Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)

Externally-Led Patient-Focused Drug Development (EL-PFDD) Meeting

Meeting Date: Tuesday, June 11, 2024, 9:30 am to 4:00 pm ET

Report date: October 9, 2024

SADS Foundation EL-PFDD SPONSORS

Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) *Voice of the Patient* Report

The Sudden Arrhythmia Death Syndromes Foundation or SADS Foundation exists to save the lives and support the families of children and adults who are genetically predisposed to sudden death due to heart rhythm abnormalities. This *Voice of the Patient* report was prepared on behalf of the SADS Foundation as a summary of the input shared by families and caregivers living with CPVT during an Externally-Led Patient Focused Drug Development (EL-PFDD) meeting, conducted virtually on June 11, 2024.

Authors and Collaborators: This report was prepared and submitted on behalf of SADS by Alice Lara, RN, BSN, CEO & President; Marcia Baker, MS Ed, Program Director; Anna Goodson, Communication Director; and Genevie Echols, RCIS, Family Support Director, all from the SADS Foundation, and by Chrystal Palaty, medical writer.

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

Disclosures: The SADS Foundation is a 501(c)(3) nonprofit organization. The Foundation receives funding from pharmaceutical and life science companies in the form of unrestricted and restricted grants and sponsorship of programs and events.

James Valentine, JD, MHS 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.

SADS Foundation contracted with Chrystal Palaty, PhD from Metaphase Health Research Consulting Inc. for assistance in writing this report.

Technical services: Provided by Dudley Digital Works.

Funding: Support for the CPVT EL-PFDD meeting was provided by Solid Biosciences, Thryv Therapeutics and Cardurion Pharmaceuticals. In return for financial support, these organizations were acknowledged at the beginning of the meeting and their logos were displayed during the meeting break. These companies did not have any input in design, planning, coordination, or execution of the meeting or in the writing of this report.

Report Version Date: October 9, 2024. **Revision statement**: This document was not revised and/or modified in any way after October 9, 2024.

Point of Contact: Please contact Marcia Baker, MS Ed, Program Director (SADS@SADS.org) for questions related to this report.

Acknowledgements

The SADS Foundation wishes to acknowledge many important people and organizations who contributed to the success of the June 11, 2024 Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) externally-led patient focused drug development (EL-PFDD) meeting.

Thank you to all the FDA staff who attended our meeting. Thank you to Dr. Shetarra Walker, MD, MSCR, Lead Physician and Clinical Team Leader in Pediatrics in the Center for Drug Evaluation and Research at the FDA, for providing a welcome from the FDA. Thank you to Ethan Gabbour from the FDA's PFDD staff who guided us through this process over the many months of planning. We are grateful to have had this opportunity to ensure CPVT patient and family perspectives are considered in the drug development and regulatory processes.

Thank you to Dr. Arthur A. M. Wilde, for providing such an insightful clinical overview of CPVT, and for serving as a scientific advisor to the SADS Foundation for many years.

Thank you to our industry sponsors, Solid Biosciences, Thryv Therapeutics, and Cardurion Pharmaceuticals for their generous support.

Thank you to James Valentine JD, MHS and Larry Bauer RN, MA, from Hyman, Phelps and McNamara, whose assistance in planning and moderating the EL-PFDD meeting was invaluable. We could not have done this without you.

Thank you to the Dudley Digital Works Media team for their production planning and all the behind the scenes work in making sure our meeting was a success.

The EL-PFDD meeting was the result of many months of planning and hard work. Thank you to everyone who has had a hand in preparing for this meeting, including the SADS Foundation volunteers and staff who have given countless hours including, but not limited to CEO Alice Lara, Program Director Marcia Baker, Communications Director Anna Goodson, Development Director Jan Schiller, Technology and Administrative Director Erin Waite, and Family Support Director Genevie Echols.

Thank you to the many representatives from industry, federal agencies, and physician scientists from across the world who attended our meeting and who, on a daily basis, are striving towards a better understanding of the basic and translational science behind CPVT and are helping to move us closer to future clinical trials. Our hope is that this meeting will encourage future research and successful new product development for people living with CPVT who urgently need better treatment options.

Most importantly, the SADS Foundation would like to thank and acknowledge our CPVT community members who took the time to attend this meeting. Thank you to our speakers, panelists and callers for so honestly sharing how CPVT and its current treatments affect you on a day-to-day basis. This meeting would not have been possible without each one of you.

Key CPVT Insights

CPVT is a very rare genetic cardiac channelopathy. CPVT has an estimated prevalence of 1:10,000. CPVT is usually inherited in an autosomal dominant fashion and may affect many members of the same family. However, some have de novo gene variations.

CPVT takes an enormous toll. Many have experienced the sudden and unexpected loss of children, parents and siblings due to sudden cardiac arrest.

CPVT and its therapies are characterized by severe health concerns: cardiac arrest, light-headedness and fainting, abnormal heart rhythm and fatigue, impaired exercise tolerance, weight loss or gain, seizures and other secondary effects from seizures, cardiac arrests and falls.

CPVT diagnosis can be lengthy and complicated. Diagnosis often happens only after another family member experiences a cardiac arrest.

CPVT and its therapies diminish quality of life. Biking or playing sports, stamina, and attending social events with family and friends are all impacted. Work, careers and attending school are also impacted, as psychologic stress, medication side-effects and restrictions on physical activities limit work and career aspirations and diminish school performance.

CPVT is accompanied by constant worries about premature death, cardiac arrest, passing the gene on to other family members, as well as fears for the uncertain future of affected family members. These worries result in anxiety and depression due to the disease, as well as current therapies, and lack of therapies that target the disease itself.

Most individuals living with CPVT require multiple medical therapies to manage their disease. Beta blockers and sodium channel blockers, avoiding sports and other lifestyle modifications, ICD implantation and left cardiac sympathetic denervation (LCSD) are the main CPVT treatment approaches. The CPVT-associated anxiety and PTSD necessitates counseling, antidepressants and anti-anxiety medications.

Most reported that CPVT treatments worked to a great extent or somewhat. Despite treatment successes, such as the reduction in incidence of sudden cardiac death, CPVT treatment drawbacks are significant and include side effects from current pharmacological therapies that may be life limiting and cause impaired physical function, chronic pain from device surgeries and LCSD, and device failures that result in medical complications and negative impacts on both physical and mental health. For those living with CPVT, current treatments aren't always successful in improving quality of life, social, or physical function. Current therapies also leave anxiety, depression, and PTSD unaddressed.

The CPVT community needs a treatment to address the root cause of the disease and to improve quality of life. The community needs a treatment that allows them to participate in sports/physical activities, prevents arrhythmias and cardiac arrests, increases energy, improves daily functioning, and treats emotional symptoms. In addition to a cure for CPVT, the community needs a once-a-day treatment, better CPVT screening and diagnosis, and more research to increase the knowledge about this disease.

Contents

Abbreviations

These abbreviations are used throughout this report and in the submitted patient comments.

AED - automated external defibrillator

AICD - automatic implantable cardioverter defibrillator

CCU - cardiac care unit

CPR - cardiopulmonary resuscitation

CPVT - catecholaminergic polymorphic ventricular tachycardia

ECG/EKG - electrocardiogram

EP - electrophysiologist

ICD - implantable cardioverter defibrillator

LSCD - left cardiac sympathetic denervation

LQTS - long QT syndrome

NSVT - non-sustained ventricular tachycardia

PTSD - post-traumatic stress disorder

PVC - premature ventricular contraction

SCA - sudden cardiac arrest

SCD - sudden cardiac death

S-ICD - subcutaneous implantable cardioverter defibrillator

VT / v-tach - ventricular tachycardia

Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) Clinical Summary[1]

What is Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)?	CPVT is a very rare genetic cardiac channelopathy. CPVT is inherited in an autosomal dominant fashion and may affect many members of the same family. CPVT has an estimated prevalence of one in 10,000.
How does CPVT present?	The major symptoms of CPVT include abnormal heart rhythms, fainting, seizures and sudden cardiac arrest, and they are typically triggered by adrenaline, which may be induced by exercise and emotional stress or other triggers. Individuals living with CPVT may experience symptoms for years before finally receiving a correct diagnosis. Symptoms appear early in life with a median age of symptom onset is 10.8 years. Eighty percent become symptomatic by the age of 20. When untreated, CPVT can be lethal.
What causes CPVT?	CPVT is caused by genetic variants that change the release of calcium in the heart, resulting in electrical conduction changes which increase heart rhythms. *RYR2* is the gene most often implicated in CPVT, which encodes the ryanodine receptor 2 protein, responsible for calcium release in the cell. Many other genetic variants can cause this disorder (including variants in genes *CALM1, CALM2, CALM3, CASQ2, TRND, KCNJ2, CPVT1, CPVT2, CPVT3, TECRL)*. However, most of these variants are rare. Although CPVT is often inherited, it can also arise *de novo* from a new gene alteration.

[1]This information was presented by **Arthur A.M. Wilde MD, PhD, FESC, FAHA** at the June 11, 2024 CPVT EL-PFDD meeting**.** Dr. Wilde is an internationally recognized CPVT expert in cardiology and cardiogenetics at Amsterdam UMC, Interuniversity Cardiology Institute of the Netherlands, and has served as a scientific advisor to the SADS Foundation for many years.

How is CPVT diagnosed?	Individuals with CPVT have no arrhythmias at rest, which makes diagnosis challenging. Diagnosis is delayed by more than one year in almost 40% of patients, and 56% of patients initially receive a misdiagnosis. The complex diagnostic pathway for CPVT first starts with the identification of an exercise-induced polymorphic ventricular arrhythmia. Other cardiac conditions, including other ECG abnormalities (such as QTc prolongation) and structural heart diseases, are ruled out and then the age of symptom onset (under 40 years) is taken into consideration.
What therapies exist for CPVT?	Currently, there are no - targeted treatments for this condition that are approved by the FDA or other pharmaceutical regulatory bodies. Those living with CPVT are advised to avoid high level of exertion and to avoid strong emotions. Most receive beta blockers and a sodium channel blocker (flecainide). However treatment-related side effects impact quality of life and non-compliance is high. Left cardiac sympathetic denervation (LCSD) is recommended if other therapies are not successful. LCSD interrupts the left cardiac sympathetic nerve and can successfully reduce arrythmias. However, the surgery is offered only at a few specialized surgical centers and can come with complications, such as nerve pain, left-sided dryness of the body, and contralateral hyperhidrosis. An implantable cardiac defibrillator (ICD) is not recommended for most CPVT patients as the shocks cause pain and stress and are pro-arrhythmic, leading to shock storms of three or more ICD shocks in 24 hours, and even death. In one study, 25% of individuals had inappropriate shocks, and almost 30% suffered other device-related complications including lead malfunction and dislodgement, infection, cardiac perforation, and device migration.

CPVT EL-PFDD Meeting summary

The Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) Externally-Led Patient Focused Drug Development (EL-PFDD) meeting was held virtually on June 11, 2024. The meeting was an important opportunity for the Sudden Arrhythmia Death Syndromes Foundation (SADS Foundation) to share patient perspectives regarding the symptoms and daily impact of CPVT, as well as current and future approaches to therapies. The meeting was cohosted by **Genevie Echols**, RCIS, Family Support Director, the SADS Foundation, and **James Valentine**, JD, MHS, from Hyman, Phelps & McNamara, P.C.

Genevie Echols opened the meeting by welcoming all meeting attendees including the members of the US Food and Drug Administration. She introduced **Shetarra Walker**, MD, Clinical Team Leader in Pediatrics in the Center for Drug Evaluation and Research at the FDA. In her opening remarks from the FDA, Dr. Walker described how this EL-PFDD meeting will help the FDA to obtain insights from CPVT experts: the caregivers and patients living with the disease. She thanked the CPVT community for sharing their personal stories, experiences, and perspectives.

Dr. Arthur A.M. Wilde, MD, PhD, a cardiologist from the Interuniversity Cardiology Institute of the Netherlands and scientific advisor for the SADS Foundation, presented a clinical overview of CPVT which served as a scientific foundation for the meeting. **James Valentine** provided an overview of the meeting structure and invited all individuals living with CPVT to contribute their voices through online polling, calling in by phone, and by contributing written comments through the online portal.

The CPVT EL-PFDD meeting was held immediately after the Long QT Syndrome (LQTS) EL-PFDD meeting. Collectively, 240 unique viewers attended the livestream for the two events. Of these viewers, 22 were individuals living with CPVT, 11 were family members of individuals living with CPVT, 18 were parents/caregivers of individuals with CPVT. Other viewers included 16 healthcare providers, six representatives from the government, nine scientists and researchers, 17 from healthcare industry, 16 healthcare providers, six from non-profit organizations and 18 others including friends, patient advocates and consultants.

EL-PFDD meeting attendees used online polling to indicate EL-PFDD meeting demographics. The vast majority of attendees with CPVT were individuals living with CPVT (82%) and the rest (18%) were caregivers of someone living with CPVT (18%). The majority of attendees were from the United States (94%), with representation from most zones, and the rest of the attendees (6%) were from Europe.

The largest group of patients represented were 19-35 years of age (39%), followed by individuals aged 35 - 50 years (22%). Other age groups were equally represented: 13- 18 years, 51-60 years and 61 years and older (11%). A small number of individuals between the ages of 6

- 12 years (6%) were represented, but no one below the age of five years was represented. The age of CPVT diagnosis covered the entire range from 3 to over 61, with most diagnosed at the ages of 6-12 and 19–35 years of age (30%). Results of demographic polling are shown in **Appendix 1.**

The CPVT EL-PFDD meeting was structured around two key topics. The first session focused on *Living with CPVT: Symptoms and Daily Impact,* and the second session focused on *Perspectives on Current and Future Approaches for CPVT Treatments.* The meeting agenda is in **Appendix 2** and meeting discussion questions are in **Appendix 3**.

The session started with a pre-recorded panel of individuals who shared patient and caregiver perspectives on the symptoms and daily impacts of CPVT. James Valentine moderated a discussion between individuals in a live Zoom panel as well as those who dialed in by phone. Genevie Echols read out relevant comments entered through an online portal. Meeting panelists and callers are listed in **Appendix 4.**

The second session commenced with a pre-recorded panel of patients and caregivers describing different medications and medical treatments, as well as other approaches they use to address CPVT manifestations. Again, meeting attendees had an opportunity to participate in online polling, by calling in and submitting written comments. To conclude, **Larry Bauer, RN, MA** Hyman, Phelps, & McNamara provided a summary of key points. Genevie Echols closed the meeting by thanking all of the meeting attendees.

Online polling results from Topics 1 and 2 are integrated throughout the report. To include as many patient voices as possible, additional patient comments were collected through both the registration portal and by an online comment submission portal which was open for four weeks after the meeting. All submitted patient comments are included in **Appendix 5**, with selected comments included in the body of this report.

As the EL-PFDD meeting potentially elicited strong emotions for those affected by CPVT, the SADS Foundation offered a Zoom support group immediately following the EL-PFDD for affected individuals, their family members and loved ones.

The CPVT *Voice of the Patient* Report

This *Voice of the Patient* report is provided to all CPVT 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 June 11, 2024, EL-PFDD meeting reflects a wide range of CPVT experiences. However not all symptoms and impacts may be captured in this report.

The final report, the accompanying document containing the submitted comments and a video recording of the meeting are available on the SADS Foundation website at https://sads.org.

Everything is fine

By Rachelle Cook

Recently someone asked me how I get up in the morning knowing I have CPVT. The assumption being that it's so depressing I guess I should just wait around to die. I faked a polite response but I wish I hadn't. It should seem obvious that that is not an appropriate question but I was forced to give an appropriate response. I am constantly sanitizing my existence for other people's comfort, in the name of "politeness". I wanted to make a joke or maybe be just a little bit too truthful. Make them share in my feeling of discomfort. If I have to be uncomfortable, I'm taking them with me.

