



Dravet Syndrome  
Foundation

# Voice of the Patient Report

Externally-Led  
Patient Focused  
Drug Development Meeting



## Voice of the Patient Report: Living with Dravet Syndrome

Dravet Syndrome Foundation (DSF) serves the patient community through its mission of aggressively raising funds for Dravet syndrome and related epilepsies; by supporting and funding research; increasing awareness; and by providing support to affected individuals and families.

This *Voice of the Patient* report was prepared by DSF as a summary of the input shared by people and families living with Dravet syndrome during an Externally-Led Patient Focused Drug Development Meeting (EL-PFDD). This meeting was hosted virtually on February 3, 2022.

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James Valentine, Esq. and Larry Bauer, RN, MA are employed by Hyman, Phelps & McNamara, P.C., a law firm that represents patient advocacy organizations and companies that are developing therapeutics and technologies to advance health.

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## About the Dravet Syndrome Foundation

**The mission of Dravet Syndrome Foundation (DSF) is to aggressively raise funds for Dravet syndrome and related epilepsies; to support and fund research; increase awareness; and to provide support to affected individuals and families.**

When a group of parents started the Dravet Syndrome Foundation (DSF) in 2009, there were no treatments specifically for Dravet syndrome. These parents set their sights high - to advance understanding of this little-known disease, to create new treatments and specialized care for their children, and to find a cure.

In the ensuing years, the fundraising and commitment of the Dravet syndrome community has enabled DSF to support fundamental research in the laboratory that has led to groundbreaking discoveries. **DSF is the largest non-governmental research funder for Dravet syndrome-specific research.** By expanding our knowledge of the underlying biology of the disease, researchers have paved the way for creating new treatments. DSF also recognizes that by opening lines of communication and working closely with all of our community stakeholders - including patient families, advocacy organizations, clinicians, researchers, and industry partners - that we can assure rapid distribution of information and avoid duplication of efforts.

DSF's steadfast commitment to advancing Dravet syndrome research, as well as our community's engagement throughout the clinical trial and drug development process has helped enable three new treatments for the disease, with several additional clinical trials already underway or soon starting. While we are pleased with the progress we have seen in the last decade, there is still much we have to do.

By organizing this EL-PFDD Meeting, we were able to assure that we have captured the patient family perspective that will provide appropriate context for the FDA when making regulatory decisions on new drugs for treating Dravet syndrome. We recognize that this is a unique and important opportunity for our patient community to share about the symptoms that matter most to them; the impact Dravet syndrome has on patients' daily lives; and patients' experiences with currently available treatments and what unmet needs remain. We appreciate the opportunity and are pleased to have these important perspectives captured in this *Voice of the Patient* report.



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## Executive Summary and Key Meeting Insights

Dravet Syndrome Foundation (DSF) hosted the Dravet Syndrome Externally-Led Patient Focused Drug Development (EL-PFDD) meeting on February 3, 2022. This meeting was held to provide a patient and caregiver perspective of the symptoms and burdens associated with Dravet syndrome (DS) in daily life, as well as the massive unmet treatment needs experienced by families who live with DS every day. The meeting was held virtually to enable as many community members to participate as possible and to allow many different voices to be heard.

This EL-PFDD meeting was modeled after the work of the FDA's Patient Focused Drug Development (PFDD) initiative. PFDD is a systematic way of gathering patient perspectives on their condition and on available treatments. The information gathered at the meeting is presented in this *Voice of the Patient* report, a high-level summary of the perspectives generously shared by the families and caregivers of individuals living with DS, who participated in the February 3, 2022, EL-PFDD meeting. The report also includes selected comments that were submitted through an online portal as well as data captured by DSF's survey, *Caregiver Opinions about Disease Modifying Therapies for Dravet Syndrome*, which was held and promoted concurrently with the EL-PFDD meeting process.

The information in the *Voice of the Patient* report may be used to guide therapeutic development and inform the FDA's benefit-risk evaluations when assessing therapies to address DS. The hope is that this information will catalyze better treatments and ultimately a cure for those affected by DS.

DSF has provided this report to the FDA, government agencies, regulatory authorities, medical products developers, academics, and clinicians, and it is publicly available for the many stakeholders in the DS community, including DSF's international partnering advocacy organizations. Note that the input received from the February 3, 2022, EL-PFDD meeting reflects a wide range of DS experiences, however not all symptoms and impacts may be captured in this report.

### Key meeting themes and insights:

**(1) Dravet syndrome is characterized by intractable seizures.** The different types of seizures change with time, and the consequences of some seizures are catastrophic. Seizures are a persistent threat, impair development, and interfere in activities of daily living. Even with multiple medications, most patients experience regular breakthrough seizures.

**(2) Dravet syndrome is MORE than seizures: many other significant Dravet syndrome-related symptoms exist.** These can include developmental delays and regression, speech and language impairment, sleep disturbances, disruptive behaviors, problems with balance and gait, and many others. The incidence and severity of these symptoms vary from one individual to the next.



**(3) Dravet syndrome symptoms, including seizures, are influenced by a complex interplay of factors.** Maturation and puberty, medications, disease progression, sleep, and environmental triggers can all contribute.

**(4) Life with Dravet syndrome is extremely unpredictable.** All aspects of life are affected, not only for the individual living with DS, but for their parents and siblings. Rigid schedules, rigorous advance planning, and extreme flexibility are required to manage seizure triggers and behaviors. As a result, DS patient families miss out on the activities, celebrations, holidays, and events that most take for granted. The lack of social interaction/relationships, lack of independence, and communication are major challenges.

**(5) Individuals with Dravet syndrome will require constant supervision and care for their entire lives.** The syndrome is progressive, and many symptoms can become more severe with age. Parents worry about ongoing care and access to resources for their children, as well as premature mortality, disease progression, worsening cognition, and intellectual impairment.

**(6) All patients with Dravet syndrome require polytherapy to treat their symptoms, particularly seizures.** Patients typically try many different medications and suffer significant medical consequences such as side effects, impacts on development, or cognition. Parents and caregivers agonize over potentially life-altering treatment decisions. As medication endpoints are subjective and it can take a long time to observe changes, it can be difficult to tell if treatments are working.

**(7) Most medications are targeted at controlling seizures, few address other symptoms or the disease itself.** Current medications treat some but not all symptoms, and only control disease symptoms “somewhat”. As medications lose efficacy, which most do, seizures resume. Quality of life is impacted. Even with multiple medications and a plethora of therapies, most patients experience many symptoms and have few evidence-based approaches to use.

**(8) Families living with Dravet syndrome have great unmet treatment needs and desperately require new therapies.** Patients with DS need therapies that improve quality of life. In addition to controlling or preventing seizures, families living with DS would like therapies to address developmental delays and regression, sudden unexpected death in epilepsy patients or SUDEP, speech and language impairment, sleep disruption, and disruptive behaviors. Disease modifying therapies are needed, including treatments for those with different genetic mutations. Medications are required for individuals at different points in their lives (including adults).

**(9) The majority of caregivers to individuals with Dravet syndrome would be willing to consider a variety of disease-modifying therapies.** Survey results demonstrated that caregivers would prioritize a less permanent therapy that would not exclude their loved ones from receiving similar therapies in the future, over a one-time treatment. Caregivers would also prefer less invasive administration options for their loved ones. Despite these preferences, over half of caregivers would still consider a permanent and invasive therapy if it offered a definite major improvement in seizures, even without affecting other symptoms.



## Introduction and Meeting Overview

### Clinical overview of Dravet syndrome<sup>1</sup>

Dravet syndrome (DS) is a severe developmental and epileptic encephalopathy, characterized by intractable seizures. The symptoms and impacts of this rare disease reverberate through nearly every aspect of patients' and their families' lives.

DS is marked by an onset of seizures, usually between five and eight months of age, after previous normal development. The initial seizure is often prolonged and uncontrollable, and in many cases associated with fever. Additional febrile and afebrile seizures emerge over the next months and years, including but not limited to tonic-clonic, hemiclonic, myoclonic, absence seizures, and episodes of status epilepticus. Seizures during sleep become more frequent as patients age.

DS is characterized by an alarming 15-20% mortality rate by adulthood. Sudden unexpected death in epilepsy or SUDEP is a significant risk, and is responsible for over half, or 53% of premature death. SUDEP remains highly prevalent throughout the patient's lifespan. A third, or 36% of deaths occur as a result of an acute encephalopathy in the setting of status epilepticus, and another 10% are due to drowning.

While seizures are a defining characteristic, DS includes many non-seizure-related comorbidities. Although most children with DS experience normal development in their first year, some degree of developmental delay emerges for all patients by age four or five years. These can include motor impairment, speech impairment, learning difficulties, autism, and other behavioral disturbances. Other comorbidities emerge and evolve with time and include gait and balance issues, hypotonia, hyperthermia, sleep disturbances, and nutritional issues.

Variants in the *SCN1A* gene are the most common genetic cause of DS, which encodes the Nav1.1 sodium channel. Since the first variant was identified in 2001, over 1700 different *SCN1A* gene variants have been described, and 85-90% of patients have an identified *SCN1A* gene variant. The variants occur across the gene, most commonly in the voltage-sensitive regions or in the pore-forming regions of the protein. Although over half of the gene variants result in shortened or deleted protein and 30-40% cause the production of an incorrect protein structure, the genotype-phenotype correlations are very poor, so these different variants are not related to different symptoms or disease severity.

DS occurs 1 in 15,700 births, which equates to about 225 new cases per year in the United States. However, it is likely that many patients remain undiagnosed.

DS involves a complex diagnostic journey. At present, at least half of the patients are diagnosed between six and 12 months. This is an improvement, as patients were often diagnosed more

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<sup>1</sup> Most of this content was extracted from the February 3, 2022 presentation by Dr. Joseph Sullivan, Associate Professor of Neurology and Pediatrics and the Director of the University of California San Francisco Pediatric Epilepsy Center.



than four years after their first seizure. Genetic testing is now recommended for children who experience seizure onset at less than 18 months of age with no other known cause, in addition to features consistent with a DS phenotype. Testing is now conducted with epilepsy gene panels to identify *SCN1A* gene variants. Even in 2022, about 10% of patients fit the DS phenotype, but yet do not have any known *SCN1A* gene variants.

Therapies and treatment approaches for DS will be described from the patient and family perspective in this report.

## Meeting summary

The Dravet Syndrome Externally-Led Patient Focused Drug Development (EL-PFDD) meeting was held virtually on February 3, 2022. The meeting represented an important opportunity for Dravet Syndrome Foundation (DSF) to share patient and family perspectives on the challenges and unmet treatment needs of those living with DS. The Dravet Syndrome EL-PFDD meeting was co-moderated by Veronica Hood, PhD, DSF Scientific Director, and by James Valentine, JD, MHS, from Hyman, Phelps and McNamara.

Dr. Hood opened the meeting by welcoming and thanking meeting participants for their attendance. She acknowledged the true disease experts - caregivers and patient families - and thanked them for their courage for speaking up on behalf of those they loved who were unable to voice their own needs. She described some of DSF's successes and thanked the FDA for their participation and industry partners and researchers for continuing to work for a cure.

Michelle Campbell, PhD, the Senior Clinical Analyst for Stakeholder Engagement in the Office of Neuroscience within the Center for Drug Evaluation and Research, offered some remarks on behalf of the FDA. Dr. Campbell defined the FDA's role which is to protect and promote public health by evaluating the safety, effectiveness, and quality of new products. She described the FDA's commitment to better understand rare diseases, to identify unmet needs and opportunities to accelerate rare disease drug developments, and to evaluate the benefits and risks of any new therapies in development.

Dr. Joseph Sullivan, a Professor of Neurology and Pediatrics and the Director of the University of California San Francisco Pediatric Epilepsy Center provided a high-level clinical overview of DS and its manifestations. He described the genetics, the typical diagnostic pathway, and the epidemiology of the syndrome. He presented the currently available treatments for DS as well as some of the novel therapies in development. He concluded by describing DS therapeutic challenges.

Dr. Hood and James Valentine provided an overview of the meeting structure and encouraged families and caregivers of individuals living with DS to contribute to the dialogue via online polling, calling in by phone, and contributing written comments using the online portal.

Online polling was used to determine the demographics of the meeting attendees who were representing those living with DS and are presented in **Appendix 1**. The majority of poll



respondents (63%), were located in the US Eastern Time Zone, followed by the US Central Time Zone, with 26% from the US Central, Mountain, and Pacific time zones combined. The remaining 11% of attendees were from Europe, Canada, and from the US Alaska Daylight Time Zone. Half, or 51% of people living with DS represented at the meeting were female, 47% were male and 2% identified as other. Poll respondents representing children with DS aged 0-5 years old were the largest group of individuals in attendance, represented by 40% of poll respondents and children aged 6-10 years and teens aged 11-18 years were represented by 20% and 22% of poll respondents, respectively. Adults aged 19-30 years and adults aged 31-50 years were represented by 14% and 4% of poll respondents, respectively and there was no representation of adults with DS aged 51 years and older. Most, 94%, of the poll respondents represented individuals with variants in the *SCN1A* gene, 4% had a clinical diagnosis of DS but not a genetic diagnosis, 2% were unsure of the genetic diagnosis. The demographics of the patients represented in the caregiver survey were similar to the demographics of those represented by poll respondents and are summarized in **Appendix 2**.

The meeting was attended by 252, including 110 parents, 18 caregivers, 14 friends, and 11 family members (including siblings and grandparents) of individuals living with DS. In addition, there meeting was attended by 17 FDA representatives, 56 industry representatives, five scientists, five healthcare providers, six representatives from non-profit groups, and 10 others (consultants, media, law firms).

The Dravet Syndrome EL-PFDD meeting was structured around two key topics. The morning session was structured around Topic 1: *Living with Dravet Syndrome: Disease Symptoms and Daily Impacts*. The afternoon session addressed Topic 2: *Current Challenges to Treating Dravet Syndrome*. The meeting agenda is in **Appendix 3**, and the questions provided for meeting discussion are in **Appendix 4**.

The morning session continued with five pre-recorded caregivers who were selected to represent a range of experiences of families living with DS. Caregivers described the terror they felt when their child experienced their first seizure. They talked about the ominous emergence of other symptoms and health concerns, and they shared distressing stories of developmental regressions and behavior challenges. They described their diagnostic journeys, and some spoke of profound fear, heartbreak, and grief. Most described how their entire family had to adapt and accommodate to the unpredictability of DS, and they talked about muted celebrations and missed vacations. Caregivers of adults living with DS spoke of disease progression and their regret at having to put their loved ones into residential care. Many expressed deep fears for the future as their family member aged and perhaps outlived their caregivers. All spoke about their deep love and support for their loved one.

James Valentine moderated a discussion between several people who served on a live Zoom panel as well as people who dialed in by phone. Additional relevant comments entered through an online submission form were read by Dr. Hood. The names of panelists and callers are listed



in **Appendix 5**. As a reflection of the severity of DS, not one of the panelists, speakers, or callers were individuals living with DS, but were all caregivers and family members speaking on their behalf.

The afternoon session opened with a pre-recorded panel of five caregivers who described different medical therapies and other treatments they use to address seizures and other disease manifestations. Caregivers described having to administer multiple medications to control seizures and the excessive number of treatment approaches attempted. They described the cycle of hope and disappointment as new therapies were added to the combination, and the impacts to their loved ones, including bewildering side effects which were challenging to attribute or to mitigate. They described valiant efforts to adapt their homes and to obtain equipment, care support, and other solutions to address the progressing disease. They described the profound challenges of clinical trial participation in this group of patients, and concluded by describing their wishes and hopes for treatments and the trade-offs that they are willing to accept for their loved ones. Again, meeting attendees participated in online polling, called in and submitted written comments which were added to the moderated discussion by James Valentine and Dr. Hood. At the end of the meeting, Larry Bauer provided a reflective summary of the key messages he had heard throughout the meeting and Dr. Hood concluded the meeting by thanking all the participants and attendees.

The online polling results from Topic 1 and Topic 2 are included in **Appendices 6 and 7**, respectively. To include as many voices as possible, an online comment submission portal was open for four weeks after the meeting. Selected comments are included in the body of this report, and all submitted comments are included in **Appendix 8**. Again, it is important to note that all submitted quotes were by caregivers and family members, speaking on behalf of their loved ones. The results of the *Caregiver Opinions about Disease Modifying Therapies for Dravet Syndrome* survey are included in **Appendix 2**.

This *Voice of the Patient* report was provided to all DS stakeholders including the US FDA, other government agencies, regulatory authorities, medical products developers, academics, clinicians, and any other interested individuals. The final report, the meeting transcript, and a recording of the meeting can be found at [www.Dravet-EL-PFDD.org](http://www.Dravet-EL-PFDD.org). According to YouTube statistics, the meeting has been streamed over 891 times as of May 31, 2022.





## TOPIC 1: Living with Dravet Syndrome: Disease Symptoms and Daily Impacts

*"It's hard sometimes to try to explain DS to people. Is it seizures? It's so multifocal. Just saying, 'Oh, my son has DS.' That is so far from capturing all of what that involves." - Danielle, mother and caregiver of a three-year-old son who is living with DS*

**Seizures were selected by caregivers as the most frequent and most troublesome Dravet syndrome-related health concern, followed by speech and language impairment, and developmental delays or loss of developmental skills.**

Meeting attendees using online polling to first select all of the Dravet syndrome-related manifestations that they or their loved ones had experienced. They were then asked to select their top three most troublesome. Poll results are presented in **Appendix 6, Q1 & Q2** and described, with caregiver quotes below.

**Key theme: While Dravet syndrome is characterized by many types of seizures, many other Dravet syndrome-related symptoms exist.** Barbara described the symptoms experienced by her 26-year-old son who is living with DS. *"Seizures, of course, because they have never gone away, and while we have reduced them at times, they always change frequency, severity, and type. Every seizure is a setback. ...Aside from seizures, the list of other challenges he faces is long and includes slowed motility, sleep disruption, kidney stones, urine retention, mood swings, and autonomic storms. That list is far from complete. Almost every symptom has had a significant impact on my son's life."*

**Key theme: Dravet syndrome symptoms have a wide range of severity, and the specific constellations of symptoms are unique to each individual living with this disease.** Nathan's wife carries the *SCN1A* gene variant and has no DS phenotypic characteristics, but their five- and three-year-old sons are manifesting the disease with different severity levels.

John K.'s daughter living with DS is, *"An 18-year-old who attends her high school, dances with a ballet group, plays basketball, and baseball. Despite her significant cognitive delays and continued seizures, she's very much a teenager who enjoys life, listening to music on her iPhone, and spending time with her friends."*



**Key theme: Dravet syndrome symptoms, including seizures, are influenced by a complex interplay of disease progression, medications, maturation and puberty, sleep, and environment.** Mandee described the challenge. *“And then 12 years old, he’s headed into puberty. And so right now I’m asking, ‘Is he having more seizures because of hormones, because of puberty, or because of the progression of the disease? Or because he’s outgrowing his medication dose?’”*

## Seizures and/or status epilepticus

Seizures and/or status epilepticus were selected as one of the top three most troublesome DS-related health concerns by 90% of caregivers: 98% of caregivers reported their loved ones experiencing tonic-clonic or other convulsive seizures, 77% experienced status epilepticus, 75% experience myoclonic seizures, 64% experience absence seizures, and 38% experience atonic or drop seizures. Sophie, older sister of a 22-year-old brother living with DS reflected, *“It makes a lot of sense to me that the seizures are going to be at the top because it’s the one thing that I feel like is always in the back of everyone’s mind - that it could strike at any time and cause the most catastrophic damage.”*

**Meeting attendees described a wide range of seizure experiences, and seizure types, and how seizures changed over time.** Ross is the father of a 14-year-old with DS who, *“had his first seizure when he was three months old; it lasted over an hour. By his second birthday, he’d spent over 70 days in the hospital, often in the pediatric intensive care unit or PICU after prolonged seizures.”* He described that his son, *“suffers from nocturnal seizures and he has for most of his life. These are tonic-clonic seizures, convulsive with muscle contractions that occur in groups and during sleep or naps, or bedtime. The seizures last about five minutes long and they usually occur less than 10 minutes apart from each other.”*

Sarah M., a mother who lost her child because of DS, described how her 8-year-old son had, *“Absence seizures, a type of generalized seizure without movement, characterized by a brief lapse in awareness, staring, and facial flushing. We asked caregivers to watch for repetitive blinking, unusual movements like lip smacking or picking while in a daze, signs of a complex partial seizure. Crying spells without triggers could last for hours, sometimes terminating with a deep breath, typical of emotional gelastic seizures. ... At night, his myoclonic jerks would last for hours, seemingly did not impact his ability to rest or his attitude the next day.”* She described the seizure that took her son’s life. *“Even as a physician, I didn’t recognize [my son’s] partial seizure when it first happened. He was playing happily with one arm while the other jerked. As we drove to the hospital, this seizure progressed and he became unresponsive. The generalized seizure lasted an hour and a half despite ER intervention.”*

Gloria, mother of a nine-year-old daughter living with DS explained how in her daughter’s first year of life, she experienced, *“400-plus seizures a day and multiple emergency room trips a week.”*



Jennifer described the severity of seizures that led them to put their 19-year-old child into residential care. *"He does have seizures all day, every day. That is part of life at this point. ...The seizures were every day; he was going through about three to six doses of rescue meds weekly. On top of just his normal head dips and eye flutters, and all of those that have been happening for years. At night, he would have 20 to 40 tonic seizures that were like about 30 seconds to a minute and a half. Sometimes those would turn into obtundation status that would cluster for up to... three hours."*

**Caregivers described many different types of seizure triggers.** They described how seizures could be triggered by vaccinations, blood draws, illness, fever, crying, bright light, specific types of indoor lighting, fast moving television, water, pattern sensitivity, puberty, heat, exertion, exhaustion, excitement, and physical activity. Mikell, the caregiver for her four-year-old son living with DS said, *"I'm constantly on the lookout for new seizure triggers so I can mitigate them"*.

**Seizures interfere with development and quality of life.** Barbara described how seizures cause her son to shut down. *"A few seizures in a row can take him down for a day or two. There are days he cannot get out of bed or lift his head. He will globally shut down - everything from motility to expression of any type. There is no language, no reaction to engagement. He looks pained and uncomfortable. His physical ability to walk or sit or reach becomes non-existent. He is agitated by stimulation or conversation.... It's hard to watch and it happens over and over and over again."*

Nadia described how her three-year-old son's seizures interfere with therapy. *"We definitely can see some of the delays kicking in with all the new seizures that he's having and then not being able to attend therapies and all that other stuff that comes with the syndrome."*

Erin described how for her seven-year-old son living with DS, *"When the status isn't there, we get to see more of him. We get to see more of his personality"*.

**Seizures are a persistent threat, even when seizures decrease in frequency.** Cara's eight-year-old son, *"is currently going through an 'easier season' with DS. He is currently 14 months seizure free and of course we are so grateful for this time. However, we are not blind to the reality that this can change at any point."*

Mandee, the caregiver of a 12-year-old son living with DS, selected seizures as her first choice, even though her son, *"Has not had a status seizure since he was two years old and got diagnosed and on the right treatments. But [the threat] is always there."*

Alexis wrote, *"Seizures, even while mostly under decent control, still are a huge challenge because we don't know when they will happen, and they often happen when [our son] is in the midst of something he loves to do. He tends to have them when he is having fun and playing and excited. It's a shadow that is always looming."*

### **Developmental delay or loss of developmental skills**

Most, 91% of caregivers reported experiencing developmental delays or loss of developmental skills, and this was selected as a top three most troublesome DS-related health concern by 77%. Many



caregivers described developmental regression, however Barbara, the mother and caregiver of a 26-year-old living with DS, described her son's deterioration over many years. *"Like the day he stopped eating, sometimes decline happens so suddenly that it's shocking. Other times it's so gradual that it's hard to pinpoint exactly when it occurred."*

Around Barbara's son's third birthday, *"we realized [our son] was not meeting developmental milestones. Despite all the therapies that early intervention and preschool had offered, I can remember sitting and watching him in his classroom with the sinking realization that my sweet boy was gradually falling behind compared to his peers. I'm glad I didn't fully grasp then the challenges that would lie ahead."*

Despite this, Barbara remembers her son's childhood as a golden period. *"Those would prove to be the best years for [our son]. He went to school and we took family vacations. He could walk and play independently, and enjoyed swimming, and horseback therapy. He could eat with assistance and use basic language. He loved watching his brother play sports and spent hours playing with his service dog. I am so glad to have those memories, and happy that he was able to experience a full, meaningful childhood...Age 10 would prove to be a turning point for [our son], and the start of a slow but steady decline."*

## Sleep disturbances

Sleep disturbances were selected as a top three most troublesome DS-related health concern by 28%, and experienced by 68% of caregivers. Sleep is unpredictable for Danielle's three-year-old son who is living with DS. *"We'll have good stretches and bad stretches of sleep. We'll have three awful nights and then maybe we'll have one or two good nights, or maybe we'll have a bad week or two... it's kind of all over the map."* She has been unable to find a pattern or understand the reasons for the sleep disturbances.

**Sleep disturbances were described throughout the meeting as a challenge for the entire family.** Ross' 14-year-old son with DS has tonic-clonic seizures which occur during sleep, naps, or bedtime. *"The only consistent remedy that we found for [our son] is to not let him sleep, literally to keep him awake. He has nights like this between seven and 15 times a month. We've spent a lot of nights rearranging our plans for work and school while watching Pixar and Marvel movies on the couch. Doing our best to act normal, just like we woke up early when the rest of the family comes downstairs in the morning. After a night of 15 to 20 nocturnal seizure clusters and no sleep, we're crushed."*

Kim described how her four-year-old daughter's sleep disturbances are not just a challenge for her daughter *"but the entire family. ... She can have a few weeks where she sleeps really well, then there's days where she won't fall asleep until midnight or 1:00 AM. And then there's days where she's just up from 2:00 AM to 6:00 AM. And she's very active in jumping on the bed, so no one else can sleep. Because of nocturnal seizures and the fear of SUDEP my husband and I split every other night, one of us sleeps with her, because we're just so scared if we were to miss a seizure in the middle of the night. ...Someone's always with her."*



## Speech and language impairment

Speech and language impairment were experienced by 91% of caregivers and selected by 48% of caregivers as a top three most troublesome DS-related health concern. Barbara described how, *“At age 19, [our son] stopped talking, seemingly losing his capacity for speech overnight. Most days he is silent, and though he can understand simple conversation he is largely unable to express himself.”*

Caregivers, including Erin, commented that many of these top symptoms are often closely related. *“It's hard to separate the cognition, the communication, the speech and language, the motor [activity], because they are all wrapped up into one.”*

## Disruptive behaviors (tantrums and refusals)

Disruptive behaviors, such as tantrums and refusals, were experienced by 63% of caregivers and selected as a top three most troublesome DS-related health concern by 21%. Peiyi is a caregiver for her 18-year-old daughter living with DS and described how, *“The biggest obstacle she and the rest of family must overcome mostly involve behavior and cognition on a daily basis. Some are simple but can be exhausting to manage as time goes on.”* Her daughter requires a long time to formulate responses, does not accept assistance, and reacts poorly to sudden changes. *“She will often completely shut down. ... She'll refuse to move and refuse to listen. This usually involves her completely tensing up so that she cannot be moved and putting her hands over her ears to let you know that she's not listening.”*

Sophie, the older sibling of a 22-year-old living with DS, described her brother's behavior. *“One of the things that specifically impacts his quality of life is the refusal and defiance. It makes it really challenging for him to participate in anything outside of the house really, because you get him outside of the house, he doesn't want to come back. And so then he's laying on the ground refusing to stand up.”* Sophie remarked that, *“as he's gotten older, ... some of these behaviors that he has shown his whole life are becoming a lot more concerning, a lot more challenging to deal with for his caregivers - my parents primarily at this point - but for whoever is caring for him.”*

**Disruptive behaviors can have triggers and can sometime intensify before a seizure.** For Sophie's brother living with DS, *“We have seen somewhat of a pattern of building up to a big future event. His behavior tends to get worse... typically there's more physical aggression towards other people, he's more likely to seek you out and hit you or pinch you or pull your hair.”*

**Disruptive behaviors often involve alarming physical aggression towards caregivers, parents, and siblings.** Janice S. described how on the worst days she is often the target of her 22-year-old daughter's aggression. *“She will sometimes hit me, scream, pinch, do all the really aggressive behaviors with me. She's attacking me, physically running after me to hit me, and screaming at the top of her lungs.”*



## Problems with balance, walking, and gait

Although problems with balance, walking, and gait are experienced by 86% of caregivers, only 11% of caregivers selected this as one of their top three most troublesome DS-related health concerns. Lynn, caregiver of a five-year-old daughter living with DS described how, *"I never really understood how important walking is until I saw my daughter not able to walk, and she wasn't a light baby, she was this 16 kilo one-year-old and I'm lugging her around, and it's this dead weight."*

Barbara said, *"Slowed mobility impacts my son's ability to participate freely in activities and impacts how he feels day to day."* She explained how, *"Ironically gait and walking issues are a double-edge sword. It is difficult to watch your child lose mobility skills, however, in a somewhat backwards way of thinking, I am grateful he can't walk independently [as an adult]. It keeps him mostly safe from falling and injury. For years we would watch my son fall with no warning and we prayed he wouldn't get hurt. He wore a helmet for three years. Now, he sits most of the day, or we always have a handle on him."*

## Autistic-like behavior

Autistic-like behavior, things like difficult social interactions or patterned or repetitive movements, are experienced by 43% of caregivers, and are a top three concern of only 8% of caregivers. Kristi described her son's challenges. *"He deals with sensory processing disorder and fine tremors. The sensory processing disorder can be so difficult to navigate on top of everything else."*

Mandee described some of her 12-years-old son's behavior, and how due to a combination of, *"Autism and speech. He's been non-verbal since he was 18 months."* Because he is unable to communicate verbally, she says he uses rough physical interactions to communicate his needs. Mandee describes, *"[He gets] physical. He'll push me, he'll pull me."* She expressed worry over him injuring himself or her.

