research and successful new product development for people living with ARPKD who urgently need treatment options.

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ARPKD EL-PFDD MEETING INSIGHTS

1. **Autosomal Recessive Polycystic Kidney Disease (ARPKD) is a rare genetic disorder.** The clinical course of ARPKD is highly variable and can present any time from before birth to adulthood. An ARPKD diagnosis is traumatic, and consequences can be tragic. The disease is progressive and affects the kidneys as well as the liver.
2. **Most individuals living with ARPKD experience a large number of disease-related health concerns.** Kidney failure and high blood pressure are the most bothersome, followed by liver problems including congestive hepatic fibrosis (CHF). Many patients also experience enlarged kidneys, gastrointestinal problems, fatigue, anxiety/depression, enlarged spleen, growth failure, breathing issues, immunosuppression, pain, and premature death. Signs and symptoms worsen as kidney and liver disease in ARPKD progress.
3. **ARPKD has an incredible disease burden. The disease is progressive, and new symptoms are likely to appear.** Most children cannot fully participate in sports, school, and social activities e.g. due to fatigue and the risk of injury or pressure from their enlarged organs. Many miss out on school because of illness and frequent care appointments. Some who are living with the disease have a sense of being different and do not want to draw attention to their needs. Many find it hard to make longer term plans as their future is uncertain.
4. **ARPKD families have many worries: disease progression leading to premature death, needing a kidney and/or liver transplant or dialysis, and worsening symptoms.** Many parents worry about their child's uncertain future and some feel like their child is living on borrowed time.
5. **There are no FDA-approved treatments to stop ARPKD disease progression.** Patients will do everything they can do to spare their organs. Patients rely on many off-label medications and medical procedures for symptom management, including blood pressure medications, growth hormone, dialysis, splenectomy, prescription iron supplements, bowel medications, and sleep medications. Other approaches include a low salt diet, dietary modifications, and hydration. Those living with ARPKD require a great deal of monitoring, scans, and lab tests.
6. **Ultimately, many patients will require a kidney transplant, a liver transplant or even a combined liver-kidney transplant. The ARPKD community emphasized that transplants are not curative but a trade-off of one chronic condition for another.** Many children have received



kidney and liver transplants from their parents, but donated organs have a finite lifespan and eventually need to be replaced.

7. **ARPKD families are frustrated by the lack of treatment options.** Treatments only help somewhat or only treat some of the symptoms, and it can be challenging to tell that they are working. Most treatments have many side effects, and the amount of monitoring is excessive.
8. **The ARPKD community needs treatments that prevent progression of kidney and liver disease, to delay dialysis and transplantation.** The community needs symptom-reducing treatments, better treatments for those with both kidney and liver involvement, better ways to measure blood pressure, more information for patients and physicians, and more research, especially more clinical trials.

CLINICAL SUMMARY¹

Autosomal Recessive Polycystic Kidney Disease (ARPKD) is a rare genetic disease. It occurs in about one in 20,000 births, with an estimated 1,500 children and young adults living with ARPKD in the United States.

ARPKD can be caused by many different gene variants. The majority of patients with ARPKD have variations in the *PKHD1* gene, which encodes the fibrocystin protein, but variants in other genes can also be involved as well. The type of gene variant influences the severity of kidney and liver involvement; null gene variations, which are those that lead to the total loss of gene/protein function, are associated with worse kidney survival and earlier liver-associated complications.

ARPKD is a progressive disease that affects the kidneys as well as the liver. The severity of both liver and kidney symptoms are highly variable and there is not a clear relationship between the severity of kidney and liver disease.

ARPKD is a highly variable disease that can present any time from before birth to adulthood. Two-thirds of patients are diagnosed prenatally or in infancy, and the remaining one-third are diagnosed in childhood or adolescence.

¹ This was from the presentations of **Dr. Erum A. Hartung**, a pediatric nephrologist, an ARPKD expert and clinician scientist from the Children's Hospital of Philadelphia and **Dr. Max Liebau**, a pediatric nephrologist with training in cellular and molecular biology who was well-known for his translational research approach at the University Hospital Cologne in Germany.

An early age of presentation is a risk factor for more severe disease. Some severely affected individuals will manifest symptoms before birth, including low amniotic fluid and underdeveloped lungs. After birth, they may experience breathing problems requiring mechanical ventilatory support, kidneys may be extremely enlarged, and nephrectomy followed by dialysis is sometimes soon required. Some experience feeding difficulties, failure to thrive and developmental delays. Of those diagnosed prenatally, 15% to 30% do not survive, primarily due to lung underdevelopment. As patients age their symptoms and challenges change.

ARPKD is characterized by the development of cysts leading to kidney enlargement and progressive chronic kidney disease. Although many will have enlarged kidneys early in life, the kidneys do not necessarily continue growing throughout the lifespan. In adolescence or adulthood, kidneys of people with ARPKD can be normal size or even smaller than normal. Individuals with ARPKD may experience declines in kidney dysfunction, leading to the need for dialysis or transplant. By the age of 20 years, half individuals who were diagnosed in the perinatal period require dialysis or kidney transplantation; in contrast 85% of those who presented later in life still have some degree of kidney function at age 20.

Elevated arterial blood pressure is a common symptom and can occur throughout the lifespan. In addition to the ARPKD-specific effects, those experiencing diminished kidney function experience anemia, bone health impacts, and issues with growth or learning.

Many patients with ARPKD have liver issues which often appear later in childhood or adolescence. Congenital hepatic fibrosis (CHF) causes a range of symptoms that can include dilated bile ducts, liver fibrosis (microscopic scarring in the periportal areas leading to stiffening of the liver), and portal hypertension (impaired blood flow from internal organs such as the spleen, esophagus, and stomach to the liver). Some patients experience only mild laboratory or imaging abnormalities, whereas others have more severe symptoms such as ascending cholangitis (bile duct infections), an enlarged spleen resulting in low platelet and white blood cell counts, and bleeding from dilated veins in the esophagus and stomach (esophageal or gastric varices). Patients may require surgical treatment such as shunting to treat portal hypertension, and some will need a liver transplant.



Current ARPKD treatments only manage disease symptoms and cannot prevent or stop the declining kidney and liver function. The development of targeted therapies for this disease are limited by ARPKD's rare disease status and clinical variability. Currently, a number of international research collaborations are underway to better understand how different genetic variants influence the clinical course of ARPKD, to identify detailed patient subgroups, to identify risk factors associated with the early need for dialysis dependency, and to determine which patients could potentially benefit the most from early interventions. New treatments will need to independently target the lung, kidney, and liver disease aspects of ARPKD, while considering safety aspects for all organs.

PKD Foundation together with the Critical Path Institute, PKD researchers, representatives of the pharmaceutical industry, regulatory agencies, and patient representatives have established the PKD Outcomes Consortium (PKDOC). PKDOC is focused on both autosomal dominant PKD (ADPKD) as well as ARPKD, with the aim of transferring potential new therapies from research to the clinic. The identification of some overlapping disease mechanisms between ADPKD and ARPKD, means that novel treatments for ADPKD may also be candidates for further study in ARPKD. As a result of this work, the first trials of tolvaptan for treatment of kidney disease in patients with ARPKD are now underway.



MEETING SUMMARY

The Autosomal Recessive Polycystic Kidney Disease (ARPKD) Externally-Led Patient Focused Drug Development (EL-PFDD) was held virtually on August 29, 2023. The meeting was an important opportunity for the Polycystic Kidney Disease Foundation (PKDF) to share patient perspectives regarding the symptoms and daily impact of ARPKD, as well as current and future approaches to therapies. The virtual meeting format allowed many ARPKD community members to participate through live online polls, telephone call-ins, and by providing written comments through an online portal. The meeting was cohosted by **Susan Bushnell**, the CEO and President of the PKD Foundation, and **James Valentine**, Esq. from Hyman, Phelps & McNamara, P.C.

Susan Bushnell opened the meeting by welcoming all meeting attendees including the members of the US Food and Drug Administration (FDA). She introduced **Dr. Kirtida Mistry**, a pediatric nephrologist in the Center for Drug Evaluation and Research at the FDA. In her opening remarks, Dr. Mistry described how this EL-PFDD meeting will help the FDA to obtain insights from the true ARPKD experts, patients living with the disease and their caregivers. She encouraged patients and families to engage in this process and thanked the ARPKD community for participating.

Dr. Erum Hartung, MD, MTR, a pediatric nephrologist who is an ARPKD expert and clinician scientist from the Children's Hospital of Philadelphia presented a clinical overview of ARPKD which served as a foundation for the first half of the meeting. **James Valentine** provided an overview of the meeting which was structured around two key topics. The morning session focused on *Living with ARPKD: Symptoms and Daily Impact*, and the afternoon session focused on *Perspectives on Current and Future Treatments for ARPKD*.

The morning session continued with a pre-recorded panel of individuals who shared patient and caregiver perspectives on the symptoms and daily impacts of ARPKD. James Valentine moderated a discussion between individuals in a live Zoom panel as well as those who dialed in by phone, and Susan Bushnell read out relevant comments entered through an online portal.



The afternoon session started with a presentation focused on the current state of research and therapies in ARPKD by **Dr. Max Liebau, MD**, a pediatric nephrologist who is an ARPKD expert and clinician scientist at the University Hospital Cologne, Germany. The afternoon continued with a pre-recorded panel of patients and caregivers as they described different medications and medical treatments as well as other approaches they use to address ARPKD manifestations. Again, meeting attendees had an opportunity to participate in online polling, to call in and submit written comments. To conclude, **Larry Bauer, RN, MA** Hyman, Phelps, & McNamara provided a summary of key points and **Susan Bushnell** thanked all of the meeting attendees for their participation.

One-hundred and twenty-eight viewers attended the livestream, including 13 individuals living with ARPKD, 34 parent/caregivers, nine other family members, two friends, one teacher, 16 members from the FDA, 19 scientists/researchers, seven from the healthcare industry, three healthcare providers, 18 from non-profit organizations, and six others.

EL-PFDD meeting attendees used online polling to indicate meeting demographics. The majority of attendees (84%) were caregivers of someone with ARPKD, and the rest (16%) were individuals living with ARPKD. All of the attendees were from continental USA, with half from the US Eastern time zone. There were also participants from Central, Mountain, and Pacific time zones. The individuals living with ARPKD represented at the meeting were split between genders (52% male, 48% female). All age groups were represented at the meeting, with slightly more from the 6-10-year-old age group and the 19-30-year-old age groups. As a reminder of the severity of ARPKD, some attendees were representing children who had passed away.

The meeting agenda is in **Appendix 1**, results of demographic polling are shown in **Appendix 2**, meeting discussion questions are in **Appendix 3**, meeting panelists and callers are listed in **Appendix 4**, and online polling results from topics 1 and 2 are presented in **Appendix 5**.

To include as many patient voices and perspectives as possible, patient comments were collected through an online comment submission portal before, during, and for four weeks after the meeting. All submitted patient comments are included **Appendix 6**, with selected comments included in the body of this report.



This *Voice of the Patient* report is provided to all ARPKD community supporters including the US FDA, other government agencies, regulatory authorities, medical products developers, academics, clinicians, and any other interested individuals. The input received from the August 29, 2023, EL-PFDD meeting reflects a wide range of ARPKD experiences, however not all symptoms and impacts may be captured in this report.

The final reports of the EL-PFDD meeting, the video recording of the meeting are available on the PKD Foundation website at [ARPKD PFDD 2023 | PKD Foundation \(pkdcure.org\)](#).

An ARPKD Adjunct Scientific Workshop was held several months after the meeting and the key scientific insights from that meeting are captured in a separate report.



Topic 1 - LIVING WITH ARPKD: SYMPTOMS AND DAILY IMPACT

Patients and caregivers shared their perspectives and experiences of living with ARPKD through pre-recorded presentations, moderated discussion, online polling, and submitted comments. They described ARPKD-related health effects, the impacts of ARPKD on activities of daily living, and their worries and fears for the future. Several key insights emerged that were not captured in online polling are highlighted below.

An ARPKD diagnosis is traumatic, and consequences can be tragic, especially when the disease manifests *in utero* or early in life.

“In the third trimester of my first pregnancy, a routine ultrasound discovered that both of my son Steven's kidneys were large and echogenic, and I no longer had any measurable amniotic fluid. The doctor delivered the devastating news that Steven likely had ARPKD, and without amniotic fluid for the remainder of my pregnancy, he would not survive.” - Lindsey A., parent of a 12-year-old son who has had a kidney transplant

“My son was diagnosed prenatally and given no hope for survival with low amniotic fluid, which is essential for lung development. After exhausting second opinions and research, funeral arrangements were made. When I had no amniotic fluid remaining, I was induced.” - Colleen, parent of an adult son who has had two liver and kidney transplants

“For children like CJ who present with ARPKD in the neonatal period, the risks are high and prognosis can be grave. One in three do not survive. It is quite literally life or death for these babies. CJ narrowly avoided being a part of the statistic, but he was not unscathed. I can tell you that time, it was the hardest of my life, and I hope for a day that no other babies and their families have to endure the same.” - Ashley A., parent of a three-and-a-half-year-old son who has had a kidney transplant



ARPKD is a genetic disease, that impacts the entire family. Some families have several affected family members. The disease is heterogeneous, even among family members.

"Through genetic testing, the diagnosis was confirmed. Genetic testing also revealed our younger daughter has ARPKD as well. Our son was found to be a carrier of the gene and can pass it on to his own children." - Lisa, parent of 13 and 9-year-old daughters living with ARPKD

Michelle's sons have different symptoms, and differing levels of liver involvement. *"Navigating the two of them and the different medications and the different doctors and the different symptoms is one of our biggest [challenges]."* - Michelle, parent of 23- and 17-year-old sons living with ARPKD

Most living with ARPKD experience a large number of disease-related health concerns. Kidney failure and high blood pressure are often the most bothersome.

Meeting attendees first selected all of the ARPKD-related health effects that they or their loved one ever had, then selected the top three most burdensome. Most experience many health effects; each individual selected an average of 5.9 different symptoms. Poll question results are shown in **Appendix 5, Q1 and Q2** and illustrated below with selected patient quotes.

"Its hard to put into words which symptom or issue has the most significant impact on my child's life living with ARPKD as there are so many. Some include severe anemia, fatigue, high blood pressure, electrolyte issues, etc. [My daughter] is currently at about 25% kidney function along with enlarged spleen and portal hypertension." - Anonymous, parent of a daughter living with ARPKD Kidney failure

"My child was diagnosed with enlarged echogenic kidneys, no amniotic fluid, and enlarged liver and spleen, and experienced issues with lung development, failure to thrive, dialysis, adrenal insufficiency, seizures, high blood pressure, pulmonary hypertension, feeding issues, and gross motor delays." - Stephen, parent of a child living with ARPKD

Kidney failure and enlarged kidneys. Kidney failure was selected by meeting participants as the most burdensome ARPKD health concern.



Kidney function gradually declines for all living with ARPKD, and eventually many require dialysis or a transplant. Other kidney issues can include acidosis (the inability to excrete acid through the kidneys), hyponatremia (low sodium levels in infancy), and urine concentration defects (resulting in the production of large amounts of urine, which may lead to frequent urination or bedwetting). Kidney issues can manifest early, and some severely affected infants are born with enlarged kidneys which can interfere in lung function. These enlarged kidneys may have to be removed for survival, and infants receive dialysis until they can receive a transplant, often from a parent.

Eric was born with massive kidneys which barely functioned. “Eric’s kidneys continued to grow, causing him incredible discomfort. They also continued to fail, so both had to be removed. It was the first of several major surgeries leading to his successful kidney transplant at age 13 months.” - Beth and Mike, parents of a son who passed away at the age of 10 years from ARPKD complications

“Our oldest didn’t have any decline in kidney function until he was 16 years old, but now we’ve seen a bigger decline. From 16 to 23, [his kidney function] has gone down a fair amount. He’s hovering around 60% now.” - Michelle, parent of 23- and 17-year-old sons living with ARPKD

“Since [ARPKD] begins early in fetal development, he had significant kidney and liver involvement at birth. ...My son experienced acute renal failure, and on his 23rd birthday, began hemodialysis. 11 months later, he was offered a kidney and liver transplant.” - Colleen, parent of an adult son who has had two liver and kidney transplants

High blood pressure. High blood pressure was the most frequently reported health concern. Blood pressure issues sometimes start at birth, yet can be very hard to monitor and difficult to control in infants and small children. When blood pressure is poorly controlled, high blood pressure can lead to heart problems such as left ventricular hypertrophy or thickening of the heart muscle.