Here's what I wanted to say:

I get up because I don't have a choice.

I contemplate my mortality at least twice a day when I take the pills that allow me to survive, hopefully. The fun part is that the only way to know they're working properly is that you're not dead yet. You're alive, until you're not.

I feel like I'm constantly waiting. Death is inevitable. I know this more than other people. I also know if it's CPVT that takes me I won't get to say goodbye and neither will the people I love. I will simply cease to exist. I think about scenarios. I hope that I'm alone and my loved ones aren't the ones to find me. I don't want them to live with "what ifs" or "if onlys" though I know they will no matter what.

When I was first diagnosed, I read an oft-cited statistic in a medical journal that 50% of people with CPVT die before age 30. I know that technically that's people who are undiagnosed but it still feels like a looming expiration date.

I am expected to be grateful to be alive all the time. It is exhausting. I have to remind myself that my survival is not in exchange for my worthiness. I don't need to earn my survival. I don't need to prove to the universe that I am worthy of keeping alive. I don't think I can stop trying, just in case I'm wrong.

When people I know die, especially of heart related causes, I have to remind myself that I didn't cause their death. My life saved at 15 does not equal theirs at 19 or 25 or … I hate feeling guilty for being alive, but I expect that feeling will never go away.

My whole life feels like risk management. "Would I be ok to die doing this?" Usually the answer is no but sometimes yes. You can't avoid all risk. You won't be living, merely surviving.

Since we're all adults here: a friendly reminder that sex is an adrenaline producing activity and therefore, a risk for me. How would you live like that?

I can't talk about this in therapy because I end up consoling my therapist, and everyone else to be honest. I would know. I've made 3 therapists cry. Therapy isn't prepared for situations where sudden death is just life.

The cardiologists think "these people are alive and stable so they are fine. Thriving. Case closed." The fact that anyone was surprised when studies were released showing SADS patients had anxiety and depression about being diagnosed with a condition that by its very nature is sudden, unpredictable and usually catastrophic defies any words I could tell you.

This life is heavy. Sometimes it's like a backpack filled with rocks, manageable and just an inconvenience. Other times it's a pair of cement shoes trying to drown me.

I often forget that I can set the weight down even if just for a moment. I don't want to ask for help carrying it because I don't want others to see the weight or God forbid have to live with this weight like I do.

But that's not polite so if you ask me I will say "yes, everything is just fine."

Rachelle Cook is a 27-year-old living with CPVT. She read this poem at the EL-PFDD meeting and provided permission to reproduce it in the CPVT Voice of the Patient report.

Session 1 – CPVT Symptoms & Daily Impact

During the EL-PFDD meeting, patients and caregivers shared their perspectives and experiences of living with CPVT through presentations, online polling, moderated discussion and submitted comments. They described CPVT-related health effects that they experienced, impacts of CPVT on activities of daily living, and their worries and fears for the future.

Several key insights emerged that were not captured in online polling. These are highlighted with the grey headings and described with patient quotes below.

CPVT takes an enormous toll. Many have experienced the sudden loss of family members.

They described the sudden and unexpected loss of their children, their parents and of their siblings.

> *"Every morning we're greeted with the same bittersweet reality. Bitter is just a taste of the eternal emotion of losing a child. Sweet is the ever-present gratitude one of our children came back to life after being pronounced dead."* - Jen, 46-year-old living with CPVT and parent of two sons, one who passed away from CPVT at 10 years of age

> Pam lost both of her children, Matthew age 17 and Brittany, age 36, to sudden cardiac arrest. "*Like many families with this rare genetic disease, the first symptom is sudden death*." - Pam, 82-year-old living with CPVT, parent and grandmother of family members living with CPVT

> *"I was six years old when my mom died, and my sister was almost eight. I remember the months following her death. My dad and grandma were fearful for my sister and me. Were we candidates for sudden death?* - Kennedy, 29-year-old living with CPVT

CPVT diagnosis can be lengthy and complicated.

Diagnosis often happens only after other family members experience a cardiac arrest. Some of those living with CPVT are misdiagnosed with other conditions including long QT syndrome. Sometimes the causative genetic alteration is hard to identify. While some families have many members diagnosed with CPVT, other families may only have one individual with CPVT.

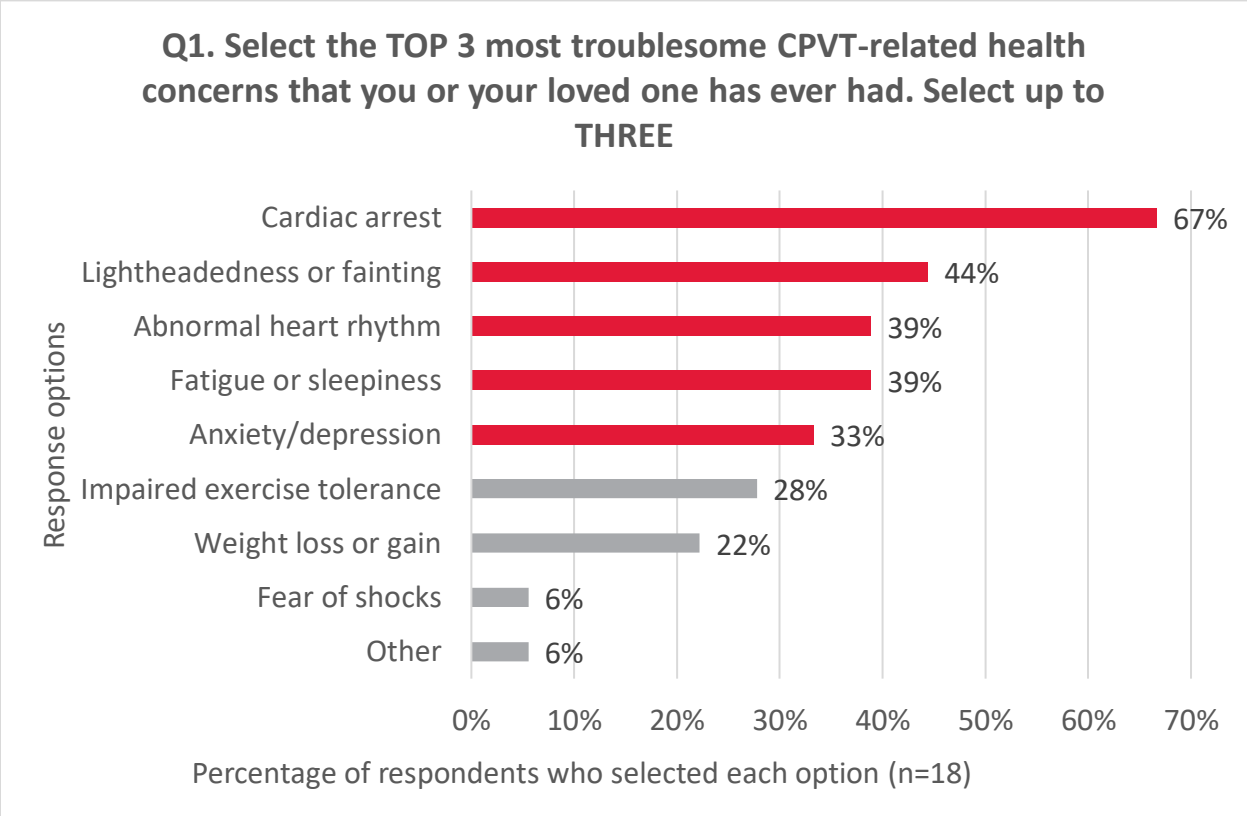
> *"I went into cardiac arrest at 29. After testing and an ICD being implanted, they sent me home with no diagnosis. … Two years ago, our 11-year-old daughter passed out suddenly after running up a hill. … Two weeks later our son who was 13 went into cardiac arrest while swimming at camp. They did CPR quickly and used a defibrillator, but he was pronounced dead two days later at the hospital. They tested him and he had the RYR2 gene, our daughters and I have the gene as well. We finally got answers, but it*

took our son dying for that to happen." - Dawn, living with CPVT and parent of children living with CPVT including a son who passed away at 13 years of age

Pam's granddaughter experienced a cardiac arrest at the age of 17, *"Kennedy's near-death experience was the catalyst to solving our medical mystery. …DNA testing involved samples from me, Kennedy, a cousin in Nebraska, and an autopsy DNA sample from Brittany, Kennedy's mom and myself of course. Results showed all DNA samples with a CPVT variant of unknown significance on the RYR2-F13L. We had found the smoking gun. Medical mystery solved."* - Pam, 82-year-old living with CPVT, family member of others living with CPVT

CPVT and its therapies are characterized by severe health concerns: cardiac arrest, light-headedness and fainting, abnormal heart rhythm and fatigue

Meeting attendees used online polling to select the top three CPVT-related health effects that they experience. Poll results are shown below and illustrated with selected patient quotes.



Poll respondents include patients, parents and caregivers who chose to participate in online polling. 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 but are intended to complement the patient comments made during and after the meeting. Poll responses selected by more than 33% of poll respondents are shown in **red**.

Cardiac arrest

Many individuals living with CPVT experienced no symptoms prior to their sudden cardiac arrest. Many expressed gratitude for the quick actions of teachers, bystanders and first responders who saved their lives and their family member's lives.

> "*Sammy had no symptoms. … In our children's cases an adrenaline rush due to fear seems to set off CPVT symptoms like fainting, seizures, and cardiac arrest."* - Jen, 46-year-old living with CPVT and parent of two sons, one who passed away from CPVT at 10 years of age

> *"I had a cardiac arrest while in my weight-lifting class doing pull-ups. After several repetitions, I collapsed and immediately went into cardiac arrest. Fortunately, two of my instructors performed CPR chest compressions as well as mouth-to-mouth resuscitation. … My teachers relentlessly kept up CPR until paramedics arrived, reviving my cardiac rhythm. … I will forever be thankful to my teachers for saving my life with CPR."* - Kennedy, 29-year-old living with CPVT

> Janai's son suffered a sudden cardiac arrest when he was five years of age. *"He was given 90 minutes of CPR and was placed on ECMO for seven days with a 2% chance of making it. After a week on life support, he woke up, survived and thankfully didn't suffer any brain injury."* - Janai, parent of a 12-year-old son living with CPVT

Syncope, light-headedness or fainting

Many living with CPVT have experienced syncopal episodes or the loss of consciousness. Often, this happened during physical activity. Some individuals are first investigated for neurological issues before having a cardiac work-up.

> *"We're lucky that Cian never had cardiac arrest. He only had several episodes of syncope and some seizure activity before he was diagnosed. … His first event, he passed out playing basketball when he was 10. Running down the court, he just fell and completely passed out. He's actually had episodes when he hasn't been active, too, which is kind of scary. He's had some at night where he had some seizure activity, and he had an episode getting in the shower as well."* - Suzanne, parent of a 17-year-old son living with CPVT

> Rachel's daughter experienced her first syncopal episode on a roller coaster when she was seven years old. "*Two seconds into that ride, I pulled myself over to take a look at her and all I saw was her lips went white and her eyes rolled back. She was unconscious for the whole ride. The ride ended, the seat opened up, and she was a wet little noodle. She'd been incontinent, she was still unconscious. Carried her off, and by miracles, she came to and was nauseated and confused."* - Rachel, parent of a 19-year-old daughter living with CPVT

Abnormal heart rhythm

Many living with CPVT experience abnormal heart rhythms such as non-sustained ventricular tachycardias, quiet slow heart rates, and bigeminy which is having an extra heartbeat between each normal one.

> *"I have had lots of non-sustained ventricular tachycardia (NSVT) events at all times of the day before, during, after work. While my ICD didn't need to shock me for any of these due to their brevity, I would still feel the symptoms that they came with. I have to wonder about the situation possibly getting worse and if I should call an ambulance or go to the hospital."* - Shanief, 34-year-old living with CPVT

> Allison experiences unpredictable, abnormal heart rhythms. *"I went through periods of my life where they happened so frequently that I had to stop doing any type of competitive sport or working out, but then there would be times where I'd go through long stretches, and I wouldn't have it at all. … Still to this day, I will feel those abnormal heart rhythms."* - Allison H., living with CPVT for over 20 years

> *"At my treadmill test, I was about six minutes into the test when the doctor pushed the emergency stop, spun around and shoved me into a chair that magically appeared under me. She immediately applied carotid pressure as she watched me slip into ventricular tachycardia. My irregular beat resolved spontaneously, and I was sent home with orders to avoid any stress or excess physical activity."* - Thomas, 54-year-old living with CPVT

Fatigue or sleepiness

Many experience profound fatigue or sleepiness as a side-effect from medications. Many have to take a lot of naps and rests during the day.

> *"My son is 17 and he is on high doses of nadolol and flecainide and he is still sleeping. It is 2:45 PM where we live. And this is one of the rare days that he doesn't have a lot on his schedule, and he has not gotten up for the day yet. That is the kind of fatigue we're talking about."* - Jen, 46-year-old living with CPVT and parent of two sons, one who passed away from CPVT at 10 years of age

> *"I didn't even tolerate 40 milligrams [of nadolol]. I had severe fatigue, barely making it through the school day, and I still needed to take a two-hour nap after school every day."* - Rachelle, 27-year-old living with CPVT

Anxiety, depression and fear of shocks

Many living with CPVT as well as their parents and family members, experience anxiety and depression. Many experience grief from having to give up activities they love, and others have PTSD from previous cardiac episodes and ICD shocks.

"*This life is heavy. Sometimes it's like a backpack filled with rocks, manageable and just an inconvenience. Other times it's a pair of cement shoes trying to drown me.*" - Excerpt from the poem "Everything is Fine", by Rachelle, 27-year-old living with CPVT

"*It's now 16 years after my diagnosis and I am still grieving the lifestyle that I lost. Not a day goes by when I don't think about my diagnosis. I have to face my own mortality every single time I take the pills that are required to keep me alive. I lie awake at night worrying about what will happen when I die.*" - Jocelyn, 27-year-old living with CPVT

Greg's ICD was implanted when he was only a child. *"That's the thing that really, for a long time, made me afraid, just not knowing when a shock would happen because sometimes, I was literally sitting and watching TV and it wasn't related to an actual arrhythmia. … There's definitely a lot of still just almost anxiety towards some intense activity. There's something that just prevents you from feeling totally comfortable with it."* - Greg, living with CPVT for 28 years

Impaired exercise tolerance

Treatment-related side effects including shortness of breath and lack of stamina, interfere with physical activity.

"Previously competed in a triathlon, then half marathons, but now unable to run it all due to shortness of breath and PVCs." - Nancy, living with CPVT

Weight loss or gain

Lisa was very athletic until her CPVT diagnosis. *"I'd like to get back into activities, but between the beta blockers and the inactivity, I gained 40 pounds over two years. … Now I've suddenly got a lot more complications because the weight adds its own set of stuff going on."*- Lisa, 66-year-old living with CPVT

Other CPVT-related health concerns – seizures and secondary injuries

Some individuals living with CPVT experienced **seizures** and were even misdiagnosed with epilepsy. **Secondary effects** from seizures, cardiac arrests and falls can include traumatic brain injury, learning impairments, short-term memory issues, bruises and cuts.