## Heat-induced temperature dysregulation

Hyperthermia, dysregulated temperature control, was experienced by 41% of caregivers, is a top three concern of 3%, and was mentioned often in comments. Patients have a tendency to overheat easily, and notably, hyperthermia is a common seizure trigger for individuals with DS. For Jessica, *"Hyperthermia has such a great impact on my son because he cannot go to recess with his peers, play sports, and often cannot even go outside during the summers here in Florida. Even with adaptive clothing (ice vest) he has been unable to tolerate a day at the beach, fishing with his dad, or attending outdoor events."*

## Growth and nutrition issues

Growth and nutrition issues were experienced by over half, or 55% of caregivers, and were selected as a top three concern by 3% of caregivers. Some patients require nutritional



supplementation through feeding tubes due to poor growth, sometimes related to appetite suppression from medications. Barbara said, *"You briefly mentioned growth/nutrition issues but along with that is gastric motility, urine retention, constipation, slow gastric emptying. Many of these children require feeding therapy or feeding tubes at some point in life."*

For some patients, nutrition issues are related to vomiting. Jennifer described of her son, *"He would vomit up all the food he'd eaten for three days because it wasn't processing. Every study we joined, every possible option out there ... would trigger cyclical vomiting syndrome. Then after his seizures, he would begin vomiting every few minutes."*

### Other Dravet syndrome-related health concerns

Almost a third, or 32% of caregivers selected "other", and 3% of caregivers selected this as one of their top three most troublesome DS-related health concerns. These are described below and include: aspiration, injuries from falling or from seizures, lack of fine motor skills, reduced level of alertness or consciousness, dysautonomia, bowel and toileting issues, kidney stones.

**Aspiration.** The accidental intake of saliva, food, or water into the airway or lungs was described by many caregivers. This can happen during normal drinking or eating in patients with poor muscle tone, during seizures, or sometimes after vomiting. Michelle F.'s daughter, now 19 years old, has aspirated multiple times. *"She aspirated seven years ago. Then she aspirated again in 2018. That year, she aspirated two more times which landed her in the hospital for one year. As a result, [she] is now NPO (nothing by mouth) with a GJ tube."*

Stephanie's six-year-old son living with DS requires a feeding tube due to aspiration and poor muscle tone. *"We had to advance it from a G (gastric) tube to a GJ (gastro-jenunal) tube. Currently he has a little backpack with a pump he carries around with him for about 18 hours a day. It's a significant quality of life issue, but ... it has completely changed his life. ... The GJ tube has really helped to control aspiration and vomiting, that it's helped lessen his propensity for illness and therefore lessened the seizure frequency."* She explained how, *"He would get a cold or a little illness or pneumonia from the aspiration, from the fever caused by the illness he'd have a gigantic seizure, possibly aspirate again during the seizure. And we were caught in this loop. ...I'd say that's been a big win. We're looking at now what quality of life improvements we can make in terms of that GJ tube. ... [We are] hoping to convert him back to a G tube so he can have more time off the backpack and would not need a continuous infusion."*

**Injuries from falling or from seizures.** Many caregivers, including Silke, described a, *"Risk of injury from the seizures and from orthopedic problems."*

Diane described injuries including, *"Head injuries with falls during seizures."*

Eduardo wrote that, for his daughter, *"We have to keep her away from sharp corners, because of fear of a myoclonic that would tumble her to the ground."*



**Lack of fine motor skills.** Lynn, mother of a five-year-old daughter living with DS described how, *“It’s the simple things, like even getting a bottle of water, or reaching out for something.”*

**Reduced level of alertness or consciousness.** Obtundation status is a dulled or reduced level of consciousness presenting along with myoclonic jerks. Claire wrote that, *“obtundation status is another area that, for us, is far more difficult to manage than typical seizures. There doesn’t seem to be much consensus on how to treat obtundation status, or even a well-defined definition of what it is.”*

**Dysautonomia.** Dysautonomia is a dysregulation of the autonomic nervous system which can interfere with heartbeat, breathing, digestion and temperature regulation. This can include paroxysmal sympathetic hyperactivity or autonomic storms which are characterized by fever, tachycardia, high blood pressure, tachypnea, excessive sweating, and dystonic posturing. Barbara said, *“We also have significant issues with dysautonomia and autonomic storms, especially with age, starting in the teen years. ... Dysautonomia affects him just as much, if not more [than seizures], and is a challenge to treat or prevent.”*

**Bowel and toileting issues.** While some individuals with DS may only experience seizure-related incontinence, some are not toilet-trained and require diapers. Adult patients can be particularly challenging as they are harder to change. Mande described that, *“This morning I had to change all of [our son’s] sheets because his diapers didn’t hold and he had just had a seizure and I couldn’t move him.”*

**Hypotonia (poor muscle tone) and frequent and long-term infections.**

Hypotonia or poor muscle tone is experienced by 68% of people with DS and was selected as a top three concern by 2% of caregivers. Frequent and long-term infections are experienced by 34% of people with DS and were selected as a top three concern by 2% of caregivers. There were few quotes for either symptom.

**Day to day life with Dravet syndrome is extremely unpredictable. Families are profoundly impacted, especially with participating in social engagements and events.**

Meeting attendees used online polling to select the top three activities that are most important, that their loved one is not able to do, or struggles with due to DS. Poll results are presented in **Appendix 6, Q3** and described, with quotes from parents and caregivers, below. Key themes identified during the meeting are in bold below.



**Key Theme: Life with Dravet syndrome is extremely unpredictable. Rigid schedules and a great deal of advance planning are required to manage seizure triggers and behaviors.**

Gloria described how, *"DS is never ending. Just when you get used to something, everything changes. ... It feels like you're on a rollercoaster you can never get off of. Being flexible can be exhausting."*

Erin, a caregiver described how living with DS, *"the seasons change"*, a metaphor that was repeated by many of the meeting participants. *"We happen to be in a season of not having status seizures, but we're always living in that fear of them returning."* Currently Erin's son is experiencing some stability.

Barbara wrote, *"I think one of the hardest things is loss of spontaneity. We can't go anywhere without planning - food, toileting, rescue meds, oxygen, et cetera. - Not to mention that it has to be a 'good' day, which is impossible to predict. Seizures can ruin a day in a minute."*

Peiyi, mother of an 18-year-old daughter living with DS, described daily management. *"Like many other children with disability, [our daughter] likes to have a consistent schedule to follow each day and thrives best when she knows exactly what is going to happen, and exactly what is expected of her. This type of schedule maybe considered overly rigid by other people, but it is necessary for her to function well."*

**Key theme: All aspects of life are profoundly affected, not only for the individual living with DS but for their parents and siblings.**

Amy said, *"Nothing is as it ought to be when you have a child with DS."* She described the impact on her neurotypical son when her daughter with DS had a seizure. *"Our eldest, is shuffled off to the TV room safely away from our anxiety or so we continually tell ourselves. Knowing that at 11 years old, he sees, he knows. The weight on him is evident. He was there ... the last time she had a status seizure when her little body was limp on her side, foaming at the mouth, unresponsive. He saw us rush about. One of us administering rescue meds that could not touch her seizure. The other throwing on clothing while calling an ambulance and packing a bag. There was no one for him. Now any hint of panic in the house makes his eyes widen and his hands tremble. This heartbreak spares no one."*

Zaheen wrote, *"Living with DS is not only hard for the patient but also for the family, too. You can't go outside in summer because of heat (trigger). You can't go outside in winter. If the weather is good, you are good and you plan go to outside - maybe that day is seizure day."*

Jennifer MK. wrote, *"Our entire life has been impacted by this diagnosis. Our family has been disrupted. Our livelihood has been impacted. Our future is unknown, and the unknown can be so consuming."*



Mikell described the long-term impact on her husband and herself of caring for a four-year-old son living with DS. *“One day, my husband actually ended up in the ER himself with an anxiety attack. It was a horrible, horrible six months stretch, culminating with [our son] wrapping up his last day of the school year with a seizure after which he stopped breathing for almost a full minute. I found myself speeding to school on a FaceTime call, listening to his teachers asking me if they needed to start CPR.”*

Jennifer M. described how, *“My DS son's two older siblings have been in psychotherapy off and on for years with PTSD from their experiences growing up with, and assisting with the care of, [their brother].”*

**Key theme: Families often have to avoid events and celebration that others take for granted, because too much excitement can trigger seizures.** Sarah M., who lost her 8-year-old son because of DS, said that their family used to joke that, *“We were allergic to fun. The excitement for getting ready for a Halloween or birthday party could trigger seizures, so we opened presents and birthday gifts over a month.”*

Bethany described how, *“My 14-year-old daughter's biggest seizure trigger is joy and excitement. We have to balance fun activities with risk of seizures.”*

Sarah J. described how even laughter can trigger a seizure, *“As a baby he'd laugh hard and have a GTC (general tonic-clonic) seizure. Today he can laugh hard with no issue - and become excited. He's less sensitive now, thank God, but we're still the 'fun police'.”*

Amy described the heartbreak and grief experienced by many parents of children living with DS. *“When you have a sick child, you are an alien. You feel unseen in every milestone, every holiday. Every typical simple pleasure of childhood is marked by either complete absence or panicked vigilance... Every child you see in a swing, every baby her age you see toddling about the park, you look at with envy.”* She further described how her 22-month-old daughter living with DS and her family were excluded from Halloween festivities. *“The park was packed with families everywhere.... My daughter would have a seizure from the excitement, from the sounds, and the sights. ... A baby girl, Ramona's age, dressed as a peacock on her father's shoulders delighted at the scene. Dogs were dressed up for their annual Halloween costume competition, a stage, and speakers. I pushed through the crowds, tears rolling down my cheeks. My daughter can't be here for any of this.”*



## Participating in social engagements and events

Participating in social engagements and events is the top activity impacted by DS, selected by 54% of the caregivers. Lucy wrote, *"One of the worst parts is the social isolation. Because illness and excitement frequently cause seizures, we avoid meeting people, going places, socializing. Because when an outing starts with a seizure and a two hour 'sleep off', or worse, it leads to illness and hospitalization. It never seems worth it. But everyone needs socializing, so it's emotionally very difficult."*

Sophie, older sibling of a 22-year-old brother living with DS said, *"the social isolation has really stood out to me ... socializing with peers, but also just participating in social activities. I think both the seizures and the behavior contribute to his inability to do those things and the communication."*

Jennifer described her son, who is 19-years-old. *"He was not able to leave the home for any social interaction. It would trigger status seizures regardless of every new therapy ... He was at the point where he was getting no socialization other than our small family and any caregivers."*

**DS patient families struggle to maintain a normal life.** Barbara described that during her son's childhood, *"We did our best to balance the constant stress of seizures and hospitalizations with creating a normal life for our family."*

Shannon, mother of three children including a 16-year-old with DS. *"We try to keep her life as normal as possible, especially for her siblings. We still try to take vacations and we go for hikes, and we know the more we keep her moving. We're hoping that will help her physical stamina and stability and that she can keep those muscles strong."*

## Self care and chores

Self care and chores was the second choice, selected by 41% of caregivers as a top impact of DS. Most individuals with DS will require care and constant supervision for the rest of their lives. Kate expressed an expectation for her 11-year-old daughter living with DS, *"She's years behind her peers, both physically and cognitively, and will stay dependent on others for care for the rest of her life."*

Barbara described how her 26-year-old living with DS, *"Is fully dependent on others for care, requires 24/7 supervision, and functions at a toddler level."*

Many, including Jennifer, described how adult patients require residential care. Jennifer described that due to a series of complex medical and behavior issues, she was, *"In the unfortunate and humiliating position to have had to place our child into residential care. He's 19 at this point, he's six one and 195 pounds. ... If it were just his size that was the problem, we would have done everything to keep him at home. ... He's a bit of a beast to care for, especially when he has behaviors."*



## Having a conversation and socializing with peers or siblings

Having a conversation was selected by 40%, and socializing with peers or siblings was selected by 38% of caregivers as one of the top three activities impacted by DS. Danielle described her wish to have a conversation with her three-year-old son. *"It's weird to say he's nonverbal because he makes an awful lot of noise throughout the day. But he doesn't really have meaningful words. ... You can tell he wants to communicate with us and tell us things and he just can't get it out. I see that I don't know what he wants sometimes."* She described how her son's language impairment, *"limits also our ability to utilize caregivers."*

Sophie described her 22-year-old brother living with DS, *"He's just a very social young adult, and he wants to have friends. But he doesn't know how to have friends, or how to communicate. He definitely connects better with younger children, because that's the level that he is at. But what scenarios are available that a 22-year-old man is hanging out with young kids? It's not really an option."*

For Shannon's 16-year-old daughter with DS, *"She was with a higher functioning group, and she doesn't understand that she's different than those kids. She wants to form relationships and she tries, but she doesn't always connect with them and doesn't understand why they're not connecting with her, which is both a blessing and a curse."*

Janice S. described that it wasn't conversation skills, but her 22-year-old daughter's aggression that interferes with sibling relationships. *"It impacts everyone in the family. I live with my mother and my mentally ill brother. We have another child who has Down syndrome. My son is terrified of her when she gets to be this way. That is probably the hardest part for me, is my child who has Down syndrome, who's sweet and loving and kind, is terrified of her. It makes a very interesting dynamic in the family to have that impact on him."*

## Sleeping

Sleeping was selected by 25% of caregivers as one of the top three activities impacted by DS. Morgan wrote that for her son, *"Every single night, he has seizures in his sleep. In addition to all of the other comorbidities of DS, he's robbed of the basic human necessity of getting a good night's sleep. This impacts our entire family, as it is hard to function on so little sleep day after day."*

Unfortunately, the lack of sleep can increase seizures. Danielle explained, *"Exhaustion lowers that seizure threshold... It's really been impactful. ...And it can be very hard to get through the days. And the nights are becoming at some point almost dreadful."*

For Nichelle, *"Sleep is a major challenge for my seven-year-old son with DS. It always takes him at least 1-2 hours to fall asleep and he often wakes up multiple times throughout the night."* She described having to use multiple monitoring devices, *"Which also equates to poor, fragmented sleep for myself and my husband as the alarms sound an average of 10-20 times per night which affects our jobs, our marriage, and our other family members."*



## Attending school or having a job

Attending school or having a job was selected by 21% of caregivers as one of the top three activities impacted by DS. Many individuals living with DS need special or alternative education programs. Kate described how when her daughter was only three, she was unable to attend preschool, *"Because of her extensive therapy needs and because her seizures were still uncontrolled. ...Instead, services would be provided in the home five days a week."* Now, at the age of 11, Kate's daughter, *"Attends a specialized school for medically and developmentally complex children with the assistance of a nurse. She still receives multiple therapies during the day. Only making small occasional gains in her development, means there is no end in sight for these services."*

For Sophie's 22-year-old brother living with DS. *"School was always hard for him. He always did half days at school, because the medications would make him really tired, so he'd go home early for a nap. I'm imagining that as he's getting older, and we're looking for day programs or something like that for him, that's going to be the same challenge. And behavior is going to impact his ability to participate in those things."*

For Shannon's 16-year-old with DS, *"Thankfully she loves going to school. And so that's never an issue. She's always very happy to get up and get on that school bus and go to school. But a lot of days she comes home tired, and she takes naps. And with the naps come seizures, her seizures right now are only when she's sleeping."*

Because of the demands of caring for their loved ones with DS, many caregivers do not work outside the home. As Barbara described, *"I am first and foremost his mother, I am also his guardian, advocate, and full-time caregiver."*

Diane described some of the challenges for parents. *"Many of us become single parents, with constantly losing jobs due to having to leave or cancelling at the last minute when our children seize and need us. Families can be plunged into poverty, and care providers quit, due to fear of the seizures, behavioral problems, and not wanting the liability when the child is injured from falls while seizing."*

## Participating in sports and recreational activities

Participating in sports and recreational activities was selected by 21% of caregivers as one of the top three activities impacted by DS, as supervision is necessary, and participation can be significantly limited. Erin described how she takes her seven-year-old son living with DS, *"To major sporting event games when we can. We're working around nap schedules, and making sure we pack the extra medication. He, right now, is thrilled to be able to cheer. But we always have an exit strategy. What happens should a seizure occur?"*

Erin continued. *"He would love to be able to go to some little day camps. But without having one-on-one supervision, which camps don't provide, and we are not eligible for additional services at this time."* She celebrated how he was able to ride a bike. *"That's a huge, huge thing for him and for those in our community. But I won't let him be on his bike unless I'm right there with him."*



Even going to the playground can be problematic. For Eduardo, the fear of his daughter falling limits her, *"Playing on jungle gyms with other children."*

Sarah J. described, how her son is unable to participate in physical activities, *"due to increase in likelihood of seizures."* She also described other activities that others take for granted but which they are unable to do including, *"Movies - sensitive to sound, attention span minimal - very distracted/cannot focus"* and, *"Eating out - he's a keto kid and meals are weighed, plus he's always getting medication therefore doing anything outside of the home requires a lot of preparation."*

## Travel and vacationing

Travel and vacationing were selected by 19% of caregivers as one of the top activities impacted by DS. Morgan described the specific challenges when traveling with her nine-year-old son living with DS. *"On a plane for a six-hour flight from San Diego to New York. We needed him to sleep on the plane to make it through the long flight without meltdowns, but we knew the risk was that he would have seizures in his sleep. ... There are not many words to describe the sheer terror of witnessing your three-year-old seizing at 30,000 feet in the air. We shielded him from view of flight attendants for fear they would force an emergency medical landing. He had multiple seizures during the flight, and we had to administer rescue medication to slow them down."*

For Barbara and her family, *"With an adult age and size child, our ability to take him out has dramatically lessened with time. He's hard to bring places and we no longer travel or take vacations. These limitations that DS places on our son trickle down to the whole family."*

Sarah J. explained how vacations are just, *"Too much to manage with environmental concerns, meal prep, and over-exertion/over excitement potential which provoke seizures."*

Still, many work to ensure that they are able to continue family vacations. Despite her son's DS, Tina said, *"We take [our son] almost everywhere we go. We love camping and since we have a new handicapped accessible camper he can go, seizures or not. It's getting tougher because he's non-mobile and 87 lbs but we do it!"*

## Walking and ambulating

Walking and ambulating was selected by 19% of caregivers as one of the top three activities impacted by DS. For Eduardo's daughter, *"Her walk is also unbalanced which means she is more likely to fall and hurt herself. ... She can't walk on hard surfaces."*

Several described how challenges with walking could lead to injury and how they had to adapt their homes as a result. Barbara heartbreakingly described how, *"My last memory of Jake walking independently comes from photos when he was 15."* When her son was 16, *"We modified our home for accessibility and moved him to the first floor."* She described some of the trade offs with her son's lack of mobility: *"It is a huge loss and physical burden that he lost the ability to walk independently, yet he is safer for it, because he is typically sitting or lying down when he seizes. Which is better or worse? Hard to say."*



Ross described how, *"We're disappointed when [our son's] physical activity is limited and the short walk or visit that we plan with his grandmothers must now be changed to a longer wheelchair ride."* Ross added, *"I'm saddened because the school is concerned about him walking to class, when the only safe exercise option during PE seems to be watch an iPad inside a gym."*

Tina M. simply expressed that for her son, *"I wish he could run and play at the beach like the other kids."*

### Spending time outdoors

Spending time outdoors was selected by 17% of caregivers as one of the top three activities impacted by DS. Spending time outdoors generated many comments about photosensitivity, temperature sensitivity, and risk of seizures. Some caregivers, including Kim, limit the amount of time spent outdoors. *"We used to have a timer for her to play outside for 15 minutes and sometimes that was still too long, she would have a seizure, we didn't know if it was the wind or just overexcitement."*

Erin described how her son was getting too big to pick up and carry. *"We live in a beautiful area full of outdoor activities. But you can't go hiking too far, because what if an emergency occurs and you need a quick outing? How am I going to get this seven-year-old...down the hiking trail?"*

### Other impacts

"Other" activities were selected by 5% of caregivers as one of the top three impacts of DS. The unpredictability of a life with DS and the struggle to have a normal family life, were already identified as key themes. Other impacts include experiencing heartbreak and grief, a reduced possibility of having a life partner or a family, and geographical limitations.

**Experiencing heartbreak and grief.** Amy, mother of a 22-month-old daughter living with DS described the heartbreak and complicated grief experienced by many parents and caregivers of individuals living with DS. *"They use [the word 'grief'] over and over again like your child is dead - like there's no chance at all your child could have a full and normal future - that your family has in essence crossed over into a purgatory you will never escape. But hey, these kids are often very happy. Will she live on her own or go to college or travel? Marry, have a family of her own someday? Likely not. Yes, you're grieving. No. No. We refuse to accept this."*

**Reduced possibility of having a life partner or family.** Donna wrote, *"My daughter is 30 years old, and being able to have a meaningful intimate relationship of her own is a HUGE problem, sadness. She SO wants a soul mate and this is so hard to find and / or maintain."*

Diane wrote that *"My daughter thinks she may want to have a child someday, but doesn't want to pass this [syndrome] on."* She pointed out that her daughter's DS medications, *"Would cause birth defects."*



**Geographical limitations.** For Kate, the mother of an 11-year-old daughter living with DS, *“Any plans for our family's future are now strictly dictated by our location, access to programs, therapies, and related services.”* She explained that, *“Services available to us here may not be the same for a family in a bordering town or county, and they are vastly different from state to state.”*

**Caregivers worry how their loved ones with Dravet syndrome will be cared for in the future, premature mortality, and the stress of not knowing how Dravet syndrome will progress.**

*“My list of worries is long, and if I let it consume me, it would. I can't possibly relay in five minutes the weight that I feel, but it is ever present. It's like we live in a fragile house of cards that could collapse at any moment. The foundation of this house is our capacity to provide for Jake's long-term physical, medical, social, and emotional needs. If for any reason we were to lose that capacity, his life would be undeniably altered, and the fear of that keeps me up at night because I cannot see a sustainable, acceptable alternative.”* – Barbara, mother of an adult son with DS

Meeting attendees used online polling to select their top three worries about their or their loved one's future. Poll results are presented in **Appendix 6, Q4** and described, with caregiver quotes, below. Most of these worries are closely related to the progression of DS and how care becomes much more challenging as their loved one gets older. Barbara summarized, *“DS is lifelong, and the burden of care only grows. NOT the burden of loving our child, but the burden of care, driven by DS as a lifelong disease, that impacts everyone in the family physically, emotionally, and financially.”*

**How they will be cared for and maintain access to resources as they get older**

The top concern for the future, selected by 77% of caregivers, was how loved ones with DS will be cared for and maintain access to resources as they get older. Emily wondered, *“I worry about how I will be able to continue to care for her needs financially, as a widowed single mom on a very limited budget. I worry about how I will continue to care for her physically, as she is growing and getting bigger and heavier. As she grows, it is becoming more and more difficult to assist her in walking when she needs it, move her during seizures if necessary, and also move her while she is postictal. I also worry for myself, how I will continue to bear the burden of 24/7 caregiving, with very little help, and how I will not have significant burnout.”*

Danielle's son is only three-years-old. *“I am already worried about how he's going to be cared for and maintain access to resources as he gets older. ... I feel like you have to always be fighting to make sure you get what you need”. ...She described how she wants “to make sure that I'm doing everything for him that will help him thrive and live the best life he can live.”*



Many, like Mandee, expressed a worry that her son will outlive his care providers. *"I'm the only one in the whole planet who knows everything about him, and all the details about him. ... there is absolutely no one on the planet who can take my place... He's the youngest of our family. He might outlive all of us."*

Barbara wrote, *"What worries me most is his total need for care, and who will provide it in a loving and caring way that meets our standards of care. What will happen if he outlives us? What will the burden be on his sibling in the future? How can we plan well for his future, knowing that he will never get better?"*

Eduardo's fears for their daughter include, *"Her ability to continue going to school, continue learning and developing, ability to live independently, and whether she can have friends that appreciate her. We're also worried about who will take care of her as we grow older and to not try and put that burden on her younger, neurotypical sister."*

### **Parents are worried that the burden of care will eventually fall on other siblings.**

Shannon, mother of three children, the oldest daughter is a 16-year-old with DS. *"A few weeks ago, she had a seizure on the couch. I asked my 13-year-old son, I said, 'Hey, go check and see if [your sister] is breathing...' My eight-year-old looked at me, 'Why wouldn't she be breathing, Mommy?' I was like, 'Well, sometimes that happens with a seizure. She may stop breathing.' He was like, 'But you never told me that was a thing.' That led to some hard conversations with her siblings, too, about we don't want you to have the burden of having to take care of her, but at some point, we're all going to have to, in the future, come up with a plan for what happens when we're not here."*

**Caregivers worried about eventually requiring residential care for their patients.** Janice S. wrote that her, *"Biggest concern is her residential options in the future, if needed. Most of the facilities I have visited are not appropriate. The CILA's (Community Integrated Living Arrangement) do not have the nursing/supervision needed. The Intermediate Care Facilities (ICFs) where nursing and supervision are available do not have residents that are her age (youngest residents in 60s). Even the day program where she is has a long wait list, an interview process, and a probation period where they can decide if they will accept her or not. Her behavior issues will also limit the facilities that will accept her. The best facilities can be picky on who they take as well."*

### **Premature mortality including Sudden Unexpected Death in Epilepsy (SUDEP)**

Premature mortality including SUDEP was the second most concern selected by 71% of caregivers, because, as Sarah M. explained, *"20% of children with DS don't make it to 18 years old."* As a parent who lost her 8-year-old son because of DS, she would know. She described how, *"He had not had a big seizure for four months... We had a very normal evening. We ate dinner, gave bedtime meds and tucked AJ into my bed with the seizure monitor underneath him. When he started to seize, we heard the bed alarm from the monitor. We administered Diastat after five minutes, and then again when it didn't stop. We were unable to stop this seizure. It had been more than five years since this happened. The paramedics struggled with IV access, the ambulance was delayed coming from out of state, and AJ's heart stopped during transit. My husband called from the*



*ambulance, and I arrived at the ER from the hospital where I trained, and recognized the code blue team surrounding my child. He was pronounced dead after 1:00 AM."*

The fear of premature mortality was shared by many. Mandee worried about her 12-year-old son dying unexpectedly. *"Every morning, I wake up and just am so joyful to see his smile. It is a miracle to wake up and see him every morning."*

Ross, father of a 14-year-old son living with DS, expressed his deepest wish. *"We want [him] to grow up and grow old."*

### **The stress of not knowing how Dravet syndrome will progress, including worsening cognitive and intellectual impairment and worsening movement and balance problems**

The stress of not knowing how DS will progress was the third most common worry selected by 58% of caregivers, while worsening cognitive and intellectual impairment was selected by 40% and worsening movement and balance problems were selected by 19% of caregivers.