“Eric developed life-threatening hypertension and electrolyte imbalances. It made our hearts ache not being able to hold him at all for the first few days, and it made our hearts break that we could not



alter the course of this brutal disease.” - Beth and Mike, parents of a son who passed away at the age of 10 years from ARPKD complications

“He’s had high blood pressure since he was born, so he’s been on a high blood pressure medicine since he was about four months old and they’ve had to titrate it up, and his blood pressure [measurements] are always high.” - Lindsey B., parent of a six-year-old son living with ARPKD

Sometimes the high blood pressure is what leads to an ARPKD diagnosis. *“When she was four, we went in for a standard checkup and the doctor saw her blood pressure and said, ‘Something’s not right here.’ We followed it until we learned about her kidneys and what was going on. We had never experienced or heard of anything like that.” - Joe, parent of a six-year-old daughter living with ARPKD*

Liver problems including an enlarged spleen. Liver problems are one of the most bothersome ARPKD-related health concerns. Congenital hepatic fibrosis (CHF) in ARPKD is associated with dilated bile ducts, periportal fibrosis, portal hypertension, esophageal varices, liver cysts, and fluid accumulation or ascites. Portal hypertension results in an enlarged spleen which can affect platelet counts and white blood cell counts, resulting in immunosuppression and blood clotting issues. Cholangitis (bile duct inflammation) is rare and presents atypically in those with ARPKD.

Many patients experience both kidney and liver issues, and the complications of one dysfunctional organ can severely impact the health and the treatment of the other organ.

“I’ve always had a heavier involvement with my liver. ... Right now, I’m not at a place where I’m ready for transplant, but I have the high blood pressure, the portal hypertension. I’ve had esophageal varices, a lot of that was resolved with the splenectomy and I had a devascularization, so a lot of that was rerouted.” - Shawna, 24-year-old, living with ARPKD

“Unfortunately, [the enlarged spleen] was not the only life-threatening concern. Eric also had esophageal varices that could bleed at any time. ...He had problems with his bile duct that could lead to cholangitis, which is a life-threatening infection, and he had blood clotting dysfunction and several other liver concerns.” Eric also



experienced ascites and immune suppression. - Beth and Mike, parents of a son who passed away at the age of 10 years from ARPKD complications

Amy's daughter experiences liver symptoms on a weekly basis
"Enlarged spleen, decreased activity, worry of variceal bleed... That's always in the back of our head, so it really limits what we can do and where she's allowed to go."- Amy, parent of an 11-year-old daughter living with ARPKD

"Some families have said that one doctor will suggest the possibility of cholangitis, only to be immediately dismissed by another doctor." - Alix, parent of an 11-year-old son living with ARPKD

Gastrointestinal (GI) issues (nausea/vomiting/diarrhea/poor appetite). GI

issues were also selected as one of the most bothersome ARPKD-related health concerns. Many of these GI issues are related to liver and kidney dysfunction, and can include abdominal pain and bloating, reflux, nausea, and vomiting. Enlarged kidneys and abdomen create difficulties with eating and feeding. Because of bile issues, some children are unable absorb and digest fat which can lead to diarrhea and malnutrition.

"Kai vomited every night. He vomited every day. He would smell something from across the room and vomit. He would get the hiccups and vomit. Too many tickles, vomit. Something would make him cry and he'd vomit. ...On his second birthday, I remember doing some quick math to calculate that he had vomited upwards of 7,000 times in his short life." – Kelsey, parent of a son who has had a kidney and liver transplant

"In our son's first year of life the hardest symptom was enlarged kidneys that limited our son to eat by mouth. This caused endless vomiting, lack of weight gain, and constant worry." - Alee, parent of a son living with ARPKD

"When his kidney function really declined, he didn't want to eat anything. Food didn't really taste good to him. He just wanted to eat carbs." - Erin, parent of an 11-year-old son who has had a kidney transplant



Fatigue. Fatigue was a frequently experienced ARPKD-related health concern.

“I get very tired easily, which stinks because when my friends want to hang out, I want to hang out with them. But due to my kidneys, I'm just usually too exhausted.” - Jaina, 13-year-old living with ARPKD

“A big thing right now is fatigue. ... I feel like I always have a level of fatigue. ... There are definitely days I wake up and I know I'm just going to be tired all day long.” - Shawna, 24-year-old living with ARPKD

“We noticed in the past probably two years ... that any sort of activity, like going on vacation tour to a theme park or anything like that, ... her abdomen is so large that it's just exhausting and painful and she gets those side stitches.” - Ashley B., parent of a six-year-old daughter living with ARPKD

Anxiety/depression. Patients with ARPKD and their families experience ARPKD-related stress, anxiety, and depression. Some expressed grief about the diagnosis of a chronic, progressive disease.

“My younger son definitely has had a lot of anxiety surrounding the disease, especially when he was younger. When he was about eight or nine, he had a lot of panic attacks. We really think it's because of the disease, because at the time, he was having a lot of appointments, he was having a lot of issues.” - Michelle, parent of 23- and 17-year-old sons living with ARPKD

“We normalized and embraced our experience as a family, but the stress was overwhelming at times.” - Beth and Mike, parents of a son who passed away at the age of 10 years from ARPKD complications

“We are just barely coming to terms with the fact that she has challenges with her kidneys. I've tried to, for the most part, avoid [worrying about] the liver. I can't even comprehend that now, because we're still adjusting to understanding what it means for kidneys.” - Joe, parent of a six-year-old daughter living with ARPKD

Growth failure/small stature. Many children with kidney dysfunction also experience problems with growth. Some parents attributed slow growth to poor feeding.



“Steven also has adrenal insufficiency, meaning he does not grow like a normal kid. He's small for his age and at a time when other boys are shooting up like weeds, he's not.” – Lindsey A., parent of a 12-year-old son who has had a kidney transplant

“He also has the issues with being very petite. He was average size when he was first born. In the NICU, they commented, ‘He's a big baby, because all that we see are little teeny-weeny tiny ones!’ Him being normal-sized, looked big to them, but he just has grown so slowly. ... His brother teases him for it, because that's what brothers do unfortunately.” - Lindsey B., parent of a six-year-old son living with ARPKD

“He was growing very slowly as he was unable to take anything by mouth. His breathing prohibiting this. He received fortified breast milk by feeding tube, but he was only able to tolerate small amounts, as his kidneys left little room for his stomach to expand.” - Ashley A., parent of a three-and-a-half-year-old son who has had a kidney transplant

Shortness of breath/breathing problems. Some severely affected infants are born with underdeveloped lungs, caused by a lack of amniotic fluid in utero, as well as the enlarged kidneys which leave little space. Respiratory problems can lead to death in severely affected infants.

“My daughter died shortly after birth due to respiratory failure from polycystic (and non-functional) kidneys and very low amniotic fluid. She was diagnosed at 36 weeks (this was 30 years ago) and born at 37 weeks.” – Connie, parent of a daughter who passed away from ARPKD shortly after birth

“Although it had been a normal term pregnancy and non-complicated birth, Eric immediately became critically ill. His kidneys were so enormous that his lungs were unable to expand, and he could not breathe.” - Beth and Mike, parents of a son who passed away at the age of 10 years from ARPKD complications

Urinary tract infections. Many individuals living with ARPKD experience multiple urinary tract infections that can affect the kidneys and can become septic.



“Every time he has a fever, we have to watch how high it gets. ... If he has a fever of 102, we have to go to the emergency room to rule out a urinary tract infection, which may affect his kidneys. He can't take most medications that would reduce these fevers, so we have to hope that Tylenol will help.” - Julie, parent of a five-year-old son living with ARPKD

“A year prior to his death, Eric had two hospitalizations for UTIs with sepsis that caused significant ascites or fluid accumulation. Definitely the liver not working right.” - Beth and Mike, parents of a son who passed away at the age of 10 years from ARPKD complications

Patients experience many other ARPKD-related health concerns.

Puffiness or swelling (edema) was a symptom selected in the polls but there were few related comments made during the meeting. Other ARPKD-related health concerns described during the EL-PFDD meeting include **premature death; pain; enlarged abdomen; immunosuppression, frequent infections and illness;** and **cognitive and behavior issues.** Other symptoms include chronic itching; eczema; self-esteem issues due to changes to appearance and extensive; cardiac issues; pulmonary hypertension, developmental delays including issues with fine and gross motor skills; seizures; strokes; fainting; hypermobility issues; and poor temperature regulation.

Premature death. Many infants and children pass away due to complications of ARPKD.

“When I was 30 weeks and six days, the ultrasound shown that [our son, Porter] was in distress, and we had to have an emergency caesarean section. By this point in the pregnancy, his kidneys had grown and lost too much function and despite trying, there was nothing more the team could do. He survived for a few hours before we lost him.” - Julie, parent of a son who passed away a few hours after birth from ARPKD

“Eric would be 19 years old now had he not died of complications from ARPKD right before his 10th birthday. ...After almost nine years of essentially no major kidney complications, Eric developed post transplant lymphoproliferative disease or PTLN, a form of lymphoma. Although the lymphoma occurred as a result of immunosuppression



following Eric's kidney transplant, it was absolutely the advancing liver disease that made it so he could not tolerate the chemotherapy.” - Beth and Mike, parents of a son who passed away at the age of 10 years from ARPKD complications

Pain. Many living with ARPKD experience bodily and abdominal pain because of their symptoms and procedures yet are unable to take many common pain medications. Many are too young to verbalize their pain.

“I was the one hovering over this sweet crying baby, shushing him and repeatedly singing songs of comfort because I couldn't pick him up to hold him during [peritoneal dialysis] drain cycles as he cramped and writhed with discomfort.” - Kelsey, parent of a son who has had a kidney and liver transplant

“The worst days were when Eric was in pain or anguish from the effects of his disease.” - Beth and Mike, parents of a son who passed away at the age of 10 years from ARPKD complications

“I still have pain in my body, and at times, all I can do is try to cope because I can't even take ibuprofen from muscle and joint pain like people without kidney disease can.” - Jaina, 13-year-old living with ARPKD

Extended abdomen. Many living with ARPKD have extended abdomens from their enlarged kidneys, liver, and spleen, which often persists into childhood.

“My son has a kidney transplant now, but he definitely has a big belly, and it's definitely related to his liver being big, and his spleen is big, and his platelet count is trending down.” - Chris, parent of a three-and-a-half-year-old son who has had a kidney transplant

“I had a really difficult time when my son was a small baby, looking at the size of his stomach. To this day I avoid putting him in pants because I know they will just fall off.” – Alee, parent of a son living with ARPKD

“Although his football size diseased kidneys had been removed, his belly was still descended because of an enlarged spleen due to advancing portal hypertension. From birth, we were warned that



trauma to the spleen could be life-threatening.”- Beth and Mike, parents of a son who passed away at the age of 10 years from ARPKD complications

Immunosuppression, frequent illness, and infections. Poor organ function and immunosuppressive drugs following a transplant can result in more frequent and severe illness and infections.

“My child had underdeveloped lungs, so it seemed he caught every respiratory bug out there.” - Colin, parent of a son living with ARPKD

“At two and a half months, she began to have multiple urinary tract infections and terrible fevers. She was hospitalized several times and had multiple tests done, but the results were inconclusive. She seemed to outgrow the infections, but always had multiple unexplained fevers each year.” - Lisa, parent of 13 and 9-year-old daughters living with ARPKD

A viral infection resulted in a dual organ transplant for Colleen’s son. *“[The viral infection] reaped havoc. It was horrifying to witness, rapid kidney and liver failure that included liver enzymes in the thousands, jaundice, and pitting edema that wept and saturated thick pads within an hour. He experienced confusion, was difficult to awake at times, and would moan the pain when his abdomen became rock hard from ascites. This required several liters of drainage every few days.” - Colleen, parent of an adult son who has had two liver and kidney transplants*

Cognitive and behavior issues. Several parents and caregivers described behavioral problems and cognitive challenges including ADHD and autistic-like tendencies.

“Steven has also been diagnosed with ADHD. While I can't prove a correlation between ARPKD and ADHD, I wholeheartedly believe his cognitive function was impacted by all of what he's been through related to the ARPKD.” – Lindsey A., parent of a 12-year-old son who has had a kidney transplant



ARPKD has an incredible disease burden. Biking and playing sports were reported as the most impacted activities, followed by attending school, sleeping, and socializing with friends.

Meeting attendees used online polling to select the top three activities that they or their loved one are not able to do or struggle with due to ARPKD. Poll question results are shown in **Appendix 5, Q3** and are illustrated below with selected patient quotes.

The disease is progressive, and more symptoms keep appearing.

This point was made throughout the meeting but not captured in the polls. Patients described how the disease robbed them of their childhoods, while their parents and caregivers just tried their best to keep things normal.

“This disease is like death by a thousand cuts. As soon as you reach an equilibrium with a new symptom/ problem, there is something else to deal with.” - Ellen, parent of a child with ARPKD

“Living with ARPKD is not linear. There are a lot of ups and downs. Symptoms can change, treatments can change, and each patient has their own set of unique challenges with this ugly disease.” - Shawna, 24-year-old, living with ARPKD

“I lost a bit of my childhood because of this disease. We all did.” - Jaina, 13-year-old living with ARPKD

“The challenge for me as a parent is to figure out a balance as far as living a normal life and giving my children a typical childhood while managing the day-to-day of having children with chronic kidney disease.”- Michelle, parent of 23- and 17-year-old sons living with ARPKD

Several parents and caregivers mentioned how reassuring it was to see Shawna, an adult who is thriving with this disease, participating in the Session 1 zoom panel.

Biking or playing sports. Biking and playing sports were the top activities impacted by ARPKD. Patients described having to avoid or sit out of many childhood activities due to fatigue, the risk of rupturing their spleen, or



because of pressure on their enlarged organs. This can sometimes make them feel singled out and self-conscious.

“For the first five years, the top treatment was to keep my spleen from rupturing and to control my blood pressure. This sounds easy but try telling a five-year-old this means no sports, no gym class, no carnival rides, no bike rides, no roller-skating, and the list goes on.” - Shawna, 24-year-old, living with ARPKD

“I’m limited to many activities that I wish I could do, such as jumping horses and riding roller-coasters that have lap bars only. It’s pretty common for me just to not feel well and not really feel like eating much.” - Jaina, 13-year-old living with ARPKD

“Some things that I can’t do since I have bad kidneys but have always dreamed of are gymnastics.” - Chesley, nine-year-old living with ARPKD

“She is currently at about 25% kidney function along with enlarged spleen and portal hypertension. ... The enlarged spleen limits the sports and daily activities that she is able to do.” - Anonymous, parent of a daughter living with APRKD

Attending school. Many children have absences due to their symptoms, frequent illness, and doctors’ appointments. Children fall behind with schoolwork and socialization. Participation can be affected by accommodations such as access to restrooms, and the need to miss gym or outdoor activities. Sometimes other siblings also miss school if the family needs to travel to another city for monitoring or treatment.

“Aside from all the medical issues I’ve experienced growing up, having a chronic illness affects all parts of your life. I miss lots of school, and even on days I didn’t miss, getting out of bed was a struggle. Nothing prepares you for the fatigue, and on top of that, there are days you just feel so isolated, so different from your peers and not being able to participate in the same ways they are.” - Shawna, 24-year-old, living with ARPKD

“At least once a year we have to go into the city, and he has appointments all day long. He’s upset every time because he has to



miss school or camp to attend these appointments and he misses his friends.” - Julie, parent of a five-year-old son living with ARPKD

“Children miss lots of school due to doctor appointments. ... She had to miss school 15 days out of a whole month. I mean, we only go to school 22 days during the month. ... All the times that she's sick, she's missing school, and then she's missing all those social interactions and cues from her peers at school as well.” - Lisa, parent of 13- and 9-year-old daughters living with ARPKD

“My daughter ... went to a middle school this year. So brand new school, brand new teachers that don't know her, don't know her limitations. She does have to always have water, free access to the restrooms, and then gym class is an issue.” - Amy, parent of an 11-year-old daughter living with ARPKD

Sleeping. Sleeping was the third most impacted activity selected in the polls. Several parents and caregivers mentioned issues such as bedwetting, difficulty in adjusting to peritoneal dialysis, and anxiety as contributors to poor sleep; these quotes appear in other sections.

Socializing/relationships with friends and family. Fatigue and frequent illness can interfere with social engagements and relationships. Some feel excluded because they cannot participate in all the activities that their friends do or opt out because of fatigue or incontinence, and this lack of participation can impact future invitations. Many adolescents living with ARPKD have a sense of being different, and of not wanting to draw attention to their needs.

“My youngest definitely had more of a problem at night with needing to wear pull-ups and not being able to hold his urine overnight until a much later age than all of his peers. ...He never did sleepovers. He would have friends come here sometimes because he could control it a little bit more. Fourth grade, they went on this big trip that all the fourth graders did, and he wouldn't go.” - Michelle, parent of 23- and 17-year-old sons living with ARPKD

“Her friends want to go do things, and stay up late, and hang out, and sometimes she's just too exhausted, or she just doesn't feel good. ... It's hard for her friends to understand how she feels. And we're just starting to notice that they'll go do things without her because they're



just so used to her being too tired, or not feeling well. So even just socially, how this disease affects these kids is very traumatic.” - Lisa, parent of 13- and 9-year-old daughters living with ARPKD

“When they'd gotten to their teen years, not really wanting to talk about it a lot at school. The fact that they needed water more than their friends or needed the bathroom or the nurse was a little bit hard for them to figure out. Not wanting to talk to their friends about it as much and not wanting it to be as known and such a big part of their life.” - Michelle, parent of 23- and 17-year-old sons living with ARPKD

Working or having a career. Some of the older individuals living with ARPKD described having to take many days off from their employment for appointments or treatments. Some are afraid of disclosing their disease, as they worry that it will compromise career opportunities.