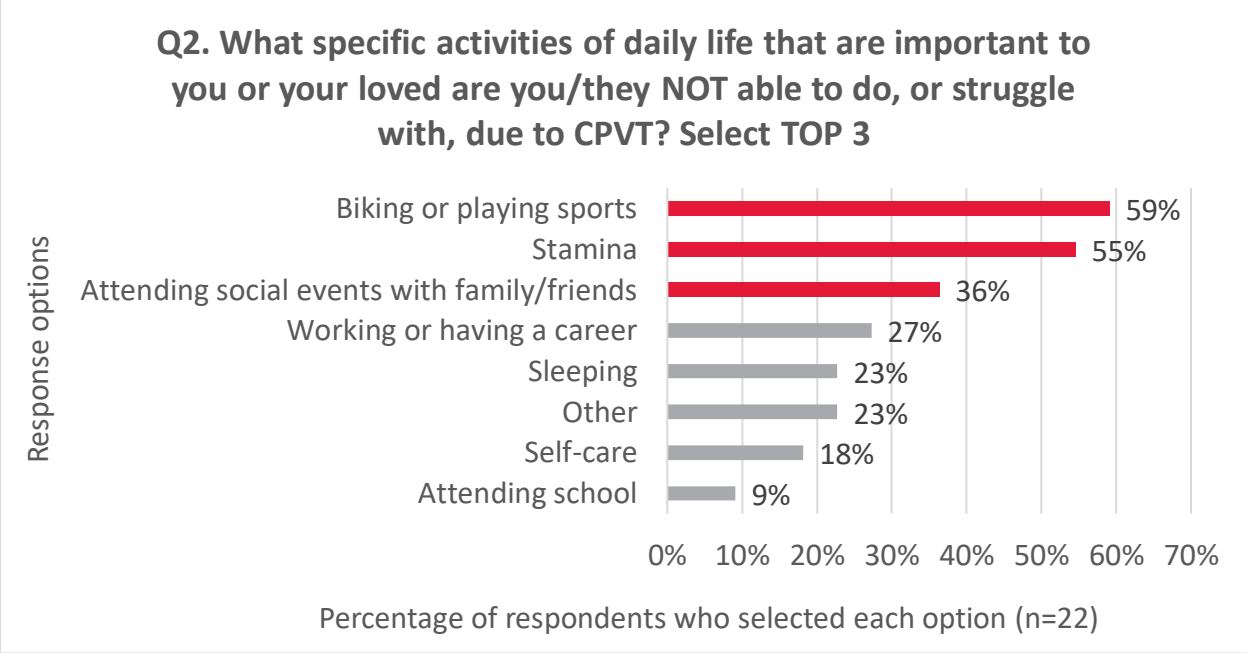
During one seizure, Jen's son fell head-first onto concrete from the high diving board, resulting in a traumatic brain injury and a brain bleed. Unfortunately, his next seizure was his last. *"Frankie felt his fourth and final seizure coming on. My husband and I rushed up the stairs to find Frankie appearing to be seizing. Though the uncontrolled motions looked odd and seemed very slow. … My husband, the first responders and hospital staff tried and tried to resuscitate him, but to no avail. Our worst nightmare was*

now our dark reality." - Jen, 46-year-old living with CPVT and parent of two sons, one who passed away from CPVT at 10 years of age

Sammy experienced paraplegia after his cardiac arrest. *"The type of paraplegia is very unique because of the lack of oxygen to his spine. So, there's hope that he may regain some functions, and he has regained some. … Today he's mostly wheelchair-bound, aside from ambulating and leg braces with a walker for short distances and in physical therapy."* - Jen, 46-year-old living with CPVT and parent of two sons, one who passed away from CPVT at 10 years of age

CPVT and its therapies diminish quality of life. Biking or playing sports, stamina, and attending social events with family and friends are all impacted

Using online polling, meeting attendees selected the top three activities that were most important to them, that they were NOT able to participate in, or struggle with, due to CPVT. The results of these poll questions are shown below and described with patient quotes.



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Biking or playing sports

As CPVT is triggered by exercise-induced adrenaline, many living with CPVT are restricted with respect to their physical activity. Being denied the activities one loves is heartbreaking.

"I was diagnosed with CPVT when I was 11 years old. I was pulled out of all sports and anything else that involved physical activity. To make matters worse, my school refused to excuse me from gym class at first and instead forced me to sit on the sidelines and watch all the other kids participate in activities that I no longer had access to. I didn't understand why I couldn't go run and play like all the other kids my age. It was devastating." - Jocelyn, 27-year-old living with CPVT

"During diagnosis and treatment, I needed to stop all activities that required exertion. At first that meant not ever being alone, not walking anywhere that a car couldn't pick me up. Could not walk the dog, could not participate in activities that I previously enjoyed: running, soccer, yoga, kayaking. Two years of restricted activity has led to weight gain, and associated health impact." - Lisa, 66-year-old living with CPVT

"I went into cardiac arrest at my swim meet last year, and the AED saved my life. After genetic testing and stress tests, it was proven I have CPVT. I can no longer participate in sports or anything that can cause an adrenaline rush." - Mindy, 12-year-old living with CPVT

Stamina

Because of their medications, many living with CPVT experience a lack of stamina and impaired exercise tolerance impacting all activities of daily life.

Allie is unable to keep up with her son. *"My toddler has been walking since he was nine months old, so he is running right now. And so it's not only this fatigue when I wake up, but it's throughout the day as well because I'm not only chasing him, but my heart rate is lower, my energy is lower, and that fatigue is really there."* - Allie, living with CPVT, and family member of others living with CPVT

Aimmy described her tiredness, dizziness and lack of stamina. *"It affected me as a child, that I felt like I would not be able to keep up with my friends."* - Aimmy, 37-year-old living with CPVT

Attending social events with family/friends

CPVT interferes with participation in recreational and social activities. Sometimes friendships suffer. Even travel is more challenging due to medications which require refrigeration and going through security with an implanted device.

Allison's daughter experiences*, "Being pulled out of all activities and anything that is remotely thrilling, like going to an adventure park or riding a roller coaster or zip lining. … Every time we had to go to her brother's soccer game or we would go on our annual*

houseboating trip, she was not able to participate. It was very traumatic for her." - Allison G., parent of an 18-year-old daughter living with CPVT

"I think [CPVT] is holding her back from friendships, either from physical activities like sports, or parents or friends not prepared or scared of a cardiac arrest." - Tom, 43-year-old living with CPVT, parent of a daughter living with CPVT

"Flecainide has to be refrigerated, so we have to carry that with us if we travel. We have increased airport security problems because of that. And my youngest son has an implanted loop recorder, so when traveling with the airport security, he has to be pulled over to the side and wanded." - Julie, living with CPVT and parent of two sons, ages 15 and 11, living with CPVT

Working or having a career

Extreme fatigue and light-headedness cause challenges at work. Others wonder about whether to disclose their CPVT to employers and colleagues.

Because of a high dose of metoprolol, *"I was just feeling like a zombie. I couldn't focus. I'd be in meetings and everyone from work is watching, and I'd be drifting off. I was always tired. The person I used to be was a stranger, that used to get a whole bunch done, and I really would have to force myself to get out of a chair."*- Lisa, 66-year-old living with CPVT

"When do I tell my employer about my CPVT and what aspects do I share with them? On one hand, I want them to understand, and on the other hand, I do not want to scare them." - Aimmy, 37-year-old living with CPVT

Sleeping

Sleep is a priority for those with CPVT, as many are so tired all the time. Some struggle with insomnia due to medication side-effects and chronic pain.

"During sleep, my heart rate gets so low because of the nadolol and because of those beta blockers, that the energy when you wake up is not there. And so not only do I wake up and not have this energy, it's throughout the day." - Allie, living with CPVT, and family member of others living with CPVT

"I also have insomnia, which is likely from long-term use of beta blockers. My sleep doctor really struggled to find a sleep medication that I could take between the QT prolonging of flecainide in combination with my other medications for chronic pain, and many sleep medications can't be taken if you take beta blockers. We actually didn't find anything, so I'm back taking doxylamine and hoping there will become another option without as many long-term side effects." - Rachelle, 27-year-old living with CPVT

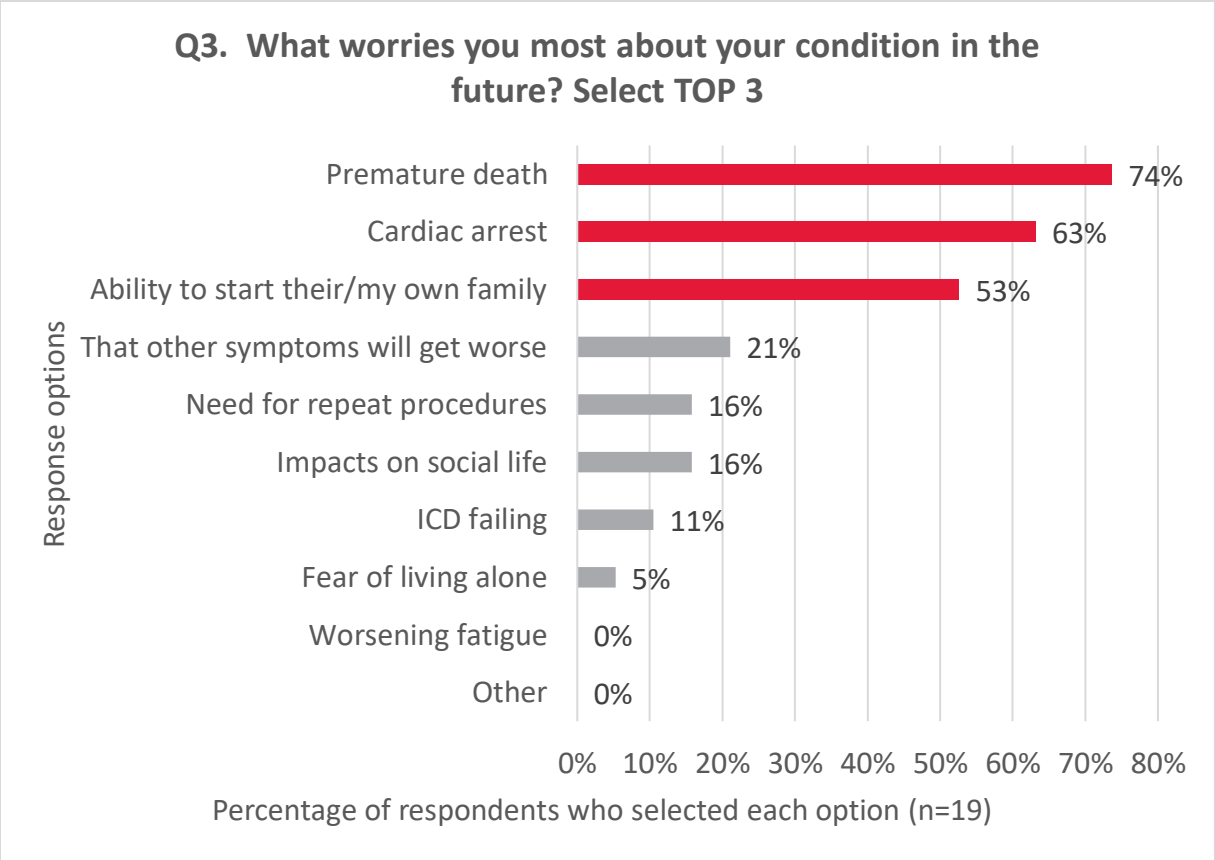
Other impacts

Those living with CPVT selected other CPVT impacts in the polls including **self-care** such as taking showers and **attending school.** Many are too tired or are not trusted to care for children and grandchildren alone, nor can they drive for a certain period of time after experiencing a cardiac event. Some also choose not to drive because of the fear of having a cardiac event while driving. CPVT impacts every life decision that is made.

> *"In addition to the anxiety and depression that comes along with CPVT, the current treatment options have side effects that make my life more difficult. My body has struggled to tolerate beta blockers. At one point, I couldn't even stand long enough to take a shower without my blood pressure becoming so low that it made me ill*." - Jocelyn, 27-year-old living with CPVT
>
> *"Specific activities that I am unable to do: take care of my grandchildren."* - Angela, living with CPVT
>
> "*We can talk about CPVT in silo and how we're going to treat it and how we're going to manage it, but what you need to think about is how it affects every other decision that you make in your life."* - Allison H., living with CPVT for over 20 years

CPVT is accompanied by constant worries about premature death, cardiac arrest and passing the gene on to other family members

Meeting attendees used online polling to indicate their top three worries about their condition in the future. Poll results are shown below and illustrated with patient quotes.



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Premature death

Many worry that they, or their family members, will die prematurely. This is closely related to worries about medication no longer working, and a lack of medication compliance. Some worry about their children continuing to take their medications correctly as they become independent.

> *"I fear that my medication will stop working and I will die of SCA. I do not currently have an ICD."* - Angela, living with CPVT

> *"Just like everyone else has said, you've got this fear. Every time either one of the boys sleeps 30 minutes, an hour longer, I'm like, 'Okay, am I going to walk in and they're not going to be there anymore?' That's the big fear. Then I have to pull myself back and say,*

'Okay, we're medication-compliant. We're doing everything that we should be doing.' But it's still there. I fear for them." - Julie, living with CPVT and parent of two sons, ages 15 and 11, living with CPVT

"What I didn't know until about seven months into my conservative treatment plan was the suffering of my wife of 20 years. She worried every minute I was out of contact during my days. I work in the medical field (specifically, in surgery), so I would be out of contact for hours. Unbeknownst to me these hours were filled with dread for my poor wife, so a year after my event, I called my EP and got on the schedule for an AICD implantation." - Thomas, 54-year-old living with CPVT

Cardiac arrest

Many individuals worry about experiencing a cardiac arrest, and some are afraid to be alone for that reason. They worry about whether an AED is available and the presence of experienced people in case they have an event. Some carry an AED with them wherever they go.

Shanief worries about having a cardiac arrest. *"I find myself being more aware of my surroundings now, like knowing where the nearest AEDs are in any building that I enter."* - Shanief, 34-year-old living with CPVT

"He's afraid that his heart might stop again. At first, … he was afraid to take a shower. He was afraid to be in any room alone, because he didn't want to be alone should something happen. So, we just took turns just keeping an eye on him until he felt sure of himself that he was going to be okay, … that it wasn't going to happen again." - Eva, wife and parent of family members living with CPVT

"We have that constant nagging in the back of our head. … Is there going to be another event? What's going to happen? And especially as the younger kids are growing up and what is in store for them as they enter adulthood … there's so many fears out there that we live with." - Allison G., parent of an 18-year-old daughter living with CPVT

Ability to start their/my own family or passing this on to family.

Many living with CPVT worry about passing the gene variant on to other family members. As CPVT is rare and information and evidence for best care practices is lacking, some physicians mistakenly believe that if the mother has CPVT, the pregnancy is extremely high risk.

"My biggest personal fear is as someone who hopes to have children one day, how can I ensure that they do not inherit CPVT? Do I pursue in vitro fertilization and then genetic testing prior to implantation? Or do I take a 50/50 chance and hope my child will not inherit the CPVT mutation?" - Kennedy, 29-year-old living with CPVT

"The idea of passing this on to your kids. I don't have any kids right now, but planning and dealing with how do you anticipate their care, I think, is really complicated." - Greg, living with CPVT for 28 years

"*We actually had to move to another state in my third trimester to have a specialized care team who specialized in CPVT because nobody in our area had treated it, let alone dealt with somebody who was pregnant. I had to stop certain medications because they weren't deemed safe for pregnancy. Actually, they were just deemed unknown because CPVT is so rare. It was a risk we couldn't take."* - Allison H., living with CPVT for over 20 years

Fears for the future living with CPVT

CPVT is a condition characterized by uncertainty. Individuals living with CPVT, and their family members worry **that symptoms will get worse, that the ICD will fail, triggering the need for repeat procedures, impacts on social life**, and the **fear of living alone**. They worry about how their disease will change as they age, if their medication will eventually stop working, whether their children will be okay once they move away from home.