Caregivers of adults with DS described their observations of disease progression. Barbara, the mother of a 26-year-old living with DS said, *"Over time, we have seen slow, steady decline in all areas, from speech, to mobility, endurance, loss of energy, tolerance for stimulation, stamina, etc."*

Barbara continued, *"DS does not get easier with age. In fact, it gets harder. ...We recently celebrated [our son's] 26th birthday in the face of rare, life-threatening disease. ... Each year is a victory that we don't take for granted. Yet, it is also cause for reflection. Because the truth is while we celebrate another year, we recognize the profound toll that DS has taken on [our son], and we are painfully aware with the passage of time of how increasingly fragile and vulnerable he is."*

Angie observed that her daughter was experiencing, *"What seems to be a loss of energy and endurance over the years, resulting in her getting less out of her days and thus an overall lower quality of life."*

Silke described how her child's symptoms progressed with time. *"A lot more seizures, cognitive decline, mobility challenges, linguistic degradation."*

Ross described how his 14-year-old son with DS is experiencing *"a progressive deterioration in his gait. He walks almost on his ankles with a wide crouch stance, knees bent, hips and legs sort of rotated inward."*

### **The burden of uncontrolled seizures and status epilepticus, and long-term effects of seizures**

The burden of uncontrolled seizures and status epilepticus were selected by 19% of caregivers as a top three worry. Tyler described his worries, *"One of the major challenges we deal with*



*concerns keeping our son (aged three) safe at night. He has many seizures that do not stop unless there is a medical rescue. This presents the risk of an hours long seizure that could easily cause brain damage or death."*

Jennifer MK. described some other fears related to seizures. *"We fear her vomiting from the seizure, which has led to aspiration."*

**Other worries – Caregivers worry if they are doing enough**

Other worries were selected by 5% of caregivers as a top three worry and were primarily about whether they are doing enough to care for their loved ones. Danielle worried about treatment for her three-year-old son who is still nonverbal. *"Is the speech support he's getting enough? Should I be pushing for more? Will it make a difference? Will it not?"* She relies on the experts to evaluate and make decisions, and worries that they may underestimate his need. *"If they catch him on a good day, maybe they don't think he needs as much as he needs."*

Mikell described her worries for her four-year-old son living with DS. *"When it comes to decisions about [our son's] care, I am absolutely terrified of guessing wrong... where my experiments and my failures are on my own son's fragile body, I fear failure."* She agonized about taking many months to realize that a medication was creating a side effect for her son. *"It took me six months, six months of data that I needed to make that connection, six months of the three-and-a-half years my son had been alive. 14% of his life spent finding out that the medication that was supposed to help was making our entire family live miserable lives."*

**Worsening nutrition issues and chronic infections**

Worsening nutrition issues and chronic infections were each selected by 2% of the caregivers as the top three worries for the future. When Barbara's son was 10 years old, *"We discovered that [our son] was aspirating, and it became necessary to place a feeding tube. Months later, he woke up one day and never ate by mouth again."*





## TOPIC 2: Current Challenges to Treating Dravet Syndrome

*“Every day, our family - and we are far from alone - is counting on science, is counting on progress, is hoping for now. There's no other way to live with this. ...“Where is the cure for this maddening disease? We know that it's coming, but will it come in time for my girl?” -*

*Amy, mother of a 22-month-old daughter living with DS*

**All patients with Dravet syndrome require polytherapy to treat their symptoms, particularly seizures.**

Caregivers of patients living with DS used online polling to select all medications and medical treatments that they had tried. Each poll respondent selected an average of 8.2 different medications that they had tried. Poll results are presented in **Appendix 7, Q1** and described with caregiver quotes, below.

**Key theme: All individuals living with Dravet syndrome require multiple medications and treatment approaches, many used in combination.**

*Tina described how, “I’m very frustrated that he’s on five medications and still has some pretty bad seizures! ...Treatment right now: Fintepla, clobazam, carbamazepine, zonisamide, and clonazepam daily. Clonazepam and Nayzilam as rescue. VNS.”*

*Kate described how many medications her 11-year-old daughter requires. “Two prescription seizure medications, one prescription sleep medication, one prescription for neurogenic bladder. She gets two drugs from specialty pharmacies that are sent through the mail and that’s in addition to her over-the-counter supplements. We have to give this treatment during five different dosing windows throughout the day.”*

*Eduardo wrote, “We are currently taking four medications, have regular neuro appointments, have physical and speech therapy, and see a range of other specialists (ENT, developmental physician, cardiologist (for Fintepla), and a few more.”*

**Key theme: Treatment is highly individualized. The medications and treatments that work for one do not work for all.** *Nicole said, “With DS we all know not one medication, regimen or treatment works universally; it’s always trial and error to find the right [combination].”*

### Seizure rescue medications

Seizure rescue medications including benzodiazepines such as diazepam, midazolam (Nayzilam), lorazepam (Ativan), or clonazepam (Klonopin) are the most commonly used medical treatment for symptoms of DS, selected by 98% of the caregivers. Some meeting participants



described how frequently they needed to use these medications. For Morgan's son, *"When he was three, his seizures started rapidly worsening in frequency and duration, and we were using rescue medication almost every day to stop them. We knew we needed to do something drastic to help him, because he had already failed several first- and second-line therapies for DS."*

Tina said, *"Our worst days are definitely the ones when he has clusters of "non-epileptic" myoclonics and has to get midazolam. He's pretty much out for the day so he can't do much."*

John described the downsides. *"One medication is unlikely to be enough. We've been dealing with multiple anti-epileptic drugs for [our daughter] from the beginning. This makes it hard to manage side effects, as well as to understand how to sequence her cycle medications. But this is our reality. ... [Our daughter] is currently on all three [FDA-]approved medications and has tried all four. As I said, one drug is unlikely to be enough."*

### Levetiracetam (Keppra)

Levetiracetam (Keppra) is an anti-seizure medication and the second most common medical treatment for DS, selected by 89% of the caregivers. Many used this treatment, often in combination with other medications. Kristi described a downside. *"Our son is currently on Keppra and clobazam, both have behavioral side effects, though we are told Keppra is a definite source of aggressive behavior, and we deal with a wide spectrum of behaviors right now."*

### Clobazam (Onfi)

Clobazam (Onfi) is the third most common medical treatment for DS, selected by 79% of caregivers. Several reported successes with Onfi, including Jari, mother of a 13-year-old daughter living with DS. *"We're better off today than what we were before. I mean, we would have hundreds or thousands of myoclonics or atonics a day, and now we're at about 10 tonic-clonics a week, which is good for us."*

Suellen said that of all the medications her child has tried, *"Onfi seems to be the only med with positive control and limited side effects."*

John described how, for his 18-year-old daughter, *"Our next option was to import [clobazam, prior to approval in the US] from Canada and to combine with stiripentol. At that point, we did see some good results in the beginning and gave us some hope."*

Sasha described a side effect in her daughter. *"Clobazam has helped [the seizures] but made her more aggressive."*

### Cannabidiol/CBD (Epidiolex)

Cannabidiol/CBD (Epidiolex) was the fourth most common medical treatment for DS, selected by 77% of caregivers. Marla said, *"[Our daughter] has had the best seizure control so far since Epidiolex was added."*



For Gloria's daughter, *"Our experience with Epidiolex was good and the side effects were minimal. Her seizure count decreased to approximately 25 a week, and we felt as if we met [our daughter] finally for the first time. So we started planning [her] life. However, over the next three years, her seizure activity began to increase by around 50%, along with new myoclonic and atypical absence seizures so we had to find another alternative."*

John described how his daughter living with DS, *"Was entered into the Epidiolex clinical trial prior to approval, and this was one of the best years of our lives. [Our daughter] had a seizure-free interval of one year, five months, and a day. As excited as we were, as wonderful as that time was, it did end. We started to see increased seizure frequency, and that became unmanageable."*

The medication is not without downsides. Mikell described how she was encouraged to double the dose for her four-year-old son living with DS. A few weeks later he, *"Began having seizures at school for the first time, ... at which point his neurologist had us max the dose."* This dose increase made Mikell's son, *"Incredibly sensitive to light and overexertion."*

### **Ketogenic diet, Modified Atkins Diet, or clinically-managed diet**

A ketogenic diet, Modified Atkins Diet, or other clinically-managed diet has been used at some period by 68% of individuals with DS. Many reported experiencing benefits with this approach, including Barbara. *"At age 18 months, we placed [our son] on a ketogenic diet, which lessened his seizures dramatically and allowed him to be temporarily medication free. This honeymoon lasted for almost two years, ... we were relieved to see our son gain back his vibrancy."*

When Kim's daughter was diagnosed with DS at six months, they chose the ketogenic diet instead of medications, but it was hard to tell how well it worked. *"We like to think that the ketogenic diet, which she's still on today, has helped prevent some other seizure types because she has never had absence seizures or clonic jerks. We know that the ketogenic diet can help with development and cognition."*

Nadia described how the ketogenic diet provides her three-year-old son with seizure control and helps him recover from seizures. *"Keto was a huge game changer for us. It gave us significant seizure control and great cognitive and developmental gains."* She described how after starting the diet, he no longer required rescue medications. After having a seizure, *"He would bounce back a lot quicker. ... He would take like a little 20–30-minute nap and then get up and go back to his daily activities."*

Many described the downsides of the ketogenic diet: taking the joy out of eating, the length of time required to adapt to the diet, aspiration, and suppression of medication levels.

Jennifer MK.'s daughter is on a ketogenic diet to minimize seizures. *"It has really taken the joy out of food that we once had. Thinking, prepping, and feeding our 21-month-old is such a chore. It takes so much time and energy; however, the reality of having seizures is so scary and harder so we do it for her."*



Stephanie described how adjusting to the ketogenic diet for her six-year-old son living with DS took about a year and a half, *"From when we started the diet, got the ratio to where we wanted it, and then really gave it some time to determine whether it was helping seizures. ... There were a lot of unintended side effects that came along with the diet, particularly aspiration."* The high fat ketogenic diet can cause aspiration in those who have reflux. Stephanie's son ended up with a feeding tube, at which point they discovered that, *"the diet was also suppressing some of the medication level, all of that became clearer to us after coming off the diet."*

### Fenfluramine (Fintepla)

Fenfluramine (Fintepla) was selected by 66% of caregivers and many reported success at limiting seizures. Jeannette described other benefits for her son besides controlling seizures. *"Although, all medications work at some level to lessen his seizure frequency, it was not until starting Fintepla that we noticed the most change. [Our son] began to have more alertness to his surroundings, and - as a non-verbal child-trying to sound words for the first time."*

For Tina's son, *"Fintepla by far has been the best treatment. And since starting...he hasn't had any grand mal seizures, status epilepticus, or hospitalizations."* Before starting this medication, she reported how her son was in the hospital, *"about three times a year for five days at a time."*

Downsides include the requirement for regular cardiac monitoring and loss of appetite for some. Gloria said, *"[Our daughter's] struggles to keep weight on during the introduction of Fintepla meant her already low appetite decreased. Unfortunately, Fintepla did not give her the continuous seizure freedom that we had hoped for, and she still struggles with her verbal skills with her current speaking word count at 25 words."*

### Other medications not included in the poll responses

Well over half, or 58%, of caregivers reported using medications not listed in the poll responses. Caregivers described other anti-seizure medications including valproate and sodium valproate (Depakote or Depakene), acetazolamide, Fycompa (perampanel), Lamictal (lamotrigine), Felbatol (felbamate). They listed pain medications and sedatives including ibuprofen, propofol, Ativan (lorazepam) as well as intravenous immunoglobulin therapy (IVIG). Barbara added to the list, *"Antibiotics, some have success with contraindicated meds, homeopathic/osteopathic treatments."*

**Valproate and sodium valproate (Depakote or Depakene).** For Kim's four-year-old daughter with DS, *"The drug that actually really made an impact in her seizures was Depakote. She had a little over a hundred seizures in 2020, and then last year she had 33. ... But really we've only seen ... a direct impact related to seizures."*

Nathan, father of two sons with DS, agreed. *"So we've gone through a litany of different medications with [our son], and we find that Depakote ... is probably the strongest drug for him."*



Jari, the mother of a 13-year-old daughter living with DS described a downside. *“Depakote was terrific for us, but it also killed off all her platelets to the point where we were in the oncology department.”* Other caregivers described side effects including liver injury, loss of appetite, and the development of an allergy to the drug.

**Ibuprofen.** On her worst days Barbara uses ibuprofen with Ativan for her son, *“just to keep him quiet and comfortable and allow him to rest.”*

**Propofol.** Sarah M., who lost her 8-year-old son because of DS, said, *“Our seizures were so resistant to typical interventions like Ativan and Diastat [benzodiazepines], that we carried a handwritten note from our neurologist to start propofol, an anesthetic that required intubation preparations to protect his airway.”*

**Intravenous immunoglobulin therapy (IVIG).** Kate H. described trying IVIG for her daughter. *“We have seen success reducing seizures using IVIG treatments. IVIG infusions have helped keep our daughter’s immunity high and inflammatory response low. Common colds and flu no longer become major seizure events for us. Unfortunately, IVIG is considered an off-label use for intractable epilepsy and is hard to get covered by insurance.”*

### Topiramate (Topamax)

Topiramate (Topamax) was used by 49% of caregivers. Like the other medications, it comes with benefits and downsides. When Nathan’s eldest son (now five) received his diagnosis, *“We went on a regimen of Depakote and then Topamax and it actually worked extremely well. The seizures were ... kept at bay.”* Nathan felt that his son, *“Wasn’t talking really very well, he just seemed to not be keeping up with his peers in that aspect. When we got him off of Topamax and put him on different medications, he brightened up almost instantaneously.”*

Marla’s daughter lost her appetite, but she wasn’t sure if it was due to her medication. *“We are currently weaning off Topamax which seemed to affect her appetite. Most meals were stressful - trying to get her to eat anything without screaming through meals and throwing food on the floor. ... Now that she is almost completely weaned off Topamax this week, her appetite has drastically improved, and it is a relief to watch her eat all the food served to her without fussing.”*

### Medications to aid with sleep

Medications to aid with sleep were used by 38% of caregivers, but were not described nor discussed in great detail.

### Stiripentol (Diacomit)

Stiripentol (Diacomit) was used by 34% of caregivers and generated many comments. When Janice S.’s now 22-year-old daughter was first diagnosed at the age of four, she, *“Was started on stiripentol and Depakote, which was our life-changing seizure medication. It really helped her with*



*the status seizures. Her average seizure went down to 20 minutes, which was life-changing for our family."*

John went to great lengths to obtain stiripentol for his 18-year-old daughter living with DS. *"Our family continued to be aggressive. We looked to import stiripentol from France as a compassionate use drug, as we were out of options. ... While we did see some impact, it also quickly waned."*

Gloria described the downsides for her nine-year-old daughter. *"Once added, stiripentol brought with it an overnight change. We didn't see the happy and smiling [girl] anymore. She was an angry wide-eyed child that rarely slept. She was irritable with everything and everyone around her, her appetite suddenly increased as she became obsessed with eating, and only playing with certain toys. She stopped making eye contact with us all together and struggled even more to communicate. She cried every day. And without the verbal skills to express her needs, she became anxious about all the things that used to bring her joy. She was changed and not for the better. The light in her eyes was gone."*

### Zonisamide (Zonegran)

Zonisamide (Zonegran) was selected by 26% of the caregivers. This was only one of the anti-seizure medications that John's 18-year-old daughter living with DS had tried. *"[She] spent the next five years trying and failing different medications, such as Tegretol, Depakote, Zonegran, Topamax, Lamictal, Felbatol, and Keppra."*

### Medications to manage behaviors or psychiatric issues

Medications to manage behaviors or psychiatric issues were selected by 25% of the poll respondents. For Janice S.'s 22-year-old daughter with DS, *"We have her on a small dose of a behavior medication called citalopram, and now we're also on Fintepla."*

### Investigational medicines

Investigational medicines, available through a clinical trial or expanded access, were used by 23% of poll respondents. Morgan, mother of a nine-year-old son living with DS described how, *"As a parent, there's a feeling of desperation to find something to help them, and this often means looking outside the box at therapies that are not yet approved."* She described numerous challenges of participating in clinical trials, including cross-country travel, blood draws, and multiple tests. *"The decision to participate in a clinical trial is not one that can be taken lightly. While there is a chance their condition could improve, there is also a chance that you could put them through all of this, and their condition could worsen."*

Morgan continued. *"We had to consider the enormous risks of the trial, the burden on his fragile body of having to travel across the country once a month during cold and flu season, and the overwhelming cost of travel, which was not reimbursed by the sponsor. We had to weigh these risks against limited available evidence that this drug would significantly reduce the number of seizures he was having to improve his quality of life. There was also a lack of guarantee at the time of enrollment on how long the open-label portion would last, so we could put him through all of this and possibly lose access to the drug after only a few months."*



Mandee agreed. *"Drug trials and new treatments usually require lots of extra medical tests and travel, both of which are nearly impossible for my son and our family to comply with."*

Gloria's daughter enrolled in a clinical trial at the age of two. *"Being included in a double-blind placebo trial gave us no guarantees. We were scared to do the wrong thing, but even more afraid to do nothing."*

### Vagus nerve stimulating (VNS) device

A VNS was used by 15% of caregivers. Matthew described that, *"The VNS really was a game changer for my son. Before the VNS, nearly every seizure was a status seizure, which would be 10 plus minutes that would stop only with rescue medication. With the VNS, status seizures are much more rare. We still have to use multiple other anti-epileptic drugs for reasonable seizure control, but the VNS offers significant protection against the more severe seizures."*

For Jennifer's 19-year-old son living with DS, the addition of the VNS reduced the rescue medications to once a week. *"One of the very newest therapies has actually made a big difference in that combined with the smarter VNS."*

### Ethosuximide (Zarontin)

Ethosuximide (Zarontin) was used by only 6% of caregivers and was not discussed during the meeting or in comments.

**Besides medication and treatments, individuals with Dravet syndrome require a great deal of therapy and support to manage symptoms.**

Caregivers for individuals living with DS selected all non-medication-related treatments and approaches that they tried to manage DS symptoms. Caregivers selected an average of 5.3 different choices. Poll results are presented in **Appendix 7, Q2** and described with caregiver quotes, below. Similar to the question above, not one caregiver selected that they are currently not using anything to help manage symptoms.

### Therapies – speech, physical (PT), occupational (OT), behavioral or psychotherapy

Most caregivers have tried multiple types of therapy, including speech therapy, selected by 92% of caregivers and physical therapy and/or occupational therapy, selected by 90% of caregivers. In addition, behavioral or psychotherapy was selected by 41% of caregivers. Therapy for Kate's daughter, *"Began early at only three months old. I began driving [our daughter] to an outpatient pediatric therapy center for physical therapy through our state's early intervention program. Within a few months, we also received a referral for occupational therapy."* After having a gastrostomy tube placed, *"We then added feeding, speech, and language therapy to her roster."*



Lynn, mother of a five-year-old daughter living with DS, described many different therapies. *“Physiotherapy has definitely helped her during a certain age. As of now, I think OT is helping her the most. Speech [therapy] has been on and off.”* She described the resulting improvements to fine motor skills they observed as a result of OT and PT. *“I see her using her hands a lot more... And now, the past couple of months, she started feeding herself and just having your child eat by herself, it's a break, it's a wonder. ... even carrying things across the room, balancing herself.”* She also described how PT improved mobility. *“The PT gave her some core strength and then she started walking ... even though she was ataxic, it was a bit of independence.”*

Many described receiving therapy through school. When Kate's daughter turned three, she *“Was officially school-aged and was transferred from the early intervention program into our school district's Committee on Preschool Special Education or CPSE program. The school performed evaluation tests on [our daughter], and she was given PT, OT, speech and language, feeding, a teacher for the visually impaired, and a special education itinerant teacher or SEIT.”*

Jennifer described therapies and resources at her 19-year-old son's residential program. *“They have recreation programs, they have therapy pools... they have all the lifts and the walkers and standers and the exercise machinery and multiple people to handle him and his behaviors.”* She described how, *“We have seen a lot of improvements in his life. ... He was able to reverse the curvature in his spine just enough, which very rarely happens that he hasn't had to have rods placed. His bowels are normal.”*

### Use of sleep and seizure-monitoring devices

Use of sleep and seizure-monitoring devices were reported by 69% of caregivers. Tyler wrote that, *“When [our son] was very young we discovered a [pulse oximeter-like product] sold to the public under the brand name Owlet. We also noticed that a seizure would cause his heart rate to spike. One night, we checked the Owlet and noticed our son's heartrate was really high. We checked on him and discovered him having a seizure. We were able to get him to a hospital and he recovered fully. Since then, we have found other devices as well that allow us to customize the heart rate or oxygen saturation that will trigger an alarm. These devices are not perfect, but they keep my son alive.”*

Nichelle described the devices that she uses to monitor her son with DS. *“We use several monitoring devices (pulse ox, seizure monitors and video monitors).”*

### Dietary changes

Other dietary changes, excluding ketogenic diet and clinically-managed diets, were selected by 57% of caregivers. Mande described how, *“Diet therapy, homeopathics, vitamins, and herbal supplements have been the most helpful treatments for my son.”*



## CBD or other cannabis supplements

CBD or other cannabis supplements, including medical marijuana, were selected by 51% of caregivers. Janice S., mother of a 22-year-old daughter with DS described using both topical and oral formulations. *“Medical marijuana has been a game changer. ... Medical marijuana really helps her behavior.”*

## Other approaches

A total of 39% of caregivers have tried other approaches to manage the symptoms of DS. They described their experiences with personal equipment and home modifications, lifestyle management approaches, and alternate therapy approaches.

**Personal equipment and home modifications.** Kate described the specialized equipment that her 11-year-old daughter requires, *“Including a transport wheelchair, a seating system, a motorized chairlift, an electric hospital bed with three-foot safety rails, a stander, a gait trainer, a toileting chair, a bath chair, and we are currently remodeling a bathroom to be fully handicap accessible. As prescribed by her specialist, we have two suction machines, oxygen tanks and oxygen concentrator, a pulse oximeter, a cough assist machine, a nebulizer machine, and a feeding pump. We receive ongoing monthly shipments from durable medical equipment companies, including incontinence, respiratory, gastronomy, and infusion supplies.”*

Janice S. wrote that, due to behavior issues, *“We have locks on our doors and fridge to keep [our daughter] safe and to keep our valuables safe.”*

**Lifestyle management including sleep, moderate exercise, and structured activity including school.** Kristi said, *“We also have to stick to a pretty rigorous schedule/routine for him to help him navigate his days and nights better. ...We also limit outside play for [our son] depending on the heat or cold and make him rest in between play time. We try to make sure he drinks a lot of water throughout the day.”*

For Kim’s four-year-old daughter with DS, *“Sleep and making sure she has enough sleep is another form of treatment control.”*

Jeannette wrote, *“Physical activity has helped my child to sleep longer at night. A walk around the neighborhood of one or two blocks in the evening helps to reduce the number of times he wakes up at night and helps him sleep longer than his usual. However, also careful not to exhaust him because that has a counter effect which will bring on seizures while he sleeps.”*

**Alternate therapy approaches including comfort therapies, medic therapy, and aquatic therapy.** Barbara said, *“We are managing DS with a combination of medications, diet, VNS, and comfort therapies including massage and music.”* She added, *“I wish EVERY family living with Dravet syndrome had access to palliative care to help manage symptoms, provide comfort, and address the needs of the whole family.”*



For Kate's daughter, *"A little known technique called medic [vibrational] therapy" was a breakthrough. "Medic was developed in the 1970s specifically for infants diagnosed with brain injuries. I have never seen the muscles in her legs shake with effort as they did in these sessions. It left her exhausted, but it was this therapist that got [our daughter] to take her first steps at eight years old. She can now take forward steps while someone holds her hands. This has improved the quality of her life immensely as she can now assist with weight-bearing transfers and take steps around her home and around the classroom."*

Emily's daughter loves aquatic therapy. *"She does both aquatic PT and OT weekly and will soon start adaptive swim lessons to continue working on water safety. ... Although she still has significant ataxia and muscle weakness, she has gained so much strength and confidence and she will be completing an adaptive triathlon this spring. She looks forward to these therapies every week."*

### Hippotherapy

Hippotherapy, or equine-assisted therapy, was selected by 35% of caregivers. Kate explained, *"Hippotherapy is therapy on a horse with a certified PT or OT and one or two additional spotters."* This has been beneficial for her 11-year-old daughter with DS. *"Smokey's deliberate and rambling gait would shake [our daughter] up from head to toe, and the effect on her core strength was remarkable. Two years after starting hippotherapy, [our daughter] rolled over and started sitting up at four-and-a-half years old. Two years later, [she] pulled herself up and out of her wheelchair and stood up by herself."*

Emily added, *"My daughter started hippotherapy at the age of three and it has changed her life. Her muscle strength has improved so much over the past six years. When she first started at three years old, she couldn't even sit upright on her horse for five minutes without being physically exhausted. Six years later, she rides well for 45 minutes weekly, trotting, standing while riding, and even learning to independently steer her horse."*

### Walking aids

The use of walking aids was selected by 33% of caregivers and includes a range of interventions. Peiyi, mother of an 18-year-old daughter living with DS said, *"She walks with the ankle braces to increase stability."*

Barbara's son requires much more. *"With loss of mobility comes a plethora of necessary durable medical equipment - adaptive chair, wheelchair, stroller, commode, shower chair, hospital bed, changing table - not to mention a ramp for accessibility and car that can accommodate him."*

### Seizure alert dogs and acupuncture

Seizure alert dogs were selected by 20% of caregivers, and acupuncture was selected by 4% of caregivers.



### Current regimens control disease symptoms and seizures only “somewhat”.

Poll respondents were asked, “How well does your current regimen control your loved one’s disease overall, including seizures and other symptoms?” Most, 68%, reported that the current regimen controls seizures and disease symptoms “somewhat”. Sixteen percent of caregivers reported that the current regimen controls their patients’ disease “to a great extent”, and 15% reported that their current regimen controls the disease “very little”. Only 2% reported that the current regimen controlled the disease “not at all”. Again, none of the caregivers reported that they are not using anything for disease control. Results are in **Appendix 7, Q4**.

**Key theme: Changing medications can be a slow process and determining if they work is challenging.** DS endpoints are subjective, so it is often hard to determine if treatments are working. Nathan, the father of two young sons with DS described this as a, *“Subjective game of how well our kids are doing based on that particular moment in time.”* He added, *“The hard thing, is that with DS, you don’t honestly know if the medication’s working or maybe it’s just a really calm time period for the child.”*

Mikell, mother of a four-year-old son living with Dravet syndrome described how the long feedback loop for DS medications makes determining efficacy even harder. *“The feedback loop is months long. We have to titrate up to a target dose over many weeks, it may be a month or two before you can even begin to see what’s going on. And then of course, if things have become worse, you can’t just stop [the treatment], you have to wean.”*

During the meeting, caregivers described the full range of experiences. Jennifer MK described how her daughter’s regimen, which includes Keppra, Epidiolex, and Depakote as well as the ketogenic diet, is allowing her to develop. *“Our daughter is walking, talking and growing right now which is beautiful. The therapies have been amazing for her developmental growth.”*

Unfortunately, as many caregivers described, most medications used to treat DS symptoms eventually lose efficacy, and seizures resume. John described that after an initial success, his 18-year-old daughter, *“Lost some of her seizure control with [her medication] combination.”* He described multiple attempts to control his daughter’s seizures. *“Each time, trying and failing. These were big events and ones that gave our family stress. You never knew if the medication was going to help, work less, or have more side effects, and this was a source of stress.”*

### Side effects are the biggest drawback of current Dravet syndrome treatment approaches.

Caregivers were asked “What are the biggest drawbacks of your current approaches? Select up to 3.” Poll results are presented in **Appendix 7, Q4** and described with caregiver quotes, below.