“As an adult, I feel like with work it can be a little more difficult just because you have to miss a lot more, maybe schedule your doctor's appointments, or try to schedule everything the same day or explaining, ‘Hey, I'm not just taking the day off!’” - Shawna, 24-year-old, living with ARPKD

“He just started ... his first real job after college, and having to tell them, trying to decide what he's going to tell his job, and what he's not going to tell his job. ... He's a civil engineer, so he is working at a construction site.” - Michelle, parent of 23- and 17-year-old sons living with ARPKD

Other activities impacted by ARPKD. Personal care or household chores and walking were also selected in the polls as activities impacted by ARPKD. Other ARPKD impacts described at the meeting included the **inability to make long term plans** and the impact of **extra things they need to contend with**.

Inability to make long term plans. During the meeting individuals living with ARPKD described how difficult it is to make longer term education and career plans. Others described anticipating that they will have to give up things that they love doing including caring for their pets.

“Right now, he is looking at dialysis and/or a transplant at some point, but we have no idea when. ...it is, it's hard to make long term plans and he will soon be a teenager, looking at job and education options, social



relationships, etc.” - Katy, Grandmother of a 10-year-old boy living with ARPKD

“My true love is birds. My dream is to work with birds when I get older. I study their habitat, diet, language, and I love to learn as much as I can about them. ...We have seven chickens and a bunch of pigeons at our house from our family 4-H projects. ... but I may have to find them a new home when I get my kidney transplant.” - Chesley, nine-year-old living with ARPKD

Extra things that they have to contend with. Joe described how his daughter has to do a lot of extra things, like carry an enormous container of water to school every day.

“There's all the things from on the one spectrum of not being able to do things, and then there's the other things, the extra things that she does. ... There's all these extra things that revolve around her.” - Joe, parent of a six-year-old daughter living with ARPKD

ARPKD families worry about disease progression leading to premature death, needing a kidney transplant, and needing dialysis.

Meeting participants used online polling to select their top three worries about themselves or their loved one’s condition in the future. Results are in **Appendix 5, Q4** and are illustrated with patient quotes.

The parents and caregivers of children living with ARPKD worry for their children.

“[ARPKD] is just a constant cycle of worry and concern for your child. And every parent has worries and concerns for their child, especially about their future. But as us ARPKD parents, ours is just magnified on a much larger scale. And you can't really talk about it with most other normal parents or even family because it's difficult, and people can't relate.” – Lindsey A., parent of a 12-year-old son who has had a kidney transplant

“As parents, we worry. And then to add in the extra stress as a caregiver of children with ARPKD, it's a whole different level. And for me, it's taken me a long time. I had a lot of anxiety surrounding the disease when the boys were younger and first diagnosed, and I had a



lot of panic attacks, and I was really only thinking about the future. And so it's taken me a very long time to get here, and try not to worry quite as much, and just to live in the day- to-day.” - Michelle, parent of 23- and 17-year-old sons living with ARPKD

Dying prematurely. The most selected worry from the polls was dying prematurely; many parents were told that their children were unlikely to survive, and some patients were told that they would die young. Many parents feel that they wouldn't be able to “keep” their child or that their child is on borrowed time. One parent reminded everyone that this is the first generation of kids with ARPKD who will make it to adulthood.

“20 years ago, I was told I had a fatal condition, and I wouldn't be here today. - Shawna, 24-year-old living with ARPKD

“At the time of [my son's] birth, ARPKD babies routinely passed away. That was the expectation, not the exception. I feared he would die his first year of life.”- Colleen, parent of an adult son who has had two liver and kidney transplants

“When my daughter was diagnosed, she was six months old. I just thought, ‘Oh my gosh. I don't get to keep her, my poor baby,’ without really understanding the disease. Thankfully I've gotten to keep her, but there's always that little voice in the back of my head that's like, ‘But for how long?’ The dying prematurely thing is very, very scary.” - Amy, parent of an 11-year-old daughter living with ARPKD

“Obviously the premature death is the root of everything, but everything else is just a part of that journey. ...When we first found out a couple of years ago, I went from feeling like she was the healthiest child in the world to feeling like I was on borrowed time.” - Joe, parent of a six-year-old daughter living with ARPKD

Needing a kidney transplant or dialysis, or a liver transplant. The second and third most selected worries in the online poll were worries about needing a kidney transplant, followed by worries about needing dialysis. The average lifespan of a transplanted kidney or liver is only about 10-20 years, so those who have already endured a first transplant worry about needing a second. As many parents have already donated a kidney and part of their liver to their child, they worry about finding other potential donors.



"I think besides obviously the premature death, I worry about dialysis. It's difficult on people's bodies. It lowers life expectancy. It's painful and you hope that the place you're going to is doing all the things they're supposed to be." - Lindsey B., parent of a six-year-old son living with ARPKD

"The hardest part about having ARPKD is always having to worry about my kidneys, what I'm allowed to eat, and not eat, remembering to take all my medications, and all the blood draws and tests I have to get done each year." - Chesley, nine-year-old living with ARPKD

"One day, mommy's kidney will probably stop working and you'll need a new one. As we know, kidneys are not easy to come by. You might also, by the way, need a new liver, which is even scarier. This is the part of ARPKD that really doesn't get much attention." - Jordan, parent of a nine-year-old son who has had a kidney transplant

Many also worry about the liver failing and needing to be transplanted.

"He hasn't had a liver transplant, but we do think he'll need one, one day and it's kind of like waiting for the other shoe to drop with what's going to happen with his liver." - Erin, parent of an 11-year-old son who has had a kidney transplant

"The fear of a GI bleed and the uncertainty of the liver side of this disease that could happen at any minute I think is what has more of an impact on our life than anything. [Kidney's function] can typically be tracked and measured over time. But knowing that the liver can cause life threatening complications (such as a GI bleed or a cholangitis episodes) at any minute has us living in fear of this happening any day." - Anonymous, parent of a daughter living with ARPKD

That my symptoms will get worse. Worries about symptoms getting worse was selected low in the polls, but there were so many comments about disease progression during the meeting. Parents and caregivers worried about high blood pressure, the risk of heart failure, and the unknown. Some worried about whether each new symptom is related to ARPKD disease progression.



“How painful is it for a kidney to go through this? Is she going to be suffering? Is she going to be crying? Is she going to be in pain? Is she going to be all of these different things?” ... It's just so much psychological strain and pressure that goes beyond just the physical attributes that we worry about.” - Joe, parent of a six-year-old daughter living with ARPKD

“I have short-term worries of, ‘Is this lab draw going to show more declining function? Is this scope going to show worsening esophageal varices? Are we going to be heading for shunt surgery in the future?’” - Amy, parent of an 11-year-old daughter living with ARPKD

“Every doctor appointment that we go to could be the one where his blood pressure requires medication. Every ultrasound could be the one that shows his ARPKD symptoms have progressed, and we have new concerns. Every round of blood work could be the one that shows kidney function is declining and we need to start talking about dialysis or transplant. We have no idea what the future will hold or what we should be preparing for, and we have no idea if we're going to have an option that will help him when we need one.” - Julie, parent of a five-year-old son living with ARPKD

Needing to quit my schooling/job. This worry reflects the challenges of planning for a future with a chronic, progressive disease.

“I really want to be a veterinarian when I grow up. I'm trying really hard to get good grades. I'm in advanced math and I'm taking college credit plus courses. I'm very smart and study hard in all of my classes. However, that might not even be possible to achieve my goal after getting new kidneys and liver. When I get my transplant, I won't be able to see my chickens and pigeons for a year or more, which will be really sad.” - Jaina, 13-year-old living with ARPKD

“The biggest thing for me is just work, and school, and just my symptoms getting worse. And obviously dying prematurely is also very nerve wracking. I am older, but thankfully I've had a pretty mild progression. So those are all worries that we all have. You just got to take it day by day and see where it goes.” - Shawna, 24-year-old, living with ARPKD



"I have long-term worries, 'Is she going to get to, ... go to college, and have those experiences, and grow up, and get married, and have babies?" - Amy, parent of an 11-year-old daughter living with ARPKD

Other ARPKD-related worries. Injury to kidney or spleen, needing extended care, and worsening impaired thinking/memory were also selected in the polls, but there were few related comments. Parents, caregivers, and patients shared many other worries including **worries whether they are making the best medical decisions, worries about passing the gene to future generations, worries about their children's future happiness and well-being.**

Worries whether they are making the best medical decisions. This also includes worries about whether their children will make the best medical decisions for themselves as they get older.

Jennifer's son is facing a transplant consultation. *"I think at this point now, the biggest fear is 'are we making all the right decisions?' Medicine is an art sometimes more than a science, as much as we wish it were more exact, and you have to place your trust in these doctors and the surgeons and everything. You just worry that you're making the right decisions ...in response to the care that they need"* - Jennifer, parent of a 19-year-old son living with ARPKD

Michelle worries about her children caring more for themselves with less involvement from her. *"They have to think about these specialists and these doctors that they have to make appointments with. ... It's a lot to think about as a young adult. I wouldn't want to think about all of that. What medications? "Oh my gosh, did I take my today? Did I refill my prescription? Can I have this? Can I take Tylenol this many times? Can I have one sip of an alcoholic drink? I mean, it's a lot."* - Michelle, parent of 23- and 17-year-old sons living with ARPKD

Worries about passing the gene to future children. Some families made a difficult decision to not have more children and worry about passing the gene to future generations.

Connie's daughter died shortly after birth due from complications of ARPKD. *"My other 2 children (now in their late 20/early 30s) have not been tested and due to insurance questions are unwilling to be tested.*



However, they are concerned for any future kids of theirs.” - Connie, parent of a daughter who passed away from ARPKD shortly after birth

Worries about their children’s future well-being and happiness. Many parents worry about whether their children will be independent and find happiness, love, and fulfillment in the future.

“His symptoms have become better with time, he has ‘grown into’ his kidneys, but I still have my moments wondering whether he will be able to live a fulfilled life like other children.” - Alee, parent of a son living with ARPKD



Topic 2 - PERSPECTIVE ON CURRENT AND FUTURE APPROACHES TO TREATMENT

Through online polling, moderated discussion and submitted comments, caregivers, parents, and patients living with ARPKD described all the different medications, medical treatments as well as non-medical approaches that they had tried for ARPKD-related symptom management. They described the most significant drawbacks associated with each approach and articulated their hopes for future ARPKD treatments. Several key insights emerged throughout the meeting that were not captured in the polls.

There are no FDA-approved treatments to stop ARPKD disease progression. Instead, patients living with ARPKD rely on many medications and extensive medical care for symptom management.

“On my journey with ARPKD, I've never had one continuous specific treatment. Symptom management has always been the top priority. Which symptoms I'm managing has changed drastically over the 20 years I've experienced with this disease.” - Shawna, 24-year-old living with ARPKD

“I'm now on 10 different meds a day, including four blood pressure meds and growth hormone shots. My little sister Chesley takes four pills a day. We have yearly ultrasounds and MRIs, quarterly blood draws, and lowered immune systems. We both have a team of specialists including nephrology, GI, cardiology, neurology, endocrinology, dermatology, and in the past, PT, and mental health.” - Jaina, 13-year-old living with ARPKD

“It felt like a miracle when Eric came home from the neonatal ICU. ... His bedroom did resemble a hospital room with equipment for dialysis, tube feeding, vital signs, dozens of medications. It was wonderful to be home, but it would not be long before we were basically living in the hospital again.” - Beth and Mike, parents of a son who passed away at the age of 10 years from ARPKD complications

A transplant is not a definitive treatment.

This point was emphasized throughout the meeting.



“A transplant is not a cure, but is trading one chronic condition for another. ... Multiple transplants are likely needed, and you introduce the risks for rejection and cancer.” - Alee, parent of a son living with ARPKD

“It's so crucial for people to understand that transplant is not a cure, it's a treatment, and this treatment has very real and very scary side effects, physical, mental, and emotional” - Lindsey A., parent of a 12-year-old son who has had a kidney transplant

Blood pressure medications are required by almost all patients with ARPKD, followed by prescription iron and other medications.

Using online polling, EL-PFDD meeting attendees selected all the medications or medical treatments that they or their loved one used (currently or previously) to treat symptoms associated with ARPKD, CHF or other related conditions. Poll responses are in **Appendix 5, Q5** and illustrated below with patient quotes.

Blood pressure medication. Most participants reported using medications to control blood pressure, and many mentioned requiring multiple blood pressure medications, and the need to treat blood pressure aggressively to protect the kidneys. Some switched from liquid to pill formulations as children grew.

After his birth, “My son was whisked away after a weak cry and remained hospitalized for three weeks for breathing and blood pressure issues. He was eventually discharged home with three hypertension meds for BP readings in the 200 over 100 range.” - Colleen, parent of an adult son who has had two liver and kidney transplants

“Being very aggressive in that treatment, and even trying to strive for the lower end of what's considered normal for our kids has maintained the quality of their kidney function for longer periods of time.” - Elizabeth, parent of a 13-year-old daughter and nine-year-old son living with ARPKD

Blood pressure medication downsides. Many infants and young children cannot stay still when their blood pressure is being measured, and in many



cases, the blood pressure cuffs are too large for their tiny arms. As a result, blood pressure measurements can be inaccurate and blood pressure may not be optimally controlled. Additional medications need to be added as the disease progressed and some described side effects including coughing.

"The blood pressure has always been tricky for us. The squeezing hurts and then he gets upset and we can't get a good reading when he gets upset, so we have to start over again and then he gets upset again." - Julie, parent of a five-year-old son living with ARPKD

"Our big issue is that with Nico, we can never get his blood pressure ever. Most appointments, he struggles so much that they don't think the reading is accurate. ... However, we don't always know what it is. I've tried to do it at home. He's just so tiny. He fights it." - Brittany, parent of a son recently diagnosed with ARPKD

"I was sent a DINAMAP, an automated blood pressure machine typically used in the intensive care units to obtain accurate blood pressure readings. This was provided by our insurance company to titrate hypertension meds and avoid hospitalizations. There were many med changes in his first year of life with growth and development." - Colleen, parent of an adult son who has had two liver and kidney transplants

Growth hormone. Almost half of poll respondents indicated that they had used growth hormone. Most reported successes.

When his son was a newborn, *"We would inject you with growth hormone every night so you could gain strength and maybe even outgrow your big kidneys."*- Jordan, parent of a nine-year-old son who has had a kidney transplant

"Our younger son had major growth problems and needed to be on growth hormone. He was tiny from the beginning and then fell off the charts when he was four, and we finally started growth hormone at the age of seven. Ironically, he's now the tallest of our three boys, so the growth hormone worked, which was amazing. He's very proud of that." - Michelle, parent of 23- and 17-year-old sons living with ARPKD



“Eventually, he was placed on growth hormone and experienced great success with no side effects. He excelled in school, played sports, and was a happy child.” - Colleen, parent of an adult son who has had two liver and kidney transplants

Growth hormone downsides. The medication must be injected daily, which can be very difficult for patients to learn to do themselves.

“He takes a growth hormone injection every night, but it's a very slow and long process and it took months of exposure therapy and years of coaching for him to be comfortable enough to handle the daily injections.” – Lindsey A., parent of a 12-year-old son who has had a kidney transplant

“We actually took a break for a year because it was taking a huge toll on her mental health to be administering shots to herself.” - Elizabeth, parent of a 13-year-old daughter and nine-year-old son living with ARPKD

Kidney transplant. Infants and children with ARPKD may need to receive a kidney donated by their parents.

“They took out your two sick kidneys and replaced it with mom's healthy, healthy kidney, and almost immediately you were healthier, stronger, and ...it was just an amazing transformation. But still, it's not easy. You have shots, you've got labs, you have doctor's visits, you get sick easily. Transplant life is better than the alternative, but it's still not ideal.” - Jordan, parent of a nine-year-old son who has had a kidney transplant

“A family friend donated her kidney to Steven in an almost identical match. Fitting a kidney from a six-foot-tall woman into a little two-year-old boy was a miracle in and of itself. Steven struggled immensely during his recovery. He had issues with anesthesia and pain medication and spent 13 days in the hospital recovering, but once we were discharged with his new large cocktail of medications, things started looking up.” - Lindsey A., parent of a 12-year-old son who has had a kidney transplant



“He’s been living with his transplanted kidney for three years now. And I just wanted to comment on how much of a change that was once he got his transplanted kidney and how life became much easier. And although we do still rely on meds, he takes them less frequently and in a pill form and just twice a day. But really it is trading one set of complications and challenges for another.” - Erin, parent of an 11-year-old son who has had a kidney transplant

Kidney transplant downsides. As emphasized throughout the meeting, a kidney transplant is not a cure. Kidney transplant patients require a great deal of monitoring, and they can experience immunosuppression from antirejection drugs. Transplanted kidneys have a finite lifespan and a second or even a third transplant may be required. A kidney transplant doesn’t protect the liver and doesn’t address all of the symptoms.