"I just am concerned moving forward in the future. He's only 17 years old, and how much higher can we go on his [medication] dose? And how long will that really be effective for him?"- Suzanne, parent of a 17-year-old son living with CPVT

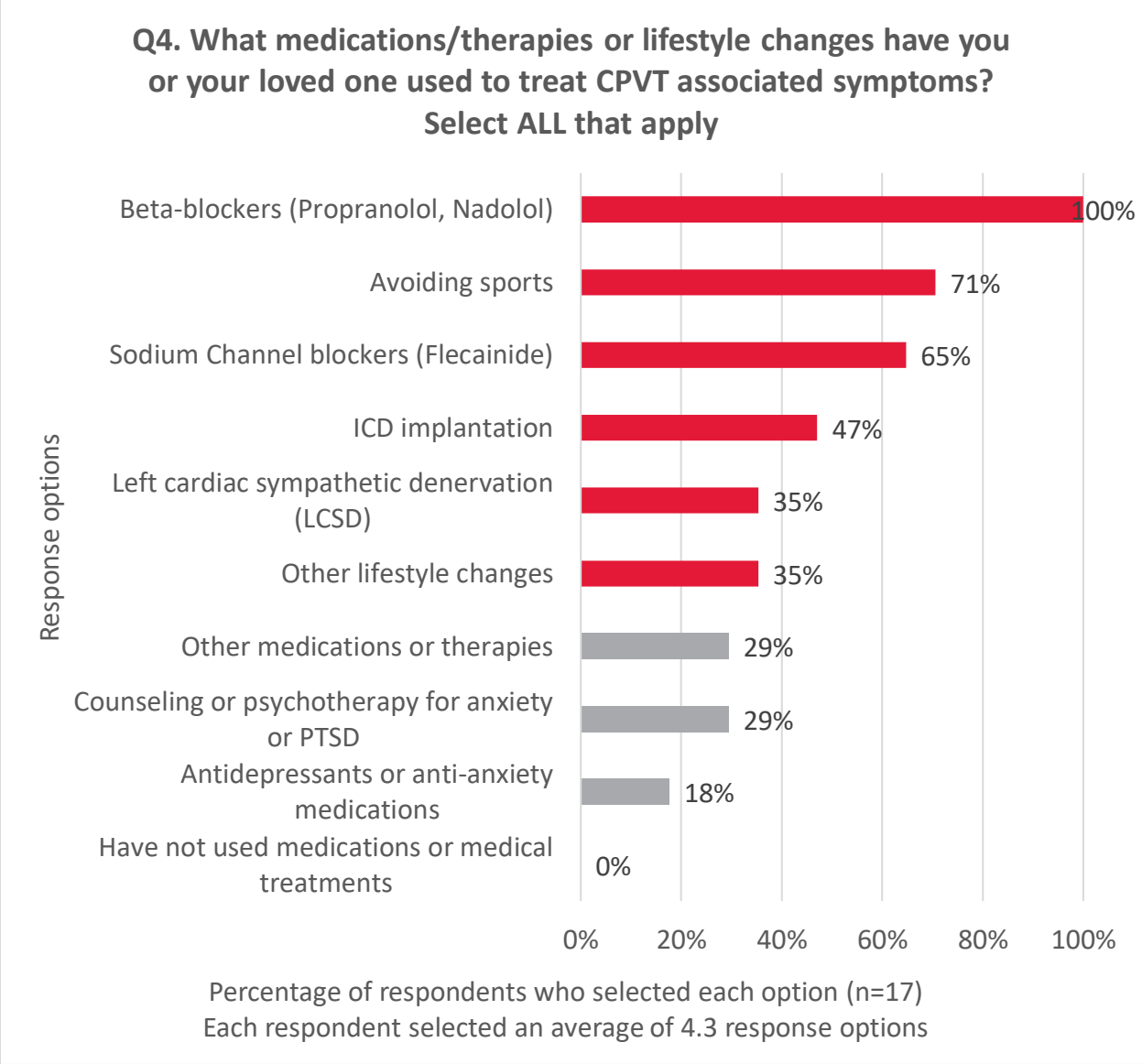
"The diagnostic burden, underlying impact on our life has been fear. Even though we've been dealing with this for 12 years, the fear doesn't go away. I think I carried that fear more than my daughter." - Rachel, parent of a 19-year-old daughter living with CPVT

Session 2 – Current and future treatments for CPVT

Through online polling, moderated discussion and submitted comments, patients and caregivers described all the different medications and therapies and lifestyle changes that they used to manage CPVT-related symptoms. They described the most significant drawbacks associated with each approach and articulated their hopes for future ideal CPVT treatments.

Most individuals living with CPVT require multiple medical therapies to manage their disease

Using online polling, individuals living with CPVT indicated all the medical therapies that they had used to treat CPVT-related symptoms. Significantly, *all* of the individuals polled reported that they required medications or medical treatments. Each respondent selected an average of 4.3 treatment approaches. Sometimes each family member requires a different treatment. Poll responses are listed below and described with patient quotes.



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Beta blockers (propranolol, nadolol)

Beta blockers are prescribed to all individuals living with CPVT, even for those who are asymptomatic. Some may still experience cardiac symptoms even when they are on beta blockers. Beta blocker downsides can include lethargy, fatigue, and brain fog. As a result, some are not adherent to their medications.

> *"For a year, I chose drug therapy with a large dose of nadolol. This conservative route was somewhat effective. The side effects were not great. Low blood pressure and a resting heartbeat of 35 made life fairly miserable."* - Thomas, 54-year-old living with CPVT

> *"Since my diagnosis, I have tried a number of medications at various dosages to attempt to get the upper hand of my arrhythmia. I have had been on a number of beta blockers, including metoprolol, sotalol, nadolol. There were times where the effects of the beta blockers were insufferable. When I was taking 300-milligram doses of metoprolol, I felt extremely lethargic no matter how much sleep I got. Beta blockers almost make it nearly impossible for me to get my heartbeat over 120 beats per minute even during intense exercise."* - Shanief, 34-year-old living with CPVT

> *"Beta blockers have always slowed me down to where naps were very common growing up. Now I create work for myself during meetings to stay engaged and awake."* - Tom, 43-year-old living with CPVT, parent of a daughter living with CPVT

Avoiding sports

Because activity-related adrenaline often triggers CPVT, those living with the condition need to control their heart rate. Exercise restrictions and avoiding sports can lead to depression and other health problems.

> *"Before beta blockers, I was participating in athletics for up to five hours every day after school. …My first cardiologist's treatment strategy was restricting me from all activity and starting me on 40 milligrams of nadolol."* - Rachelle, 27-year-old living with CPVT

> *"She was immediately pulled out of sports. That's when her events all happened, was during exercise or anxiety. She was a competitive dancer and a competitive soccer player, and so that piece was incredibly devastating to her. And of all of my children, she was the most active, … most athletic, most energetic, the biggest thrill seeker. …It was extremely devastating to her."* - Allison G., parent of an 18-year-old daughter living with CPVT

> *"It's important to realize that although exercise restrictions are one of the mainstays of treatment for CPVT, it's not without consequences. There are a lot of health complications associated with having a sedentary lifestyle. I'm currently in medical*

school and spend every day telling patients how important it is to stay physically active, all while knowing that I'm at an increased risk for everything I'm warning them about." - Jocelyn, 27-year-old living with CPVT

Sodium channel blockers (flecainide)

Sodium channel blockers such as flecainide can be used to control arrhythmias. The dose needs to be fairly high and comes with treatment-related side effects including fatigue and contraindications with other medications. Some individuals remain symptomatic even when they are taking both a beta blocker and flecainide.

"My four children and husband have been diagnosed with CPVT. Three of my children are currently taking nadolol and flecainide. Some handle it better than others because it makes you feel tired and have low energy." - Amy, wife and parent of family members living with CPVT

"After multiple stress tests, treadmill tests, getting her put on the combination and adjusting the medications and the timings of her doses, she's now on the nadolol and the flecainide and has much better response to it." - Allison G., parent of an 18-year-old daughter living with CPVT

"Cian takes flecainide and nadolol. He's been on that since he was about 13, and so that is really the only thing that he has for CPVT. … The medication, it does control him pretty well. But he is on very high doses."- Suzanne, parent of a 17-year-old son living with CPVT

ICD implantation

Even though ICDs are not recommended because shocks can be pro-arrhythmic, many living with CPVT have one implanted. Downsides include inappropriate shocks, battery monitoring and replacement surgery, and for some, ongoing pain from the implantation.

"In the first year of living with an AICD, I was administered a therapeutic shock two separate times. I must note that my defibrillator was programmed very conservatively, so the shocks were definitely needed to sustain life." - Thomas, 54-year-old living with CPVT

"I had an ICD placed about a year after my cardiac arrest, and that was something you just don't understand [as a child]. I had some inappropriate shocks and a myriad of problems with the actual ICD." - Greg, living with CPVT for 28 years

"I have an ICD in my chest and beta blockers are my daily medication. This means monitoring of the battery as well as having surgery to replace the battery." - Kennedy, 29-year-old living with CPVT

Left cardiac sympathetic denervation (LCSD)

This surgical procedure can reduce arrythmias by interrupting the left sympathetic nerve. This procedure can only be done by a specialist team of surgeons, so travel may be required. While LCSD works well for some, downsides can include chronic pain, sweating on only one side of the body, dysautonomia, as well as surgical complications.

> *"In 1996, doctors decided to treat my condition with a new procedure being done for ventricular arrhythmia patients, left cardiac sympathetic denervation. It was an experiment at the time. They were hoping to completely resolve the condition. The risks were described as a possibility of Bell's palsy type symptoms in my face, but they knew I wouldn't sweat in my left arm or left side of my face. It was also an open surgery, which meant a much more painful and long recovery."* - Tom, 43-year-old living with CPVT, parent of a daughter living with CPVT

> "*I've had the cardiac denervation done, which has created a pain in my left arm and shoulder blade and makes my body temperature different on each side.*"- Mindy, 12-year-old living with CPVT

> Among the permanent side effects from Rachelle's LCSD surgery, the damage to the nerves to her left hand causes chronic pain and a loss of grip strength. "*Recently, I invested in battery heated gloves because the pain from my hand getting cold is so severe that it causes significant symptoms like nausea and light-headedness. The cold can also cause my left hand to become partially paralyzed. The worst part of this is that they can't do anything.* - Rachelle, 27-year-old living with CPVT

Other lifestyle changes

Those living with CPVT address their CPVT related symptoms with important lifestyle changes including remaining calm, proactive heartrate monitoring, reducing their BMI, and carrying an AED with them.

> *"Today, in my forties, I continue to take my medication, keep up with my ICD appointments, and maintain fairly calm. I had problems with weight for a decade or two after college, and through lifestyle changes, my health coach and my wife, I have been able to maintain a healthy BMI."* - Tom, 43-year-old living with CPVT, parent of a daughter living with CPVT

> *"Still to this day, I will feel those abnormal heart rhythms, and the worst thing for CPVT is adrenaline and they tell you to stay calm. That's very hard to do when you feel your heart not functioning as it should. …Trying to remain calm, not induce additional adrenaline into your system to make it worse, it's kind of this feedback loop. Easier said than done."* - Allison H., living with CPVT for over 20 years

Rachel took a preventative approach to her daughter's health. *"We created our little algorithm: get flecainide levels done, do a stress test once a year, wear a monitor for a month every six months, and that was our cookie cutter system for 12 years. What happened? … We're doing what we've always done, yet she had an event."* - Rachel, parent of a 19-year-old daughter living with CPVT

Other medication or therapies

Those living with CPVT require many other medications and therapies including **pain treatments**, **catheter ablations**, **other implanted devices**, and **physical therapy**.

Pain treatments include medications, acupuncture, ice and ketamine.

The pain from Aimmy's ICD incision was so bad that at times she could not sleep. *"I tried taking medication, acupuncture, and ice for the pain. At first, acupuncture worked for a while to ease the pain. In 2016, I then had lead extraction and repositioning of my ICD. This helped me with the pain a lot, but unfortunately due to nerves being cut during surgery, the pain in my incision would never go away."* - Aimmy, 37-year-old living with CPVT

Rachelle's LSCD causes chronic pain. *"Currently, my chronic pain is kept in check with ketamine infusions that I get every six weeks. This treatment is very expensive since it has to be given in the hospital, and I have to take the entire day off for every treatment."* - Rachelle, 27-year-old living with CPVT

Catheter ablations

"The ablation took over four hours. It took two hours to map my heart, and another 2.5 hours to attempt to eradicate to aberrant foci in my heart muscle. …The mapping was uncomfortable. The ablation was very painful. It was like a medically induced heart attack. I had crushing chest pain, left arm pain, neck pain, shortness of breath, an amazingly bad headache. … After a day in CCU, the ectopic beats returned. Runs of 5-6 PVCs triggered alarms and got me put back on 160mg of nadolol per day. My EP programmed my ICD to pace me at 55 with a top of 120." - Thomas, 54-year-old living with CPVT

Other implanted devices including loop recorders to record the heartbeat and pacemakers to help control the heartrate.

"Since he started the beta blockers, he's had one episode where he fainted, but we don't know why. So then after that, immediately he got an implanted loop recorder so we can know just in case something happened." - Eva, wife and parent of family members living with CPVT

Physical therapy

Jen's son experienced paraplegia after CPR. *"What it entails is extreme amounts of physical therapy and many different types of physical therapy that he endures every day in addition to school."* - Jen, 46-year-old living with CPVT and parent of two sons, one who passed away from CPVT at 10 years of age

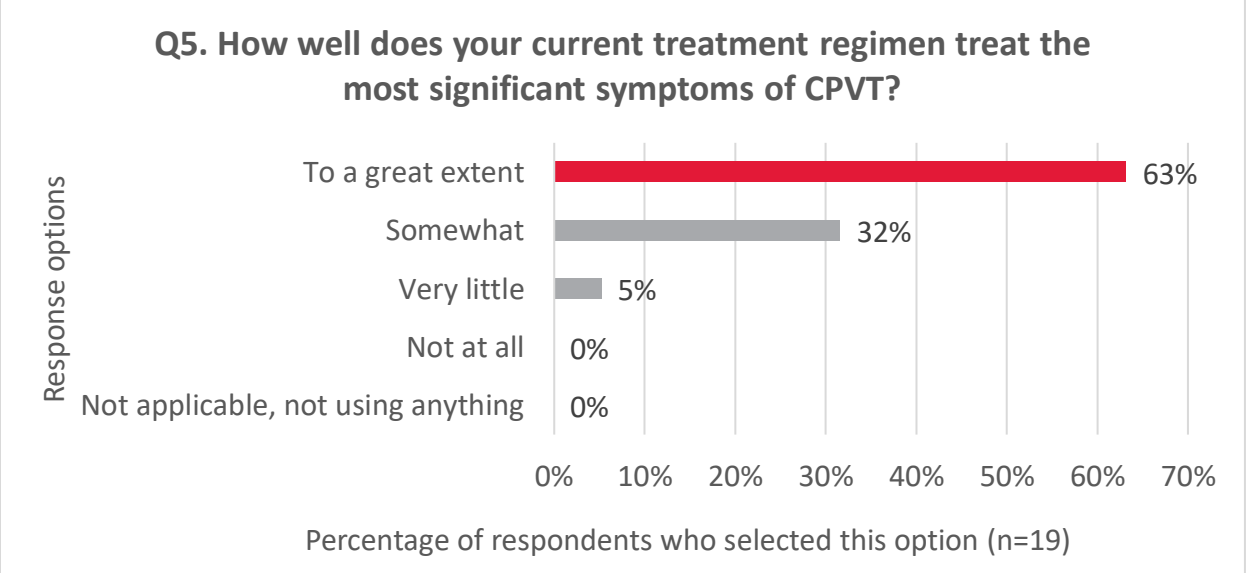
Counseling or psychotherapy for anxiety or PTSD, antidepressants or antianxiety medications.