**Key Theme: As a result of taking so many medications, patients suffer significant medical consequences such as side effects, impacts on development, or cognition.**

Diane pleaded, *"Please understand that this is a devastating condition, where we parents and guardians constantly weigh the balances of controlling seizures vs the side effects of medications that can cause dizziness and processing delays."*

As Mikell described, *"The choice to attempt a new therapy or a new medication, to change a dose or to wean it completely, it might result in glorious stretches of seizure freedom, it may do nothing at all, or it might make things worse, and worse can mean a lot of things. It can mean more seizures, but could also be impact on liver function, appetite, growth, cognition, speech, behavior, sleep, so much more. That's not to even mention the impact on our family. And if I guess wrong in making a decision about his care, the stakes are excruciatingly high.... In these situations, we agonize over backtracking, stopping, or increasing the medicine, and it's impossible to know what the right answer is at the time. And the cost of guessing wrong feels intolerably high."*

Alexis wrote about the trade-offs. *"We are stuck right now at a place where we know lowering one of his meds will help increase cognition and help him make strides towards better independence and academic ability, but if we lower any more then his seizures will increase dramatically. Finding that balance is basically impossible and extremely frustrating because we know he can do more and improve if not for the cognitive toll of the medications."*

## Side effects

Side effects are the biggest drawback of current treatment approaches, selected by 85% of caregivers. They described the many side effects that their loved ones experienced and how seizure control medications compromised other aspects or quality of life. As Morgan wrote, *"We have experienced everything from rapid weight loss, hair loss, tremors, elevated liver enzymes, severe aggression, insomnia, loss of appetite, heat sensitivity, decline in cognition, vomiting and diarrhea, and worsening seizures - just to name a few. Sometimes these side effects are irreversible, which is a terrifying thought when you are using these medications to treat your young child."* Many side effects were already described along with specific medications in a previous section (starting on page 26). Others include sedation and sleeping, mood and behavior changes, photosensitivity, loss or increase of appetite, and increasing medication doses.

**Sedation and sleeping.** Silke said that current treatments cause, *"Sedation, slowing down in his overall thinking and actions."*

Lynn described how a combination of many medications has affected her five-year-old daughter living with DS. *"I have a zombie of a child on my hands, who's just sleeping 16, 18 hours a day, who was just not responding to anything. She's losing her cognitive ability. She's losing ... the person that she is."*



For Tina's son, *"Way too many medications are causing him to sleep a lot. And he isn't the super happy and smiley boy that he was. And it's very sad."*

Donna said, *"My daughter sleeps too much (with medications). She sleeps half her day a way sometimes, and once she is sleeping is hard to wake. She misses out on a lot.... Not sure if [it can be attributed to] DS or medications or both."*

**Mood and behavior changes.** Nathan described the side effects that his two sons with DS, age five and three, experienced. *"Sometimes the behavioral changes, the potential aggression, certain medicines have caused problems with speech. Certain medicines have caused issues with behavior. I mean, as a five-year-old when he wakes up crying in the morning and it just seems like sad all day - you know that the medicine's not his medicine. So you have to go move on to something else."*

Jari described how treatments for her 13-year-old daughter living with DS, *"Some of these medications cause negative behaviors and our daughter is also autistic, so she will harm herself. And we really need to decide whether the new medication will cause more harm than minimizing her seizures."*

**Photosensitivity.** Mikell described how increasing her four-year-old son's Epidiolex doses affected him. *"[He] became so incredibly sensitive to light and overexertion. We had blackout curtains over every window in our house, shades on our car windows, along with the sun hat and dark sunglasses for him for even the briefest excursion outside the house."*

Caregivers often felt uncertain if side effects could be attributed to a specific medication, a combination of medications, a new symptom of DS progression, or a combination of all three. As Mikell, explained, *"When we try new treatments, it's because something is changing about [his] seizure frequency, severity, or triggers, or types of seizures. So when we change something at the medication, it's really hard to figure out whether or not any new things we see are from that change or because we're just seeing the ongoing disease progression for DS."*

**Increasing medication doses.** Janice S., the mother of a 22-year-old daughter, described how waning efficacy meant that the drug doses needed to be increased. *"We tend to keep increasing the dosage on medications. And then what would happen with [our daughter] is she'd become allergic or toxic to the medication. So sometimes I think it's better to go on a lower dose if it's working and not continue to get to a therapeutic level necessarily."*

Lynn had a similar experience and described how her five-year-old daughter living with DS became ill from very high levels of medications. *"She was taking a few steps before all of this happened and [suddenly] she's lost her ability to stand. She's also lost her ability to walk. And I'm thinking this is DS. But it turns out it wasn't DS. She was in toxic states of a medication level. So now we're bringing down the medication levels. I'm seeing my child sort of wake up. And now I'm confused. How much is the meds? How much is DS?"*



### Only treats some and not all of the symptoms

The second most frequently selected treatment drawback selected by 77% of caregivers, is that current approaches only treat some, and not all of the symptoms. Again, trade-offs were often described. Darien wrote, *"When we try one treatment, it may "help" one seizure type, but it increases the frequency or severity of another seizure type. We try another treatment and see improvement in one area, but then another area declines. It's a constant battle between good and bad, yet no outcome yields the most optimal results."*

Matthew said, *"Dravet syndrome is pretty unique in terms of how it impacts the quality of life. As it does with our son, it includes a severe mental disability (e.g., nonverbal), physical disability (e.g., primarily wheelchair bound), and medical fragility (e.g., photosensitivity can trigger life-threatening seizures in almost any environment). There are strategies to address and improve quality of life as against each of these challenges separately, but addressing all three is extremely difficult."*

Jari, mother of a 13-year-old daughter living with DS reported success with one medication, *"Which has been terrific for us, but again, it doesn't treat all the symptoms. So, do we make the decision to try something new? Or do we stay where we're at? Because I think the side effects sometimes is too much for us to make that transition."*

### Not very effective at treating target symptom or symptoms

The third most selected drawback is that treatments are not very effective at treating target symptoms, selected by 44% of caregivers. Adrienne wrote, *"Nocturnal seizures and light sensitivity are the symptoms that have the biggest impact on my son. Treatments such as drugs only reduce these symptoms."*

For some caregivers, even a partial reduction in seizures is a benefit. Peiyi, mother of an 18-year-old daughter living with DS reported on their success. *"Like most Dravet syndrome patient families, we have gone through a lot of medications and countless therapy sessions. All this effort helped. ... we are thrilled that the seizures are now controlled at one episode every 30 to 40 days on average."*

### High cost, high co-pay, or not being covered by insurance

High cost, high co-pay, or not being covered by insurance was selected as a top three drawback by 21% of caregivers. Sasha described financial difficulties because of her daughter's DS. *"Her father changed jobs and did not have work for five weeks with no prescription coverage. Epidiolex was \$17,000 with a GoodRX coupon - we were lucky Greenwich Biosciences [the drug manufacturer] helped us, but what about other medications that she takes?"*

Kristi said, *"It frustrates me that we have to navigate challenges with insurance all the time for medications, and wondering if supply for his medications will ever stop."*

Mikell, the mother of a four-year-old son living with DS said, *"I have my employer's pharmacy benefits account manager on speed dial, so that insurance coverage is less of a roadblock."*



### Requires too much effort and/or time commitment

Requires too much effort and/or time commitment was selected as a top three drawback by 18% of caregivers. Sarah J. simply stated, *"We spend hours each day in speech/occupational/physical therapy."*

Several mentioned difficulties in subjecting patients to frequent testing, including Amy, who described how going to the pediatrician was torture for her 22-month-old daughter, *"After five hospital stays and every test you can imagine - from spinal taps, MRI, CT scans, nights with EEG leads on her head, echocardiograms every six months for one of her medications, the constant blood draws, - [our daughter] fairly doesn't trust doctors and howls and fights like a boxer at even the most benign examination."*

Jari, the mother of a 13-year-old daughter living with DS described her drawbacks, *"The frequent blood draws, the trips to the hospital to follow up on the efficacy of the drugs that you're utilizing."*

Kate described the challenge of administering medications many times a day. *"It has become very common and very accepted that Dravet patients are going to be on multiple medications indefinitely. And that creates a really high burden for caregivers. It creates a lot of stress and anxiety in Dravet syndrome patient families."*

Kate explained the burdens of individual insurance approval processes for each medication, refill limits, and approvals from doctors' offices. *"Some of those require specific blood tests or cardiac monitoring to obtain. So this is a really, really difficult lifestyle to manage aside from all of those logistics but when you add that into it, especially maybe to a family with two working parents, or perhaps a single parent. I mean, the more variables you have in these treatment options, the more room there is for error."*

### Route of administration

Route of administration was identified as a top drawback by 10% of caregivers. Adrienne pointed out that, *"Treatments can be difficult to administer if not formulated for a child (for example, Depakote sprinkle capsules)."*

Janice S. described how challenging it can be to administer oral medications to her 22-year-old daughter. *"In the past, if her behavior was so bad, I couldn't get her regular medication in."* She described using a medical marijuana wrist cream which would make her daughter more amenable to taking oral medications.

### Limited availability or accessibility

Limited availability or accessibility was selected by 5% of caregivers. Lynn, mother of a five-year-old daughter living with DS described the lengths they went to obtain medications. *"We are originally from India and we relocated to Canada when she was two for better access to treatment and hopefully newer medications."*



Bethany described that, *“Why can we only get the newer medications (Fintepla, Epidiolex) through specialty pharmacies even though they are now FDA approved? It takes multiple monthly phone calls, being home to sign for deliveries, and causes missed doses when orders/deliveries don’t happen in time.”*

Janice S. said *“[the medications] that I’ve worked really hard to find that are very effective for her sometimes are not available.” ... “The difficulty with medical marijuana is it’s not FDA approved. And so there’s no regulation... about what the suppliers have on hand, the cost.”*

## Other drawbacks

Only 2% of caregivers reported other drawbacks to treatments for DS.

**The top choices for new therapies are treatments for seizures and/or status epilepticus, in addition to addressing developmental delays and loss of developmental skills, and speech and language impairment.**

*“An ideal treatment for DS would eliminate [our daughter’s] seizures, help her to be able to regulate her temperature so that she can go outside anytime she wanted, open up her cognition so that she can be on grade level with her peers and be able to talk to us and physically be able to walk and do all of her activities of daily living including being able to eat solid foods.”* – Sasha, mother of a four-year-old daughter with DS

### **Key theme: Disease-modifying therapies for Dravet syndrome are urgently needed.**

Rachel said, *“The next DS drug needs to be disease modifying and improve cognition. ... I agree with others that it would be amazing if this disease modifying treatment could eliminate all of the other medications and treatments we need to use to manage our son’s quality of life.”*

Mikell, mother of a four-year-old son living with DS, agreed. *“As long as we’re simply treating symptoms, families like mine will go through this trial and error over and over and over. We are grateful for newer DS-specific drugs, but realistically we need disease-modifying therapies that will change the course of DS progression and whose effects will be long enough in duration that will actually be worth the time, quality of life, and psychological investment for families to try them.”*

Tina wrote in to remind everyone that disease modifying therapies need to be developed for people with different genetic variants. *“The gene therapy sounds pretty promising but since our son has THR226MET (a different genetic variant), he can not participate in the trial at this time so we will be patient and see what happens.”*



Caregivers were asked, “Which aspects of your condition would you rank as most important for a possible new drug today? Select your TOP 3”. There was high concordance between poll and survey responses. Poll responses are presented in **Appendix 7, Q5** and survey responses are in **Appendix 2, Q7**, and highlights are presented below with caregiver quotes.

## Seizures and/or status epilepticus

*I think we're all striving for seizure freedom.” – Stephanie, mother of a six-year-old boy living with DS.*

Treatments for seizures and/or status epilepticus are the top choice for symptoms to be addressed by new therapies, selected by 82% of caregivers who responded to the poll, and similarly this was also selected by 93% of caregivers who responded to the survey, as a top symptom to be addressed specifically by disease modifying therapies. Caregivers were adamant that seizure reduction could not compromise quality of life or other aspects. Jari, mother of a 13-year-old daughter living with DS, “*Our top treatment goal would be to minimize or reduce or completely get rid of seizures. There's no doubt about that. But we're very clear that we won't sacrifice quality of life.*”

Caregivers felt that reducing seizures would allow their children to develop in other ways. Stephanie, mother of a six-year-old son living with DS shared, “*My top goal would be to control seizures. My son has had a really nice long break from convulsive seizures, but he has been plagued with dozens of other types every day. ... I think that if we could help alleviate that seizure burden for him, he would make more progress developmentally. And I think he would acquire more language. I think it would probably improve his behavior.*” She explained how, “*This is still a critical developmental time period for him. So, I think he has a lot to gain from time-sensitive improvements and seizure control.*”

Nathan, father of two young sons living with DS said, “*I would absolutely love to never see a seizure again. ... Nobody wants to have seizures.*” He explained how vigilant he is when he goes to the pool or the park. “*I'm always very nervous they're going to have a seizure. ...That's what I'm always watching like a hawk for.*”

## Developmental delay or loss of developmental skills

Developmental delay or loss of developmental skills were the second most selected symptom to be addressed, selected by 74% of caregivers who responded to the online poll and 72% of caregivers responding to the survey. Caregivers felt that increasing cognition would help foster their loved ones’ independence and quality of life. For Cara, “*A top treatment goal at this point would be directed at comorbidities. Something that would allow the body and mind to continue to develop and grow (even when seizure freedom isn't happening). I think this would help behavior significantly and quality of life in general for all DS patients and their families.*”

Short of a cure, Sarah J. said, “*I'd like [my son] to be more participatory in every way - academically and physically. DS limits him developmentally and recreationally.*”



Aimee expressed her wish for future treatments. *“Developmentally, we would love to get him to a state where we could transition him from diapers to being able to use the toilet.”*

Tina said, *“His brain can’t develop properly or at all for that matter if he’s seizing every day.”*

Rachel discussed trade-offs. *“I would even accept living with some level of ‘manageable’ seizures that do not significantly impact quality of life, if my son could have significant cognitive gains.”*

Kim described what she wanted for her four-year-old daughter. *“Something that really helps with her cognition. She’s so smart and I feel like there’s so much there, but she needs a treatment to let her live to her full potential.”*

### **Risk of SUDEP**

The risk of SUDEP was the third most popular choice for a symptom to be addressed, selected by 41% of caregivers responding to the survey, but was not provided as a response option in the polls. Sophie, older sibling of a 22-year-old brother living with DS described a trade-off. *“I think most people would agree that if we have to live with poor communication forever of our loved one with Dravet, we’ll do that as long as a seizure doesn’t take them from us.”*

Amanda said, *“My ultimate fear is losing my child to SUDEP. Every day we wake up not knowing if today will be the day he starts clustering again, will he start having status seizures again or will DS take his life?”*

Emily wrote. *“One of my biggest fears as my daughter (who is 9) gets older is that she is going to die, either from a complication from a seizure or from SUDEP.”*

### **Speech and language impairment**

Speech and language impairment was selected as a top symptom to be improved by 42% of caregivers responding to the online poll and by 22% of caregivers responding to the survey. Aimee said, *“Getting rid of the seizures would be the top goal for our 12-year-old, but it would also be wonderful for him to be able to communicate with us...be able to tell us what he is feeling or needing.”*

Barbara S. expressed hopes for her son. *“I would love to see him regain some speech so he can communicate and be less frustrated.”*

### **Disruptive behaviors and autistic-like behavior**

Disruptive behaviors, including tantrums and refusal, and autistic-like behavior including difficult social interactions and patterned or repetitive movements were selected by 25% and 12% of caregivers responding to the online poll, respectively, as a top three symptom to be improved. This was also selected as a top symptom to be improved by 31% of caregivers responding to the survey.



## Dysautonomia

Dysautonomia - function of the autonomic nervous system such as temperature regulation, heart function, breathing, digestion - was the sixth most popular target, selected by 18% of caregivers responding to the survey but was not offered as a poll response option.

## Sleep disturbances

Sleep disturbances were selected by 28% of caregivers responding to the online poll and 10% of caregivers responding to the survey as one of their top three aspects of DS for new drug development. Amy said, *"It's super frustrating not to have an all-in-one device to help monitor our kids at night. Sleep is so important for the whole family and one device that monitors and records and alarms for irregular movements, something that tracks not just pulse/ox, but the quality and type of sleep (deep/REM/light) and can graph it would be so helpful. The technology is available but unfortunately no one is putting it all together for parents like us."*

Janelle wrote, *"A life without Dravet syndrome is a dream I'm scared to even wish for. It would mean we wouldn't wake to seizure - false or real - alarms in the middle of the night, often multiple times a night."*

## Problems with balance and gait

Problems with balance and gait were an aspect of DS to consider for drug development selected by 12% of caregivers responding to the online poll and 7% of caregivers responding to the survey. For Sharon, *"Mobility and endurance issues have become extremely impactful in providing much of the social and lifestyle activity that we have been able to provide our daughter in the past. The aging process (currently aged 31) has been very difficult, and we have hopes that we can keep her as healthy as possible physically which is becoming a real concern. Our hope is that some of the new treatment options may result in enhanced improvement in extremities."*

## Growth and nutrition issues; hypotonia; and frequent and long-term infections

The following aspects of DS received the fewest votes during the polling/survey processes: growth and nutrition issues (5%/1%); hypotonia (poor muscle tone) (2%/1%); and frequent and long-term infections (2%/2%). There were few comments.

## Other aspects of Dravet syndrome for therapeutic development

Although other aspects of DS were selected by 7% of caregivers as a possible focus for drug development, many different options were described including more options for adult individuals living with DS, a reduction in side effects, new clinical trial endpoints to better ways to measure and predict treatment success, better treatment algorithms, and better administration options. These aspects are described below with caregiver quotes.



**More options for adult patients with Dravet syndrome.** During the meeting, many caregivers expressed concern that there were fewer treatments in development for their loved ones who are adults. Sharon wrote, *“As we look to the new treatment plans, could we please consider the adult population in the clinical trials or compassionate use protocols? Particularly if there is hope in slowing degeneration of the DS patient who has reached adult age but still retains physical function.”*

Michele W. pointed out that many trials do not include adults and expressed other care gaps. *“Adult DS patients having underlying issues (gastrointestinal, genitourinary, ortho) dismissed as “just DS” when even the experts don’t really know what DS looks like as adults.”* She continued, *“I am concerned we do not have enough doctors who truly understand adults with disabilities, let alone DS. ...I want to know more about the long-term effects of the AEDs on our adult [patients].”*

Donna wrote, *“I pray too, that our 30-year-old daughter ... will be included in a treatment plan that will give her a better quality of life (yes, even at that age of 30 and beyond).”*

Clare wrote, *“As the number of adults with DS is increasing, it can feel like a whole new syndrome as new co-morbidities appear, and little research to understand the best course of action. The development of Parkinsonian-like symptoms is one example, with changes in gait, behavior, posture. So should we be looking at adding Parkinson medications?”*

Caregivers also described a challenge with finding health care providers as their loved ones transitioned from the pediatric system. Jessica noted, *“There seem to be very few adult neurologists with knowledge of DS treatment.”*

**Reduction in side effects.** Jennifer W. asked for a therapy to, *“prevent seizures WITHOUT all the crazy other side effects”.*

Lynn, the mother of a five-year-old daughter living with DS, described how, *“If you’re going to treat her seizures, it should be something that I’m not worried that I’m going to lose her kidney, or her lungs, or her brain, or her heart, or her liver. Minimizing the impacts to other body parts.”*

**New clinical trial endpoints that better align with meaningful outcomes for patients.**

Nadia wrote, *“we were looking for more trials to include primary endpoints beyond reduction in tonic-clonic seizures. As patients grow older, they may no longer see tonic-clonics, but other life-altering seizure types - such as myoclonics, absences - prevail. These patients are often excluded from clinical trials as they do not meet the inclusion criteria of tonic-clonics.”*

Caregivers discussed what they considered would be a significant clinical impact in terms of treatments. Stephanie said, *“Meaningful seizure reduction for me - to take a risk on a new treatment - maybe even as low as a 20% improvement, I think would be meaningful.”*



Lynn, the mother of a five-year-old daughter living with DS, described how, *“For me personally, I can take one seizure that is self-resolving every week. So, one seizure a week is something that I don't mind accepting and just moving on with our lives.”*

**Clearer treatment algorithms.** Ted, the grandfather of a four-year-old child living with DS said, *“Wouldn't it be wonderful if we had a treatment algorithm where we had all the data for all the patients and what worked and what didn't work, because I don't believe there's a good algorithm. ... there's really no good treatment algorithm as it relates to age. And as the brain matures and the body matures, we heard about puberty. There needs to be a better algorithm to help the clinical practitioners in recommending and prescribing treatments for this patient population.”*

Bethany agreed. *“Even if we keep using the same rescue medications, we need to know the best timing, the best combinations, the best route to give medications.”*

**Better administration options including monotherapies.** Jennifer MK wrote that she would like different administration options. *“Can't all meds just dissolve or be sprayed in the nose or one time or monthly injections? What I would love is easy administration for any medicine that is currently in existence and will be created in the future.”* She also suggested monotherapy and nutrition/supplement patches instead of pills.

Kate, mother of an 11-year-old daughter living with DS said, *“There's so many medications being used to treat one patient and we really need a monotherapy for DS patients.”*

Ted (caller), grandparent of a four-year-old child living with DS, also wanted a single, streamlined therapy to reduce drug-drug interactions. *“By having a single therapy, or even two, instead of the multiple ones we have today, I'm sure you can eliminate side effects.”*

Alexis wrote: *“An ideal treatment for DS would be something he doesn't have to take daily, if possible, that improves seizures dramatically without the need for multiple drugs and without the side effects we currently have to contend with.”*

### **Administration for disease-modifying therapies: Caregivers would prefer less permanent and less invasive options**

DSF held and promoted a survey, *Caregiver Opinions about Disease Modifying Therapies for Dravet Syndrome*, concurrently with the EL-PFDD meeting process. Caregivers responding to the survey were asked about therapy scenarios surrounding varying administration methods and levels of improvement in disease symptoms. The survey responses are complex and can best be reviewed in **Appendix 2, Q8-12**. Overall, caregivers to individuals with DS indicated a preference for therapies that were less invasive and less permanent, allowing patients to try other options if desired. For regular intravenous injections that would not be a permanent therapy, the majority of responses would consider the therapy even at the lowest level of



benefit (“possible improvement” in seizures only), but for the remaining therapy scenarios caregiver preference progressively shifted towards “definite improvement” in seizures or seizures and at least one other symptom. Notably, over half (67%) of caregivers would still consider a one-time treatment of a more invasive option (administered directly to the brain) for their loved one with DS if it showed major improvement in just treating seizures alone.

### **Incorporating Patient Input into a Benefit-Risk Assessment Framework**

*“I know that we often talk about benefit and risk of medication, but it's also important to note that the risk of having no options at all is also real.” – John, father of an 18-year-old daughter living with Dravet syndrome.*

The FDA uses a Benefit-Risk Assessment Framework which includes decision factors such as the analysis of condition, current treatment options, benefit, risk, and risk management. The Framework provides an important context for drug regulatory decision-making and includes valuable information for weighing the specific benefits and risks of a particular medical product under review.

**Table 1** speaks to the challenge of having a lifelong disease burden that patients living with DS 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 this unique condition for key reviewers in the FDA Centers and Divisions who would be evaluating new treatments for DS. The data resulting from this meeting may help inform the development of DS-specific clinically meaningful endpoints for current and future clinical trials, as well as encourage additional researchers and industry to investigate options for treatments.

The information presented captures the perspectives of caregivers caring for patients living with DS presented at the February 3, 2022, meeting. It also includes information from the caregiver survey and polling results, as well as comments submitted before, during, and after the meeting through the online portal.

Note that the information in this sample framework is likely to evolve over time.





**TABLE 1 Dravet syndrome Benefit-Risk Table**

	EVIDENCE AND UNCERTAINTIES	CONCLUSIONS AND REASONS
ANALYSIS OF CONDITION/ IMPACTS ON ACTIVITIES OF DAILY LIVING	<p><b>Dravet syndrome is MORE than just seizures.</b> Seizures are a persistent threat, impair development, and interfere in all activities of daily living. Different types of seizures change over time, and the consequences can be catastrophic.</p> <p>Other significant symptoms of DS include developmental delays and regression, speech and language impairment, sleep disturbances, disruptive behaviors, problems with balance and gait, and many others.</p> <p>The incidence and severity of these symptoms vary from one individual to the next.</p> <p>DS symptoms are influenced by a complex interplay of factors: maturation, puberty, medications, disease progression, sleep, and environmental triggers can all contribute.</p>	<p><b>Life with Dravet syndrome is extremely unpredictable.</b> All aspects of life are affected, not only for the individual living with DS, but for their parents and siblings. Rigid schedules, rigorous advance planning, and extreme flexibility are required to manage seizure triggers and behaviors. DS patient families miss out on the daily activities, holidays, and celebrations that most take for granted.</p> <p><b>Most individuals with Dravet syndrome will require constant supervision and care for their entire lives, and will never live independently.</b> The syndrome is progressive, and symptoms can become more severe with age. Parents worry about ongoing care and access to resources for their children, as well as premature mortality, disease progression, worsening cognition, and intellectual impairment.</p>
CURRENT TREATMENT OPTIONS/ PROSPECTS FOR FUTURE TREATMENTS	<p>All patients with DS require polytherapy to treat their symptoms, particularly seizures. Individuals living with DS require a great deal of therapies and other supportive approaches. Even with multiple medications and a plethora of therapies, most patients experience many symptoms.</p> <p><b>Most medications are targeted at controlling seizures. Few address other symptoms or the disease itself. Current medications are accompanied by a plethora of side effects and can have developmental or cognitive impacts.</b> Therapy treats some but not all symptoms, and only control disease symptoms “somewhat”. As medications lose efficacy, which most do, seizures resume, and quality of life is impacted.</p> <p>Medication endpoints are subjective, it can take a long time to observe changes, and it is difficult to tell if treatments are working. Parents and caregivers agonize over potentially life-altering treatment decisions.</p>	<p><b>Patients living with Dravet syndrome have great unmet treatment needs and desperately need new treatments.</b> In addition to controlling or preventing seizures and/or status epilepticus, patients living with DS need therapies to address developmental delays and regression, risk of SUDEP, speech and language impairment, sleep disruption, and disruptive behaviors. Clinical trial participation is particularly challenging for individuals living with DS and their families.</p> <p><b>Individuals living with Dravet syndrome need more treatment options.</b> This includes disease modifying therapies, including treatments for those with different genetic mutations, and medications for individuals at different points in their lives (including adults).</p> <p><b>Caregivers hope for disease-modifying therapies that can treat multiple symptoms of DS.</b> Caregivers would prioritize a less permanent therapy that would not exclude their loved ones from receiving similar therapies in the future, over a one-time treatment. Caregivers would prefer less invasive administration options. Over half would consider a permanent and invasive therapy if it offered a major improvement in seizures, even without affecting other symptoms.</p>
	<i>See the Voice of the Patient report for a more detailed narrative.</i>	



## Conclusion

*“Our hope will always be to give [our daughter] a life without limits and, most important, no seizures. [Our daughter] should have a life where she can play outside, make friends, and learn, where being excited doesn't mean a trip to the hospital or missing family events. An extraordinary life without seizures is all we want. Thank you.” - Gloria, mother of a nine-year-old daughter living with Dravet syndrome.*

The February 3, 2022, Dravet Syndrome EL-PFDD meeting will help to advance DSF's mission to aggressively raise funds for Dravet syndrome and related epilepsies; to support and fund research; increase awareness; and to provide support to affected individuals and families.

This meeting provided an opportunity for the FDA, government agencies, regulatory authorities, pharmaceutical and biotechnology companies, scientists, and health care professionals to hear directly from the parents and caregivers of people with DS. Caregivers and parents of individuals with DS described the disease manifestations and experiences, the impacts on their activities and daily lives, and worries related to living with Dravet syndrome. They described the medications and therapeutic approaches that were required, and how these do not alleviate disease symptoms. The large numbers and combinations of medications cause many additional side-effects and sooner or later, stop working.

The participants at this EL-PFDD demonstrated that short of a cure, reducing seizures is a top choice for a therapeutic, followed by preventing developmental delay, reducing the risk of SUDEP, improvements to speech and language impairment, and addressing disruptive behaviors. Individuals living with DS need more treatment options including disease-modifying therapies and treatments for those with different genetic mutations. Adult DS patients, who are not included in many of the clinical trials for current treatments, also need medications.

DSF is grateful for this opportunity to share our voices through this *Voice of the Patient* report and sincerely thanks the patients and families that are navigating life with Dravet syndrome and who shared their insights and experiences at the EL-PFDD meeting, submitted online comments, and participated in the caregiver survey. Your input was invaluable and the positive impacts of your feedback will be felt for many years to come.