“Since transplant, there have been many struggles and those struggles ebb and flow each year. Steven is now 12 years old and just celebrated his 10-year kidney transplant anniversary. It’s an incredible milestone, but he’s also currently undergoing treatment for donor-specific antibody mediated rejection. It’s confusing and hard for a 12-year-old to understand why he needs to do this treatment and why this is happening to him.” - Lindsey A., parent of a 12-year-old son who has had a kidney transplant

“Transplants are miraculous, but they have all their own issues. Transplant, your immune system is weaker, it puts you at all sorts of risks for other diseases like cancer.” - Jordan, parent of a nine-year-old son who has had a kidney transplant

Kidney dialysis. Kidney dialysis can replace the blood filtration function in failing kidneys. Peritoneal dialysis is used on infant patients, especially after their enlarged kidneys have been removed. Dialysis downsides are that it is highly invasive, needs a lot of medical supervision, is chronic, and only a temporary solution.

Kai’s first two years were “nothing short of traumatic. I don’t know how many of you have ever come across a baby on dialysis, but let me tell you, it’s horrific. ... Peritoneal dialysis requires intense training of the parents, and I was tasked with connecting and disconnecting Kai’s



dialysis cyler every night. I was the masked medical staff that made him cry.” - Kelsey, parent of a son who has had a kidney and liver transplant

After Steven’s double nephrectomy, “He spent every night on dialysis for 12 hours. ...It took an entire year for his body to normalize to the peritoneal dialysis and for him to sleep through the night. He didn’t take his first steps until he was one year and 10 months old. The following year was spent preparing for transplant, which finally occurred on May 9th, 2013.” – Lindsey A., parent of a 12-year-old son who has had a kidney transplant

“When [my son] turned six, his kidney function declined, really very low and he had a nephrectomy and was put on dialysis. And then received a transplant from me... right before he turned seven.” - Erin, parent of an 11-year-old son who has had a kidney transplant

“Medical providers are told that ondansetron is the best remedy for nausea caused by peritoneal dialysis, but let me tell you, it did nothing and you’ll never understand how many tears the parents that these children cry over empathy for their baby’s suffering.” - Kelsey, parent of a son who has had a kidney and liver transplant

Splenectomy. A splenectomy may be necessary to remove an enlarged spleen. Although a splenectomy can solve spleen issues, it does nothing to mitigate liver problems and often results in immune suppression and blood clotting issues.

“When I was a teenager, the vein of my spleen clotted off. At this point, it was time to remove my spleen. Once they removed it, I had an entirely different set of problems. My platelets skyrocketed. I had to start Anagrelide to get them under control. I underwent a round of vaccines and started taking penicillin from my weakened immune system. I had to have four endoscopies the next year to address the varices that popped up after my surgery.” - Shawna, 24-year-old, living with ARPKD

Liver transplant. Several parents and caregivers who spoke at the EL-PFDD had children who had experienced a liver transplant and many more worry



that a liver transplant is in their future. Some patients require more than one liver transplant, including Colleen's son, who had to have both his donated kidney and liver replaced as a result of a viral infection.

"When nothing more could be done, he was placed on a transplant list with a MELD (Model for End-Stage Liver Disease) score of 39 and was gifted with a new liver and kidney within 12 hours. He was incredibly fortunate to survive that harrowing ordeal." - Colleen, parent of an adult son who has had two liver and kidney transplants

Other medications mentioned in the polls. According to poll responses, over three quarters of those living with ARPKD require **prescription iron supplements**, half have used **bowel medications** (omeprazole, laxatives, anti-diarrhea). **Corticosteroids** (prednisone, methylprednisolone) are often administered before birth to help babies' lungs mature. Some have used **sleep medications**, and several reported using **antidepressants or anti-anxiety medications**. Very few of these medications were discussed during the meeting.

"We dosed Kai with max levels of lansoprazole, omeprazole, famotidine. Any other antiacid we could get our hands on to fight the burning in his throat, that would still come often, sometimes with small amounts of blood in his vomit." - Kelsey, parent of a son who has had a kidney and liver transplant

Other medical procedures or medications not mentioned in the polls. Many other medications and medical procedures were mentioned throughout the EL-PFDD meeting including, **extensive monitoring, surgical interventions, feeding and breathing supports, many additional medications, and participation in clinical studies.**

Extensive monitoring. Patients, caregivers, and parents described blood pressure monitoring, blood work for kidney and liver function, endoscopies for varices, as well as MRIs and other tests.

Katy's grandson has mild disease. *"We are doing what we can with diet, frequent lab and imaging, and blood pressure control."* - Katy, Grandmother of a 10-year-old boy living with ARPKD

"I have imaging done to check the nodules on my liver and whether they appear cancerous. ...I still continue my regular MRIs, blood work,



and checkups every six months. ...Every year or so, I would have to undergo an endoscopy to check the size of the varices to see if new ones had formed, and if I had to have any banding to prevent bleeding.” - Shawna, 24-year-old living with ARPKD

Surgical interventions. In addition to transplants and splenectomies, many individuals living with ARPKD have had multiple surgical procedures. A nephrectomy removes enlarged or dysfunctional kidneys and may be necessary to allow the lungs to expand. Endoscopic banding procedures or shunt surgeries may be necessary divert blood from the liver to deal with varices. Others require surgeries to install gastric-tubes, ports, and catheters to repair hernias.

“When his breathing got worse, and he, again, had to be reintubated and placed back on the ventilator, we made the difficult decision to proceed with nephrectomy to try it and save his life. Difficult not only because we were committing him to dialysis, and eventually hopefully a transplant, but also incredibly difficult because he had rapidly become so critical. We were not sure whether he would survive the surgery. ‘On the precipice,’ his surgeon said.” - Ashley A., parent of a three-and-a-half-year-old son who has had a kidney transplant

“At the same time his kidneys were removed, a gastric tube was placed in his stomach and a PD catheter was placed in his abdomen for dialysis. ... Steven spent his first year of life in and out of the hospital, including additional four surgeries to repair hernias, put in a Mediport for blood draws and IV access, and to replace his PD catheter.” - Lindsey A., parent of a 12-year-old son who has had a kidney transplant

Ashley’s daughter has had multiple endoscopies to monitor and band her varices. *“It’s not only difficult and risky to do, but it’s also emotionally upsetting to my daughter. And it’s scary because now that we’ve had a few, she knows what’s involved.” - Ashley B., parent of a six-year-old daughter living with ARPKD*

Breathing supports. Many parents and caregivers described breathing supports including non-invasive respiratory support, tracheostomy, and ventilators.



Ashley's son required life support at birth. *"His lungs, underdeveloped from the large cystic kidneys he had developed in utero, were struggling to oxygenate his body, despite the life support from the ventilator."* - Ashley A., parent of a three-and-a-half-year-old son who has had a kidney transplant

"After spending nearly a month on a ventilator and three months inpatient, we were finally able to bring him home." - Kelsey, parent of a son who has had a kidney and liver transplant

Many additional medications. Many additional medications are required including: pain medications; recombinant erythropoietin and other drugs for anemia; medications to lower platelet levels; blood thinners such as rivaroxaban; drugs to treat reflux and vomiting; ursodiol to treat primary biliary cholangitis; medications including dupilumab for itching and eczema; prophylactic antibiotics, IVIg, and other medications for immune support.

"I was admitted to the ER with severe abdominal pain. I had two large blood clots, one in the portal vein and one in my mesenteric vein. I was started on Xarelto [rivaroxaban] and will likely continue for the rest of my life." - Shawna, 24-year-old, living with ARPKD

"But the liver, it's so terrifying. ...My daughter's 13 and was listed for dual transplant when she was five. She stabilized because we put another medication in, a prophylactic one. And, along with the ursodiol, ... to help manage and mitigate any symptoms that the liver has." - Elizabeth, parent of a 13-year-old daughter and nine-year-old son living with ARPKD

"Dupixent [dupilumab] ... changed our lives. In a matter of hours, I was able to change a diaper without pinning Kai's arms down with my feet to prevent scratching. He was suddenly able to wear short sleeves, singled layer clothing. ... What's fascinating here is that now post-transplant Dupixent hasn't been very useful. It was only when he had no kidneys and a liver that was prone to cholangitis that this was so helpful." - Kelsey, parent of a son who has had a kidney and liver transplant



Participation in clinical studies. During the EL-PFDD meeting many described how they or their children were actively participating in ARPKD natural history and imaging studies. Participants mentioned that there were some minor benefits to participants, mainly just obtaining the results of blood and DNA tests (specific gene variants), MRI results and incidental findings. This community has not experience with interventional trials, so their answers may evolve as the pipeline expands.

“If there were any incidental findings or any findings of concern, we would've been told of them. As a parent, I can see the benefits of this type of study, but it was very hard for my boys to see the benefits.” - Michelle, parent of 23- and 17-year-old sons living with ARPKD

As part of clinical studies, patients had to meet with multiple specialists (geneticists, hepatologists, dieticians, nurses) and endure multiple tests (numerous ultrasounds, MRIs, blood draws, urine tests, blood pressure checks, physical exams, MRIs, surveys, psychological testing).

Clinical study downsides include traveling and staying at the study site (sometimes for several days); tests can be unpleasant, uncomfortable, and even painful; not all children qualify to participate; not all the studies are necessarily ARPKD specific; the studies may not provide any overall benefit to the patient themselves.

“I'm currently involved in a clinical research study with Cleveland Clinic. The study focuses on using imaging to gather information and determine how ARPKD progresses. I would like to get involved with more observational studies if the opportunity came up. However, I'm not comfortable participating in drug trials until I start to see a decline in my liver and kidney functions.” - Shawna, 24-year-old, living with ARPKD

In addition to many medications and medical treatments, those living with ARPKD rely on dietary modifications including a low salt diet and dietary supplements as well as many other approaches.

Meeting attendees used online polling to select all the approaches, besides medications and treatments that they were using currently or previously to help manage symptoms of ARPKD, CHF or other related conditions. Each



respondent selected an average of 3.8 options. Poll results are shown in **Appendix 5, Q6** and illustrated below with patient quotes.

Low salt diet as well as other dietary modifications including excessive hydration. Many Patients with ARPKD adhere to a low salt or low potassium diets to create less demand on the kidneys. Most patients have been instructed to hydrate excessively to create less demand on the kidneys. Parents and caregivers of children with larger bellies space out meals to optimize nutrient intake. Some patients select foods to minimize reflux or to prevent variceal bleeding.

“I was diagnosed with severe acid reflux and had to be cautious of which foods I ate to avoid being in pain. I was fortunate that my checkups were routine after the splenectomy up until I was in college.”
- Shawna, 24-year-old, living with ARPKD

“Over the years, my sons have tried to eat a low sodium diet, and also to drink a lot of water. Max drinks a gallon of water a day. Gabe has a harder time drinking that much water.” - Michelle, parent of 23- and 17-year-old sons living with ARPKD

When Alix’s son was only five, the doctors, *“were just trying to get him to drink as close to two liters of water as possible. I know adults that can't do that. ... That was the extent of what was available and what we could do, but we had to do something.”* - Alix, parent of an 11-year-old son living with ARPKD

Dietary modification and hydration downsides. Adhering to a low salt diet is difficult. There is no way to know if dietary modifications and hydration actually prevent or slow further kidney dysfunction, and these interventions do not protect the liver.

“Right now, our main focus again is just making sure he has enough water. I told this to someone yesterday, and they said, ‘I'd be really concerned if I left the doctor, and they said the best thing you can do is drink more water.’ But that is what we try and do, and just keep him at a healthy weight and a healthy diet.” - Alix, parent of an 11-year-old son living with ARPKD



Carolina focuses on a low sodium diet featuring fruits and vegetables at home, but her son wants to buy food at the school cafeteria and go out to eat with friends and family. *“All the moms will agree, we do our best at home, but it's the age that they eat out and they go to birthday parties.”* - Frank and Carolina, parents of a six-year-old son living with ARPKD

Dietary supplements. Patients and caregivers also reported using supplements including probiotics, vitamin K, multivitamins, renal vitamins, calcium, and nutritional support for those who are unable to absorb fat due to biliary disease. Some have reported experiencing vitamin deficiencies.

“I was more susceptible to bleeding because I had lower platelet counts due to the enlarged spleen. To help with this, my doctors put me on vitamin K to help with the clotting.” - Shawna, 24-year-old living with ARPKD

“He's got a lot of vitamin deficiencies related to him not absorbing his fat-soluble vitamins.” - Chris, parent of a three-and-a-half-year-old son who has had a kidney transplant

“My daughter was on sodium supplements as an infant as well as Bicitra [sodium citrate/citric acid] for hyponatremia and acidosis.” - Ashley B., parent of a six-year-old daughter living with ARPKD

Supplement downsides: People living with ARPKD must be very careful about avoiding anything that may further compromise organ function.

Counseling or psychotherapy. Almost half of those living with ARPKD selected counseling or psychotherapy in the polls as a way that they have tried to address ARPKD impacts. Therapy, along with other interventions have been helpful for some.

“She does a lot of different things that help. As a 13-year-old girl who is affected by this disease, it's very impactful for her at this age. Different things like that just to help with calming, just learning how to manage and mentally and emotionally deal with this disease as well and what it means for her.” - Elizabeth, parent of a 13-year-old daughter and nine-year-old son living with ARPKD



“When he was about eight or nine, he had a lot of panic attacks. We really think it's because of the disease, because at the time, he was having a lot of appointments, he was having a lot of issues. ...He had a lot of anxiety and then, over the years, he's had therapy, which has really helped.” - Michelle, parent of 23- and 17-year-old sons living with ARPKD

Physical and speech therapy. Many described receiving physical, speech, or occupational therapy for early intervention or to address developmental gaps. Even with these therapies, parents worry about their children's future.

“My son has been in PT and OT since he started school, and so it's almost like he's constantly trying just to keep up just physically and just with some of these things in school. And luckily, we've had fantastic physical therapists and occupational therapists and speech therapists. And he really tries so hard. ... I think early interventions and having the diagnosis and then also having that support structure within the schools to be able to assist and do that has been really helpful.” - Alix, parent of an 11-year-old son living with ARPKD

“By two years of age, he did not speak and required speech therapy.” - Colleen, parent of an adult son who has had two liver and kidney transplants

Spleen guard. Some respondents reported wearing a spleen guard around the abdomen to protect the spleen from damage or rupture.

“Soccer became his favorite sport. And this was made possible with a spleen guard, a hard piece of molded plastic individually fitted over the abdomen to protect his enlarged spleen that was displaced below his rib cage. These were periodically replaced with growth.” - Colleen, parent of an adult son who has had two liver and kidney transplants

“To add an extra layer of protection, I had a spleen guard I wore every single day everywhere I went. ... I was more susceptible to bleeding because I had lower platelet counts due to the enlarged spleen.” - Shawna, 24-year-old living with ARPKD

Feeding tube and feeding therapy. Some families described how their children had gastric tubes installed or other feeding supports to ensure that



they received enough nutrition. Sometimes feeding therapy is later required to adapt to eating by mouth.

After his double nephrectomy, Steven, “was fed via G-tube three times a day and overnight.” – Lindsey A., parent of a 12-year-old son who has had a kidney transplant

“We have gone through over a year of feeding therapy to get him to eat by mouth today, but the worry is still there, that the physical limitation of enlarged kidneys will keep him from eating enough.” - Alee, parent of a son living with ARPKD

Other ARPKD management approaches. CBD and **acupuncture** were also reported by some respondents. Some are not currently using any treatment.

“Max has also tried acupuncture over the years. Unfortunately, it's hard to know if the acupuncture, low sodium diet, and water intake has helped at all.” - Michelle, parent of 23- and 17-year-old sons living with ARPKD

Other symptom management approaches described during the meeting, include obtaining **support from the ARPKD community, preparing children to care for themselves in the future, taking the best care of themselves,** and **therapy dogs.**

Support through online communities. Many parents acknowledged the ARPKD community for providing both support and information. For many, the online ARPKD community is their primary source of information for learning about ARPKD symptoms and care approaches.

“Over the past few years, we have had the privilege of finding friends and the parents of other ARPKD babies with similar severity to Kai. They have become our community of support and truly our families. We commiserate during the late-night tears and wakeful hours when everyone else is fast asleep. I was able to find comfort with these families and this was often the only way I was able to truly discover which of Kai's symptoms fell within normal range.” - Kelsey, parent of a son who has had a kidney and liver transplant



After Elizabeth's daughter was diagnosed, *"We really had no clue, and we were not given a very good diagnosis at all whatsoever. But reaching out to people, we gained a little bit of hope, and we were able to be set up with providers who are knowledgeable."* - Elizabeth, parent of a 13-year-old daughter and nine-year-old son living with ARPKD

"I find hope by connecting with other parents and really following medical research and donating to organizations. And that helps me. It brings me some peace because it gives me that little sense of control over this thing that I have no control over." - Lindsey B., parent of a six-year-old son living with ARPKD

A downside of connecting with the community is finding out what can happen.