"My husband and I remain on antianxiety and anti-depressant medications due to the trauma our family has experienced because of CPVT, traumas and deaths that could have been prevented with a correct diagnosis." - Jen, 46-year-old living with CPVT and parent of two sons, one who passed away from CPVT at 10 years of age

"I can't talk about this in therapy because I end up consoling my therapist, and everyone else to be honest. I would know. I've made three therapists cry. Therapy isn't prepared for situations where sudden death is just life." - Excerpt from the poem "Everything is Fine", by Rachelle, 27-year-old living with CPVT

Most reported that CPVT treatments worked to a great extent or somewhat

Many living with CPVT reported that their current treatments regimen works to "a great extent" or "somewhat" to control the most significant symptoms of CPVT. Poll responses are listed below and described with patient quotes.



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To a great extent

Many reported that their treatment worked well at preventing cardiac arrests, fainting, and arrythmias.

> *"My son was diagnosed at the age of seven. He's on nadolol and flecainide at this time. … We've been very fortunate. We've not had another event."* - Josef, parent of a 10-year-old son living with CPVT

> "*My son did amazing with the [LCSD] surgery and is doing very well and will hopefully be cleared next week for high school sports for his senior year."* - Amy, wife and parent of family members living with CPVT

> *"In terms of how CPVT continues to affect my daily life, the defibrillator in my chest is a very secure reminder for me that life is extremely precious even amidst the unknown. I lost my mom, I lost my uncle, but I'm still here. And for that, I will forever be grateful."* - Kennedy, 29-year-old living with CPVT

Somewhat

Many indicated that their treatments work "somewhat, in that while there were beneficial aspects to the treatment, there were also significant treatment-related side effects. Others are reluctant to trust the medications to protect them or their loved ones in the future.

> *"I am doing so much better since being on meds. I have a clearer head, I can walk to my car without bigeminy, I do have days of being somewhat dizzy with bradycardia."* - Angela, living with CPVT

> *"My brother with LCSD surgery, has had a couple side effects. We were actually at a parade and he was only sweating from half of his face, which is a little bit crazy to watch. But he ultimately has gotten to go back to sports, we got to the end goal with him, for him to be more active, but there definitely is some high costs when it comes to the treatment of CPVT."* - Allie, living with CPVT, and family member of others living with CPVT

> Josef reported that his son's treatment, "*It's working great at this point, but again, as we get to puberty, as we get to college, which someone alluded to earlier, we take it a day at a time. And he's 89 pounds and nine years old right now, and we'll just continue to roll with it as we go."* - Josef, parent of a 10-year-old son living with CPVT

Very little or not at all

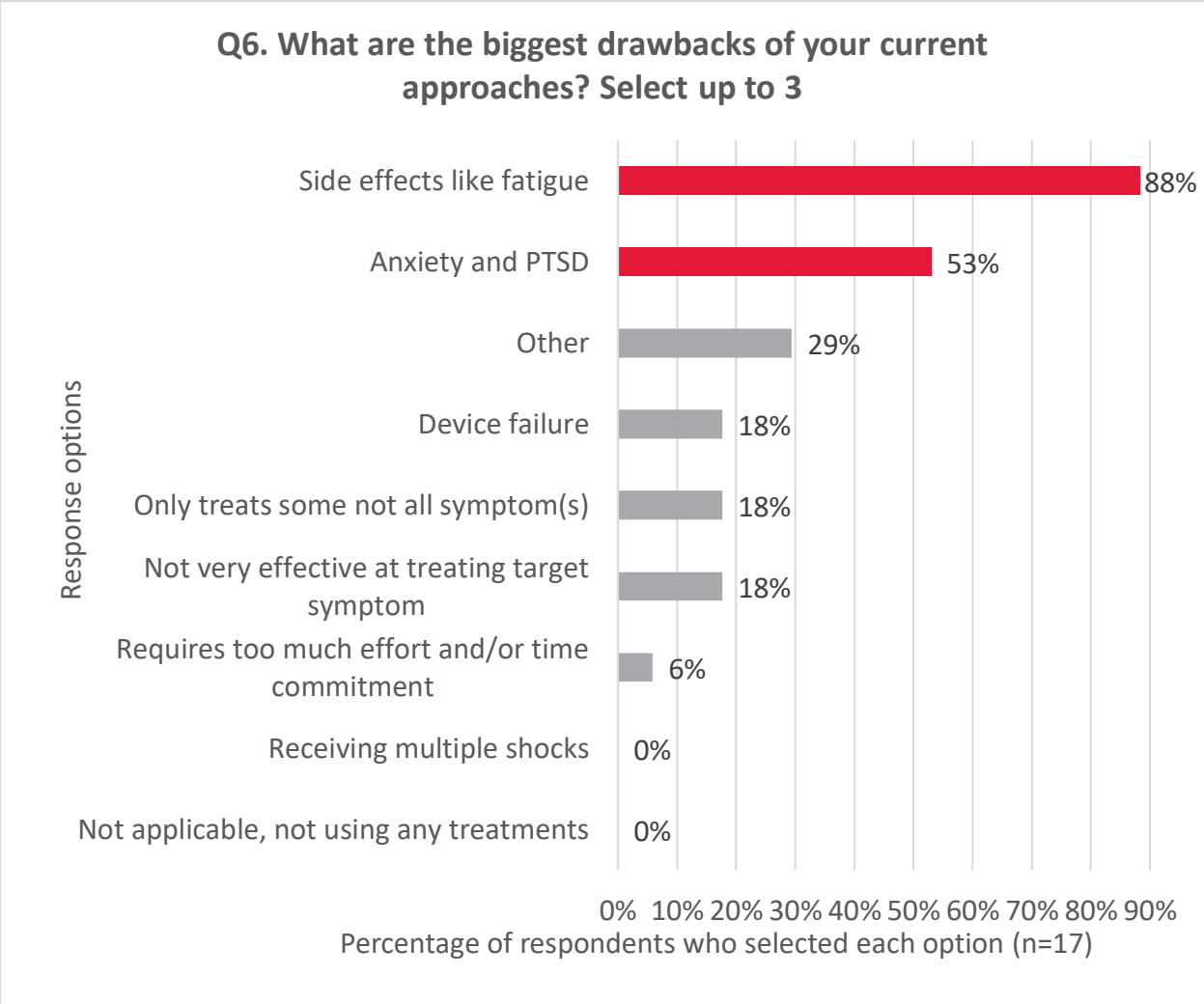
Some had very little success with treatment. This is consistent with some of the results of the following poll, where individuals living with CPVT and their families indicated that their treatment **only treats some, not all, symptom(s)** and **not very effective at treating target symptom**.

Shanief had two unsuccessful cardiac ablations. *"After the first procedure, the doctor explained to me that they were unable to reproduce the arrhythmia and that I wouldn't experience any more arrhythmias. They also said I could stop taking my heart medications, so I did. But I continued to have cardiac events, which meant the ablations did not mitigate the issue. I gave up on ablations months later when the second procedure had the same outcome as the first."* - Shanief, 34-year-old living with CPVT

Tom had an LSCD, *"I still remember waking up in pain. We went two decades thinking it was a failure because the episodes did not stop. I use my pacemaker 95% of the time and have been shocked from the defibrillator between 60 and 70 times."* - Tom, 43-year-old living with CPVT, parent of a daughter living with CPVT

Despite treatment success, CPVT treatment drawbacks are significant and include side effects, anxiety and PTSD, chronic pain, device failure and others.

Individuals living with CPVT indicated the downsides of their current treatment approaches using online polling. Poll responses are listed below and described with patient quotes.



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Side effects like fatigue

The many treatment-related side effects experienced by those with CPVT were described along with treatments on pages 25-30. These included fatigue and pain.

> *"The side effects of [propranolol and nadolol] were very difficult to deal with. Her energy was drained drastically. After a full day of school, she would come home and have to just*

sleep two to three hours before even having any energy to do her homework." - Kerwin, parent of a daughter who passed away from CPVT

"*My flecainide and nadolol make my heart rate so slow that I'm sluggish and tired and I'm only 12 years old.*"- Mindy, 12-year-old living with CPVT

"My personal symptoms with nadolol is the extreme fatigue. I am a mom of a super busy toddler, and having fatigue is not easy in your day-to-day life with a toddler. Toddlers just go, go, go, and it's hard to keep up with him when you feel that fatigue in your day-to-day life." - Allie, living with CPVT, and family member of others living with CPVT

Anxiety and PTSD

Medical treatments for CPVT can lead to anxiety as well as PTSD. Being forced to reduce physical activity can be traumatizing for those who are athletic.

Propranolol and nadolol affected Kerwin's daughter*. "She became very temperamental and depressed, and this was so uncommon, because Morgan was just a joyful, bubbly personality that would fill every room, but she just was lethargic and depressed, and that was so uncommon for her."* - Kerwin, parent of a daughter who passed away from CPVT

Eva's husband received an S-ICD after experiencing a sudden cardiac arrest. *"So since then, … he did have a lot of anxiety about driving, about being home alone. It's been a few years now, so he's gotten better with it."* - Eva, wife and parent of family members living with CPVT

Allison's family had to stop all sports activities, which was hardest on her daughter. *"It was completely devastating to her. …But she has definitely gone through all of the cycles of grief with this lifestyle loss. And I think to some extent, our entire family has as well, because our entire family lifestyle was centered around sports and physical activity."* - Allison G., parent of an 18-year-old daughter living with CPVT

Other drawbacks of current treatment choices

Other drawbacks of current treatment approaches include **chronic pain**, and **medication contraindications**.

Chronic pain can result from surgical interventions such as ICD implantation, LSCD and catheter ablations, as described throughout this report. Thomas decided not to pursue a treatment after learning about this treatment-related side effect.

"The only option I have left is denervation. Having researched the procedure and spoken with multiple denervation patients, this is hardly an option at all. The die is set for me. I'm 57 and have lived a full productive life." - Thomas, 54-year-old living with CPVT

Medication contraindications.

"My son had a cold that he struggled with forever. I can take Robitussin or DayQuil or NyQuil, whatever it would take, and that takes care of it. Well, my son can't take those for his condition. And at the end of the day, the things that he does take do have their side effects." - Josef, parent of a 10-year-old son living with CPVT

Other drawbacks identified by the CPVT community

Other drawbacks of current treatment approaches include the **lack of CPVT knowledge**, and **difficulties obtaining genetic testing**.

Lack of CPVT knowledge. Many patients had to educate their physicians about CPVT. Some felt that the lack of specialist knowledge about CPVT may have compromised care and outcomes.

"We later learned his top neurologist and epilepsy expert had never heard of CPVT or the correlation between seizures and CPVT." - Jen, 46-year-old living with CPVT and parent of two sons, one who passed away from CPVT at 10 years of age

Difficulties obtaining genetic testing. Not all gene variants are included in next generation screening panels and insurance may not cover all family members to get tested.

"She was tested genetically, and the RYR2 [gene test] was a part of it, but we haven't been tested. And at the time, our health insurance didn't even support or approve her testing. … We had to have our doctor write letters just to get the testing." - Kerwin, parent of a daughter who passed away from CPVT

Device failure

Many have experienced ICD failure or malfunction, fractured leads, and devices becoming obsolete. Some have had multiple surgeries to replace and even remove their devices.

"I'm on my fifth ICD, had difficulties with the lead extraction in 1998, and moved the device from the left side of my chest to the right." - Tom, 43-year-old living with CPVT, parent of a daughter living with CPVT

"He was initially fitted with an ICD and had this for six years until recently when they removed it and inserted a loop recorder instead. This was … recommended due to the malfunctioning of ICD's and the inappropriate shocks that they can give." - Janai, parent of a 12-year-old son living with CPVT

"*Although I know research has gone a long way for ICD, I'm still frustrated at times as to why ICD only lasts 10 to 15 years."* - Aimmy, 37-year-old living with CPVT

Requires too much effort and/or time commitment

Many spoke about how much time and effort it requires to take these medications each day. Some described how having medications compounded takes extra time.

> *"My son has to take [medication] twice a day. He has to remember to do it, with the tiredness and things like that."* - Suzanne, parent of a 17-year-old son living with CPVT

> *"He transitioned this year from compound medication to pills. He's so proud of that piece of it, and it gives us more of a peace of mind because it's more consistently made, versus being less accessible or having only one compounding pharmacy within our whole area that's in our insurance network."* - Josef, parent of a 10-year-old son living with CPVT

Receiving multiple shocks

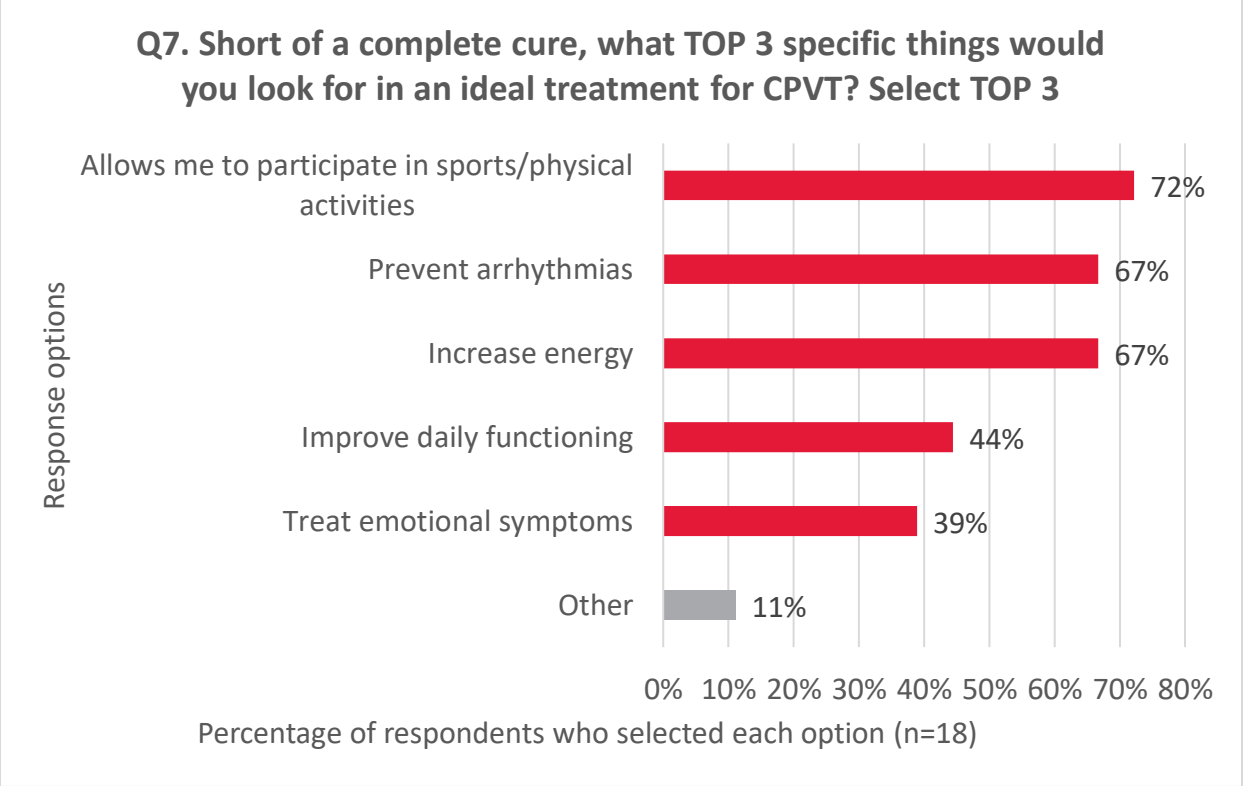
Although this poll option was not selected as anyone's top three choices, many described receiving multiple shocks from their ICD.