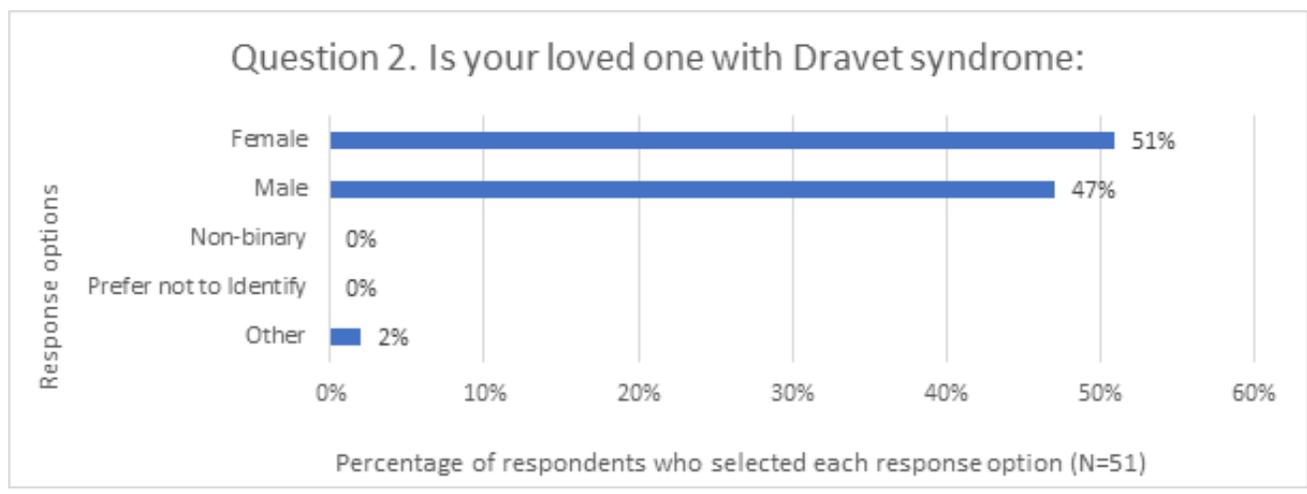
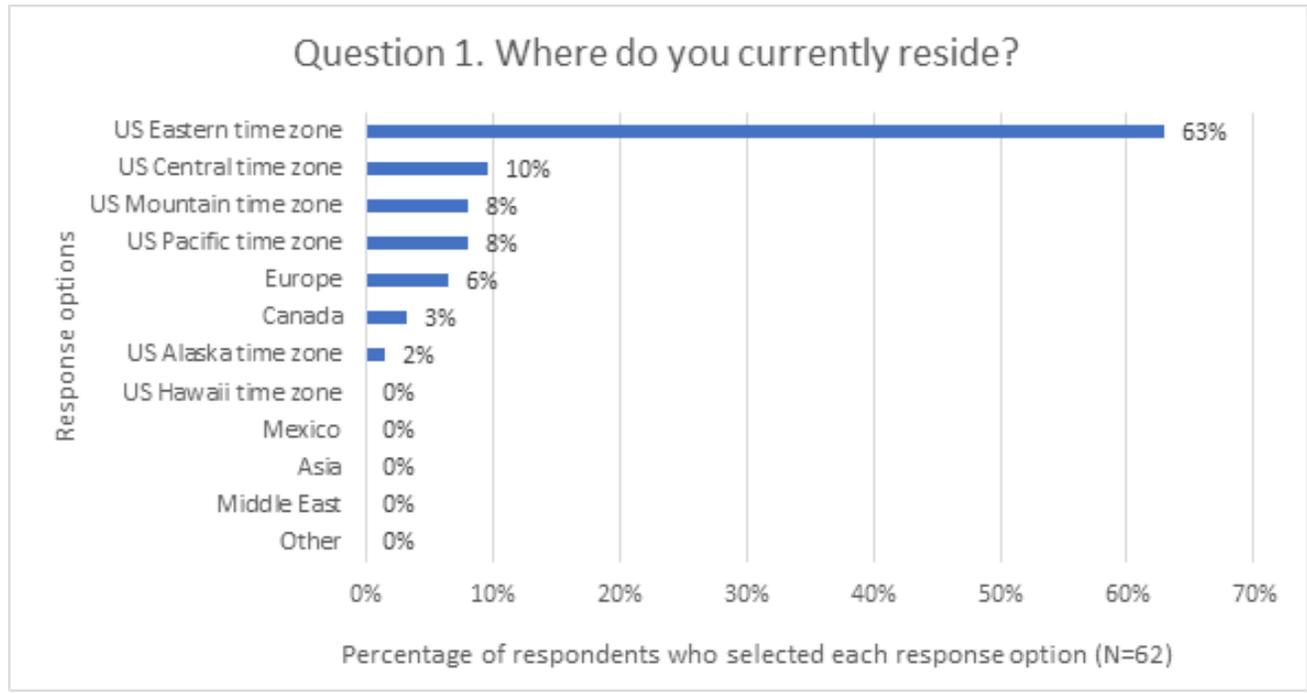
*“We need better solutions and better therapies in order to fully succeed in Dravet syndrome. ...We did our absolute best for [our son] and offered him the best therapies available. The fact that even a well-controlled Dravet syndrome patient is not protected from sudden death is a tragedy.” -Sarah M., mother who lost her 8-year-old son due to Dravet syndrome*

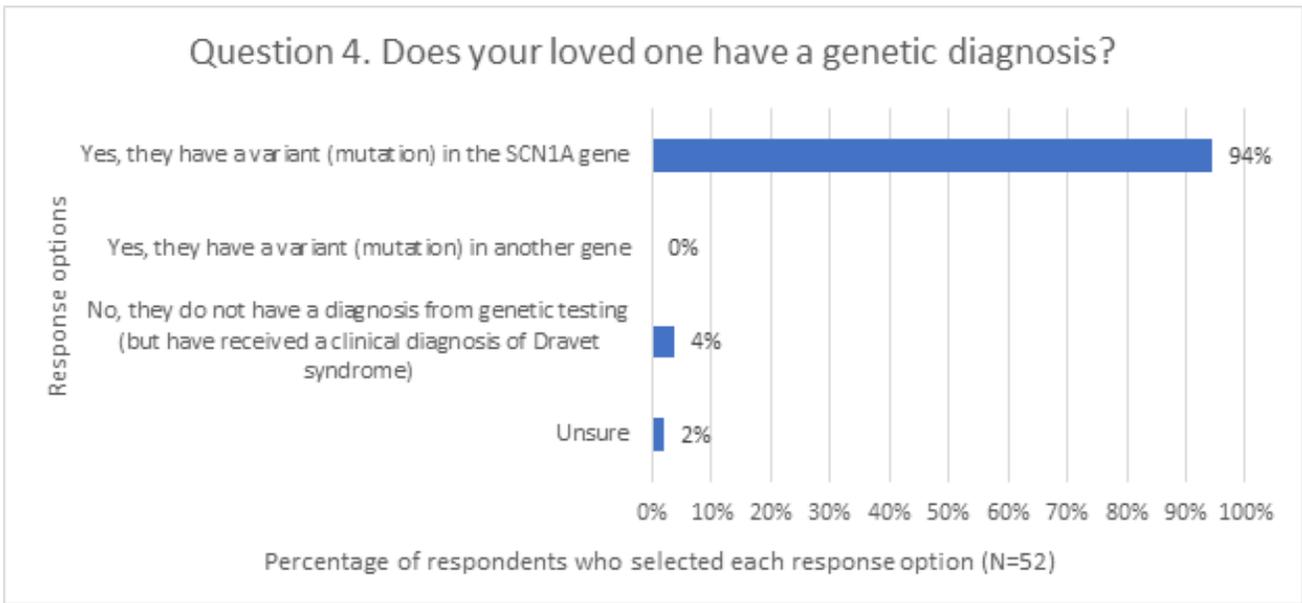
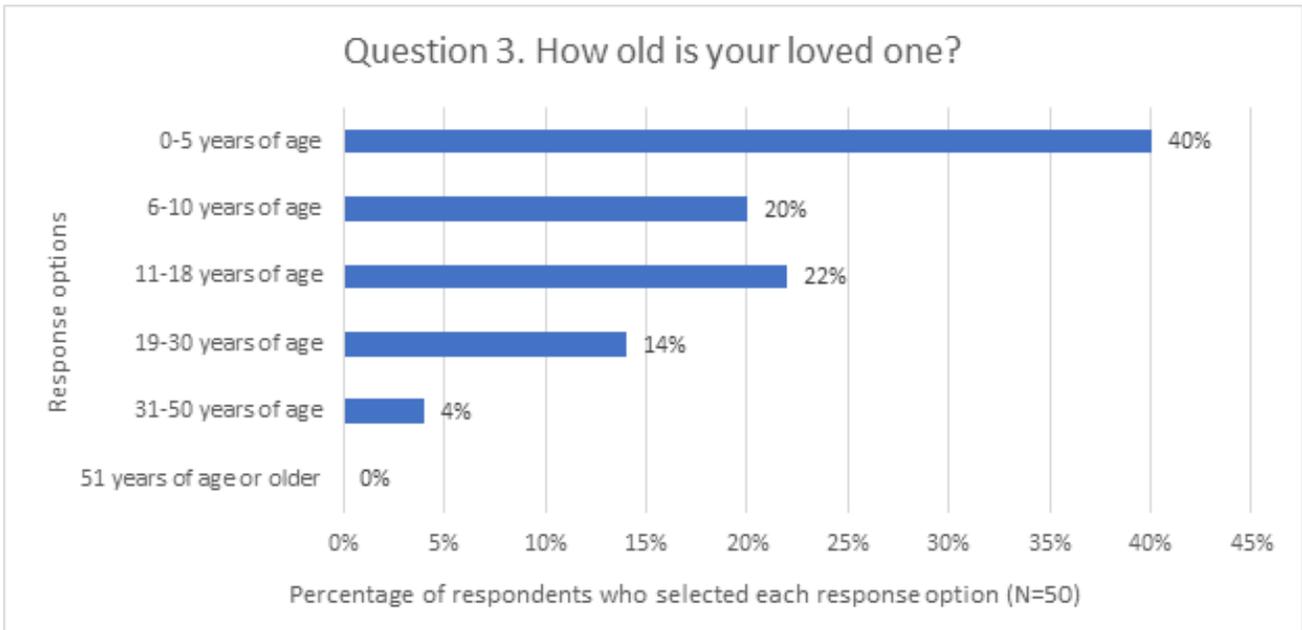


### Appendix 1: Demographics

These graphs include those attendees who chose to participate in online voting. The number of caregivers 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 EL-PFDD meeting and is intended to complement the live and pre-recorded comments throughout the meeting.







## Appendix 2: Caregiver Survey Results

DSF held and promoted a survey, *Caregiver Opinions about Disease Modifying Therapies for Dravet Syndrome*, concurrently with the EL-PFDD meeting process. The main goal of the survey was to better understand caregiver thoughts and preferences surrounding administration, permanency, and symptom treatment for considering disease-modifying therapies.

The survey was developed and shared by DSF via their website, on the webpage dedicated to the EL-PFDD meeting, by emails promoting the EL-PFDD meeting, through DSF social media channels, and in DSF-moderated online caregiver support groups.

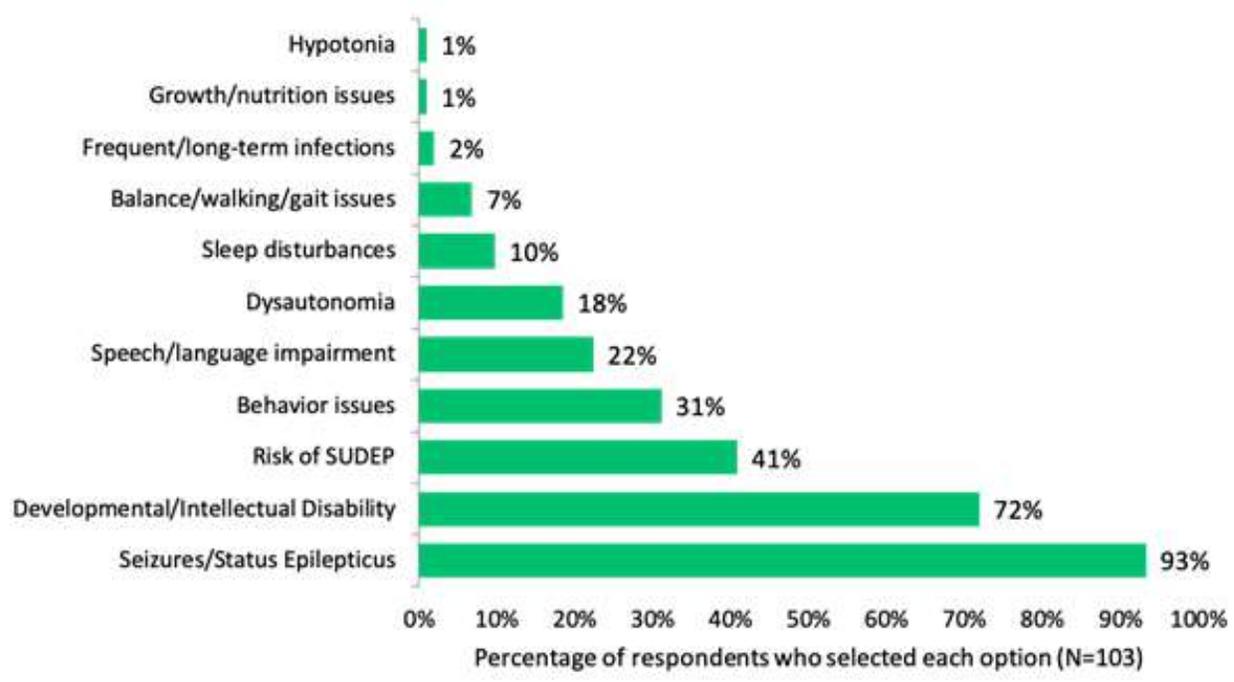
The first survey question verified participants were willing to participate in the survey with the intention that their de-identified responses would be utilized to support data from the EL-PFDD meeting for DS within the *Voice of the Patient* report as well as through other public channels utilized to share information by DSF.

Responses were received from 114 individuals that identified themselves as the primary caregiver to an individual with DS. Demographic data was very similar to the polling of the live audience. Caregivers represented individuals with DS that were 53% male and 47% female. The majority of responses (97%) indicated the individual with DS had an SCN1A gene variant, and the remainder (3%) had no identified genetic variant. The majority of individuals with DS represented were between the ages of 0-5 years (37%), 25% were between 6-10 years, 22% were between 11-18 years, 11% were between 19-30 years, and 6% were between 31-50 years. There were no responses from caregivers to individuals with DS older than 51 years. The majority of individuals with DS represented (89%) were located in the United States; the remaining were from Europe (6%), Canada (3%), India (2%), and Australia (1%).



When caregivers were asked in Question 7 to select the top 3 symptoms or comorbidities they would most like to see treated with a disease-modifying therapy for their loved one with DS, the top choices were seizures or status epilepticus (93%), developmental and/or intellectual disability (72%), risk of SUDEP (41%), and behavior issues (31%).

**Question 7: What 3 symptoms or comorbidities would you most like to see treated with a disease-modifying therapy? Please choose your TOP 3 options.**



Questions 8-12 of the survey focused on hypothetical scenarios for application of disease-modifying therapies. Caregivers were informed that a disease-modifying therapy would target the underlying cause of DS, namely the loss of SCN1A gene expression, including therapies that work at various molecular levels (DNA, RNA) and that may require different levels of invasive administration.

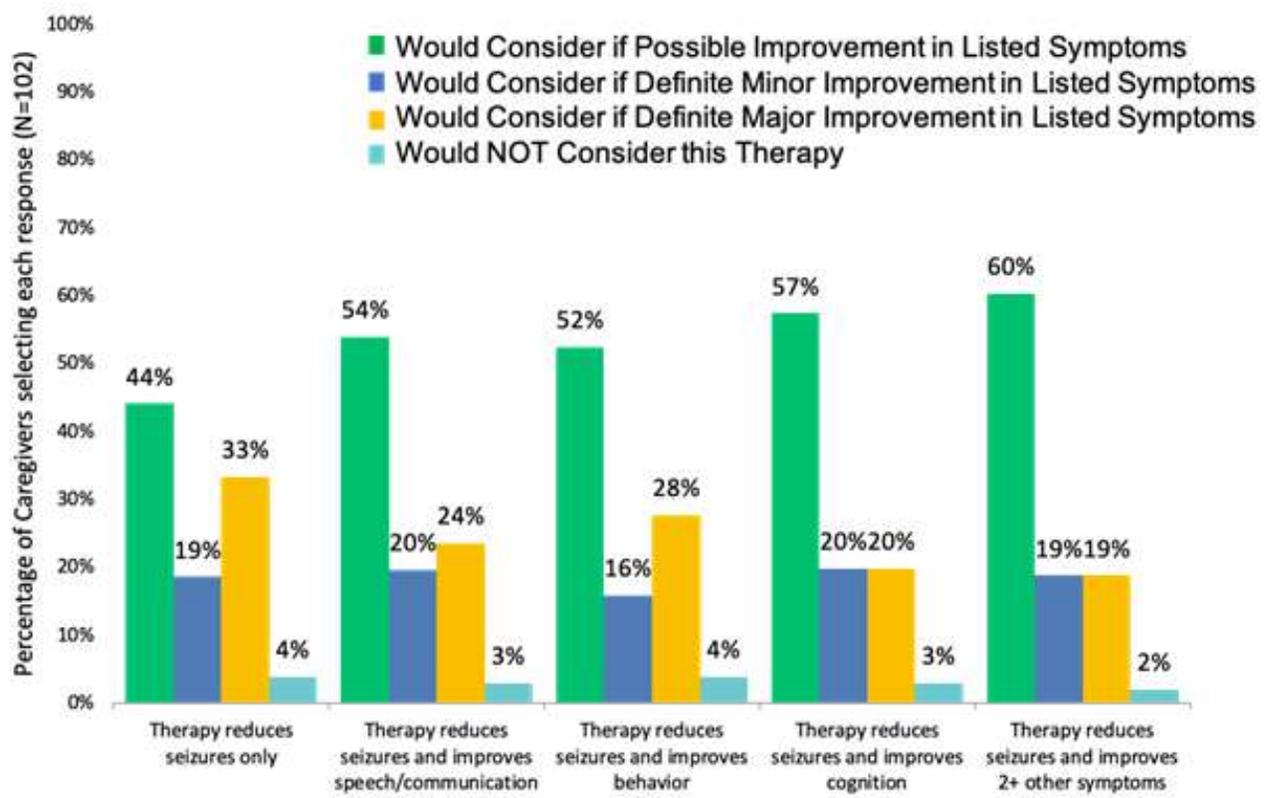
Caregivers were asked under what level of benefit (possible improvement, definite minor improvement, definite major improvement) they would consider a new disease-modifying therapy in the context of therapy permanency (one-time, versus regular administration every 3-6 months), methods of administration (intravenous, intrathecal, or injection to the brain), and number of symptoms treated (seizures only, seizures and speech/communication, seizures and behavior, seizures and cognition, or seizures and 2+ other symptoms).



In Question 8, caregivers were asked to consider a disease-modifying therapy that requires a **regular intravenous (IV) injection** that would be administered directly to a vein such as in an arm or leg, given once every 3-6 months. Note that caregivers responding to this survey were informed that this type of therapy likely would have a "wash-out period" before another disease-modifying approach could be tried.

- The majority of responses would consider this regular IV therapy if there was at least *possible improvement in seizures and at least one other symptom* (52-60%).
- Even if the therapy provided *possible improvement in seizures only*, 44% of caregivers would still consider this therapy.
- Only a few (2-4%) *would not consider this therapy*.

**Question 8:** For this question, please consider a disease-modifying therapy that requires **regular intravenous injections given once every 3-6 months**. An intravenous (IV) injection would be administered directly to a vein such as in an arm or leg. This type of therapy likely would have a "wash-out period" before another disease-modifying approach could be tried.

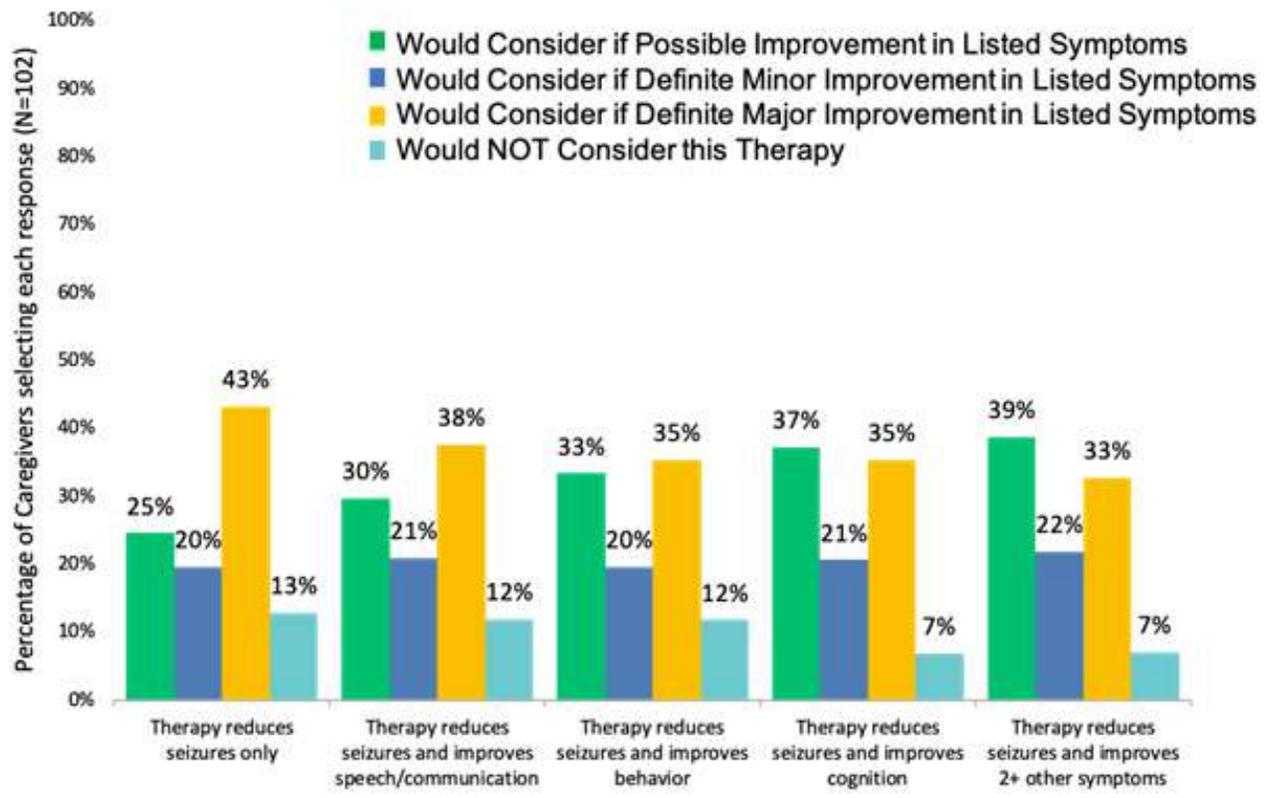




In Question 9, caregivers were asked to consider a disease-modifying therapy that requires **regular intrathecal (IT) injections** (a shot into the spinal cord similar to a lumbar puncture) given once every 3-6 months. Note that caregivers responding to this survey were informed that this type of therapy likely would have a "wash-out period" before another disease-modifying approach could be tried.

- Compared to Question 8 regarding a regular IV injection, there was preference from caregivers to see a greater level of benefit before considering a therapy requiring a regular IT injection. However, many caregivers would still consider this therapy if it provided a *definite major improvement in seizures only* (43%), and an additional 45% would consider it if it provided possible or *definite minor improvement in seizures only*.
- Responses were split in whether they would consider the treatment if it showed *definite major improvement* (30-39%) or *possible improvement* (33-38%) in seizures, plus at least one other symptom.
- Depending upon the level of impact on specified symptoms, 7-13% of responses indicated they would not consider this therapy.

**Question 9:** For this question, please consider a disease-modifying therapy that requires **regular intrathecal injections given once every 3-6 months**. An intrathecal injection is a shot into the spinal cord similar to a lumbar puncture. This type of therapy likely would have a "wash-out period" before another disease-modifying approach could be tried.

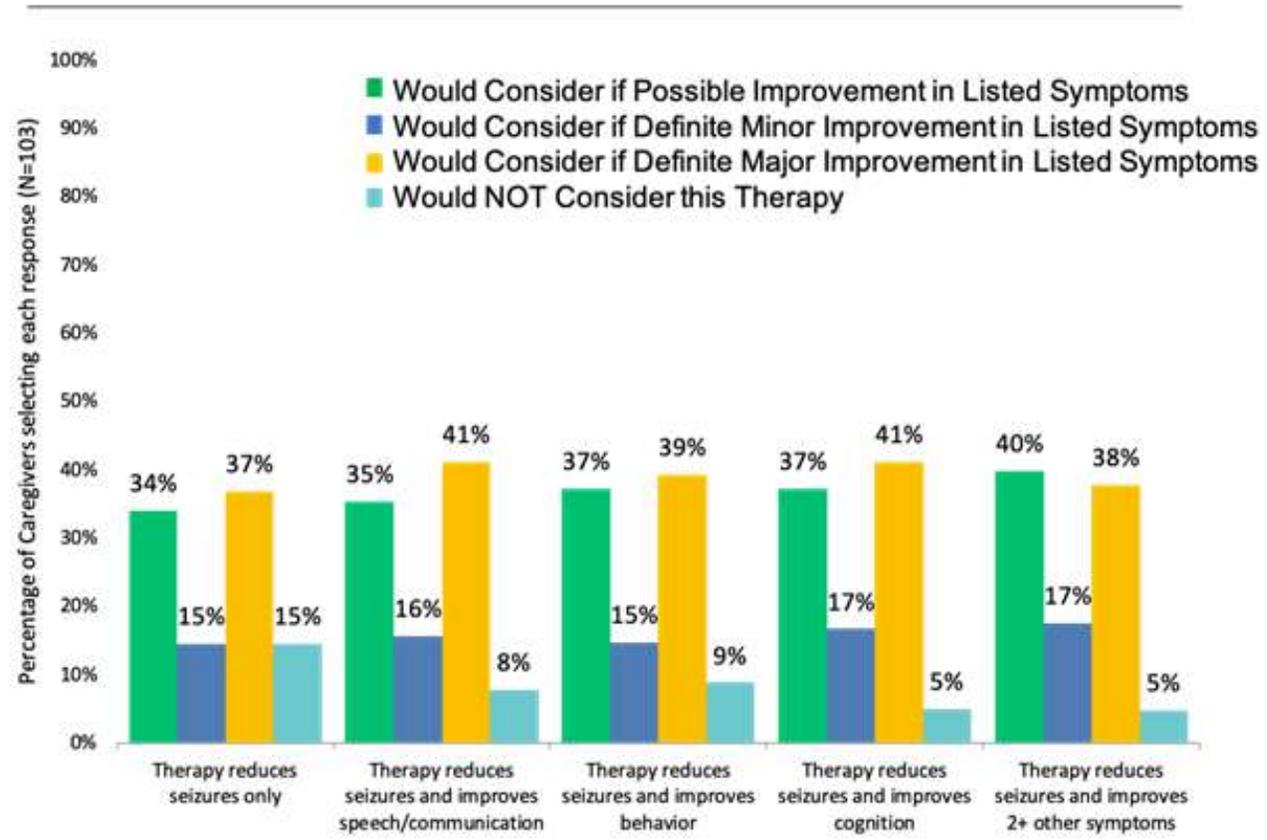




In Question 10, caregivers were asked to consider a disease-modifying therapy that requires a **one-time intravenous (IV) injection** administered directly to a vein such as in an arm or leg. Caregivers were informed that a one-time therapy may limit the ability to try another kind of disease-modifying therapy in the future.

- As with the preferences surrounding a regular IT injection in Question 9, the majority of responses indicated caregivers would consider this type of one-time IV treatment if it offered a *definite major improvement* (37%) or *possible improvement* (34%) in seizures only, or *definite major improvement* (38-41%) or *possible improvement* (35-40=%) in seizures plus at least one other symptom.
- Depending upon the level of impact on symptoms, only 5-15% of responses indicated they would not consider this therapy.

Question 10: For this question, please consider a disease-modifying therapy that requires a **one-time intravenous (IV) injection**. An intravenous (IV) injection would be administered directly to a vein such as in an arm or leg. A one-time therapy may limit the ability to try another kind of disease-modifying therapy in the future.