"Sometimes the internet is a wonderful place, but it can also be a really scary place. ... watching children in our community pass away waiting for transplants, or from other issues. And so that of course adds to the worry. And also seeing adults struggling through this disease as well, frequent hospitalizations, and infections. ... Seeing that is hard, but you can also learn from it, and prepare yourself." - Lindsey A., parent of a 12-year-old son who has had a kidney transplant

Preparing children to care for themselves. Caregivers want to ensure that their children take the best care of themselves, including taking their medication correctly, as they get older.

"Now that my oldest is going to adult care, he has to take more of this on versus me doing all of the appointments for him, and getting his medications, and monitoring. ... Mom being a little bit less involved. How we can figure that out, making us all happy with the doctor's appointments, knowing what medications they need to be on, and advocating for themselves." - Michelle, parent of 23- and 17-year-old sons living with ARPKD

"The next step for us is really understanding how to give her the best sort of support socially, psychologically, and then also prepare her for, ... the unknown. All of these things that could come, that they're not surprises to her, that she's ready and able to deal with them." - Joe, parent of a six-year-old daughter living with ARPKD



Taking the best care of themselves and therapy dogs

Shawna gets enough sleep, stays hydrated, exercises, and recognizes when her body needs to rest. *“I have been working out more, I try to be consistent at least three times a week. I do Orangetheory, but there's some days that ... I just know that no matter what I do, no matter how much water I've drank, I can just tell that my body is just not ready for that today, so I just maybe walk instead or just relax a little and just let my body rest. Just listening to what's going on.”* - Shawna, 24-year-old, living with ARPKD

“She's trained her dog to be her therapy dog. And I know that this helps lower her blood pressure and calm her. And she doesn't take him to school, but she does take him to a lot of different places.” - Lisa, parent of 13 and 9-year-old daughters living with ARPKD

There is an enormous unmet need for effective ARPKD treatments.

Meeting attendees used online polling to first indicate how well their current treatment regimen treats the most significant ARPKD symptoms, and to select the top three biggest drawbacks of their or their loved one's current treatment approaches. The results of both polls are shown in **Appendix 5 Q7 & Q8**, and the top response of both were consistent.

Treatments only help somewhat, treats some but not all symptoms, or are not very effective at treating target symptoms. In response to the first question, more than half of poll respondents stated that their treatment helped **somewhat**, and in the second poll, they specified that their treatment regimen **only treats some but not all symptoms** and are **not very effective at treating target symptom**. Parents and caregivers are frustrated by the lack of treatment options for ARPKD, that treatments are ineffective, and by not being able to tell if the treatments are making any difference.

“She's on four blood pressure medicines a day. She takes some in the morning, some at night. ...I feel that the blood pressure medicines help definitely somewhat, but not enough to ever get it to where her blood pressure is supposed to be. ...Sadly, none of this is a treatment.” - Lisa, parent of 13- and 9-year-old daughters living with ARPKD

“Except for improvements in generalized care for prenatal, renal and transplant, treatment for this disease has not changed since my son's



birth. There are no specific treatments for ARPKD.”- Colleen, parent of an adult son who has had two liver and kidney transplants

“There wasn't a medication to get rid of the varices. The only way that I could manage this was by avoiding foods that could be sharp like potato chips and by having a plan of action to stop the bleeding if they ruptured.” - Shawna, 24-year-old, living with ARPKD

A minor percentage of ARPKD families indicated that their medical treatment helped to a great extent, however most were families whose children had kidney transplants. They again reminded others that sometimes a transplant doesn't solve all the medical issues.

“Despite all of his [kidney transplant] challenges, Steven's living his best 12-year-old life. He rides the bus to school, attends the same classes as his peers, plays sports, loves cars and his dog. Without knowing his past, you'd have no idea this boy has braved so much in his short life.” – Lindsey A., parent of a 12-year-old son who has had a kidney transplant

“I was able to donate a kidney to him when he was 16 months old. Soon, he was sitting up, trying to mobilize, alert and curious, and playing like he never had before. The fog had been lifted. He finally walked at two years old. Although his is not an easy life, it is a full wonderful life, and he's the absolute light of our lives.” - Ashley A., parent of a three-and-a-half-year-old son who has had a kidney transplant

After her son's transplant, *“He really turned into a different kid in a lot of ways. He had a lot more energy, he was a lot more just alert, and he also got his appetite back. ... And I'd say diet and energy level were the biggest things [to improve his] quality of life.” - Erin, parent of an 11-year-old son who has had a kidney transplant*

Side effects. Medications and medical treatments side effects can sometimes impact other important organs, making treatments feel like a trade off.



“Some medicines I have to take have a ton of side effects that affect our quality of life, including headaches, nausea, dizziness, and I have even fainted several times.” - Jaina, 13-year-old living with ARPKD

“When he was 17, the doctor started him on a medication to help with portal hypertension, but nobody told him that this would affect him being able to push himself when running. His times got worse. It really affected him mentally until we finally asked the doctor, who confirmed that that was a problem.” - Jennifer, parent of a 19-year-old son living with ARPKD

“The more blood pressure medicines you take, the worse your kidneys get because they're damaging your organs. It's kind of a trade-off to see, well, how is her heart doing? Is her heart okay now? Then we're going to stay at four before we add another one. ...To add one more medication, you have to weigh the risks with the benefits.” - Lisa, parent of 13- and 9-year-old daughters living with ARPKD

Requires too much effort and/or time commitment. Patients living with ARPKD have to endure a great deal of medical testing and monitoring including regular blood tests, urinalysis, ultrasounds to monitor the abdomen and kidneys, as well as blood pressure monitoring. Some younger patients are terrified and resistant. Many families live far away from kidney or liver centers, so must travel several times a year for check-ups and testing. ARPKD related healthcare takes time and effort to manage all the different medications and to get younger children to take them at the right time.

“I've never known a life without having giant kidneys. I go to the doctor a lot and get a bunch of blood draws. I always try to be tough when I have to have blood draws and scans.” - Chesley, nine-year-old living with ARPKD

“For about the first six years of his life, his treatment was 13 different medications. ... That was really challenging because some were refrigerated, some were not. They all expired at different times, and it was constantly juggling these meds. A lot of them didn't taste great. ...They had to be taken at different points throughout the day, was a challenge.” - Erin, parent of an 11-year-old son who has had a kidney transplant



“During these appointments, he needs to have his blood work to check his kidney function. I’m sure you can imagine how fun it is to explain to the toddler why they have to let the nice person stick the needle in their arm.” - Julie, parent of a five-year-old son living with ARPKD

Route of administration. Administering large amounts of medications to small children can be challenging, especially if children have a lot of belly pain, nausea, and vomiting. Teaching and trusting adolescents and young adults to take their medications on their own is also a challenge.

“She’s on three blood pressure medicines, she’s on ursodiol, she’s on iron, all of these twice a day. ... It’s not an uncommon thing for her to take her medications and then vomit them up later.... And so that’s our biggest problem right now is that the pain and the uncomfortable aspect of having such a large abdomen and how that impacts with her medications.” - Ashley B., parent of a six-year-old daughter living with ARPKD

“Taking 12 pills a day is hard to remember to do, and then I have to make sure I eat with them, and I still get sick to my stomach almost every single morning and night of my life. I know all of my medicines by name and I’m very responsible and mature.” - Jaina, 13-year-old living with ARPKD

Jordan told his son, *“You did an amazing job of taking your meds, six, eight, 10 pills every day. You’ll have to take these pills for the rest of your life, no question about it. Hopefully you always will, and when you get older, you’ll continue to take your medicines because lots of teenagers forget, and they lose their kidneys as a result.” - Jordan, parent of a nine-year-old son who has had a kidney transplant*

Other treatment drawbacks. Other treatment drawbacks that not previously described in the medication section (starting on page 27) and not included as poll response options include **contraindications**, and **access challenges**. Importantly, not one person selected **not applicable as I am not using any treatments**.

Contraindications. This can include not being able to take medications or supplements excreted through the kidneys or liver.



"We always have to balance the reason for the medication and the potential adverse effects on the kidneys or liver." - Logan, parent of a 10-year-old child living with ARPKD

"I was not a suitable candidate for the medication options available to slow ARPKD. One of the medications directly impacts and could further damage my liver, and as someone who also has congenital hepatic fibrosis, this medication would not be worth the risk. The other medication would lower my blood pressure to a dangerous level."- Shawna, 24-year-old, living with ARPKD

"I don't want to introduce a supplement that isn't tested, or we don't know how it's going to impact one organ or the other. The tricky thing and the scary thing with ARPKD is that both kidney and liver are affected, so anything you ingest, whether it's a medication or food, it's going to be processed through one or the other or both. While it may help one organ, it may hurt the other organ, and finding that balance is really scary." - Alix, parent of an 11-year-old son living with ARPKD

Short of a complete cure, people living with ARPKD would like a treatment to prevent kidney and liver disease progression.

The top three choices from polling were all related to stopping or slowing kidney and/or liver disease progression, which includes delaying the time to, or avoiding dialysis or transplant. Results are in **Appendix 5 Q5** and shown below with patient quotes.

Prevent kidney disease progression, delay time to or avoid dialysis and transplant. The top three selected poll responses are all related to slowing disease progression to prevent the more severe ARPKD manifestations. Some wished that this treatment could be in a pill.

"For [my grandson's] situation, I think a huge help would be something that would slow, or preferably stop, the progression of the disease and its impact on other organs. ... If progression can be slowed, then there is more time to develop a cure before the disease has progressed to the need for a transplant or dialysis." - Katy, Grandmother of a 10-year-old boy living with ARPKD



“Anything that just extends his native kidneys, and his native liver for as long as possible, so that the medical [technology and knowledge] can catch up would be great.” - Alix, parent of an 11-year-old son living with ARPKD

“My long-term goal, I think would be, to prolong the life of the kidneys as long as possible. ... I have two kids that have this. And, I only have one kidney [to donate]. And my husband has one kidney [to donate]. And we each have half a liver [to donate]. So, I don't know how we're supposed to cover all our kids with our little bit of organs.” - Lisa, parent of 13 and 9-year-old daughters living with ARPKD

In addition, patients and families would like more research into transplant alternatives including prosthetic or synthetic organs.

“I'm just so hopeful that the medical community will be able to progress where they can make him his own kidney out of his own stem cells. That was science fiction many years ago. They're talking about this in the real world.” - Alix, parent of an 11-year-old son living with ARPKD

“Outside of a cure would be getting as advanced as finding some level of prosthetic kidneys, or prosthetic livers.” - Frank and Carolina, parents of a six-year-old son living with ARPKD

Prevent liver disease progression and delay time to transplant. Preventing liver disease progression may help to mitigate some of the liver-related symptoms including varices.

“Overall, I believe the liver side of this disease needs more understanding and treatment options.” - Anonymous, parent of a daughter living with APRKD

“We live with the knowledge and fear that ARPKD invariably affects the liver in all children. Though the cysts will not recur in his transplanted kidney, his disease continues in his liver. It may eventually lead to cirrhosis and a need for a liver transplant to survive. And there is no equivalent to dialysis for liver disease. There are currently no treatment options to help delay or stop the progression of his liver disease. And therapeutic options for the management of liver disease



and ARPKD is a critical need.” - Ashley A., parent of a three-and-a-half-year-old son who has had a kidney transplant

“I would like to see a treatment that targets and slows the progression of the liver disease (CHF) as well as ARPKD in the kidneys.” - Shawna, 24-year-old, living with ARPKD

Some mentioned the potential use of CRISPR gene editing technologies to prevent CHF.

“Gene editing techniques to where you could deliver a CRISPR package, maybe with a hepatitis virus, or an adenovirus, or something that would go to the liver, and maybe potentially alleviate a lot of the congenital hepatic fibrosis symptoms that these kids have, because the treatments aren't great.” - Chris, parent of a three-and-a-half-year-old son who has had a kidney transplant

Reduction of other symptoms including fatigue, spleen enlargement and immune suppression.

“We'd like our 10-year-old to have the energy so he shouldn't miss out on other activities.” - Logan, parent of a 10-year-old child living with ARPKD

“Would like the ability to be in public without a big risk to immunity, specifically talking post-transplant.” - Kai, individual who has had a liver transplant

“One of the things that I'd really be interested in is the decreasing the progression of varices. ... We're doing endoscopies now multiple times a year because each time we've had one, they have found them.”- Ashley B., parent of a six-year-old daughter living with ARPKD

“Treatment options for the rapidly growing kidneys that can occur with ARPKD is a critical need.” - Ashley A., parent of a three-and-a-half-year-old son who has had a kidney transplant

Other important ARPKD treatment and research needs. ARPKD families identified many additional important treatment and research needs including **better methods to measure blood pressure more accurately in**



small patients, better access to appropriate care, more research, information, and more clinical trials.

Better methods to measure blood pressure more accurately in small patients. Parents and caregivers would like there to be more awareness about the possibility of high blood pressure in infants and small children, as some felt that concerns about their child's blood pressure were dismissed.

"What I hope to the future, ... some type of monitor that can be worn similar to how a Dexcom is with diabetes, something that could monitor blood pressure. Our big issue is that we can never get his blood pressure ever." - Brittany, parent of a son recently diagnosed with ARPKD

Elizabeth's daughter's high blood pressure was dismissed and was told, *"Well, she's upset." 'She is in a weird environment where it could cause that to be higher.'* - Elizabeth, parent of a 13-year-old daughter and nine-year-old son living with ARPKD

Better access to appropriate care. ARPKD families spoke about the challenges of finding and gaining access to nephrologists and other medical specialists who are familiar with ARPKD. One parent suggested a multidisciplinary kidney clinic, where a patient could see all the specialists in one place on the same day.

"These kids go to seven, eight, sometimes, doctors. In one month, we had 15 different doctor appointments. And my poor child is trying to go to school. ... If it would be possible to have a clinic where doctors could be in the same place at the same time, that would be super helpful to make these kids just feel more of a normal life." - Lisa, parent of 13- and 9-year-old daughters living with ARPKD

"I live about three hours away from the University of North Carolina. That's where my son's nephrologist is. We don't even have a nephrologist in the town I live in, or within a 45-mile radius. For appointments, I am constantly driving about three and a half hours there, three back." - Brittany, parent of a son recently diagnosed with ARPKD

More research and information about optimal diets and lifestyles for those living with ARPKD. This research could include ways to support children who



have problems gaining weight or have difficulties digesting fat. ARPKD families would also like more resources specifically for the parents of newly diagnosed children as well as for their family physicians.

"In addition to new medications, I believe it could be beneficial to have clear more specific diet and exercise recommendations that aren't just to simply 'drink lots of water'." - Shawna, 24-year-old, living with ARPKD

"More guidance on diet. Additives and specific items to avoid. Renal diet suggestions vary widely it seems." - Edward, parent of a child living with ARPKD

Alix specifically wants more information about optimal amounts of protein for growing children and on phosphates and preservatives specifically for those with ARPKD. *"I would love more research on nutrition! ... Most advice makes people afraid of food. Give us something that we can use in a practical way and talk to us like we are resilient... Is there a way for parents to space out meals to optimize protein and nutrient intake? ... What would a child Macro chart look like?" - Alix, parent of an 11-year-old son living with ARPKD*

"There are so many new moms that we meet or pregnant women that type into the Facebook page and they ask, 'What do I do? What can I ask my doctor for?' And I wish that there was something we could say, 'Go ask your doctor for this.' [I wish we could] give them information, tips, and things to look at like steroid shots and things." - Alix, parent of an 11-year-old son living with ARPKD

More clinical trials for those living with ARPKD.

"My short-term wish would be more clinical trials. ...I know there's lots of people that are very willing to continue participating in studies if it's going to, maybe not help our children because we have to have a place where our research is showing us how to finally find that cure. We don't know what's helping and what's not." - Lisa, parent of 13- and 9-year-old daughters living with ARPKD

"It is time for science to step up and do their part. Right now, there's nothing available in the form of clinical trials. ...If there were any experimental therapies out there, we would certainly take a very hard look at them because it could mean giving you an even better quality



of life or the next generation of ARPKD kids.” - Jordan, parent of a nine-year-old son who has had a kidney transplant



INCORPORATING PATIENT INPUT INTO A BENEFIT RISK ASSESSMENT FRAMEWORK

The ARPKD EL-PFDD meeting helped to increase the understanding of how ARPKD impact patients and their loved ones. The meeting also reinforced the continued unmet medical need in this community. **Table 1** speaks to the disease burden that patients living with ARPKD endure. It serves as the proposed introductory framework for the Analysis of Condition and Current Treatment Option to be adapted and incorporated in the FDA's Benefit-Risk Assessment. This may enable a more comprehensive understanding of these disorders for key reviewers in the FDA Centers and Divisions who would be evaluating new treatments for ARPKD. The data resulting from this meeting may help inform the development of ARPKD-specific, clinically meaningful endpoints for current and future clinical trials, as well as encourage researchers and industry to investigate better treatment.