> *"Since 2013, I've had about 50 appropriate shocks, 32 of those happened on the same day, all within a half hour. The shocks surprised me each time, even though I always anticipate them. I yelp whenever my ICD fires and my vision is filled with a flash of light. Although when I have received ICD shocks in public, no one seems to hear the yelp or even notice."* - Shanief, 34-year-old living with CPVT

> *"My twelve-year-old son has CPVT and was initially fitted with an ICD. He had this for six years until they removed it due to the inappropriate shocks that they can give."* - Janai, parent of a 12-year-old son living with CPVT

The CPVT community needs a treatment to address the root cause of the disease and to improve quality of life

Individuals living with CPVT and their family members used online polling to select the top three specific things – short of a complete cure - that they would look for in an ideal CPVT treatment. Poll responses are listed below and described with patient quotes.



Poll respondents include patients, parents and caregivers who chose to participate in online polling. 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 but are intended to complement the patient comments made during and after the meeting. Poll responses selected by more than 33% of poll respondents are shown in **red**.

Allows me to participate in sports/physical activities

Being allowed to freely participate in sports and physical activities would significantly improve quality of life for those living with CPVT. However, this will likely require a cure for CPVT rather than just a treatment.

> *"I hope that one day my child and my niece who we discovered also have [CPVT] can continue to play sports without relying on an ICD to save their life."* - Valerie, living with CPVT, parent and family member of others living with CPVT

> *"Treatments do not 'cure' CPVT. The meds help me to control my heart rate, the ICD is ready to shock me if it goes up too high, but I still need to avoid activities that take my*

rate too high, and they don't address the root problem. They provide a safety net, but life is still restricted." - Lisa, 66-year-old living with CPVT

Prevent arrhythmias and cardiac arrest.

Family members want their children to be safe from cardiac arrests and from inappropriate shocks.

"Nadolol and flecainide won't prevent a cardiac arrest, necessarily." Josef wants a treatment to offer him, *"Peace of mind knowing that what we're doing is able to protect him and keep him safe …a hundred percent assured that there will be no certain cardiac arrest or anything else."* - Josef, parent of a 10-year-old son living with CPVT

"Ideal treatment would be medication management and an ICD that recognizes bidirectional VT so that the shocks are appropriate and does not trigger a v-tach storm." - Angela, living with CPVT

Increase energy

"*I really hope a new medicine can be made so I can feel better and have more energy and have a normal kid life.*" - Mindy, 12-year-old living with CPVT

"If there could be a drug that works as well as, for example, nadolol but doesn't cause that kind of fatigue, ... something that would be able to help push that energy rather than drain it would be incredibly helpful." - Jen, 46-year-old living with CPVT and parent of two sons, one who passed away from CPVT at 10 years of age

Improve daily functioning

For some, fewer side effects such fatigue would help to improve daily function. For others, not needing to carry around an AED would improve daily functioning.

"I hope in the future that we can continue to develop [treatments] that maybe don't have as many side effects as we have in our current treatments."- Allie, living with CPVT, and family member of others living with CPVT

"Something that is protective but also allows for resumption of a somewhat return to normalcy. Whether that's energy level or getting back to an activity, it's improving just the overall quality of life. - Allison G., parent of an 18-year-old daughter living with CPVT

Treat emotional symptoms

Several spoke about the need for more emotional and mental health support for those living with CPVT and their families.

"I'm wondering if we can support the whole person better through this. CPVT impacts your entire life, but you get specialized physical care only." - Lisa, 66-year-old living with CPVT

In addition to a reduction in side effects, Allie would like more support for herself and her siblings to help them, "*Working through those emotional symptoms of: not being sure if you're going to go into cardiac arrest, or the fear of taking that dance class and not knowing if you're going to collapse in the middle of the dance class. Helping with that fear, easing that fear and that burden of the fear."* - Allie, living with CPVT, and family member of others living with CPVT

Other treatment priorities

Other important things required by individuals living with CPVT and their family members include **a cure for CPVT**, **a once-a-day treatment**, **better CPVT screening and diagnosis**, **more research**, devices with better battery life, less surgeries.

A cure for CPVT. Individuals living with this condition require a treatment that addresses the cause of the disease rather than just the symptoms. Many specifically wish for gene therapy.

"My hope to see better treatments for CPVT would be an understatement. I'd like to see drug trials continue and expand to find a cure in gene therapy. It would be a dream of mine for my child and grandchildren to never experience the same things I have." - Tom, 43-year-old living with CPVT, parent of a daughter living with CPVT

Once-a-day pill or treatment.

"I wish there was a single treatment given once a day that was better at controlling the arrhythmia. Something less invasive than having an ICD for the rest of their lives. Obviously, we would love a cure but a better treatment would be welcomed." - Julie, living with CPVT and parent of two sons, ages 15 and 11, living with CPVT

Earlier screening, diagnosis and treatment

"Ability to detect CPVT across a larger population and understand prevalence and variation. Through most of my life, I had no idea of the risks that I was running when I would have a VT incident. … Hope for better detection. My genetic test did not reveal a genetic component. My father's death of VT in 2013 did not trigger testing of family, or a deeper look into the cause. He had a prior incident of VT four years prior to that, for which CPVT was also not considered." - Lisa, 66-year-old living with CPVT

More research

> *"Would like to know about long term effects of CPVT, like how the heart might change with time or how different genetic variants might result in different phenotypes with time."* - Nancy, living with CPVT

Incorporating Patient Input into a Benefit-Risk Assessment Framework

The CPVT EL-PFDD meeting helped to increase the understanding of how arrhythmogenic cardiomyopathy impacts patients and their loved ones. The meeting also reinforced the urgent need for effective therapeutics for this disorder. **Table 1** speaks to the challenge of having a lifelong (albeit with a potentially shortened lifespan) disease burden that patients living with CPVT 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 CPVT. The data resulting from this meeting may help inform the development of CPVT-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 of patients and families living with CPVT presented at the June 11, 2024 EL-PFDD. The collective hope of CPVT families is that this meeting will encourage future research and successful new product development for people living with CPVT who urgently need better treatment options. Note that the information in this sample framework is likely to evolve over time.

> *"CPVT has taken so much for me over the years: time, money, energy, exercise, ambitions, dreams. For now, I live with CPVT and just try to cope and survive."* - Shanief, 34-year-old living with CPVT
>
> *"There have got to be better options on the horizon for people diagnosed with this hidden killer. When I was told of the mortality rates of CPVT, I was astounded. Any other ailment that kills 10 percent of sufferers should get a LOT of attention."* - Thomas, 54-year-old living with CPVT
>
> "*One doctor told me recently that our daughter Morgan was born a little too soon to benefit from some of these advances today, and that really broke our hearts while at the same time we're determined to do whatever it takes to help change lives."* - Kerwin, parent of a daughter who passed away from CPVT

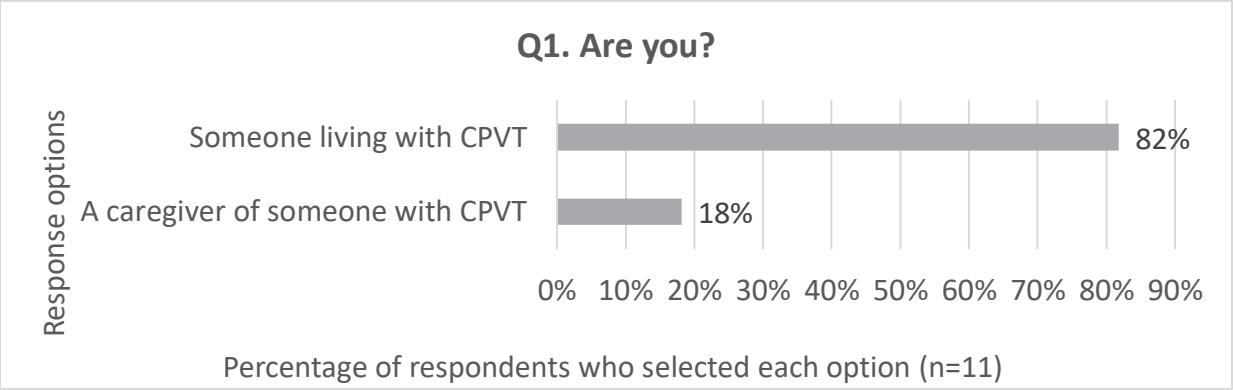
TABLE 1: Benefit-Risk Table for CPVT

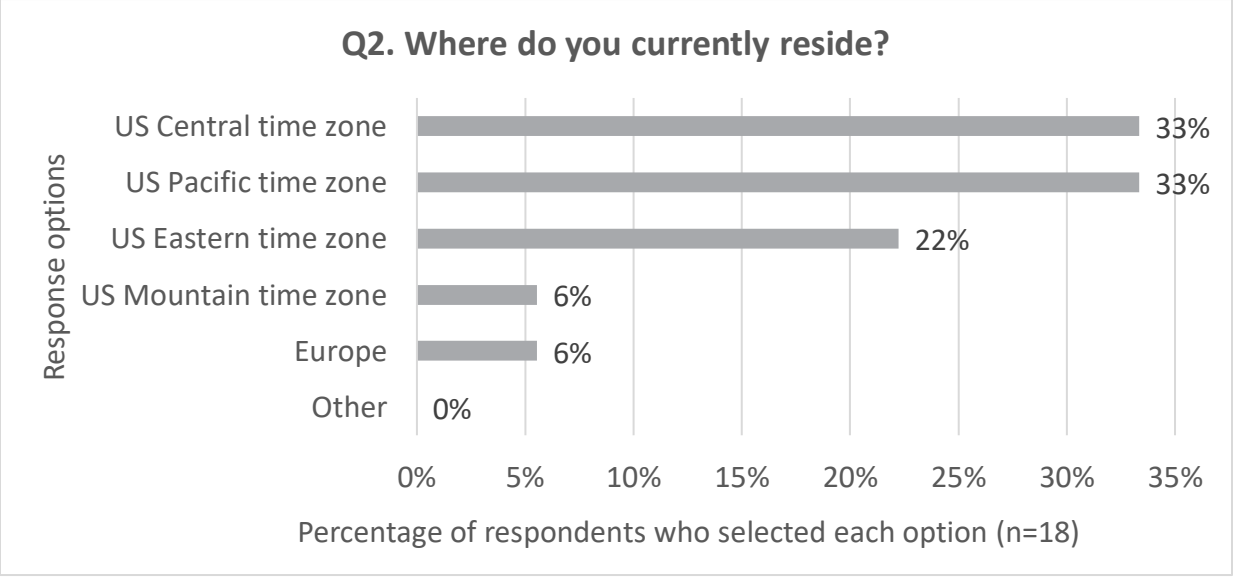
	EVIDENCE AND UNCERTAINTIES	CONCLUSIONS AND REASONS
ANALYSIS OF CONDITION/ IMPACTS ON ACTIVITIES OF DAILY LIVING	**CPVT is a very rare genetic cardiac channelopathy,** with an estimated prevalence of 1:10,000**.** CPVT is usually inherited in an autosomal dominant fashion and may affect many members of the same family. However, some have de novo gene variations. **CPVT diagnosis can be lengthy and complicated**. Diagnosis often happens only after other family members experience a cardiac arrest. **CPVT and its therapies are characterized by severe health concerns**: cardiac arrest, light-headedness and fainting, abnormal heart rhythm and fatigue, impaired exercise tolerance, weight loss or gain, seizures and other secondary effects from seizures, cardiac arrests and falls.	**CPVT takes an enormous toll.** Many have experienced the sudden and unexpected loss of children, parents and siblings. **CPVT and its therapies diminish quality of life.** Biking or playing sports, stamina, and attending social events with family and friends are all impacted. Psychologic stress, medication side-effects and restrictions on physical activities limit work and career aspirations and diminish school performance. **CPVT is accompanied by constant worries** about premature death, cardiac arrest and passing the gene on to other family members as well as fears of an uncertain future for affected family members. These worries result in anxiety and depression due to the disease, as well as current therapies, and lack of therapies that target the disease itself.
CURRENT TREATMENT OPTIONS/ PROSPECTS FOR FUTURE TREATMENTS	**Most individuals living with CPVT require multiple medical therapies to manage their disease**. This includes beta blockers and sodium channel blockers, avoiding sports and other lifestyle modifications, ICD implantation, LCSD. The CPVT-associated anxiety and PTSD necessitates counseling, antidepressants and anti-anxiety medications. **Most reported that CPVT treatments worked to a great extent or somewhat**. Despite treatment successes, CPVT treatment drawbacks are significant and include side effects from current pharmacological therapies that may be life limiting and cause impaired physical function, chronic pain from device surgeries and LCSD, and device failures that result in medical complications and negative impacts on both physical and mental health.	**The CPVT community needs a treatment to address the root cause of the disease and to improve quality of life.** The community needs a treatment that allows them to participate in sports/physical activities, to prevent arrhythmias and cardiac arrest, increase energy, improve daily functioning, treat emotional symptoms. In addition to a cure for CPVT, the community needs a once-a-day treatment, better CPVT screening and diagnosis, and more research **For those living with CPVT, current treatments aren't always successful in improving quality of life, social, or physical function. Current therapies also leave anxiety, depression, and PTSD unaddressed.**
	See the Voice of the Patient report for a more detailed narrative.	