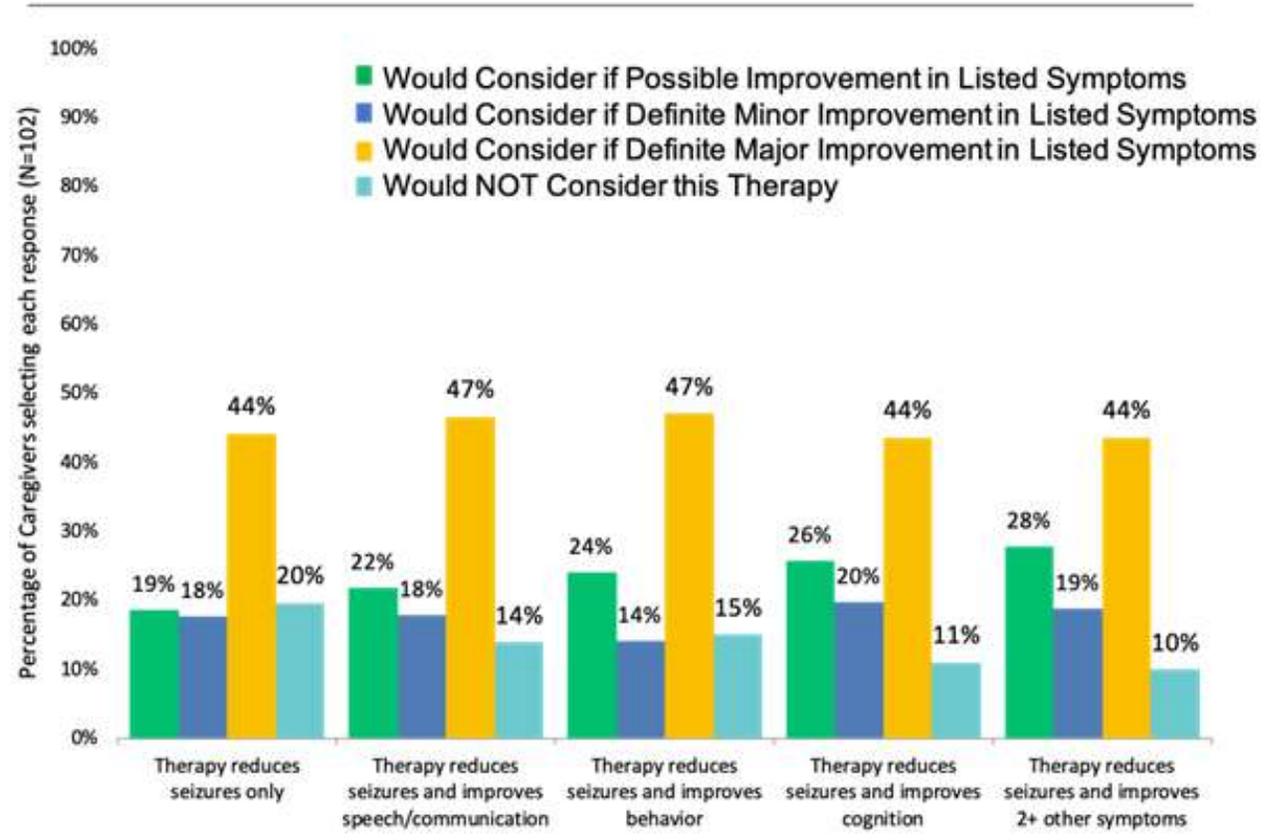




In Question 11, caregivers were asked to consider a disease-modifying therapy that requires a **one-time intrathecal (IT) injection**, and were informed that a one-time therapy may limit the ability to try another kind of disease-modifying therapy in the future.

- The majority of caregivers would consider this therapy as long as there was a *definite major improvement in seizures only (44%) or in seizures and one or more other symptoms (44-47%)*.
- Compared to the previous scenarios in Questions 8-10, fewer caregivers would consider this one-time IT therapy if there were *only possible improvement in symptoms (19-28%)*.
- Although higher compared with the previous treatment scenarios, there were still only 10-20% of caregivers that indicated they *would not consider this therapy*.

**Question 11:** For this question, please consider a disease-modifying therapy that requires a **one-time intrathecal injection**. An intrathecal injection is a shot into the spinal cord similar to a lumbar puncture. A one-time therapy may limit the ability to try another kind of disease-modifying therapy in the future.

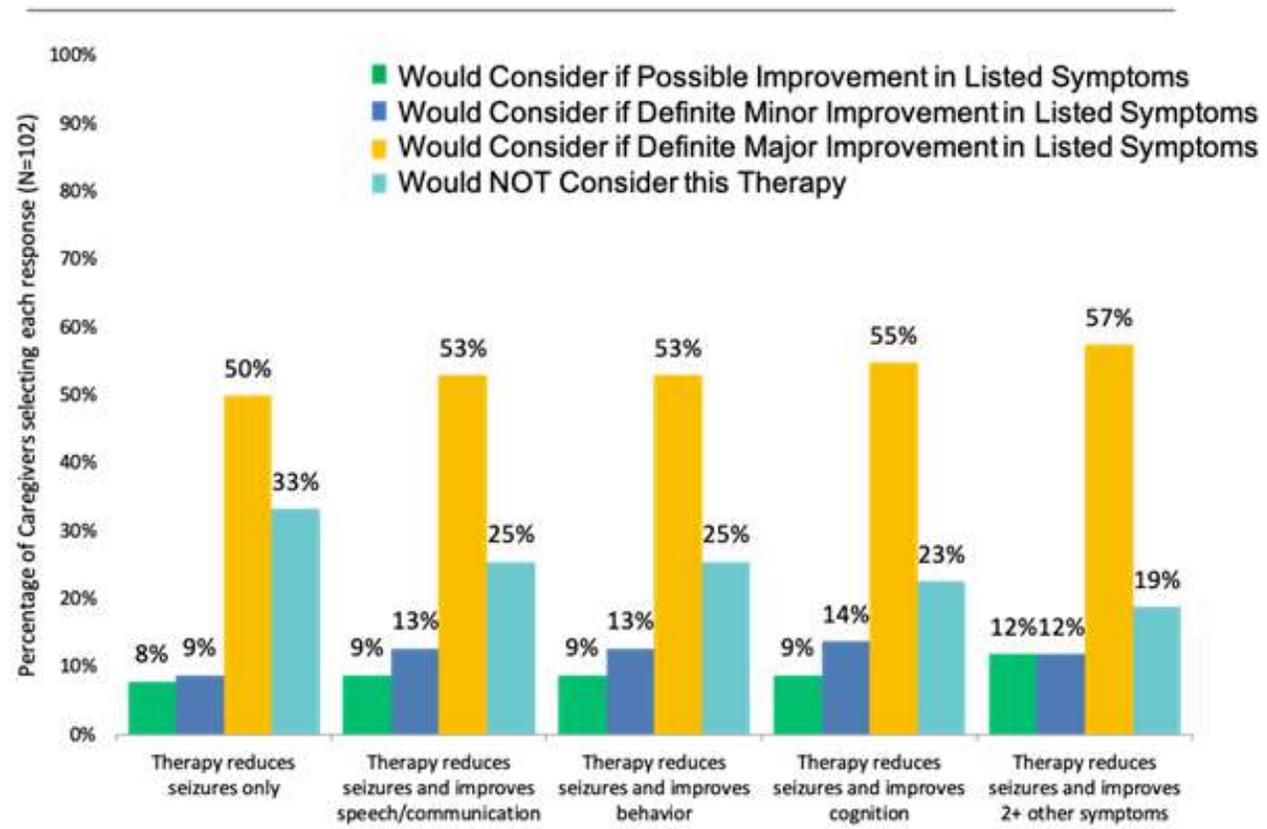




Finally, in Question 12, caregivers were asked to consider a disease-modifying therapy that requires a **one-time injection directly to the brain**, and were informed that a one-time therapy may limit the ability to try another disease-modifying therapy in the future.

- Caregivers who responded to this survey would primarily consider this therapy only if it made a *definite major improvement in seizures only* (50%) or a *definite major improvement in seizures and at least 1 other symptom* (53-57%).
- Notably, even with this more invasive and permanent treatment scenario, 67% of caregivers were still willing to consider this treatment even if it only reduced seizures (with *definite major improvements*) without impact on other symptoms.

**Question 12: For this question, please consider a disease-modifying therapy that requires a one-time injection directly to the brain. A one-time therapy may limit the ability to try another disease-modifying therapy in the future.**





## Appendix 3: Meeting Agenda

### Dravet Syndrome Externally-Led Patient Focused Drug Development Meeting

February 3, 2022

10:00 am – 3:00 pm Eastern Time

10:00 am EST **Welcoming remarks**

*Veronica Hood, PhD, Dravet Syndrome Foundation Scientific Director*

10:05 am EST **FDA Introduction to EL-PFDD**

*Michelle Campbell, PhD, Senior Clinical Analyst for Stakeholder Engagement, ON, OND, CDER, FDA*

10:15 am EST **Scientific Overview & Medical Review**

*Joseph Sullivan, MD, Professor of Neurology and Director of the Pediatric Epilepsy Center, UCSF*

10:25 am EST **Discussion Format Overview**

*James Valentine, JD, MHS, Hyman, Phelps, & McNamara, P.C., Meeting Moderator*

10:30 am EST **Demographic Polling**

#### **Session 1: Symptoms & Daily Impacts**

10:35 am EST **Introduction and Patient Testimonials**

11:00 am EST **Moderated audience discussion and polling**

12:30 pm EST **Break**

#### **Session 2: Current & Future Treatments**

1:00 pm EST **Introduction and Patient Testimonials**

1:25 pm EST **Moderated audience discussion and polling**

2:45 pm EST **Meeting summary**

*Larry Bauer, RN, MA, Hyman, Phelps, & McNamara, P.C.*

3:00 pm EST **End meeting**



## Appendix 4: Meeting Discussion Questions

### Topic 1: Living with Dravet syndrome: Disease Symptoms and Daily Impacts

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

### Topic 2: Current Challenges to Treating Dravet syndrome

- What are you currently doing to manage your loved one's Dravet syndrome symptoms?
- How well do these treatments treat the most significant symptoms and health effects of Dravet syndrome?
- What are the most significant downsides to your current treatments and how do they affect daily life?
- Short of a complete cure, what specific things would you look for in an ideal treatment for Dravet syndrome?





## Appendix 5: Panel Participants, Discussion Starters, and Callers

### Session 1: Symptoms & Daily Impacts

#### Parent/caregiver testimonials

- Amy, mother of a 22-month-old daughter living with Dravet syndrome
- Ross, father of a 14-year-old son living with Dravet syndrome
- Peiyi, mother of an 18-year-old daughter living with Dravet syndrome
- Sarah M., mother who lost her 8-year-old son because of Dravet syndrome
- Barbara, mother of a 26-year-old son living with Dravet syndrome

#### Zoom discussion starters

- Erin, mother of a 7-year-old son living with Dravet syndrome
- Sophie, older sibling of a 22-year-old brother living with Dravet syndrome
- Mande, mother of a 12-year-old son living with Dravet syndrome
- Shannon, mother of a 16-year-old daughter living with Dravet syndrome
- Danielle, mother of a 3-year-old son who is living with Dravet syndrome

#### Callers

- Jennifer, mother of a 19-year-old son living with Dravet syndrome
- Janice S., mother of a 22-year-old daughter living with Dravet syndrome

### Session 2: Current & Future Treatments

#### Parent/caregiver testimonials

- Morgan, mother of a 9-year-old son living with Dravet syndrome
- John K., father of an 18-year-old daughter living with Dravet syndrome
- Gloria, mother of a 9-year-old daughter living with Dravet syndrome
- Kate, mother of an 11-year-old daughter living with Dravet syndrome
- Mikell, mother of a 4-year-old son living with Dravet syndrome

#### Zoom discussion starters

- Lynn, mother of a 5-year-old daughter living with Dravet syndrome
- Kim, mother of a 4-year-old daughter with Dravet syndrome
- Nathan, father of two sons, ages five and three, who are both living with Dravet syndrome
- Jari, mother of a 13-year-old daughter living with Dravet syndrome
- Stephanie, mother of a 6-year-old son living with Dravet syndrome

#### Callers

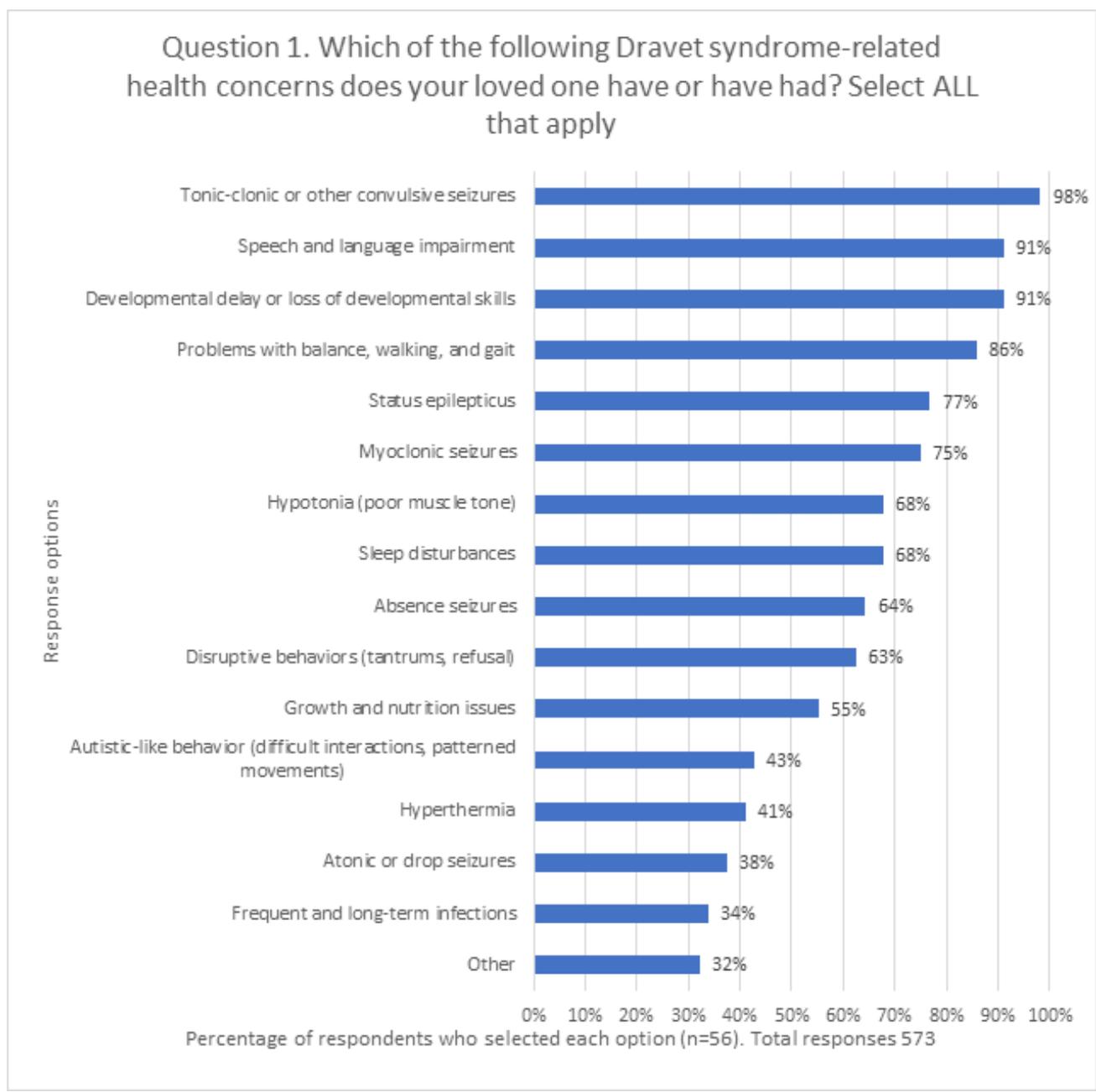
- Nadia, mother of a 3-year-old son living with Dravet syndrome
- Janice S., mother of a 22-year-old daughter living with Dravet syndrome
- Ted, grandparent of a 4-year-old granddaughter living with Dravet syndrome
- Kate, mother of an 11-year-old daughter living with Dravet syndrome



### Appendix 6: Topic 1 Polling Results

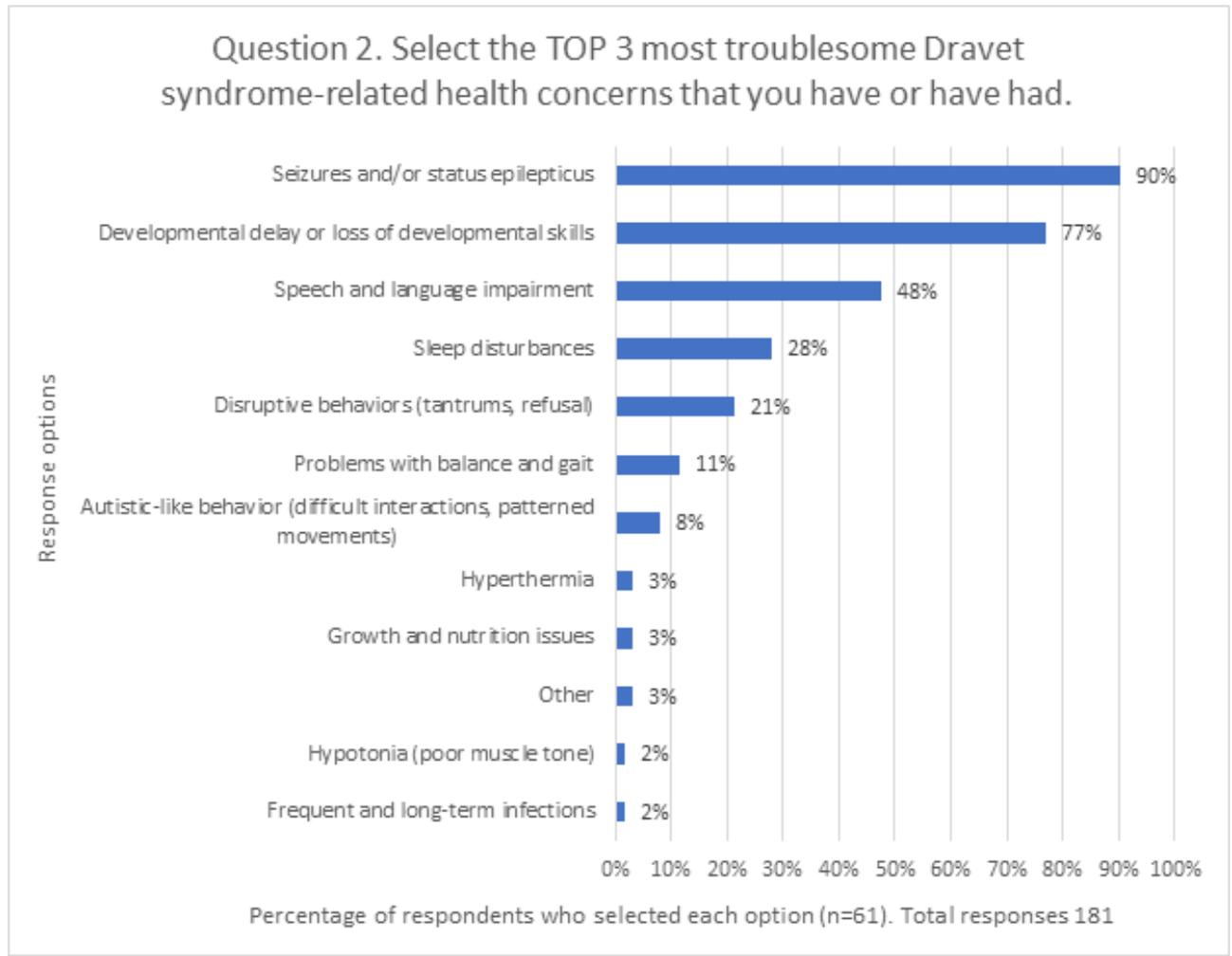
These graphs include those attendees who chose to participate in online voting. The number of patients who responded to each polling question is shown below the X axis. For most questions, poll respondents could select more than one response. The total of poll responses is also shown below the X axis.

While the response rate data for these polling questions is not considered scientific data, it provides a snapshot of who participated in the EL-PFDD meeting and is intended to complement the live and pre-recorded comments throughout the meeting.



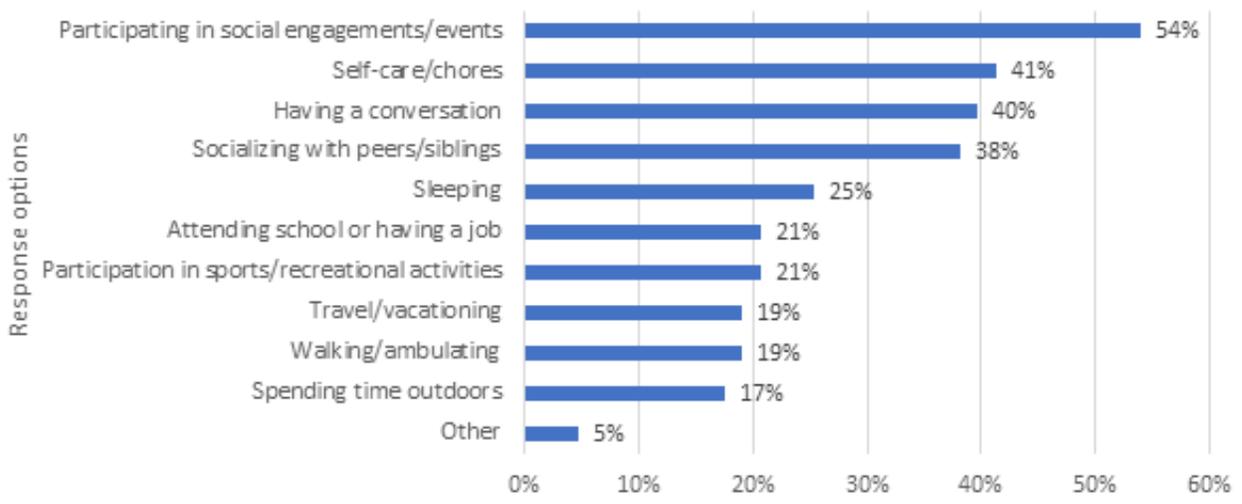


Note that respondents selected an average of 10 responses out of a possible 16.



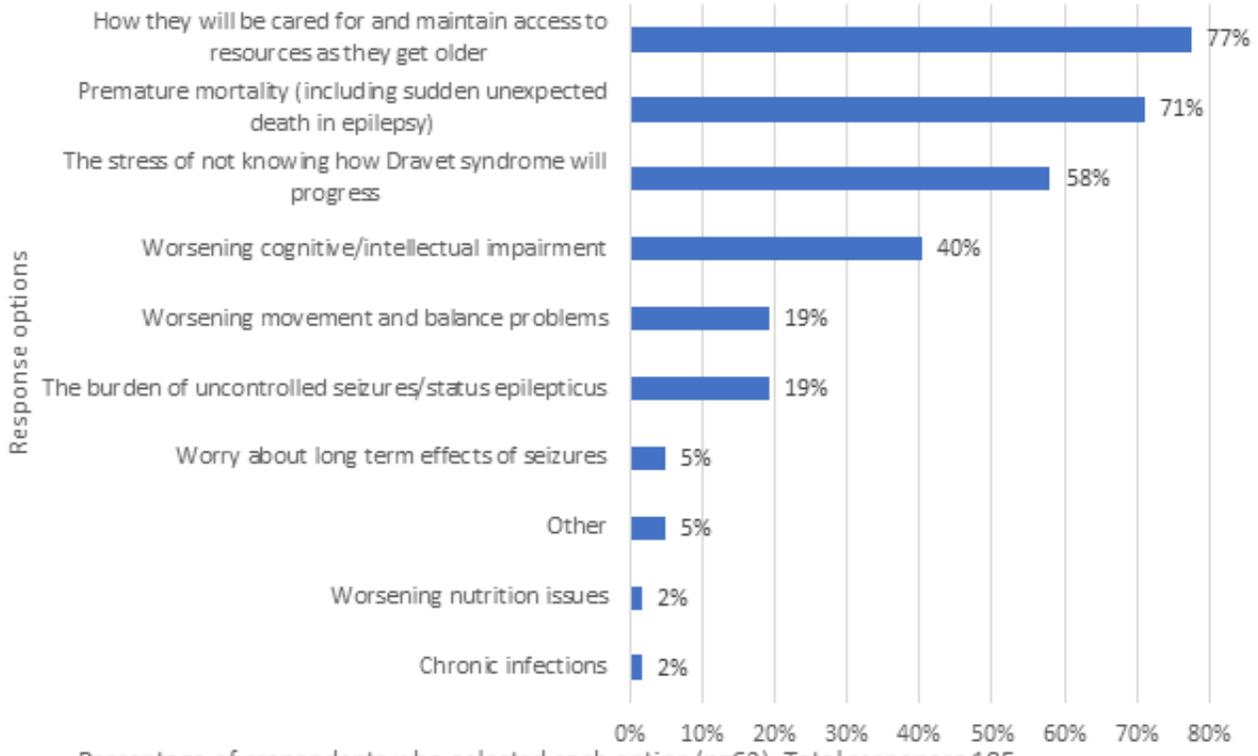


**Question 3. What specific activities are most important to you that your loved one is NOT able to do or struggles with due to Dravet syndrome? Select TOP 3**



Percentage of respondents who selected each option (n=63). Total responses 189

**Question 4. What worries you most about your or your loved one's condition in the future? Select TOP 3**



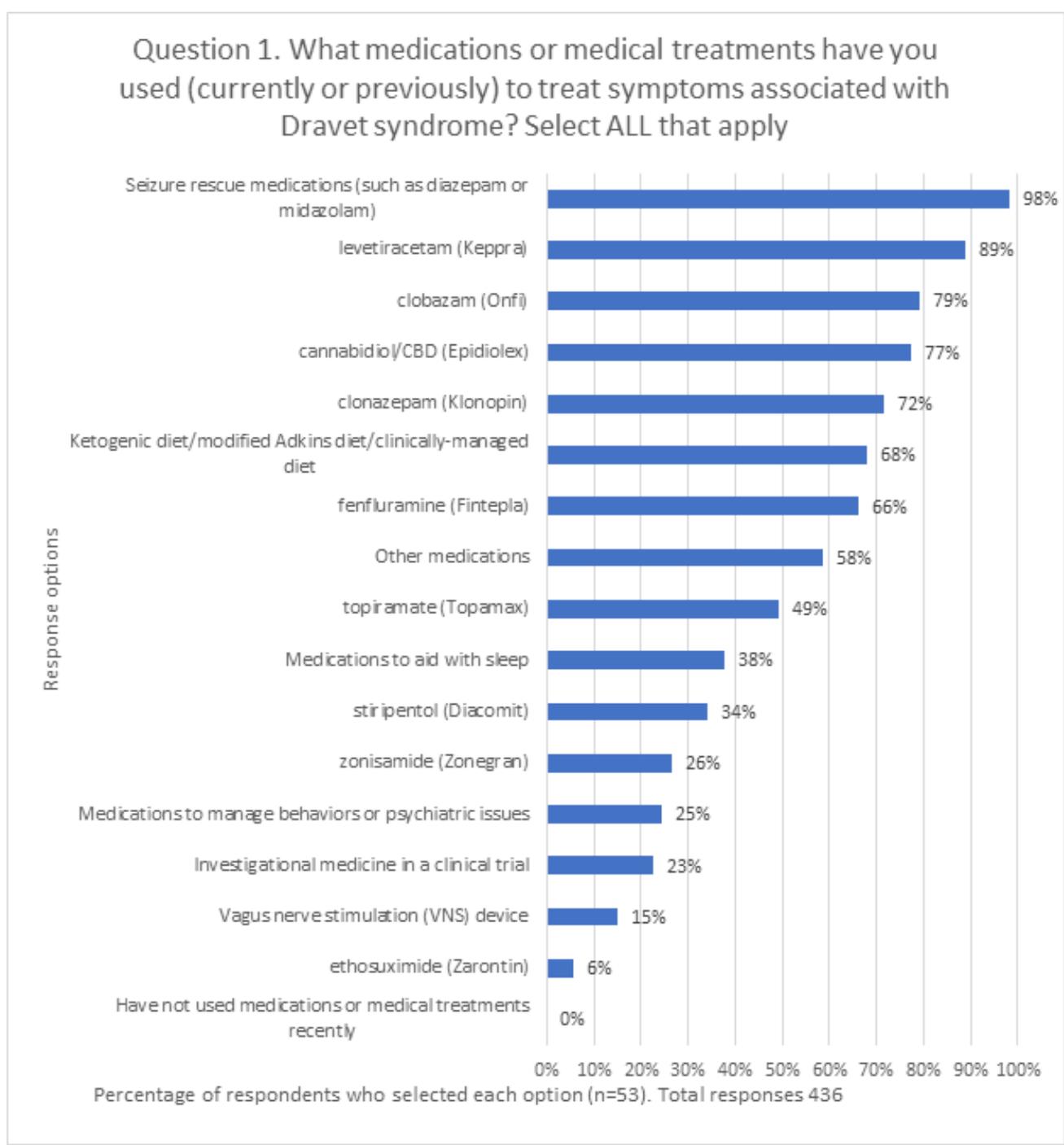
Percentage of respondents who selected each option (n=62). Total responses 185