The information presented captures the perspectives and collective hopes of people living with ARPKD for future research and successful new product development. Note that the information in this sample framework is likely to evolve over time.

"I want the world to know about our children! That children are dying of kidney disease and are dying waiting for transplants and are struggling every single day with this awful disease. Our children deserve the funding, attention, and awareness that other pediatric diseases receive." - Lindsey A., parent of a 12-year-old son who has had a kidney transplant



TABLE 1: Benefit-Risk Table for Autosomal Recessive Polycystic Kidney Disease (ARPKD)

	EVIDENCE AND UNCERTAINTIES	CONCLUSIONS AND REASONS
ANALYSIS OF CONDITION/ IMPACTS ON ACTIVITIES OF DAILY LIVING	<p>ARPKD is a rare genetic disorder. The clinical course of ARPKD is highly variable and can present any time from before birth to adulthood. An ARPKD diagnosis is traumatic, and consequences can be tragic. The disease is progressive and affects the kidneys as well as the liver.</p> <p>Most individuals living with ARPKD experience a large number of disease-related health concerns. Kidney failure and high blood pressure are the most bothersome, followed by liver problems including congestive hepatic fibrosis (CHF). Many patients also experience enlarged kidneys, gastrointestinal problems, fatigue, anxiety/depression, enlarged spleen, growth failure, breathing issues, immunosuppression, pain, and premature death. Signs and symptoms worsen as kidney and liver disease in ARPKD progress.</p>	<p>ARPKD has an incredible disease burden. The disease is progressive, and new symptoms are likely to appear. Most children cannot fully participate in sports, school, and social activities due to fatigue and the risk of injury or pressure from their enlarged organs. Many miss out on school because of illness and frequent care appointments. Some who are living with the disease have a sense of being different and do not want to draw attention to their needs. Many find it hard to make longer term plans as their future is uncertain.</p> <p>ARPKD families have many worries: disease progression leading to premature death, needing a kidney and/or liver transplant or dialysis, and worsening symptoms. Many parents worry about their child’s uncertain future and some feel like their child is living on borrowed time.</p>



CURRENT TREATMENT OPTIONS/ PROSPECTS FOR FUTURE TREATMENTS	<p>There are no FDA-approved treatments to stop ARPKD disease progression. Patients rely on many medications and medical procedures for symptom management: blood pressure medications, growth hormone, dialysis, splenectomies, prescription of iron supplements, and others. Other approaches include low salt diet, dietary modifications, and hydration. Most patients will do everything they can do to spare their organs.</p> <p>Ultimately, many patients will require a kidney transplant, a liver transplant or even a combined liver-kidney transplant. The ARPKD community emphasized that transplants are not curative but a trade off of one chronic condition for another. Many children have received kidney and liver transplants from their parents; donated organs have a finite lifespan and eventually need to be replaced.</p>	<p>ARPKD families are frustrated by the lack of treatment options. Treatments only help somewhat, only treat some of the symptoms, and it can be challenging to tell that they are working. Most treatments have many side effects, and the amount of monitoring is excessive.</p> <p>The ARPKD community needs treatments that prevent progression of kidney and liver disease, to delay dialysis and transplantation. The community needs symptom-reducing treatments, better treatments, more information and more research, especially more clinical trials.</p>
See the Voice of the Patient report for a more detailed narrative.		

Appendix 1: ARPKD EL-PFDD Meeting Agenda

Meeting date and time: August 29, 2023, 10 a.m. – 3 p.m. EST

This meeting held virtually in order to give all members the ARPKD community an opportunity to attend and participate. A recording of the meeting is available at [ARPKD PFDD 2023 | PKD Foundation \(pkdcure.org\)](https://www.pkdcure.org/ARPKD-PFDD-2023). The meeting was cohosted by Susan Bushnell, the CEO and President of the PKD Foundation, and James Valentine, Esq. from Hyman, Phelps & McNamara, P.C.

Welcome - *Susan Bushnell, PKDF President and CEO*

FDA Opening Remarks - *Dr. Kirtida Mistry*

ARPKD clinical overview - *Dr. Erum Hartung, Children’s Hospital of Philadelphia*



Session 1 – Living with ARPKD Symptoms and Daily Impact

- Patient/Caregiver Panel 1
- Audience polling & moderated discussion

ARPKD treatment overview - *Dr. Max Liebau, University Hospital of Cologne*

Session 2 – Current and Future Treatments for ARPKD

- Patient/Caregiver Panel 2
- Audience polling & moderated discussion

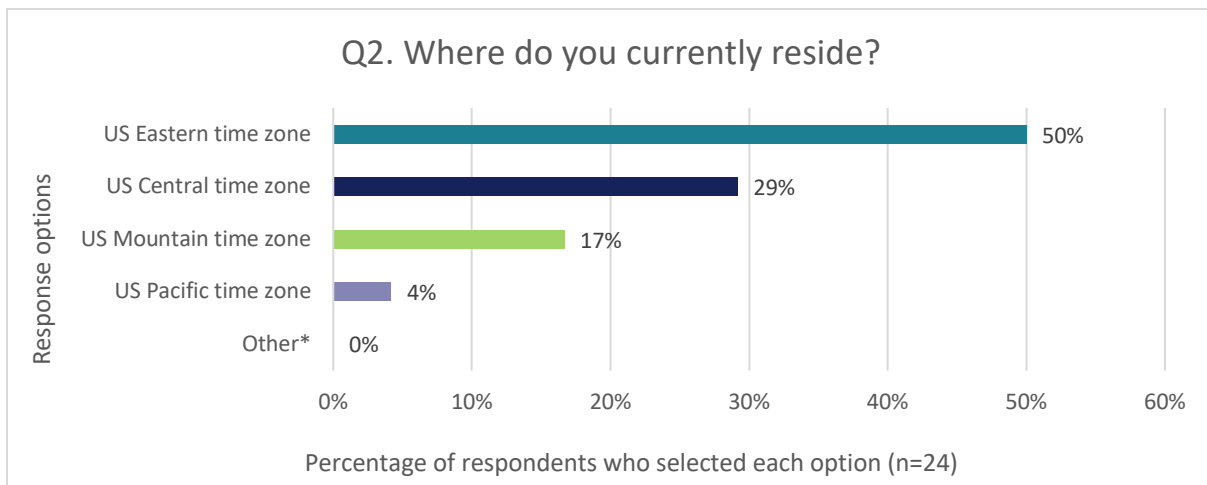
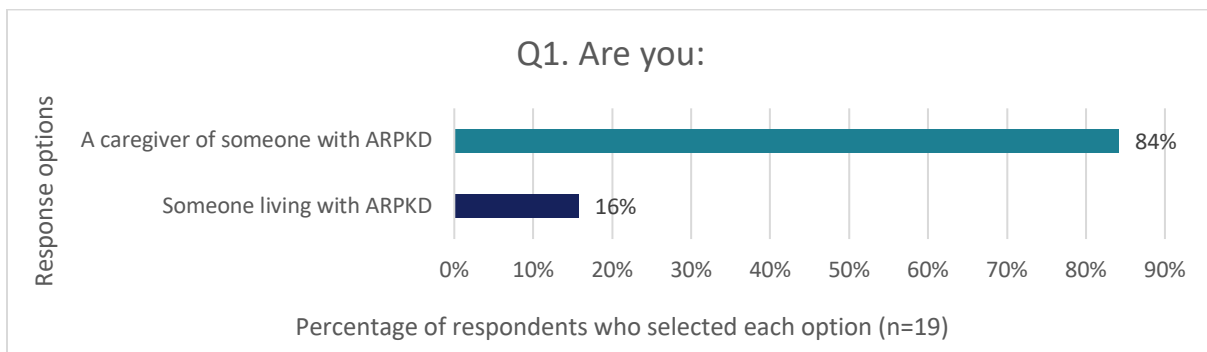
Meeting Summary - *Larry Bauer, RN, MA Hyman, Phelps, & McNamara*

Closing Remarks - *Susan Bushnell, PKDF President and CEO*

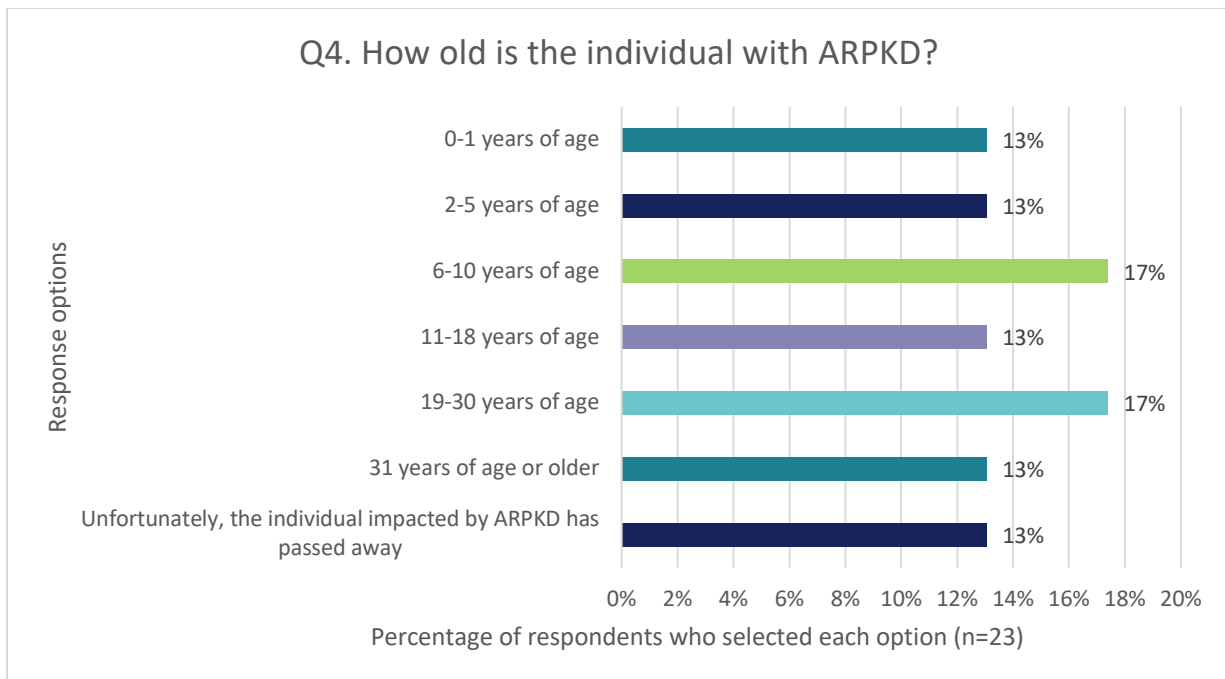
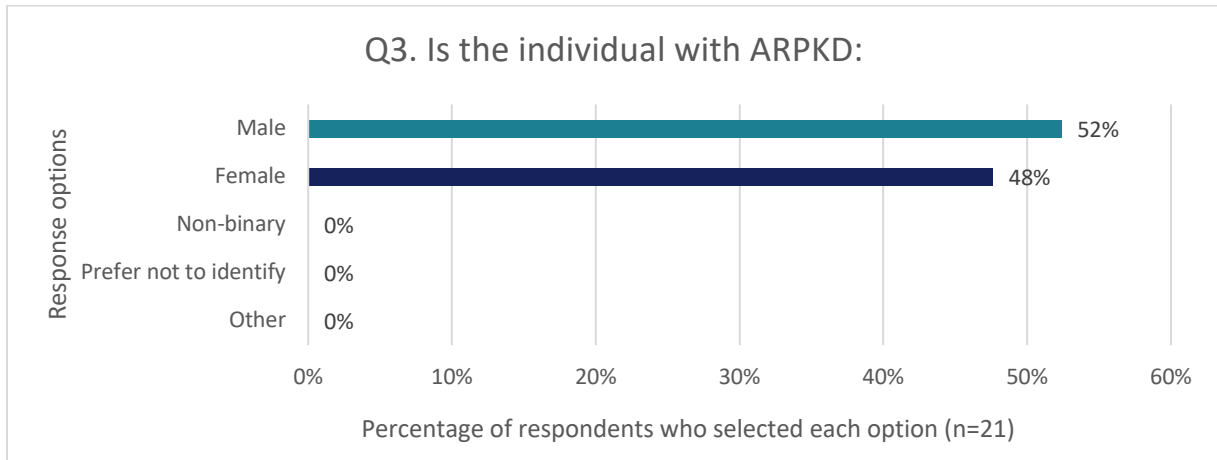
Appendix 2: Demographic questions

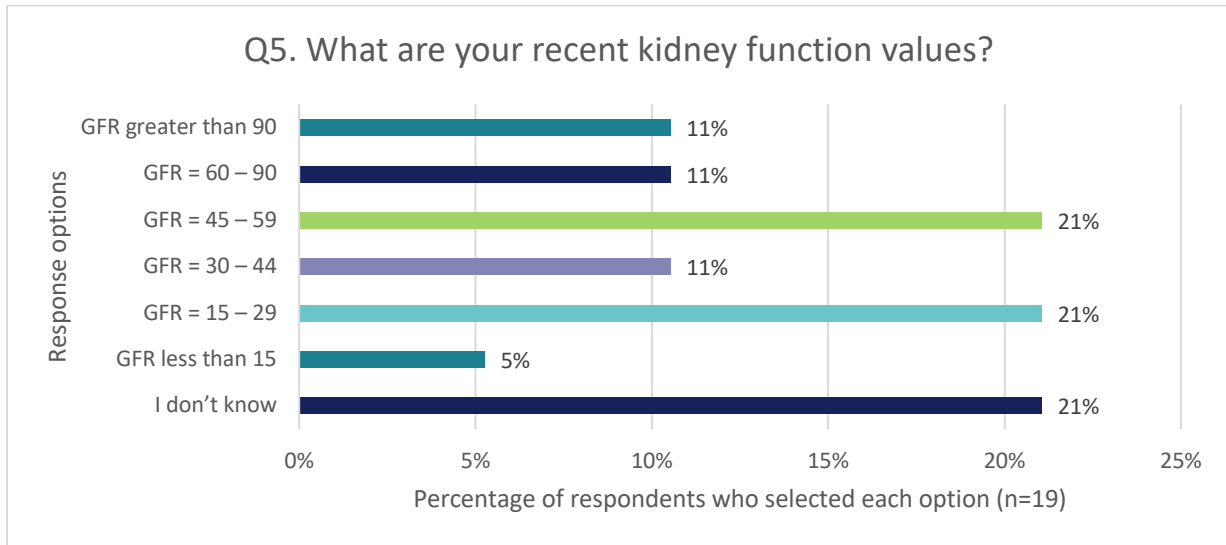
The graphs below include patients, parents, and caregivers who chose to participate in online polling at the August 29, 2023, meeting. The number of individuals who responded to each polling question is shown below the X axis (N=x).

While the response rates for these polling questions is not considered scientific data, it provides a snapshot of those who participated in the ARPKD EL-PFDD meeting. Note that meeting demographics are dynamic and may have changed as more individuals joined the meeting.



*US Alaska and Hawaiian time zones, Canada, Mexico, Europe, Asia, and Middle East were offered as poll response options but were not selected by any of the poll respondents.







Appendix 3: Meeting Discussion Questions

TOPIC 1 – LIVING WITH ARPKD: SYMPTOMS AND DAILY IMPACT

1. Of all the symptoms and health effects of ARPKD, which 1-3 symptoms have the most significant impact on you or your loved one's life?
2. How does ARPKD affect you or your loved one on best and on worst days?
3. How has your or your loved one's symptoms changed over time? How has the ability to cope with the symptoms changed over time?
4. Are there specific activities that are important to you or your loved one that you cannot do at all or as fully as you would like because of ARPKD, CHF or other related conditions?
5. What do you fear the most as you or your loved one gets older? What worries you most about you or your loved one's condition?

TOPIC 2 – PERSPECTIVE ON CURRENT AND FUTURE APPROACHES TO TREATMENT

1. What are you currently doing to manage your or your loved one's ARPKD and its symptoms?
2. How well do these treatments treat the most significant symptoms and health effects of ARPKD?
3. What are the most significant downsides to your or your loved one's current treatments and how do they affect daily life?
4. Short of a complete cure, what specific things would you look for in an ideal treatment for ARPKD? What factors would be important in deciding whether to use a new treatment?



Appendix 4: ARPKD EL-PFDD Panelist and Callers

Please note: second initials were assigned when patients, parents or caregivers shared the same first name.