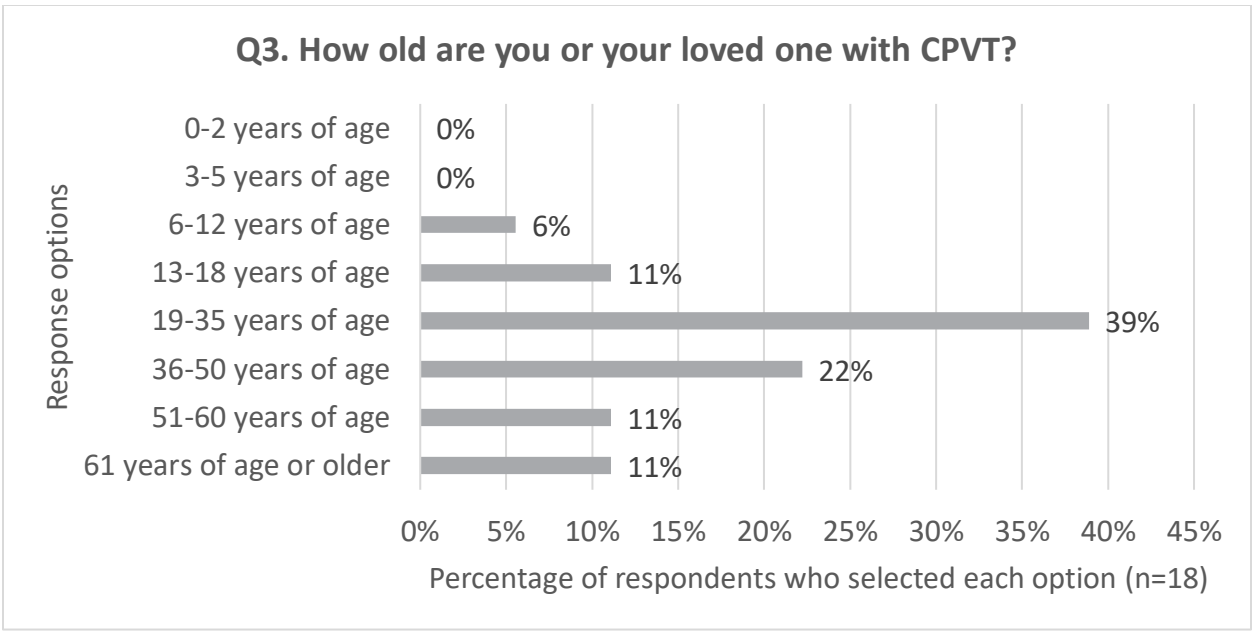
Appendix 1: Demographic Polling

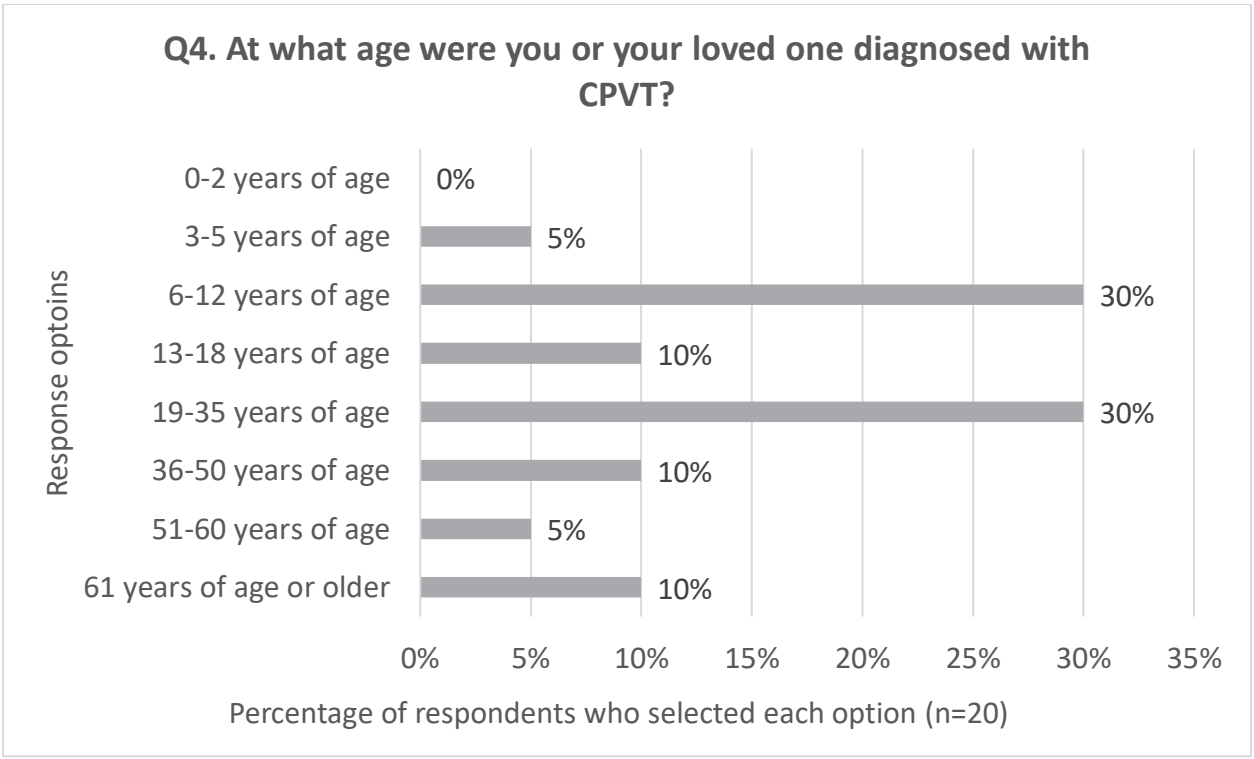
The graphs below include patients, parents and caregivers who chose to participate in online polling at the June 11, 2024 meeting. The number of individuals who responded to each polling question is shown below the X axis (N=x).

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






Q3. How old are you or your loved one with CPVT?
Response options
0-2 years of age
3-5 years of age
6-12 years of age
13-18 years of age
19-35 years of age
36-50 years of age
51-60 years of age
61 years of age or older
0%
0%
6%
11%
39%
22%
11%
11%
0% 5% 10% 15% 20% 25% 30% 35% 40% 45%
Percentage of respondents who selected each option (n=18)


Q4. At what age were you or your loved one diagnosed with CPVT?
Response optoins
0-2 years of age
3-5 years of age
6-12 years of age
13-18 years of age
19-35 years of age
36-50 years of age
51-60 years of age
61 years of age or older
0%
5%
30%
10%
30%
10%
5%
10%
0% 5% 10% 15% 20% 25% 30% 35%
Percentage of respondents who selected each option (n=20)

Appendix 2: June 11, 2024 EL-PFDD Meeting Agenda

9:30 am to 4:00 pm ET

The CPVT Patient Voice

1:00-1:10 am	Welcome: *Genevie Echols, RCIS, Family Support Director, SADS Foundation*
1:10 -9:40 am	FDA Opening Remarks and Overview: *Shetarra Walker, MD*
1:15-1:30 pm	CPVT Clinical Overview: *Arthur A.M. Wilde, MD, PhD, Amsterdam UMC, the Netherlands*
1:30-1:45 pm	Introduction and CPVT session overview: *James Valentine, JD, Hyman, Phelps & McNamara, PC, Genevie Echols, RCIS, Family Support Director, SADS Foundation*

Topic 1: Living with CPVT: symptoms and daily impacts

1:30-1:45 pm	Panel discussion - 3 panelists
1:45-2:35 pm	Audience and remote polling; Moderated audience discussion - 5 discussion starters

Topic 2: Current and future treatments for CPVT

2:35-2:50 pm	Panel discussion - 3 panelists
2:50-3:40 pm	Audience and remote polling; Moderated audience discussion - 5 discussion starters
3:40-3:45 pm	Summary of CPVT Patient Voice: *Larry Bauer, RN, MA, Sr Regulatory Drug Expert, HPM*
3:45-3:50 pm	Closing remarks: *Genevie Echols, SADS Foundation*
3:50 pm	Adjourn

Appendix 3: CPVT Discussion Topics

Topic 1 Living with CPVT: Symptoms and Daily Impact

1. How does CPVT affect you or your loved one on best and on worst days?
2. How have your or your loved one's symptoms changed over time? How has the ability to cope with the symptoms changed over time?
3. Are there specific activities that are important to you or your loved one that you/they cannot do at all or as fully because of CPVT?
4. What do you fear the most as you or your loved one gets older? What worries you most about your or your loved one's condition?

Topic 2 Current and Future Approaches to CPVT Treatment

1. What are you currently doing to manage your or your loved one's CPVT symptoms?
2. How well do these treatments treat the most significant symptoms and health effects of CPVT?
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 CPVT? What factors would be important in deciding whether to participate in a new research trial?

Appendix 4: Panelists and Callers

Session 1 Pre-recorded Panel
Pam, 82-year-old living with CPVT, family member of others living with CPVT
Kennedy, 29-year-old living with CPVT
Aimmy, 37-year-old living with CPVT
Jen, 46-year-old living with CPVT and parent of two sons, one who passed away from CPVT at 10 years of age
Sammy, 17-year-old living with CPVT

Session 1 Discussion starters
Julie, living with CPVT and parent of two sons, ages 15 and 11, living with CPVT
Eva, wife and parent of family members living with CPVT
Allison H., living with CPVT for over 20 years
Rachel, parent of a 19-year-old daughter living with CPVT
Greg, living with CPVT for 28 years

Session 1 Callers
Kerwin, parent of a daughter who passed away from CPVT

Session 2 Pre-recorded Panel
Shanief, 34-year-old living with CPVT
Rachelle, 27-year-old living with CPVT
Tom, 43-year-old living with CPVT, parent of a daughter living with CPVT

Session 2 Discussion starters
Suzanne, parent of a 17-year-old son living with CPVT
Lisa, 66-year-old living with CPVT
Josef, parent of a 10-year-old son living with CPVT
Allie, living with CPVT, and family member of others living with CPVT
Allison G., parent of an 18-year-old daughter living with CPVT

Session 2 Callers
Julie, living with CPVT and parent of two sons, ages 15 and 11, living with CPVT

Appendix 5: Additional Submitted Patient Comments

To ensure that as many voices as possible from the Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) Externally Led Patient Focused Drug Development (EL-PFDD) Meeting were heard, an online comment submission portal was open before and four weeks after the meeting. Submitted comments are presented in this appendix, and respondents are identified by their first name only. Selected comments are included in the main body of the *Voice of the Patient* report.

Multiple comments from the same patient were clustered together. Some members of the CPVT community responded specifically to the discussion questions which are presented below and italicized in the text. Note that comments were not edited or rewritten, and healthcare provider and hospital names and locations were redacted.

Eva, wife and parent of family members living with CPVT

My husband had a sudden cardiac arrest in 2016 at the age of 36 he left the hospital with an S-ICD and no explanation as to what caused this. I wanted to run tests on my son but was denied. In 2021 after requesting again for tests, my son was found to have CPVT, and we finally knew what caused my husband's SCA 5 years earlier.

Suzanne, parent of a 17-year-old son living with CPVT

My son Cian was diagnosed with CPVT in 2020 when he was 13 years old, however, his symptoms started when he was 10. He started having syncopal episodes during times of exercise and other activities. His first visit to a cardiologist was in 2019 when he was 12. He had an ECG and echocardiogram and all seemed to be normal. He was scheduled for a follow-up visit the following year. At that follow-up, he was found to have a junctional escape rhythm on his ECG. He was sent home with a Holter monitor and after the review of the Holter, he had a stress test. After his very abnormal stress test, he was sent to an electrophysiologist and was diagnosed with CPVT. He currently takes flecainide and nadolol. He also has a loop recorder implanted in his chest as a continuous ECG. He has had to adjust the way he participates in activities. He has restrictions from competitive sports activities but can participate recreationally. We also own an AED as a precaution if he has a cardiac event. In the future, it would be nice to have therapies and or treatments that don't involve remembering to take daily medications that have side effects and complications of their own.

Thomas, 54-year-old living with CPVT

On April 10, 2010 (at 44 years old) midway into a vigorous workout, I felt funny and stopped exercising. I sat down and developed tunnel vision. At this point I knew I was going to pass out and struggled to stay conscious. In any event, everything went black.

Here’s where my story gets to continue. As I lay pulseless on the gym floor, an off-duty paramedic watched my sudden collapse and jumped in to render aid. I should also note that an AED was mounted less than ten feet from where I went down. If I were running or on a bicycle, I have no doubt that my outcome could have been tragic. The medic assessed me, determined

that I had no palpable pulse, and allowed the AED to do its work. I awoke surrounded by paramedics and firefighters. I remember that the oxygen being delivered through a cannula felt wonderful. The medics determined that my abnormal rhythm dictated that they load me up and go to the nearest cardiac center asap. They put me on a backboard (I split my head open on a piece of gym equipment) and got me to the nearest catheter lab. The ER docs determined that I'd had a significant MI (heart attack) and got me to the catheter lab. I still remember the confusion in the voice of the cardiologist when she couldn't find any blockages at all. With the nitroglycerin, beta blockers, and mild sedative administered at the hospital, my rhythm had returned to normal. I was kept overnight in the CCE (Cardiac Care Unit), discharged and instructed to follow up with cardiology. I had an appointment with my confused cardiologist and referred to an electrophysiologist (EP). My EP put me on atenolol and a statin and scheduled for a treadmill the following week.

At my treadmill, I was about six minutes into the test when the doctor pushed the emergency stop, spun around and shoved me into a chair that magically appeared under me. She immediately applied carotid pressure as she watched me slip into ventricular tachycardia. My irregular beat resolved spontaneously, and I was sent home with orders to avoid any stress or excess physical activity.

I was faced with a host of options… Drugs. Atenolol wasn't working. Nadolol was next. AICD to address lethal arrhythmia.

Surgery options… Cardiac denervation. Cardiac ablation (fairly new at the time).

For a year, I chose drug therapy with a large dose (160mg) of nadolol. This conservative route was somewhat effective. The side effects were not great. Low blood pressure and a resting heartbeat of 35 made life fairly miserable.

What I didn't know until about seven months into my conservative treatment plan was the suffering of my wife of 20 years. She worried every minute I was out of contact during my days. I work in the medical field (specifically, in surgery), so I would be out of contact for hours. Unbeknownst to me these hours were filled with dread for my poor wife, so a year after my event, I called my EP and got on the schedule for an AICD implantation.

In the first year of living with an AICD, I was administered a therapeutic shock two separate times. I must note that my defibrillator was programmed very conservatively, so the shocks were definitely needed to sustain life.

Back to the drawing board.

My EP referred me to another EP that was having some success with ablation for paroxysmal VT. She recommended I have the procedure as she explained that patients die OF CPVT and not with this ailment. I went ahead and had the ablation procedure. The ablation took over four hours. It took two hours to map my heart, and another 2.5 hours to attempt to eradicate to aberrant foci in my heart muscle. I only know the timeline for my procedure because it was required that I be conscious due to the catacholaminergenic aspect of my ailment. Good times!

Suffice to say, that the mapping was uncomfortable.

The ablation was very painful. It was like a medically induced heart attack. I had crushing chest pain, left arm pain, neck pain, shortness of breath, an amazingly bad headache.

When my procedure was done, I was put in the CCU for two nights (long case, stroke risk, etc) and left off of any beta blockers.

My surgeon explained that she did her best to “put a leash on” my arrhythmia, but she had to stop ablating because of the closeness to the aortic root and the unique nature of the alternative pathways that CPVT was capable of utilizing.

After a day in CCU, the ectopic beats returned. Runs of 5-6 PVC triggered alarms and got me put back on 160mg of nadolol per day. My EP programmed my ICD to pace me at 55 with a top of 120.

As of today, I’m on my second ICD (the first was recalled!) and still dependent on a non-selective beta blocker to maintain a safe rhythm.

I get breakthrough ectopic beats once in a while. These are usually found during routine ICD interrogations. My concern over the years has never been for my wellbeing, but that of my daughter’s and my siblings’ children.

The only option I have left is denervation.

Having researched the procedure and spoken with multiple denervation patients, this is hardly an option at all.

The die is set for me. I’m 57 and have lived a full productive life.

As someone who was diagnosed later in life, my worry for the younger generation of my family is real and distressing.

There have got to be better options on the horizon for people diagnosed with this hidden killer. When I was told of the mortality rates of CPVT, I was astounded. Any other ailment that kills 10 percent of sufferers should get a LOT of attention.

I hope my story helps people understand what it’s like living with a heart that could call it quits at any moment. Research of new therapies and further testing protocols are needed to ensure early detection and intervention will give newly diagnosed patients treatment pathways that ensure a long, productive life. There have got to be better options on the horizon for people diagnosed with this hidden killer. When I was told of the mortality rates of CPVT, I was astounded. Any other ailment that kills 10 percent of sufferers should get a LOT of attention.

Jocelyn, 27-year-old living with CPVT

Comment 1

Taking beta-blockers for my CPVT makes it really hard for me to function in daily life. I'm so tired all the time that it's hard to keep up with my peers in school. They have so many extra hours per day to study and take care of themselves that I have to spend sleeping. The meds also lower my blood pressure so much that I couldn't stand for more than 15-30 mins at a time,

which made it really hard for me to have a job. I had to start an additional medication and now wear compression gear every day just to function.

Comment 2

It's important to realize that although exercise restrictions are one of the mainstays of treatment for CPVT, it's not without consequences. There are a lot of health complications associated with having a sedentary lifestyle. I'm currently in medical school and spend every day telling patients how important it is to stay physically active, all while knowing that I'm at an increased risk for everything I'm warning them about.

Comment 3

I was diagnosed with CPVT when I was 11 years old. I was pulled out of all sports and anything else that involved physical activity. To make matters worse, my school refused to excuse me from gym class at first and instead forced me to sit on the sidelines and watch all the other kids participate in activities that I no longer had access to. I didn't understand why I couldn't go run and play like all the other kids my age. It was devastating. Things haven't gotten easier with time. It's now 16 years after my diagnosis and I am still grieving the lifestyle that I lost. Not a day goes by when I don't think about my diagnosis. I have to face my own mortality every single time I take the pills that are required to keep me alive. I lie awake at night worrying about what will happen when I die.