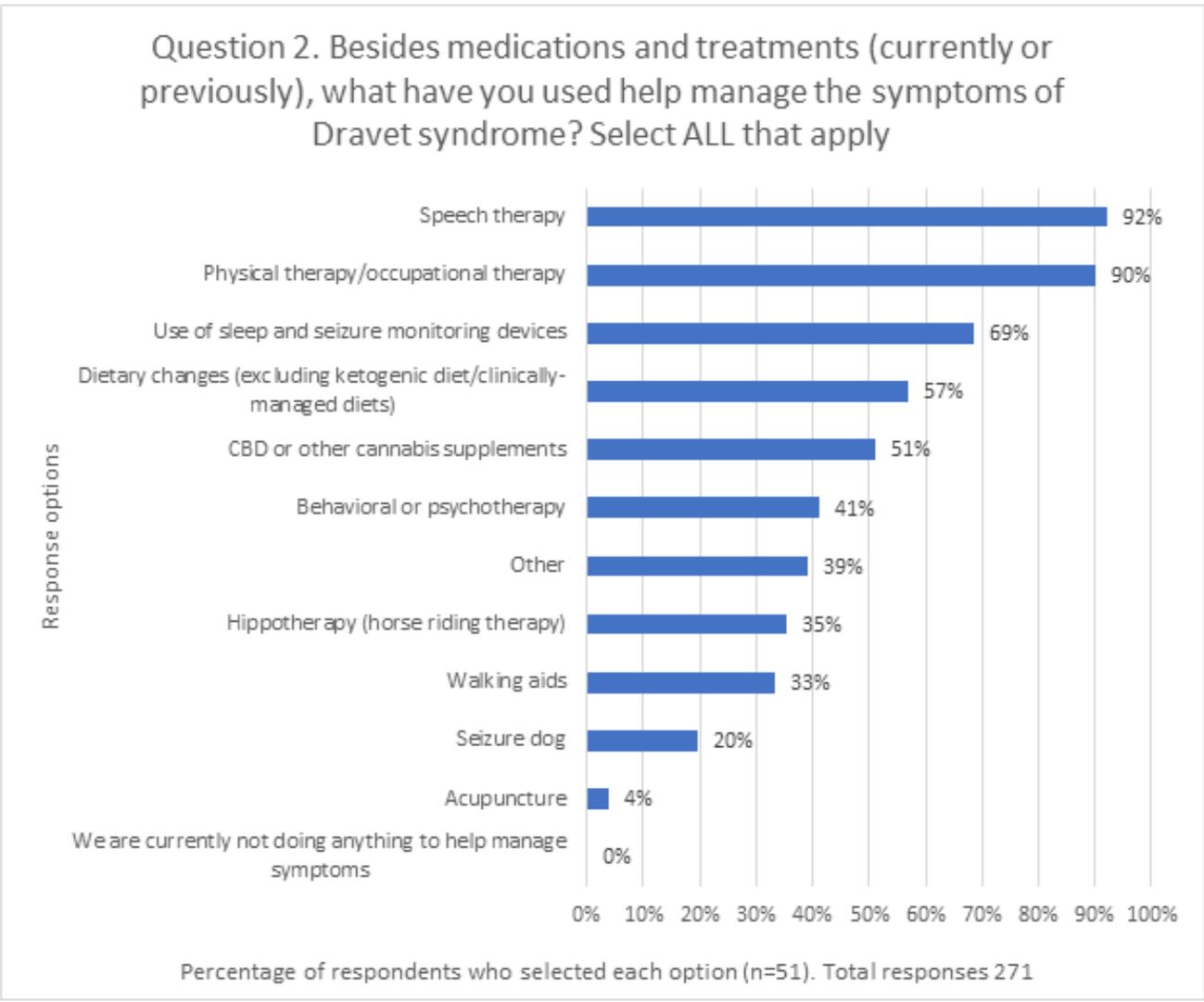
### Appendix 7: Topic 2 Polling Results

These graphs include those attendees who chose to participate in online voting. The number of patients who responded to each polling question is shown below the X axis. For most questions, poll respondents could select more than one response. The total of poll responses is also shown below the X axis.

While the response rate data for these polling questions is not considered scientific data, it provides a snapshot of who participated in the EL-PFDD meeting and is intended to complement the live and pre-recorded comments throughout the meeting.



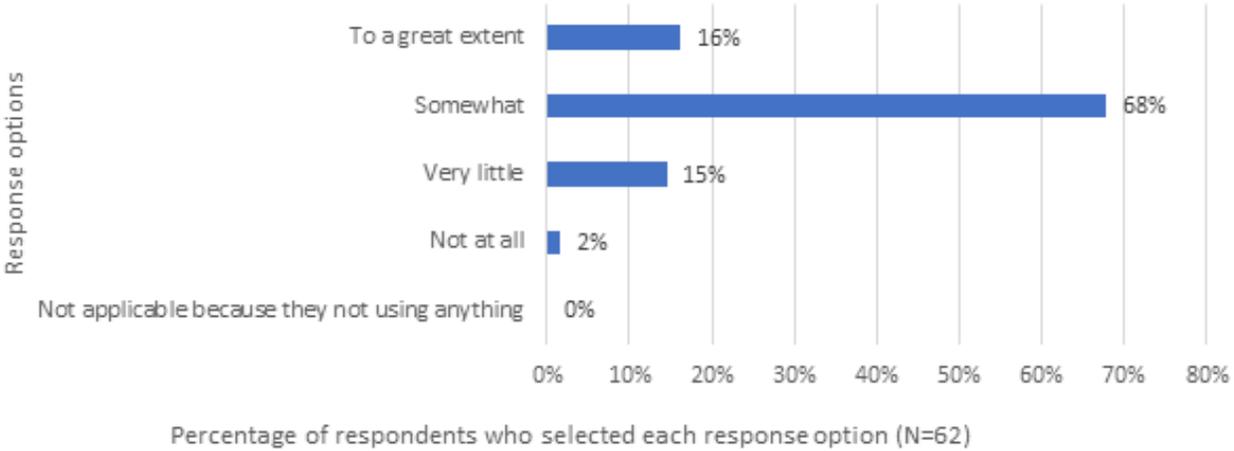
Each respondent selected an average of 8.2 different response options.



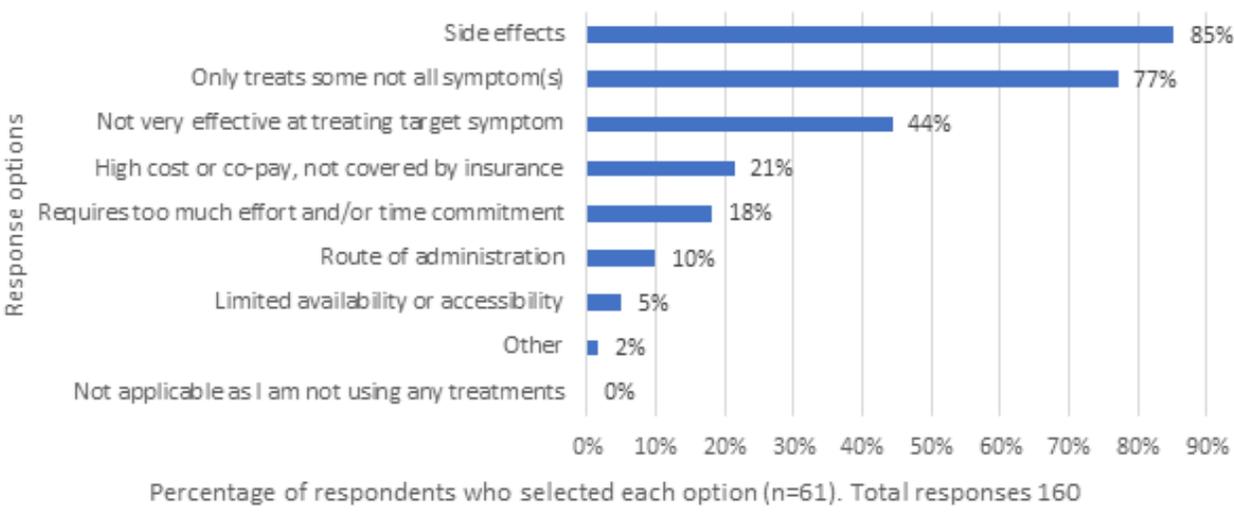
Each respondent submitted an average of 5.3 different response options.



### Question 3. How well does your current regimen control your loved one's disease overall, including seizures and other symptoms?

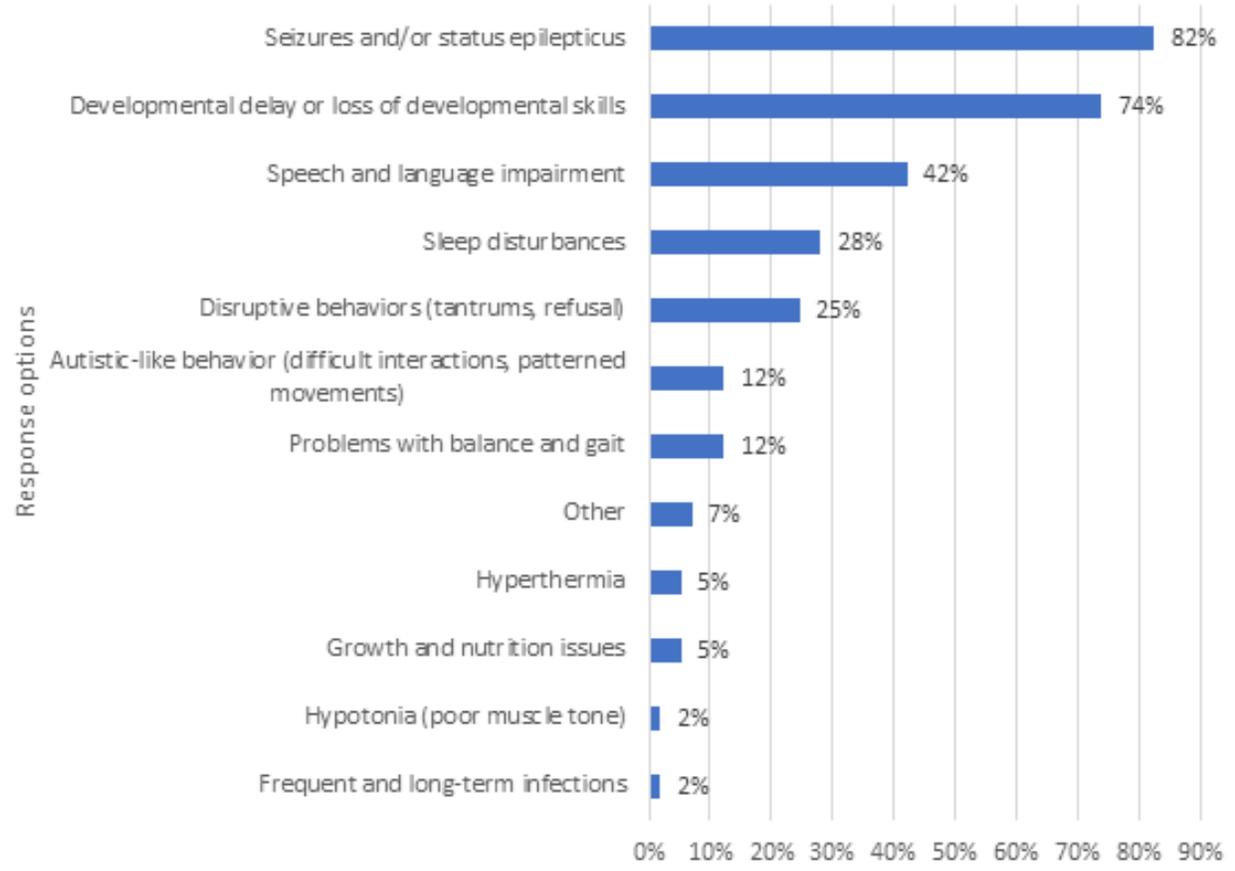


### Question 4. What are the biggest drawbacks of your current approaches? Select up to 3





### Question 5. Which aspects of your condition would you rank as most important for a possible new drug today? Select your TOP 3



Percentage of respondents who selected each option (n=57). Total responses 169



## Appendix 8: Comments Submitted Online

An online comment submission portal was open for one week before and four weeks after the Dravet Syndrome EL-PFDD meeting in order to allow as many voices as possible to respond to the Meeting Discussion Questions presented in **Appendix 4**.

The comments submitted through the online portal are presented below. Caregivers are identified by their first name and last initial only. Comments were sorted by the respondent and then in the order that they were submitted so that all comments from each individual are grouped together. The comments were edited slightly for grammar, spelling, and punctuation and those that did not address the meeting discussion questions were removed. Selected comments and excerpts are included in the main body of the *Voice of the Patient* report.

### Nicole B. - One comment

As we know new medications or interventions will be available, I would recommend the FDA to not limit the opportunities and access these kids could potentially have. With Dravet syndrome we all know not one medication, regimen, or treatment works universally; it's always trial and error to find the right mixture. By the FDA not limiting access allows more kids to seek and be accepted into treatment options to better the outcomes of these kids' lives long-term.

### Sarah J. - Six comments

#### Comment 1

Of all the symptoms of Dravet syndrome, the following 1-3 symptoms have the most significant impact:

- Seizure activity due to over-heating, over exertion
- Developmental delay/disconnect - whether due to mutation, seizure drug side effects, we spend hours each day in speech/Occupational/Physical therapy
- Lack of involvement in physical activities due to increase in likelihood of seizures

#### Comment 2

On his best days, Dominic is able to focus more typically and therefore participate in school and acquire new academic skills. This type of day coincides with minimal focal seizures. Dominic has multiple focal seizures lasting 1-3 seconds throughout the day. They do not stop him in the moment but they do cause disruption overall to the success of the day as a whole. Dominic's best days are those which he feels healthy. I find that it's 50/50 for him - feeling spry and ready to go, or feeling tired and wanting to just sit and not be encouraged to do much.

Dominic loves physical activity but exertion has proven to be a seizure trigger for him. On his best days he can swim in a pool, run around in the backyard for more than 1-2 minutes without being prompted to take a break - however at age 6, he now seems to recognize he needs more breaks if he wants to continue to feel well.



### Comment 3

Specific activities that Dominic cannot participate in due to Dravet syndrome and its comorbidities are as follows:

- Sports - any including body exertion
- Movies - sensitive to sound, attention span minimal - very distracted/cannot focus
- Eating out - he's a keto kid and meals are weighed, plus he's always getting medication therefore doing anything outside of the home requires a lot of preparation.
- Vacations - too much to manage with environmental concerns, meal prep, and over-exertion/over excitement potential which provoke seizures
- Attending concerts/plays/even school-related events
- PE Class

### Comment 4

Overtime Dominic has become less affected by heat and exertion. As a baby he'd laugh hard and have a GTC (generalized tonic-clonic seizure). Today he can laugh hard with no issue - and become excited. He's less sensitive now, thank God, but we're still the "fun police".

### Comment 5

Currently my son Dominic is on the ketogenic diet, a 3:1 ratio and has been for 6 years. He's on 3 anti-seizure drugs (Keppra/Fintepla/Onfi) in addition to many other drugs due to diet, distractibility/focus.

We're most concerned, as he ages, about his care. There needs to be one dedicated caretaker who's full-time job is to manage Dominic's medication and everyday life.

### Comment 6

Short of a cure - I'd like to see focal seizures dissipate drastically. Additionally, I'd like Dominic to be more participatory in every way - academically and physically. Dravet syndrome limits him developmentally and recreationally hugely. I want Dominic to have access to treatment that doesn't affect his lifestyle and behavior as the ketogenic diet (lifestyle) and seizure drug medications (behavior) do.

### **Tyler P. - One comment**

One of the major challenges we deal with concerns keeping our son (aged 3) safe at night. He has many seizures that do not stop unless there is a medical rescue. This presents the risk of an hours long seizure that could easily cause brain damage or death.

Gratefully, when he was very young we discovered a pulse oximeter sold to the public under the brand name Owlet. We also noticed that a seizure would cause his heart rate to spike. One night, we checked the Owlet and noticed our son's heart rate was really high (> 180 bpm). We checked on him and discovered him having a seizure. We were able to get him to a hospital and he recovered fully. Since then, we have found other devices as well that allow us to



customize the heart rate or oxygen saturation that will trigger an alarm. These devices are not perfect, but they keep my son alive.

### **Barbara S. – Seven comments**

#### Comment 1

Topic 1: Almost every symptom has had a significant impact on my son's life. Seizures, of course, because they have never gone away and while we have reduced them at times, they always change frequency, severity, and type. Every seizure is a setback. We also have significant issues with dysautonomia and autonomic storms, especially with age, starting in the teen years. Finally, slowed motility impacts my son's ability to participate freely in activities and impacts how he feels day to day. Motility including urine retention, constipation, ability to receive and process nutrition. He has been reliant on a g-tube for all intake since age 10. Over time, we have seen slow, steady decline in all areas, from speech, to mobility, endurance, loss of energy, tolerance for stimulation, stamina, etc. What worries me most is his total need of care and who will provide it in a loving and caring way that meets our standards of care. What will happen if he outlives us? What will the burden be on his sibling in the future? How can we plan well for his future knowing that he will never "get better". Most frustrating is being unable to plan or predict, no solid prognosis, his being non-verbal so he can't communicate pain or feelings, worrying that he will become "status quo" with age after so many years in the hospital setting. Worries and frustrations only seem to increase as he ages. Dravet syndrome is lifelong and the burden of care only grows. NOT the burden of loving our child, but the burden of care, driven by Dravet syndrome as a lifelong disease, that impacts everyone in the family physically, emotionally, and financially.

#### Comment 2

Topic 2: We are managing Dravet syndrome with a combination of medications, diet, VNS and comfort therapies including massage and music. We try to manage mobility issues with regular PT. All of these treatments combined have not allowed us to achieve seizure freedom, but they DO allow us to give our son the best quality of life that we can. We are open minded to new treatments but also mindful of the risk/benefit of each. Every treatment is weighed carefully, not only because we are afraid of "rocking the boat" of stability that we have achieved, but also because we are most focused on the big picture of what is best for him. It's not always just about the seizures. Downside to current treatment is that we have yet to achieve an acceptable level of seizure control, and our second most pressing issue, dysautonomia, affects him just as much, if not more, and is a challenge to treat or prevent. A cure seems unreachable to our adult population. What we always look for is quality of life. What will have the most impact on making him comfortable, safe and happy and what will ensure he does not suffer as he ages? Every symptom has a trade-off. He is tube dependent and cannot eat, yet a g-tube allows us to keep him out of the hospital and affords us the ability to give him the meds and nutrition that he needs, regardless of his ability otherwise. It is a huge loss and physical burden that he lost the ability to walk independently, yet he is safer for it, because he is typically sitting or lying down when he seizes. Which is better or worse? Hard to say. I would love to reduce seizures



and autonomic storms so he suffers less. I would love to see him regain some speech so he can communicate and be less frustrated. And most pressingly, as my son ages, I would love to see the same support and expertise of care provided to our adult community that we experienced as a pediatric patient. These patients are living longer and longer and Dravet syndrome does not get easier with age. Our adult patients need resources and support.

#### Comment 3

Topic 1: Best and worst days: On a good day, my son is joyful, calm, engaged, and active. He is able to participate in activities and is responsive to stimulation. He loves walks, bike and car rides, school activities, and visits from friends and family. He tolerates feeds, walks better, and has functional motility. The bad days are just what you might expect, the complete opposite. A few seizures in a row can take him down for a day or two. There are days he cannot get out of bed or lift his head. He will globally shut down - everything from motility to expression of any type. There is no language, no reaction to engagement. He looks pained and uncomfortable. His physical ability to walk or sit or reach becomes non-existent. He is agitated by stimulation or conversation. On these days, we are forced to keep him on Ativan and Ibuprofen just to keep him quiet and comfortable and allow him to rest. It's hard to watch and it happens over and over and over again. Good days followed by bad. Dravet syndrome for us has been an endless cycle of one step forward followed by two steps back. As he is aging, the bad days are starting to equal or even outnumber the good.

#### Comment 4

I had checked "other": Dysautonomia, dysregulation, and autonomic storms seem to be prevalent, especially as these children age from teen years to adulthood. You briefly mentioned growth/nutrition issues but along with that is motility, urine retention, constipation, slow gastric emptying. Many of these children require feeding therapy or feeding tubes at some point in life. Behavior is a concern that in our case comes and goes, mostly it's aggression and we link it to either seizure activity or my son not feeling well, but he can't tell us. Ironically, gait and walking issues are a double-edged sword. It is difficult to watch your child lose mobility skills, however, in a somewhat backwards way of thinking, I am grateful he can't walk independently at this age (adult). It keeps him mostly safe from falling and injury. For years we would watch my son fall with no warning and we prayed he wouldn't get hurt. He wore a helmet for three years. Now, he sits most of the day, or we always have a handle on him. Also worth mentioning that with loss of mobility comes a plethora of necessary durable medical equipment - adaptive chair, wheelchair, stroller, commode, shower chair, hospital bed, changing table - not to mention a ramp for accessibility and car that can accommodate him. We have it all and it's an enormous task to order, justify, fit, and find space for all of these things. It's an extra task for the caregiver that most don't think all the way through.

#### Comment 5

I think one of the hardest things is loss of spontaneity. We can't go anywhere without planning - food, toileting, rescue meds, oxygen, etc. Not to mention it has to be a "good" day which is impossible to predict. Seizures can ruin a day in a minute. With an adult age and size child, our ability to take him out has dramatically lessened with time. He's hard to bring places and we no



longer travel or take vacations. These limitations that Dravet syndrome places on our son trickle down to the whole family. In a sense, we are "trapped by our care." I worry about this all the time as he ages and we do too. What do we do about holidays? Funerals? Weddings? Families are forced to stay home, or divide and conquer. Either way it is frustrating and somewhat depressing and sad for everyone involved.

#### Comment 6

It is challenging, frustrating and time consuming to try to find the best treatment for our children of all ages. Trying to balance the side effects and risk of trying new treatments is always done with the inner fear of making things worse vs the hope of success. Don't forget the other "out of the box" treatments - some use antibiotics, some have success with contraindicated meds, homeopathic/osteopathic treatments, etc. Parents are desperate for answers, but the process of finding and trying new treatments is a challenge. As far as symptom management, I wish EVERY family living with Dravet syndrome had access to palliative care to help manage symptoms, provide comfort, and address the needs of the whole family in this light.

#### Comment 7

My son has struggled with sleep for 26 years. It is exhausting, unsafe and a struggle for both patients and parents. One of us has slept with him always. What is the long term impact of too little sleep on both the Dravet syndrome patient and the caregivers? Likely significant.

#### **Adrienne L. - One comment**

Nocturnal seizures and light sensitivity are the symptoms that have the biggest impact on my son.

Treatments such as drugs only reduce these symptoms. Additionally, the treatments can be difficult to administer if not formulated for a young child (for example, Depakote sprinkle capsules).

#### **Kristi D. - Two comments**

##### Comment 1

##### Topic 1

- The 3 most symptoms that impact my son's life are exhaustion, heat, and a new symptom over the last year is his environment.
- Dravet syndrome has started to become difficult and challenging to say the least, and my son doesn't understand why we have to say no to a lot of things since he's only 4 1/2. On our best days I get to see a glimpse of the little boy I've always known and love and on our worst days all I know to do is cry and wonder if he'll ever understand what normal looks like.



- Our son, though he never verbalizes what's going on inside him, he removes himself a lot of times from outside play and goes inside and sits and rests. We believe he recognizes something is going on but he always tries to reassure that he feels fine, but in the back of my head and in the depths of my heart I know he isn't.
- Though I believe in a loving and kind God, death is something I fear for my son. Not death in and of itself but for the reasons of Jameson not living a long and full life. Wondering if the next status seizure he has will bring him to take his last breaths on this earth. I think the thing that frustrates me most is that I will continue to have to disappoint him and tell him no to things that a typical toddler and school-aged kid is able to do. It frustrates me that we have to navigate challenges with insurance all the time for medications and wondering if supply for his meds will ever stop, as we came to a real fear of this around Thanksgiving.

Comment 2

Topic 2

- How we manage the symptoms: our son currently is on two types of seizure meds which he takes 4ml of one twice a day and the other 5ml twice a day, he's on sleeping meds to help him sleep since exhaustion is a trigger for him. We also limit outside play for him depending on the heat or cold and make him rest in between play time. We try to make sure he drinks a lot of water throughout the day. We also have to stick to a pretty rigorous schedule/routine for him to help him navigate his days and nights better.
- Our son is currently on Keppra and clobazam, both have behavioral side effects, though we are told Keppra is a definite source of aggressive behavior and we deal with a wide spectrum of behaviors right now. It's a Catch-22, he's doing ok on the two he's on, but the cost of the side effects is very hard and challenging most days to navigate. He needs constant direction of where his attention must go to and requires a balance of discipline to wrongdoings and reassurance that he's still a good person. He deals with sensory processing disorder and fine tremors. The sensory processing disorder can be so difficult to navigate on top of everything else.

**Nadia S. – One comment**

We are looking for more trials to include primary endpoints beyond reduction in tonic-clonic seizures. As patients grow older they may no longer see TCs but other life-altering seizure types such as myoclonics, absences prevail. These patients are often excluded from clinical trials as they do not meet inclusion criteria of TCs.

**Janelle P. – One comment**

A life without Dravet syndrome is a dream I'm scared to ever wish for. It would mean:

- We wouldn't wake to seizure - false or real - alarms in the middle of the night, often multiple times a night.
- My son wouldn't be on a strict medical keto diet.
- I wouldn't have to worry about my son getting 32 oz of water daily to prevent kidney stones.



- We wouldn't have to get through meal time saying "take a bite" every 3 minutes because my son is bored of his keto food.
- We wouldn't stress about his weight and growth.
- We wouldn't be afraid of my son dying in his sleep (SUDEP).
- I wouldn't worry about how to dress him for school for potential overheating seizures (he had one last year).
- My son would be able to sleep in a toddler bed and not a crib.
- My son would be able to sleep with a blanket and a real pillow at night instead of with nothing (suffocation risk).
- My son would be able to fully dress himself.
- My son would be fully potty trained.
- My son wouldn't have bags under his eyes from being so constantly exhausted from the heavy seizure meds.
- My son at 4 years old wouldn't be addicted to a benzo (we're trying to wean it).
- I wouldn't worry about missing med time twice a day to keep his med blood levels exact.
- I wouldn't worry about playing outside and he getting an overheating seizure.
- I wouldn't worry about him laughing and getting so excited that it caused a seizure.
- My 4 year old son wouldn't have to have long naps every afternoon.
- We would be able to travel with much less stress as we took 6 suitcases of medical supplies this last trip.
- We wouldn't hesitate for playdates because we were so afraid of germs.
- We wouldn't have a speech delay and the behavioral outbursts that come from the meds.
- My son would be able to sweat.
- My son wouldn't have balance issues.
- We wouldn't need PT and OT twice a week and speech therapy 3 times a week.
- We wouldn't have an IEP (Individualized Education Program).
- We wouldn't worry about living near a childrens' hospital.
- We wouldn't have to make big decisions like deciding what medications to alter at the cost of delaying his speech or making him eternally dizzy.
- We wouldn't have to add oil in his applesauce so it didn't spike his blood sugar.

We love our son and he's 1000% worth the work but it's excruciating to watch him battle this disease every day. To say it's taken a toll on our quality of life would be an understatement!

### **Tina M. - Eight comments**

#### Comment 1

I would say the 3 symptoms that impact my son's life are seizures, sedating medications, and no communication.

#### Comment 2

Our worst days are definitely the ones when he has clusters of "non-epileptic" myoclonics and has to get midazolam. He's pretty much out for the day so he can't do much. Our best days are when he starts his morning without those clusters and is alert and very happy. Seizures or not, our very best days are camping!