Session 1: Pre-Recorded Panelists

- Lisa, parent of 13- and 9-year-old daughters living with ARPKD
- Jaina, 13-year-old living with ARPKD
- Chesley, nine-year-old living with ARPKD
- Lindsey A., parent of a 12-year-old son who has had a kidney transplant
- Kelsey, parent of a son who has had a kidney and liver transplant
- Beth and Mike, parents of a son who passed away at the age of 10 years from ARPKD complications
- Julie, parent of a five-year-old son living with ARPKD and a son who passed away a few hours after birth from ARPKD

Session 1: Zoom Panel

- Amy, parent of an 11-year-old daughter living with ARPKD
- Lindsey B., parent of a six-year-old son living with ARPKD
- Joe, parent of a six-year-old daughter living with ARPKD
- Shawna, 24-year-old living with ARPKD
- Michelle, parent of 23- and 17-year-old sons living with ARPKD

Session 1: Callers

- Lisa, parent of 13- and 9-year-old daughters living with ARPKD
- Lindsey A., parent of a 12-year-old son who has had a kidney transplant
- Jennifer, parent of a 19-year-old son living with ARPKD

Session 2: Pre-Recorded Panelists

- Shawna, 24-year-old living with ARPKD
- Michelle, parent of 23- and 17-year-old sons living with ARPKD
- Jordan, parent of a nine-year-old son who has had a kidney transplant
- Colleen, parent of an adult son who has had two liver and kidney transplants
- Ashley A., parent of a three-and-a-half-year-old son who has had a kidney transplant

Session 2: Zoom Panel

- Lisa, parent of 13- and 9-year-old daughters living with ARPKD
- Alix, parent of an 11-year-old son living with ARPKD
- Elizabeth, parent of a 13-year-old daughter and nine-year-old son living with ARPKD



- Frank and Carolina, parents of a six-year-old son living with ARPKD
- Ashley B., parent of a six-year-old daughter living with ARPKD

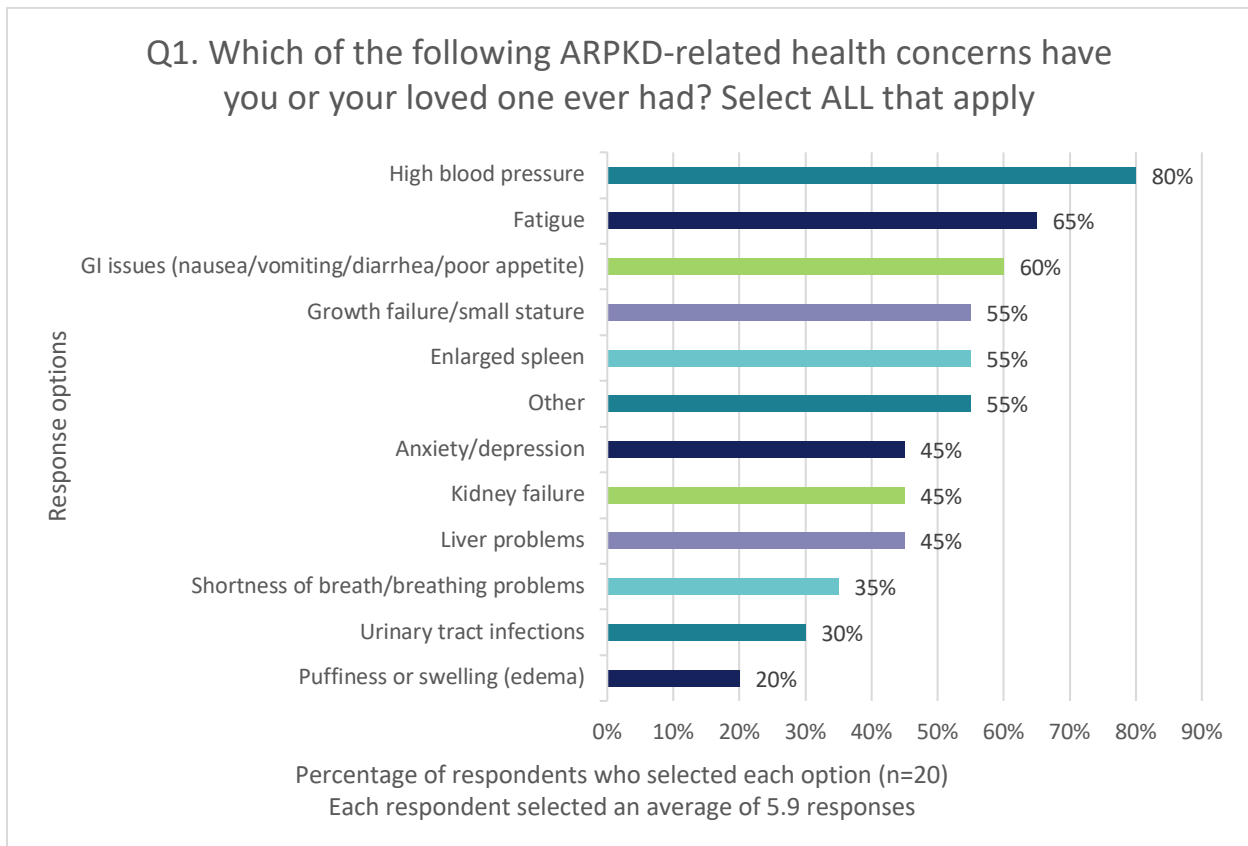
Session 2: Callers

- Erin, parent of an 11-year-old son who has had a kidney transplant
- Chris, parent of a three-and-a-half-year-old son who has had a kidney transplant
- Brittany, parent of a son recently diagnosed with ARPKD

Appendix 5: Meeting Poll Results

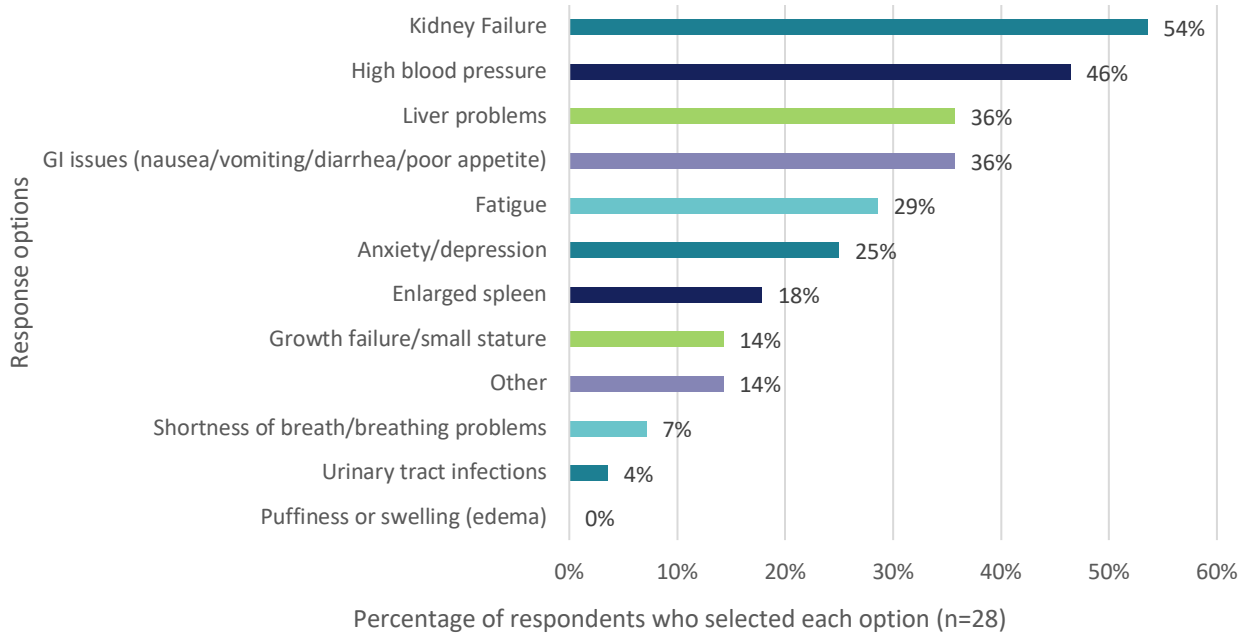
The graphs below include patients, parents, and caregivers who chose to participate in online polling during sessions 1 and 2. The number of individuals who responded to each polling question is shown below the X axis (N=x). The responses for these polling questions are not considered scientific data. These are intended to complement the patient comments made during and after the meeting.

Response options selected by more than 50% of poll respondents are shown in **turquoise**.

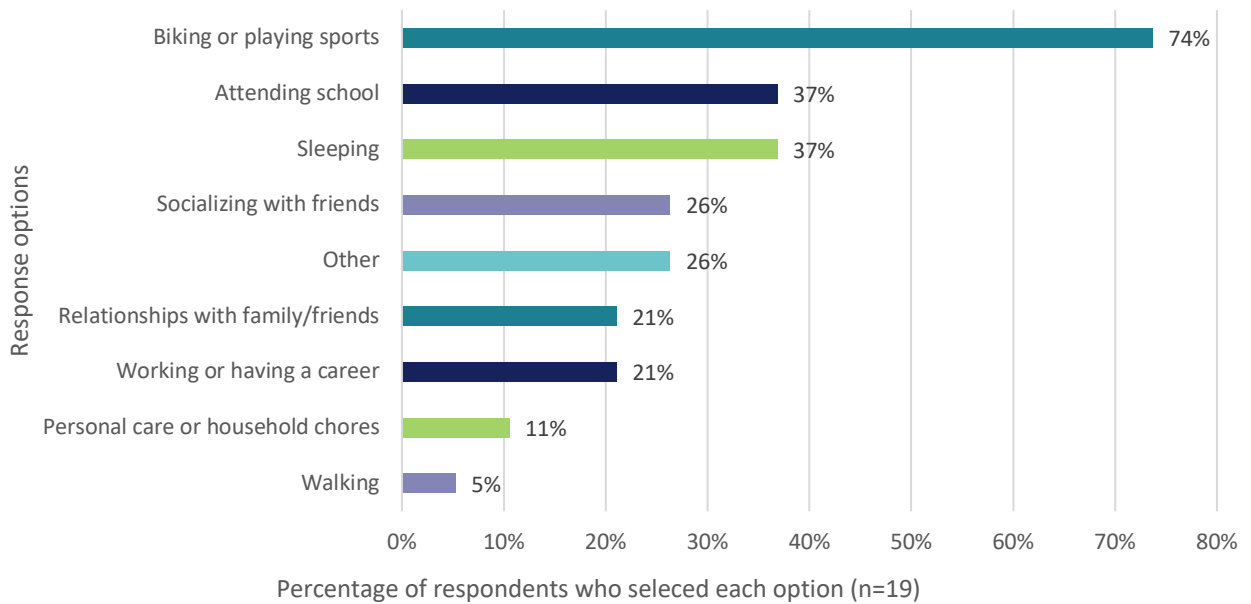




Q2. Select the TOP 3 most troublesome ARPKD-related health concerns that you or your loved one have ever had. Select up to 3

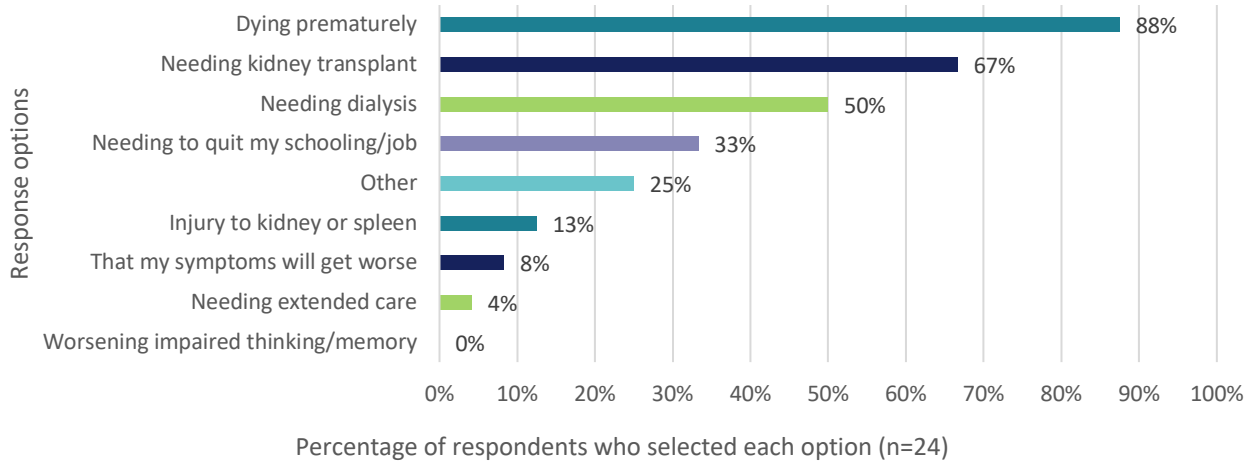


Q3. What specific activities are you or your loved one NOT able to do or struggle with due to ARPKD? Select TOP 3

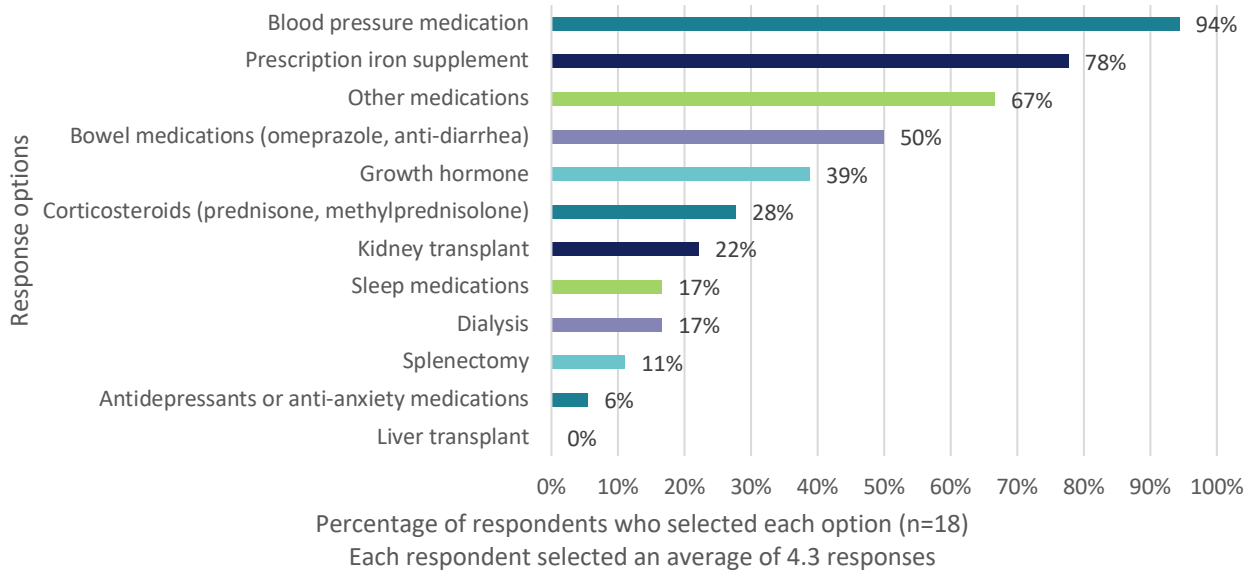




Q4. What worries you most about you or your loved one's condition in the future? Select TOP 3

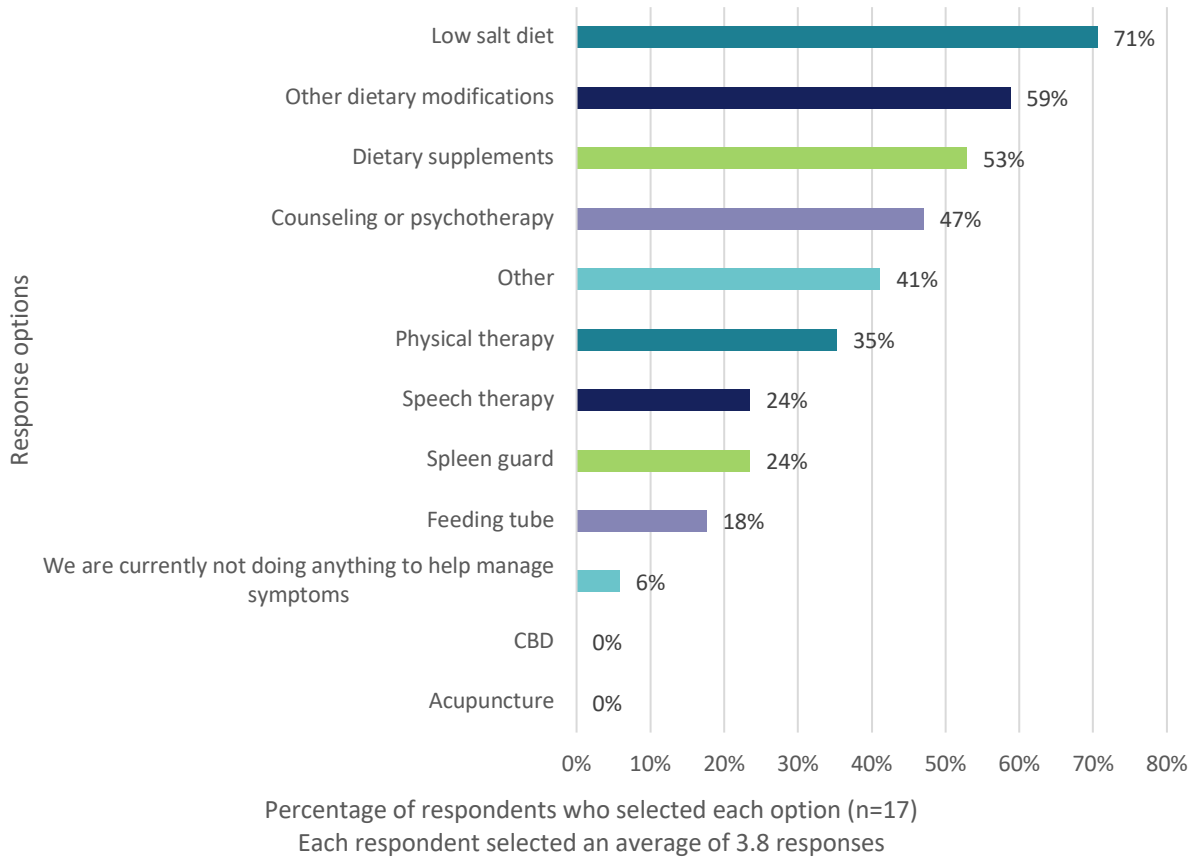


Q5. What medications or medical treatments have you used (currently/previous) to treat symptoms associated with ARPKD, CHF or other related conditions? Select ALL that apply