In addition to the anxiety and depression that comes along with CPVT, the current treatment options have side effects that make my life more difficult. My body has struggled to tolerate beta blockers. At one point, I couldn't even stand long enough to take a shower without my blood pressure becoming so low that it made me ill. I couldn't stand for more than 15-30 minutes at a time before becoming light-headed, nauseous, and would pass out if I didn't sit down. It made holding a job extremely difficult. My beta blockers have also made graduate school extremely difficult for me because of significant fatigue. I sleep 9 hours at night and take 2-3 naps throughout the day just to be able to function. I lose so much time sleeping that my peers get to spend studying or taking care of myself.

Valerie, living with CPVT, parent and family member of others living with CPVT

I had my first cardiac arrest at age 38, as I was training for my first half marathon. CPR was performed and I lived! I lived to have another child, and have another cardiac arrest. This time my body brought me back. I had an ICD inserted and went through the process of discovering I had CPVT. I now take medication that helped me finally complete that half marathon with NO shocks to my ICD. I hope that one day my child and my niece who we discovered also have it can continue to play sports without relying on an ICD to save their life.

April, living with CPVT and parent of daughters living with CPVT

My oldest daughter, Madalyn collapsed and hospitalized for a few days. Three weeks later she was diagnosed with CPVT and the rest of our family and extended family was genetically tested. Several of us were diagnosed with CPVT including myself and my youngest daughter. We now know that my cousin’s death was because he also had CPVT. Madalyn is currently taking

nadolol and flecainide. Meredith is taking nadolol and is going to have flecainide administered in the hospital next week to see how her body reacts to the medication. I'd love for my girls to not have to take medication daily if possible, but we are also extremely grateful for modern medicine.

Josef, parent of a 10-year-old son living with CPVT

On October 9th, 2021, my seven-year-old son went into sudden cardiac arrest. (Prior to this incident, my son displayed no prior symptoms or any cardiac issues in his lifetime.) We began CPR and called 911 where he was resuscitated by EMS. From there, we took an ambulance to our local hospital where he crashed multiple times.

He was then flown by helicopter to a hospital. We had to travel via car since there was not enough weight allowed on the plane. He then crashed multiple times throughout the night and was continually resuscitated by medical staff until he was transferred to [the hospital].

They made modifications when they took over his care. He was sedated for almost two weeks while they looked for answers. During that time, we did not know if any neurological damage occurred, as he was intubated with the same equipment placed in our living room

We began the journey of recovery with [the hospital] and he relearned how to walk, eat, and were thrilled that our son was still cognitive and himself upon being taken off the ventilator under medical supervision.

He was diagnosed with CPVT. Both my wife and I do not carry this gene. This was the only shown symptom we have seen with this condition. He is currently treated with a combination of medication and has a loop recorder in his chest. We visit [the hospital] twice a year to evaluate and adjust his treatment if needed.

We were very fortunate, and continue to be. We will continue to face this diagnosis as he grows up, and plan to take further steps should the current treatment become ineffective or advance with further research.

This is our new normal, and we take it a day at a time. My son is my hero, and we are so grateful for the support provided by SADS, [the hospital], his school, and our community.

Dawn, living with CPVT and parent of children living with CPVT including a son who passed away at 13 years of age

I went into cardiac arrest at 29. After testing and an ICD being implanted, they sent me home with no diagnosis. 20 years passed with surgeries to change batteries and a fractured lead.

Almost 2 years ago our 11-year-old daughter passed out suddenly after running up a hill. She woke up, but the whole thing was weird. At the ER they said to have her checked out by a cardiologist, so we made an appointment. Two weeks later our son who was 13 went into cardiac arrest while swimming at camp. They did CPR quickly and used a defibrillator, he was pronounced dead two days later at the hospital. They tested him and he had the RYR2 gene, our daughters were tested and the one who passed out had the gene, the other did not. I was

then tested and I have the gene as well. We finally got answers, but it took our son dying for that to happen.

Julie, living with CPVT and parent of two sons, ages 15 and 11, living with CPVT
My 14-year-old -son was diagnosed with atrial tachycardia two days after his first birthday. He was started on flecainide and had regular follow up with his EP for years. When he was seven and younger brother was 4, the youngest was also diagnosed with atrial tachycardia. The EP was perplexed that both boys would have the same arrhythmia that is not hereditary. We had genetic testing, cardiac MRIs and regular monitoring with no change in diagnosis.

Three years later the youngest had the first of seven syncope events, five of them were cardiac arrests requiring CPR. We saw neurology and cardiology because it appeared he was having atonic seizures and we were told it would be rare for it to be syncope with atrial tachycardia. He was put on the medicines for seizures and kept having events. After the seventh event and the ninth visit to the hospital, the neurologists pushed for more genetic testing and a long term Holter monitor. The genetic test revealed the RYR2 mutation for the youngest and he was diagnosed with CPVT.

After his results came back, the whole family was genetically tested and the older brother and me (Mom) had the mutation as well.

The youngest has been treated with flecainide, nadolol and LCSD surgery. He has an implanted loop recorder.

The oldest is on flecainide and nadolol and may soon need LCSD surgery if his latest medication increase does not give the control he needs. They take heart meds three times a day. I am on nadolol alone and am considered low risk for a SCA or syncope.

We have gone through many restrictions during the last four years and currently we are allowed most activities we would normally engage in. We live in what I call a healthy fear for CPVT/Cardiac arrest episode. We do activities but always assess how exciting it might be and whether an activity might trigger an episode and whether we are near live saving people/equipment if something does happen.

We carry an AED with us. We know CPR. Our nanny knows CPR. School personnel know CPR. The boys don't know it, but they are always around someone CPR certified and within 2 minutes of an AED.
It seems the treatments are successful for the youngest - flecainide, nadolol and LCSD. But it is strange to see him be red on one side when he's hot and totally white on the other - this is from the LCSD surgery. Nadolol and flecainide may no longer be the solution for the oldest. I hate that either one of them might have to have an ICD down the road given the cons of the device. Psychologically we have to balance fear of the condition with having a happy, active childhood for the boys. It is hard.

I wish there was a single treatment given once a day that was better at controlling the arrhythmia. Something less invasive than having an ICD for the rest of their lives. Obviously, we would love a cure but a better treatment would be welcomed.

Kerwin, parent of a daughter who passed away from CPVT
Our beloved daughter, Morgan passed away in April of 2017 from CPVT. Prior to her death, we discovered that Morgan had CPVT while responding to a near death crisis that sent us to [the Children's Hospital] two days before her 10th birthday. [Name redacted], a leader in the field attended to our daughter and immediately restricted ALL activity and placed her on beta blockers, propranolol and nadolol. Morgan's life changed drastically after the prescriptions. The side effects were very difficult to deal with. Her energy was drained drastically. After a full day of school, Morgan would come home and sleep 2-3 hours before having the energy to attempt homework. Even more challenging was the mental toll that it had on our daughter. She became very temperamental and depressed. This was so uncommon for our precious Morgan. She was usually the most bubbly, joyful person in the room.

We are thankful that the study and treatment for CPVT continues to improve, and we are doing our part through A Piece of My Heart Foundation, which we started in Morgan's honor. However, we must continue to advance and collectively share information, insights and partnerships to save lives. We were told by a leading physician in the field that our daughter Morgan was born a little too soon, so she did not benefit from the advancements. This is why we are committed to making sure that other families don't experience what we have. Let's work together with SADS and the FDA to save lives...one heart at a time!

Respectfully, Kerwin & Madelyn, A Piece of My Heart Foundation

Lisa, 66-year-old living with CPVT
History: I was diagnosed with CPVT at 62 (2020/21) due to workup for shortness of breath while exercising. Prior to this, had been actively running, playing soccer, doing yoga with no concern for heart issues. Imaging, EKG and genetic test negative, stress test showed VTs. Ongoing occasional PVCs. Activity was greatly restricted on diagnosis. Slowly working toward regaining a more active life walking and doing yoga, hoping to add more back.

Metoprolol started in 2000, ICD implanted in September 2023.

Very lucky to have never had a heart attack, never had a shock & had plenty of time to think about treatments before acting on them.

Family history: father passed of unspecified VT at 85, had a prior VT episode four years prior to that. His father died in his 50's of unspecified heart attack.

What symptoms of CPVT are the most bothersome?

Generally, I don't directly experience CPVT symptoms any more due to the efforts that go into avoiding VT. Palpitations and irregular beats are concerning. Short runs of PVCs are relatively frequent under stress.

When my heart rate gets into dangerous range, it feels like I can't get air no matter how deeply I breathe. I get dizzy if it goes on for a while. Before I knew what it was, I'd go back to running (or whatever) a minute or so later. I used to do this all the time, thinking that I was just out of shape.

I'm lucky to have not had a life-threatening heart attack yet. It's the sword of Damocles - hanging there- waiting for my heart rate to spike. Don't get angry, don't run, don't get excited, don't feel. The ICD changes the risk analysis, but the shocks have their own cost: pain, appointments, loss of permission to drive."

How does CPVT impact activities of daily life?

The medication, implanted device, and avoidance of anything that can get adrenaline up (and hence the heart rate) have the most impact on my life.

Inactivity: During diagnosis and treatment, I needed to stop all activities that required exertion. At first that meant not ever being alone, not walking anywhere that a car couldn't pick me up. Could not walk the dog, could not participate in activities that I previously enjoyed: running, soccer, yoga, kayaking. Two years of restricted activity has led to weight gain, and associated health impact.

Fear: Needed to keep a strict watch on heart rate, at first not allowing it over 120, then over time raising it to 130. With an ICD, I'm allowed to go up to 140. I wear an Apple Watch all the time to track it, and focus on the watch when exercising. Risk of exertion & need for strict control is always present: a run of VT due to exertion or emotion may resolve itself, may become ventricular tachycardia or fibrillation.

What have you done to treat or manage your CPVT? Has it helped?

Current: Beta blockers and defibrillator. Mild exercise to get weight down.

Past: Diltiazem and amlodipine (for HBP).

During and just after diagnosis: all activity stopped. Essentially, sit on the couch and try not to die. Longer term, slowly returning to activity.

Treatments do not "cure" CPVT. The meds help me to control my heart rate, the ICD is ready to shock me if it goes up too high, but I still need to avoid activities that take my rate too high and they don't address the root problem. They provide a safety net, but life is still restricted.

Medication side effects: Had previously been on a higher dosage of beta blocker, which made me very tired and groggy, with difficulty concentrating, which was a problem at work. Since the ICD, the dosage has been reduced to a more manageable level. I gained a lot of weight during this time, which is creating new issues for me.

ICD: provides a safety net, but at a cost. Recovery time from surgery, some activities limited. If I get a shock, I may not be able to drive for 6 months even if I return to baseline right away. I do not perform activities that put me at risk of a VT while seated and driving. I'm not sure that this level of restriction is reasonable for otherwise healthy people with CPVT.

What are your hopes and desires for new therapies? i.e. what symptoms do you want to see addressed?

Ability to detect CPVT across a larger population & understand prevalence and variation. Through most of my life, I had no idea of the risks that I was running when I would have a VT incident. To me that was a normal thing to occur during exercise.

Currently treatment manages the symptoms, no cure for the underlying problem.

I was lucky to have a long time to think about getting an ICD before going ahead. It's a pretty scary thing.

I'm wondering if we can support the whole person better through this. CPVT impacts your entire life, but you get specialized physical care only. It was super interesting seeing the webinar on emotional support.

Hope for better detection. My genetic test did not reveal a genetic component. My father's death of VT in 2013 did not trigger testing of family, or a deeper look into the cause. He had a prior incident of VT four years prior to that, for which CPVT was also not considered.

How much risk would you accept for a given therapeutic improvement?

About as much as the current treatments. Since quality of life is heavily influenced by the need to balance risk levels, more risk would be a tough trade.

Amy, wife and parent of family members living with CPVT

My four children and husband have been diagnosed with CPVT after my 17-year-old son went into cardiac arrest last December.

Three of four children are currently taking nadolol and flecainide, some handle it better than others because it makes you tired and have low energy.

We had to travel to Rochester, MN for my son to have the LCSD surgery performed by an experienced surgeon. We are traveling again next week for his checkup and clearance, as well as LCSD surgery performed on my 12-year-old daughter if it gets approved by insurance. I am thankful for the resources at the [the clinic], they are amazing, but it is a huge financial burden for our family every time we need to go there. There really needs to be more options for medications and more experienced/trained surgeons for the LCSD. My son did amazing with the surgery and is doing very well and will hopefully be cleared next week for high school sports for his senior year.

Gemma, parent of a 10-year-old son living with CPVT

Our son has CPVT diagnosed after a SCA aged 3. LCSD, flecainide and nadolol.

Low muscle tone, autism and ADHD.

Trouble regulating himself.

Mental impact on our 10-year-old son.

Janai, parent of a 12-year-old son living with CPVT

My 12-year-old son has CPVT and was diagnosed when he was five after suffering from a sudden cardiac arrest. He was given 90 minutes of CPR and was placed on ECMO for seven days with a 2% chance of making it. After a week on life support, he woke up, survived and thankfully didn't suffer any brain injury.

He takes nadolol and flecainide every day. He was initially fitted with an ICD and had this for six years until recently when they removed it and inserted a loop recorder instead. This was significantly advised and recommended due to the malfunctioning of ICD's and the inappropriate shocks that they can give. He has also had LCSD surgery as another form of treatment for this condition.

He is the only one in our family with CPVT (RYR2 mutation). Myself and my husband have been genetically tested and we are not carriers so this is just localised to our son only. His brother also doesn't have it and there is no family history either.

My son sees his cardiologist every six months and does a stress test and wears a Holter for 24 hours as part of his regular care.

Nancy, living with CPVT

Had first CPVT event at age 40 with ICD placed along with metoprolol, with subsequent arrhythmia events every 4-6 years. Changed to nadolol, then flecainide added when frequent PVCs developed at rest in my 50s. Previously competed in a triathlon just before first event, then half marathons, but now unable to run at all due to shortness of breath and PVCs. Initial shockable events were not due to exertion, but last two events were during running. Would like to know about long term effects of CPVT, like how the heart might change with time or how different genetic variants might result in different phenotypes with time.

Mindy, 12-year-old living with CPVT

I went into cardiac arrest at my swim meet last year during the 200 free and had to be resuscitated and the AED is what saved my life. After genetic testing and stress tests it was proven that I have CPVT. I can no longer participate in sports or anything that can cause an adrenaline rush. The flecainide and nadolol make my heart rate so slow that I'm sluggish and tired and I'm only 12 years old. I've had the cardiac denervation done which has created a pain in my left arm and shoulder blade and makes my body temperature different on each side. I really hope a NEW medicine can be made so I can feel better and have more energy and live a normal kid life!

Angela, living with CPVT

Worst symptoms: Bigeminy with shortness of breath and exhaustion.

Best days: less shortness of breath and bigeminy

Worse days: Bigeminy no matter how far I walk.

Specific activities that I am unable to do: take care of my grandchildren.

My symptoms have gotten worse over time. Bigeminy had gotten worse, fatigue, brain fog was awful!

Fear the most: I fear that my medication will stop working and I will die of SCA. I do not currently have an ICD.

The most frustrating is the unknown of when and if I will die of SCD due to my CPVT.

I am taking nadolol and flecainide. I am only able to take the most minimal dose because of bradycardia and low blood pressure.

I am doing so much better since being on meds. I have a clearer head, I can walk to my car without bigeminy, I do have days of being somewhat dizzy with bradycardia.

Downside: Tired, low blood pressure, bradycardia, and not a "cure".

Ideal treatment: would be medication management and an ICD that recognizes bidirectional VT so that the shocks are appropriate and does not trigger a v-tach storm.

Aimmy, 37-year-old living with CPVT
I would like to elaborate on the poll question of ‘what are your worries with the current treatment?’. I would say having to go through more ICD surgeries, having leads not working or breaking as a risk, having to endure more pain from surgeries, long term side effects of the medications.