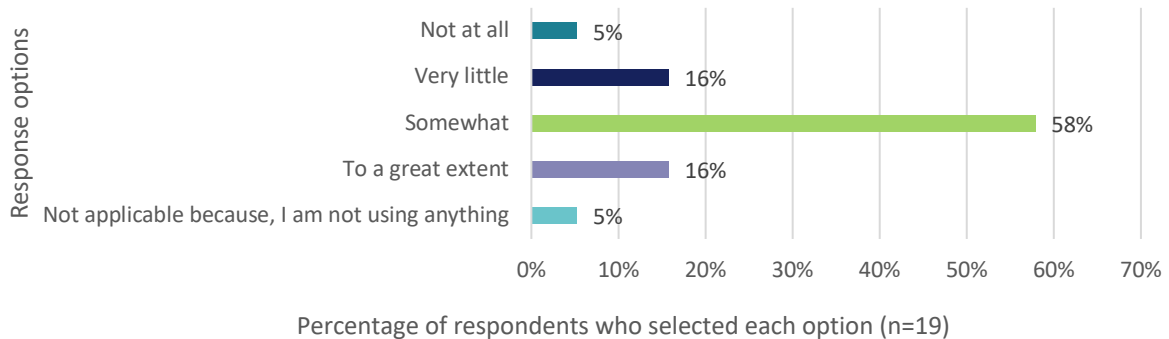




Q6. Besides medications and treatments (currently or previously), what have you or your loved one used to help manage the symptoms of ARPKD, CHF or other related conditions? Select ALL that apply

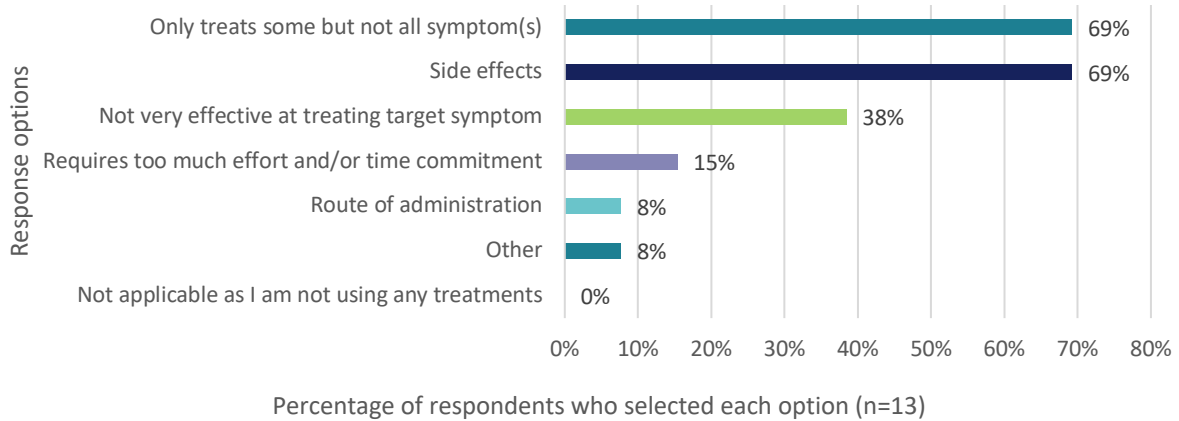


Q7. How well does your current treatment regimen treat the most significant symptoms of ARPKD?

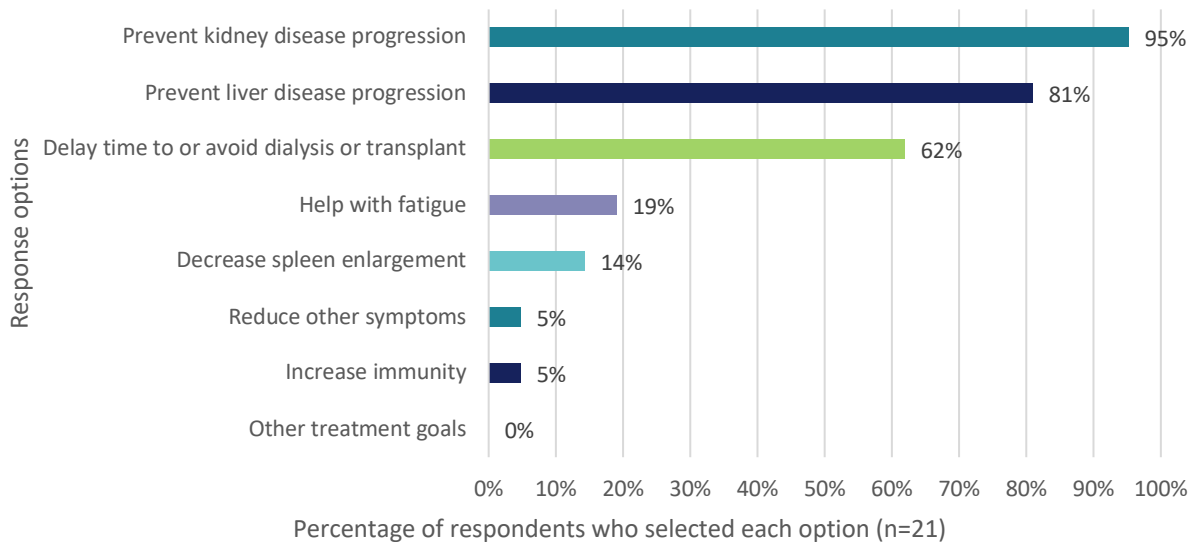




Q8. What are the biggest drawbacks of your or your loved one's current approaches? Select UP TO 3



Q9. Short of a complete cure, what specific things would you look for in an ideal treatment for ARPKD or related conditions? Select TOP 3





Appendix 6: Additional Patient Comments

To include as many patient voices and perspectives as possible, patient comments were collected through an online comment submission portal before, during, and for four weeks after the meeting. All submitted patient comments are compiled in this appendix, with selected comments included in the main body of the *Voice of the Patient* report.

Alix, parent of an 11-year-old son living with ARPKD

I would love more research on nutrition! So much of what is out there is directed at "the typical American diet" (e.g., lots of red meat, which is not typical for our family) or overweight adults with ADPKD. Most advice makes people afraid of food (e.g. the oxalates in spinach are shown to have a negative effect in mice). What am I supposed to do with that information as a parent? We've also been told not to have too much protein. How much protein should my growing child aim for in a day? Give us something that we can use in a practical way and talk to us like we are resilient. The average adult kidney can handle 25 grams of protein in an hour. What is it for kids by age, or height and weight? Is there a way for parents to space out meals to optimize protein and nutrient intake? Many families do this already for kids with larger bellies as their kids can't physically take in too much food in a sitting. What would a child Macro chart look like? The word diet can have such a negative connotation, especially for children, but personally, we are raising our son to understand that what he puts in his body matters and there are ways to be a kid and enjoy food, like pizza and cake at birthday parties, without overdoing it. Lastly, more information on phosphates and preservatives. We know these things are impacting the kidney, liver, colon, etc. What does this do to the PKD body? Especially growing kids? Thank you!!

The ARPKD/CHF Community would benefit from having more data around how Cholangitis specifically impacts AR patients who have more liver involvement. We need better testing and better treatment options.

Everything I have is anecdotal, but I've noticed a trend. Kids get reoccurring fevers, often over a series of months. The frustrating thing is most of these families' concerns about cholangitis are dismissed for two reasons; 1. Cholangitis is rare (But you're telling this to people who have kids with a rare disease) and 2. AR kids don't present like a typical cholangitis case; meaning that they don't have jaundice and their liver labs look normal. Some families



have said that one doctor will suggest the possibility of cholangitis, only to be immediately dismissed by another doctor.

My understanding is that the way to formally diagnosed is through a liver biopsy. That is extremely invasive and from what I understand, has a risk of spreading the infection.

A few people mentioned getting an MRCP test, which is an MRI that can look at the bile ducts.

The standard course of treatment is antibiotics. Unfortunately for one parent who had a child with a reoccurring case, they ended up putting in a pic line, but it still came back, and the child is now on a low-grade prophylactic antibiotic. I know the story of this parent personally. They had to weigh the choice of keeping their kid on a long-term antibiotic versus having them in the hospital every month.

Lastly one person mentioned that their child had been in and out of the hospital with low-grade fever. They felt that due to the size of the kidneys and liver the child is not able to completely expel their poop by themselves and the buildup could've been causing the problems. They said they've had success using daily laxatives, and a high dose probiotic as a preventative. Constipation and the use of laxative, and probiotics is pretty common within this group. One person specifically mentioned Symprove probiotic.

Ellen, parent of a child with ARPKD

This disease is like death by a thousand cuts. As soon as you reach an equilibrium with a new symptom/ problem, there is something else to deal with. Some issues could have been mitigated, at least somewhat, had I been aware of the possible problem (i.e. osteoporosis due to parathyroid issues and a low potassium diet). What really scares me is that as a retired science supervisor, with a biology background, I never realized that this would be a problem, so what does that mean for less educated patients. Nobody warns you of the multiple domino health issues, but really doctors and other health professionals should be more proactive in educating their patients.

Lindsey A., parent of a 12-year-old son who has had a kidney transplant

I want the world to know about our children! That children are dying of kidney disease and are dying waiting for transplants and are struggling every single



day with this awful disease. Our children deserve the funding, attention, and awareness that other pediatric diseases receive.

Ashley, parent of a daughter living with ARPKD

My daughter was on sodium supplements as an infant as well as bicitra for hyponatremia and acidosis.

Lisa, parent of 13- and 9-year-old daughters living with ARPKD

When my girls were first diagnosed and we were completely devastated, someone found this great, inspirational video on Youtube made by Devon, a girl who had ARPKD. It gave us hope for our girls that they could possibly live a semi-normal life. After doing more research, we learned she died suddenly at her home, shortly after being married. Since then, we have found so many of these kids don't make it through their 20's. I still feel like each day with our girls is a blessing and we are on borrowed time.

Anonymous, parent of a daughter living with ARPKD

Which ARPKD symptoms have the most significant impact on your life?

Its hard to put into words which symptom or issue has the most significant impact on my child's life living with ARPKD as there are so many. Some include severe anemia, fatigue, high blood pressure, electrolyte issues, etc. She is currently at about 25% kidney function along with enlarged spleen and portal hypertension. Even though at this point we have more kidney involvement- the fear of a GI bleed and the uncertainty of the liver side of this disease that could happen at any minute I think is what has more of an impact on our life than anything. When it comes to the kidneys that is something that can typically be tracked and measured over time but knowing that the liver can cause life threatening complications (such as a GI bleed or cholangitis episodes) at any minute has us living in fear of this happening any day. In addition to this, the enlarged spleen limits the sports and daily activities that she is able to do. Overall, I believe the liver side of this disease needs more understanding and treatment options.

My son, who is almost 20, never had any limitations because luckily he never had any interest in contact sports. He was a runner, so participated in track and cross country. When he was 17, the doctor started him on propranolol to help with portal hypertension but nobody told him that this would affect him being able to push himself when running. His times got worse. It really



affected him mentally until we finally asked the doctor, who confirmed that was the problem.

Connie, parent of a daughter who passed away from ARPKD shortly after birth

My daughter died shortly after birth due to respiratory failure from polycystic (and non-functional) kidneys and very low amniotic fluid. She was diagnosed at 36 weeks (this was 30 years ago) and born at 37 weeks.

My other 2 children (now in their late 20/early 30s) have not been tested and due to insurance questions are unwilling to be tested. However, they are concerned for any future kids of theirs.

Edward, parent of a child living with ARPKD

More guidance on diet. Additives and specific items to avoid. "Renal diet" suggestions vary widely it seems.

Jennifer, family friend

I have known a family with two girls with ARPKD and they have had to raise money to be able to travel for treatment and to pay for treatment and they definitely need better treatments to be able to live a normal life.

Alee, parent of a son living with ARPKD

What are you currently doing to manage your ARPKD symptoms?

My son is on two blood pressure medications and is also on a low potassium diet. We also do weekly PT and OT. We visit our local children's hospital every three months for lab work. Alee, parent of a son living with ARPKD

What do you fear the most as you get older? What worries and frustrates you most about your condition?

Trading one chronic condition for another. (ARPKD to transplant) A transplant is not a cure. Multiple transplants are likely needed, and you introduce the risks for rejection and cancer.

How have your symptoms changed over time? How has your ability to cope with the symptoms changed over time?

My son's symptoms have changed for the better overtime. I had a really difficult time when he was a small baby looking at the size of his stomach. To this day I avoid putting him in pants because I know they will just fall off.



Knowing what his kidneys were doing and would eventually do to his little innocent body were extremely hard to comprehend. His symptoms have become better with time, he has "grown into" his kidneys, but I still have my moments wondering whether he will be able to live a fulfilled life like other children.

Which ARPKD symptoms have the most significant impact on your life?

In our sons first year of life the hardest symptom was enlarged kidneys that limited our son to eat by mouth. This caused endless vomiting, lack of weight gain, and constant worry. We have gone through over a year of feeding therapy to get him to eat by mouth today, but the worry is still there that the physical limitation of enlarged kidneys keep him from eating enough.

Katy, grandmother of a 10-year-old boy living with ARPKD

My grandson is unusual in that his onset of ARPKD was late. Probably showed symptoms age 7, but not diagnosed until 8 1/2. He's now 10. For his situation, I think a huge help would be something that would slow, or preferably stop, the progression of the disease and its impact on other organs. Right now, he is looking at dialysis and/or a transplant at some point, but we have no idea when. If progression can be slowed, then there is more time to develop a cure before the disease has progressed to the need for a transplant or dialysis. As it is, it's hard to make long term plans and he will soon be a teenager, looking at job and education options, social relationships, etc. We are doing what we can with diet, frequent lab and imaging, and blood pressure control.

Michael, parent of a child living with ARPKD

Child was diagnosed at birth after a crushed lung in the birth canal.

Would like to see success in keeping the kidneys functioning without need for transplant.

Logan, parent of a 10-year-old child living with ARPKD

Our child was diagnosed with ARPKD within one year of birth with an enlarged abdomen and a urinary track infection. Thankfully progression has been fairly slow over the 10-year diagnosis; liver issues have worsened at a faster pace than kidney issues.



Medication works well to regulate blood pressure, but it doesn't tackle quality of life issues. We always have to balance the reason for the medication and the potential adverse effect of the kidneys or liver.

We'd like our 10-year-old to have the energy he should, so he doesn't miss out.

Our child was tested for the tolvaptan trial but deemed ineligible because of his liver functions. We would try again if offered.

Stephen, parent of a child living with ARPKD

Our infant was diagnosed with enlarged, echogenic kidneys, no amniotic fluid, an enlarged liver and spleen, and experienced issues with lung development, failure to thrive, dialysis, adrenal insufficiency, seizures, high blood pressure, pulmonary hypertension, feeding issues, gross motor delays.

Colin, parent of a son living with ARPKD

My child had underdeveloped lungs, so it seemed like he caught every respiratory bug out there. Portal hypertension and esophageal varices showed up in my child's early teens. We just need to watch hydration very carefully as dehydration affects him more. Would like to slowly increase platelets to moderate level or get GFR back to stage 3 level and maintain it there so transplant could be pushed off even further.

Kai, individual who has had a liver transplant

Infections were a constant issue prior to the liver transplant. Would like the ability to be in public without a big risk to immunity (post-transplant).

Robert, parent of a child living with ARPKD

Would like to slow down my child's worsening or improve azotemia, slow down formation of additional cysts in kidneys.

Shawna, 24-year-old living with ARPKD

I would like to see a treatment that targets and slows the progression of the liver disease (CHF) as well as ARPKD in the kidneys. In addition to new medications, I would like to see more research and information on what particular diet and lifestyle changes could be.