#### Comment 3

We take Ryan almost everywhere we go. We love camping and since we have a new handicapped-accessible camper he can go seizures or not. It's getting tougher because he's non-mobile and 87 lbs, but we do it! I wish he could run and play at the beach like the other kids. He's gotten much better with seizure control as he gets older.

#### Comment 4

I don't really have fears of him getting older, it's our life and he will always stay with us. It worries me that I could lose him but we can't focus on that or I'll go crazy. We just take it day by day. I'm very frustrated that he's on 5 medications and still has some pretty bad seizures!

#### Comment 5

Treatment right now: Fintepla, clobazam, carbamazepine, zonisamide, and clonazepam daily. Clonazepam and Nayzilam as rescue. VNS.

#### Comment 6

Fintepla by far has been the best treatment! Since starting 3/12/2018 he hasn't had ANY grand mal seizures, status epilepticus, or hospitalizations! We were there about 3 times a year for 5 days at a time before we got into the clinical trial.

#### Comment 7

Way too many medications are causing him to sleep a lot and he isn't the super happy and smiley boy that he was and it's very sad.

#### Comment 8

The gene therapy sounds pretty promising but since our son has THR226MET he cannot participate in the trial at this time so we will be patient and see what happens. His brain can't develop properly or at all for that matter if he's seizing every day.

### **Diane M. - Two comments**

#### Comment 1

Hi, my kids, 28 and 24, inherited the SCN1A mutation from their father, with my son on the Dravet syndrome end. Where are we with gene therapy, with taking out the flawed copy of the gene and replacing it with an unflawed one? My daughter thinks she may want to have a child someday, but doesn't want to pass this on. At this point, taking Depakote, clobazam and Epidiolex would cause birth defects. Thanks!

#### Comment 2

Please understand that this is a devastating condition, where we parents and guardians constantly weigh the balances of controlling seizures vs the side effects of medications that can cause dizziness and processing delays. It's difficult to tease out what is the problem our children at any age is the worst: head injuries with falls during seizures, behavior issues that



medicines can aggravate (ie. mood disorders such as bipolar and hyperactivity), executive functioning problems, and SUDEP. My now adult son went from an IQ of 110, assessed with neuropsychological testing after a year of hard seizures at age 3.5, to a measured IQ of 70 reported at age 4.5. Many of us become single parents, with constantly losing jobs due to having to leave or cancelling at the last minute when our children seize and need us. Families can be plunged into poverty, and care providers quit due to fear of the seizures, behavioral problems, and not wanting the liability when the child is injured from falls while seizing. Trying medication therapies and behavioral therapies with the fear that any of this can cause more problems is a constant battle. We so need a cure!!

**Silke F. – Two comments** (translated from German)

Comment 1

Of all the symptoms of Dravet syndrome, which 1-3 symptoms have the greatest impact on your loved one's life?

- The seizures (serial seizures)
- Aggressive, uncontrolled behavior
- Risk of injury from seizures, from orthopedic problems

How does Dravet syndrome affect your loved one on the best and worst of days? Describe your best days and your worst days.

- Best days: having fun, laughing and being happy with yourself
- Worst days: lying on the couch and sleeping, dozing, vegetating

Are there certain activities that are important that your loved one cannot do at all or as fully as you would like because of Dravet syndrome?

- Regular school attendance
- Peaceful sleep without seizures
- To go on vacation
- Learn to play the guitar

How have your symptoms changed over time?

- A lot more seizures
- Cognitive decline
- Mobility challenges
- Linguistic degradation

How has your loved one's ability to manage their symptoms changed over time?

- It's getting harder, he cries a lot, seems depressed.

What do you fear most as your loved one ages?

- Increasing aggression
- Harder to compromise as his size increases
- There are no accommodation options for his special needs



What worries you most about the condition of your loved one?

- The future

What frustrates you most about your loved one's condition?

- The resistance to seizure therapy
- The uncontrolled behavior

Topic 2: Current challenges in the management of Dravet syndrome

What are you currently doing to manage the symptoms of Dravet syndrome?

- Keep changing medications

How well do these treatments treat the main symptoms of Dravet syndrome?

- Bad

What are the main disadvantages of your current treatments and how do they affect the daily lives of your loved ones?

- Sedation
- Slowing down in his overall thinking and actions

Besides a complete cure, what specific things would you look for in an ideal treatment for Dravet syndrome?

- Psyche of the child

Comment 2

We use bromides for TC-seizures. That helps greatly against the status seizures.

My question: why do we have only a short seizure-free time with new medications? That means that we have a new medication it helps only for 1 to 4 months and then there is the same as before. The reason for this is very interesting for me!

**Emily Z. – Five comments**

Comment 1

Of all the symptoms of Dravet syndrome which 1-3 symptoms have the most significant impact on your loved one's life?

Prolonged and frequent seizures, dysautonomia, movement, and balance issues.

Comment 2

How does Dravet syndrome affect your loved one on best and on worst days? Describe your best days and your worst days.



On the best days, brief myoclonics and absence don't disrupt activities and pass while barely being noticed. Sunglasses and hats help ease seizures caused by sunlight. The night before has had less than 10 tonic clonic seizures and my daughter awakens on her own and is happy and ready to start the day. Her gait and balance issues hardly interfere with her activities and she is focused and content during whichever of her five therapies she happens to have that day. I almost forget that we have a pulse ox, oxygen, and rescue medications in the car, ready to be used at any time. I almost forget that it isn't "normal" for children to have five + therapies a week, to be on the phone fighting with insurance almost weekly, to be constantly scheduling doctor appointments, and driving constantly to different therapies and appointments. Her therapists comment on how well she did and how focused she is. We get her a special treat for doing so well and have nearly no behavior issues occur. She is happy to see her brother after school, we play together, have a fun bubble bath, and she goes to sleep peacefully.

On her worst days, every aspect of her (and our) lives are affected. She has had up to 60 tonic clonic seizures the night before and most likely, one of them lasted 10+ minutes, required 1-2 doses of her rescue medication, had a significant oxygen drop requiring oxygen and suction. She cries and screams for sometimes hours from pain in her head and stomach, vomits multiple times from the rescue medication, and cannot even hold her own head up, taking hours, to sometimes a full day, to recover and regain the ability to walk. She cannot speak and cries from the frustration of not being understood. Every appointment we have is cancelled and we spend the day going between the bedroom, bathroom, and living room, with me providing partial to full assistance as she tries to walk on unsteady legs. Her older teenage brother calls and texts from school, worried about how his little sister is recovering and if she's doing ok. She is highly emotional, remembers that in the last year and a half, both her father and her service dog passed away, and cries on and off. Our lives are completely put on hold and as a parent, I spend the day both grateful that she made it through and at the same time, devastated at the reality of our lives and the suffering we watch her experience.

#### Comment 3

I could not narrow it down to one fear, but rather two. One of my biggest fears as my daughter (who is 9) gets older is that she is going to die, either from a complication from a seizure or from SUDEP.

My other biggest fear is how on earth I am going to continue to care for her as she gets older and bigger. I worry about how I will be able to continue to care for her needs financially, as a widowed single mom on a very limited budget. I worry about how I will continue to care for her physically, as she is growing and getting bigger and heavier. As she grows, it is becoming more and more difficult to assist her in walking when she needs it, move her during seizures if necessary, and also move her while she is postictal. I also worry for myself, how I will continue to bear the burden of 24/7 caregiving, with very little help, and how I will not have significant burnout.

#### Comment 4

What do you fear the most as your loved one gets older?



I did already comment on this but one other thing - something I fear the most is the concern that if I die, since her father has passed away, that my older son would feel like he should care for his sister and the sadness that is our reality that he would want to care for her. He (at 16) has already told me that if something happened to me, he would take care of his sister.

#### Comment 5

We have not found any treatment options that have slowed the severe amount of seizures my daughter has daily, from 3 months old until now at 9 years old. As of now, we have focused more on quality of life (although still on medications).

Two of the best treatments we have used for "symptoms" of Dravet syndrome (not related to medications) are hippotherapy and aquatic therapy. My daughter started hippotherapy at the age of three (riding a horse and in her case, receiving OT while riding) and it has changed her life. Her muscle strength has improved so much over the past 6 years. When she first started at 3 years old, she couldn't even sit upright on her horse for 5 minutes without being physically exhausted. 6 years later, she rides well for 45 minutes weekly, trotting, standing while riding, and even learning to independently steer her horse (she does have 2 side walkers who are close to the horse and keep their arm on her thighs at all times in case she were to have a seizure and fall off the horse). Her horse is also her best friend.

The second thing we have tried is aquatic therapy. My daughter loves water and nothing makes her happier than being in the pool. However, she has NO water safety awareness at all. She does both aquatic PT and OT weekly and will soon start adaptive swim lessons to continue working on water safety (although she will likely never understand the danger of water). She wears a lifejacket during therapy and is never out of arm reach of her therapist.

Hippotherapy and aquatic therapy have been beneficial because we are using something she loves (water and horses) and getting her to work without realizing she is working. There is almost no resistance as opposed to regular PT and OT which we struggled with because it was hard or frustrating and would cause more seizures because of emotional upset. Although she still has significant ataxia and muscle weakness, she has gained so much strength and confidence and she will be completing an adaptive triathlon this spring. She looks forward to these therapies every week.

#### **Angie M. - One comment**

Seizures and development issues have the most significant impact on our 23-year-old daughter's life. Our third is her need for sleep, which I group with what seems to be a loss of energy and endurance over the years, resulting in her getting less out of her days and thus an overall lower quality of life. She goes to bed at 9 p.m. and will stay in bed till 11 or 12 if we don't get her up. Why does she need so much sleep? Is it sleep disturbances in the night that cause her to sleep so late? Does her medication need to be adjusted? Is it part of Dravet syndrome or the progress of the disease? If we get her up earlier, are we increasing her chance of seizure or causing her to feel bad? She already feels bad so often.



**Reka S. – Three comments**

Comment 1

My child has an SCN1A genetic mutation, but also two other genetic mutations. This was not an option on the poll.

Comment 2

Acetazolamide has been an excellent medication for my daughter. How well a medication works is very subjective to each family experience.

Comment 3

I'd really like to see more focus on treating the cause of the seizures. The genetic piece coming down the pipeline is great, but it would also be great if we really look at each child's triggers and treating those.

If lack of sleep increases seizures, treat that. If a child seems to be constantly ill, look into immune issues and treat that. If a child seizes with every activity, monitor cardiovascular and circulatory, and if there is an issue, treat that.

I think too often we focus only on treating the seizures with the limited anti-epileptic drugs (AEDs) available and all other trigger items get passed over as being "just another part of Dravet syndrome".

**Eduardo G. – One comment**

Topic 1:

Of all the symptoms of Dravet syndrome which 1-3 symptoms have the most significant impact on your loved one's life?

- Myoclonic seizures are probably the most impactful because it keeps Carolina from living a semi-normal life. She can't walk on hard surfaces and we have to keep her away from sharp corners because of fear of a myoclonic that would tumble her to the ground. Her walk is also unbalanced which means she is more likely to fall and hurt herself.

How does Dravet syndrome affect your loved one on best and on worst days? Describe your best days and your worst days.

- On worst days when she is sick, she is incredibly fatigued and tired and unable to walk. On sick days, myoclonic seizures are constant and we are almost guaranteed a tonic clonic seizure. These days require full attention all day.

Are there specific activities that are important that your loved one cannot do at all or as fully as you would like because of Dravet syndrome?

- Walking on a variety of (hard surfaces) surfaces and for long distances, including playing on jungle gyms with other children (fear of falling off the gym). Speech is delayed. We're worried about certain stores that have halogen lights that seem to trigger some seizures.



How have your symptoms changed over time?

- Myoclonic seizures started at around 12 months and were very difficult for a full year until we found a good balance of medicine. Myoclonics are usually under control unless sick but there are random very strong myoclonics that can tumble her over.

How has your loved one's ability to cope with the symptoms changed over time?

- She is surprisingly resilient despite all of our fears and continues pushing on.

What do you fear the most as your loved one gets older?

- Her ability to continue going to school, continue learning and developing, ability to live independently, and whether she can have friends that appreciate her. We're also worried about who will take care of her as we grow older and to not try and put that burden on her younger, neurotypical sister.

What worries you most about your loved one's condition?

- All of the above.

What frustrates you most about your loved one's condition?

- That she is otherwise a perfect, happy, and beautiful baby who wants to live a normal life. She is incredibly happy and sweet and she doesn't understand why she can't do everything her sister or other kids do.

## Topic 2: Current Challenges to Treating Dravet syndrome

What are you currently doing to manage Dravet syndrome symptoms?

- We are currently taking four medications normally, have regular neuro appointments, have physical and speech therapy, and see a range of other specialists (ENT, developmental physician, cardiologist (for Fintelpa), and a few more). We have modified our house to make sure it is as safe as possible in case our daughter has a fall (covering sharp corners, etc.). We actively manage any sickness and frequently have to take Carolina out of daycare if she is not feeling well. We limit exposure to fast moving television and we limit exposure to halogen lights in stores (seem to be a trigger).

How well do these treatments treat the most significant symptoms of Dravet syndrome?

- Her medicine mix is fairly effective right now at limiting myoclonic seizures. We also actively manage sickness to limit larger seizures (tonic clonic or complex partials). Seizures are much better managed than a year ago.

What are the most significant downsides to your current treatments and how do they affect your loved one's daily life?

- No known side effects of medicine at this moment but worried that could be impacting diet.



Short of a complete cure, what specific things would you look for in an ideal treatment for Dravet syndrome?

- Limiting myoclonic/drop seizures, better control when sick, anything that can improve muscle strength and coordination, better sleep and control of seizures at night

### **Jessica B. – Two comments**

#### Comment 1

For the top three symptoms, I selected seizures, behavior, and hyperthermia. Hyperthermia has such a great impact on my son because he cannot go to recess with his peers, play sports, and often cannot even go outside during the summers here in Florida. Even with adaptive clothing (ice vest) he has been unable to tolerate a day at the beach, fishing with his dad, or attending outdoor events. Would we not be moving away from our only family support, our family likely would have already moved across the country to allow my son some semblance of childhood and time outdoors which for any other child would be considered healthy and necessary.

#### Comment 2

Specific to my son's care as he ages:

1. There seem to be very few adult neurologists with knowledge of Dravet syndrome treatment.
2. The cutting edge gene treatments are focused on young children, regardless of the older patients' health status.
3. Who will care for my son when I die? I don't want to saddle a younger sibling with this enormous responsibility, but the prospect of a group home seems ominous.

### **Donna T. – Six comments**

#### Comment 1

Behavior is definitely more prominent an issue as children get older (and seizures are more controlled). Behavior takes a back seat to medically fragile young children as we worry about their seizures and life in general.

#### Comment 2

My daughter is 30 years old, and being able to have a meaningful intimate relationship of her own is a HUGE problem, sadness. She SO wants a soul mate and this is so hard to find and / or maintain.

#### Comment 3

Sleeping is an issue but also because my daughter sleeps too much (with medications). She sleeps ½ her day away sometimes, and once she is sleeping is hard to wake. She misses out on a lot.

#### Comment 4

My hope is that in all the upcoming ground-breaking treatments - our children with Dravet



syndrome won't be forgotten. When I heard about the exciting gene therapy that is on the horizon, I was so hopeful and excited. I pray that Dravet syndrome will have a cure and that no more children or families will have to go through what we have gone through with respect to the challenges and fears we've lived with. I pray too, that our 30-year-old daughter (the warrior that has fought so hard for 30 years) and her siblings who have stood beside her - will see a new day - that she will be included in a treatment plan that will give her a better quality of life (yes, even at that age of 30 and beyond). Being able to participate in more activities, freedom from fear of seizures and SUDEP, fear from progression of immobility, and a multitude of other uncertainties that we face with Dravet syndrome and its future. These are paramount in all of our lives (no matter your age).

We are all the biggest cheerleaders of our Dravet syndrome Warriors, and I want nothing more, than to see the day, when we are all on the sidelines, cheering our children on - young and old, as they attain THEIR dreams - what THEY determine - as being THEIR dreams (not what someone else thinks should be considered good enough).

#### Comment 5

Sleepiness has always been an issue during the day, and nighttime broken sleep or difficulty getting to sleep has always been an issue also. Not sure if Dravet syndrome or meds or both.

#### Comment 6

A CURE is our hope - for Dravet syndrome in particular. A complete cure - and it being available to every Dravet syndrome patient.

### **Jennifer MK. – Seven comments**

#### Comment 1

Prolonged seizures are top concern for our 21-month-old daughter Cora, as they usually require medical intervention. We fear her vomiting from the seizure, which has led to aspiration and potential aspiration.

#### Comment 2

The unknown of everything related to Dravet syndrome is so overwhelming, confusing, and so depressing. Our entire life has been impacted by this diagnosis. Our family has been disrupted. Our livelihood has been impacted. Our future is unknown, and the unknown can be so consuming.

#### Comment 3

One area I'd highlight is food/eating. We are on the ketogenic diet as a way to minimize seizures. It has really taken the joy out of food that we once had. Thinking, prepping, and feeding our 21-month-old is such a chore. It takes so much time and energy; however, the reality of having seizures is so scary and harder, so we do it for her. The diet can play into our inability to easily have meals together as well as engage socially because so much revolves



around her food. Even going to a friend's house for a few hours requires so much planning and bringing of supplies. It also is heartbreaking to withhold items from her, limit her intake, and alienate her from seeing what others are eating because she is too young to understand this isn't good for her right now. It's hard to manage when she fights us about the food, doesn't want what we have prepared, has a seizure and is being treated inpatient with poor understanding in the hospital, is sick and can't stomach the diet. It's sad when the one option that does help her medically, hurts her in other ways.

#### Comment 4

Before getting COVID-19 unfortunately in January, we were seizure free from 8/6/21 until 1/14/22 (161 days). She was on Keppra and Epidiolex, but it wasn't helping. We added Depakote and 3:1 keto last year. Our daughter is walking, talking, and growing right now which is beautiful. The therapies have been amazing for her developmental growth. It's great to have objective individuals to observe her and give us feedback. They have been there after most of her seizures to help us not lose anything developmentally.

#### Comment 5

Our 21-month-old fights us with her oral meds two times a day. It's awful. She loves her Klonopin (clonazepam) though. It dissolves in her mouth. Can't all meds just dissolve or be sprayed in the nose or one time or monthly injections? What I would love is easy administration for any medicine that is currently in existence and will be created in the future.

#### Comment 6

The keto diet sounds like it has been very successful for so many and has so many benefits. It would be great to understand WHY it is helpful and companies to focus on making legit meals/formulas based on ratios for medical diets (not the losing weight fad). They should maximize the positive effects of keto by making it easier and more accessible.

#### Comment 7

Monotherapy...Nutrition/supplement patches instead of pills. Better ways to monitor ketones for the keto diet - like a glucose monitoring device that diabetics have.

### **Michelle F. - Six comments**

#### Comment 1

Andrea is 19. She aspirated 7 years ago. Then she aspirated again 4 years ago in 2018. That year, she aspirated 2 more times which landed her in the hospital for one year (Aug 18 to Aug 19). This has led to:

- Growth and nutrition: Andrea is now NPO (nothing by mouth) with a GJ tube.
- Gait: Being in the hospital so long, she has lost her ability to walk and to bear weight.

With sleep, she has an enclosed bed and sleeps through the night. Or does she? Is it a quality sleep? Is she seizing? Andrea can sleep at school for up to 3 hours at school. This is concerning



because she loses valuable therapy time (academic, PT with the stander, OT which has regressed, speech) and age 22 is coming soon!

Comment 2

- Andrea cannot walk and keep up with her peers.
- Andrea is very social but only when she "controls" the topic (which is Dora the Explorer) which is not age appropriate for a 19-year-old. Also, her speech is not functional which also has an impact with peers.
- Being so focused with "Dora" has limited her with social engagements. I was asked if she wanted to participate with graduation; I said no because I know she does not understand and she would be disruptive during the ceremony.

Comment 3

Just reaffirming what everyone has said about the future. Care in the future is my major concern. I'm looking at retirement age, so a placement is required at some point. What will it look like?

Comment 4

This is more to trying to deal with the future: During the last 10 minutes of the last session, I had to deal with the company that supplies Andrea's enteral formula and related supplies. I needed to address my PCA's paperwork since the company that maintains this switched systems. There are areas that most people don't even know exist so to try to teach my older children how to navigate this world is more than I can think of (both my older children have their own issues to deal with). Just wanted to put this out there.

Comment 5

My daughter has been on Fycompa, which wasn't on the list.

Comment 6

For my daughter, she is on valproic acid, clobazam, and Fycompa. She has been seizure-free for 2 years (which is why it was upsetting that with a change in insurance, the insurance denied approval for clobazam because she's not on stiripentol -- on appeal that decision was reversed!)

**Lynne M. – Two comments**

Comment 1

Constant worry about when a seizure will hit, regulating temperature- too hot, too cold, too humid, too dry, nutrition issues.

Comment 2

We had seizure control for a long time but zero quality of life. Our daughter was a zombie: zero development and it was absolutely miserable dealing with medication side effects.

**Morgan T. – Two comments**

## Comment 1

The prevalence of his nocturnal seizures affects every aspect of our lives. This has been the hardest seizure type to treat with existing therapies. Every single night he has seizures in his sleep, so in addition to all of the other many co-morbidities of Dravet syndrome, he is robbed of the basic human necessity of getting a good night's sleep. This impacts our entire family, as it is hard to function on so little sleep day after day.

## Comment 2

One of the most frustrating parts of finding a treatment for our son is that everything we try seems to come with side effects. So often the side effect of the medication is worse than the small benefit it provides. We have experienced everything from rapid weight loss, hair loss, tremors, elevated liver enzymes, severe aggression, insomnia, loss of appetite, heat sensitivity, decline in cognition, vomiting and diarrhea, and worsening seizures- just to name a few. Sometimes these side effects are irreversible, which is a terrifying thought when you are using these medications to treat your young child, and having to make the decision for them on if the risk is worth it. We need treatment options that do not come with black box warnings and a whole list of potential side effects.

**Lucy S. – One comment**

One of the worst parts is the social isolation. Because illness and excitement frequently cause seizures, we avoid meeting people, going places, socializing, because when an outing starts with a seizure and a two-hour "sleep off", or worse, it leads to illness and hospitalization, so it never seems worth it. But everyone needs socializing, so it's emotionally very difficult.

**Yee A. – One comment**

My 19-month boy has struggled with hundreds of myoclonic seizures since 5 months old. His myoclonic seizures are mainly triggered by hand movements. Hence to prevent myoclonic jerks, we have to constantly restrict his hand movements and he is not allowed to play with his toys freely. It is awful for a 19 mo toddler who just wants to play. It is truly a parent's worst nightmare.

**Janice S. – Four comments**

## Comment 1

Emily's biggest issue right now are behaviors. She has a lot of issues transitioning from one place to another. It makes it very difficult for her to go to any programs. Her seizures are well controlled right now. I've been doing research regarding behavior with developmental delays and it has been beneficial to realize she cannot do some things (she lacks the cognitive ability to know that she will be safe where we want her to go) - it is not that she won't do them. Medical marijuana has been very helpful in alleviating her anxiety.



#### Comment 2

Biggest concern is her residential options in the future if needed. Most of the facilities I have visited are not appropriate. The CILA's (Community Integrated Living Arrangement) do not have the nursing/supervision needed. The Intermediate Care Facilities (ICFs) where nursing and supervision are available do not have residents that are her age (youngest residents in 60s). Even the day program where she is has a long wait list, an interview process, and a probation period where they can decide if they will accept her or not. Her behavior issues will also limit the facilities that will accept her. The best facilities can be picky on who they take as well.

#### Comment 3

Other things that have benefited Emily include hippotherapy and use of a CPAP machine. Although Emily was not diagnosed with sleep apnea, the CPAP machine has been a life-changer in terms of her getting to sleep and staying asleep.

#### Comment 4

Just wanted to add a few issues - we have locks on our doors and fridge to keep Emily safe and to keep our valuables safe. Emily has thrown an iPad out the car window as we drove down the highway, threw a computer downstairs, hit me so hard it gave me a concussion. Her behavior is sometimes so bad that we have considered having her placed into residential.

### **Jennifer M. - One comment**

I called in a bit ago. I thought I would add to my story that my Dravet syndrome son's two older siblings have been in psychotherapy off and on for years with PTSD from their experiences growing up with, and assisting with the care of, Stockton.

### **Bethany G. - Three comments**

#### Comment 1

My 14-year-old daughter's biggest seizure trigger is joy and excitement. We have to balance fun activities with risk of seizures.

#### Comment 2

Why can we only get the newer medications (Fintepla, Epidiolex) through specialty pharmacies even though they are now FDA-approved? It takes multiple monthly phone calls, being home to sign for deliveries, and causes missed doses when orders/deliveries don't happen in time.

#### Comment 3

We also need more than just daily medications FDA-approved. We need seizure alert devices that are tested and approved to keep our loved ones safe. We need rescue medications - even if we keep using the same rescue medications we need to know the best timing, the best combinations, the best route to give medications.

**Jen W. – One comment**

The mystery/ individual ways this syndrome affects each patient and all the ways it can progress is overwhelming. What does the future hold for my child individually? What help will he need in the future? Cost/benefits of various treatments/meds vs. cost/ benefits of risking a seizure? Is this my child's natural development or Dravet syndrome or med side effect? The rabbit hole of things that cause questions and anxiety feels endless.

**Sasha D. – Three comments**

## Comment 1

Larissa is 4 and I had her at 38 years old. It worries me a lot about how she will be cared for when she is older because we had her at an older age. Her dad has a good job now and I am a nurse so we can adequately care for her but in 20+ years things will be so much different, especially when we are not there. Her father changed jobs and did not have work for 5 weeks and no prescription coverage. Epidiolex was \$17,000 with a GoodRX coupon-we were lucky Greenwich Biosciences [the drug manufacturer] helped us, but what about other medications that she takes. We hope that her the older siblings will be there for her but we also do not want to take away from living their lives with caregiver burdens.

## Comment 2

An ideal treatment for Dravet syndrome would eliminate Larissa's seizures, help her to be able to regulate her temperature so that she can go outside anytime she wanted, opened up her cognition so that she can be on grade level with her peers, and be able to talk to us and physically be able to walk and do all of her activities of daily living including being able to eat solid foods.

## Comment 3

Larissa is four years old and when she was placed on Depakote at eight months, she lost her appetite and the ability to eat solid foods and thinned her hair. Adding CBD and then Epidiolex was the best for her-opened her cognition more and helped her to progress physically and stopped her myoclonics and kept tonic-clonic seizures to one per week. Clobazam has helped but made her more aggressive. Keto has been great for seizures but she is not eating much so she has lost a lot of weight and she is losing her hair so we are weaning the diet currently.

**Amanda P. – One comment**

My main concern with Dravet syndrome is the unpredictability. Every day we are unsure of the future. When my son was first diagnosed, I thought that if I could control the seizures his cognition wouldn't be affected, he would continue to develop normally, and I would have a very high-functioning son with Dravet syndrome. But as time goes on, I realized that regardless of what I do - keto diet, limit cognitively impairing meds, therapies - Dravet syndrome continues to have its own course.



My ultimate fear is losing my child to SUDEP. Every day we wake up not knowing if today will be the day he starts clustering again, will he start having status seizures again or will Dravet syndrome take his life.

### **Gloria R. – One comment**

Learning about Dravet syndrome is never-ending. Just when you get used to something, everything changes. Grace's seizures, schedule, appetite, and education are just a short list. It feels like you're on a rollercoaster you can never get off of. Being flexible can be exhausting.

### **Sharon C. – Three comments**

#### Comment 1

Mobility and endurance issues have become extremely impactful in providing much of the social and lifestyle activity that we have been able to provide our daughter in the past. The aging process (currently aged 31) has been very difficult, and we have hopes that we can keep her as healthy as possible physically, which is becoming a real concern. Our hope is that some of the new treatment options may result in enhanced improvement in extremities.

#### Comment 2

Comment: The extreme sensitivities of many Dravet syndrome patients with regard to medications. There is a tremendous risk at being treated with generic drugs versus name brand AED's (either take-home medications or in-hospital use). This single change in treatment can cause tremendous status episodes for many in our population, and this is difficult to convey to the non-specialized treatment medical teams.

#### Comment 3

As we look to the new treatment plans, could we please consider the adult population in the clinical trials or compassionate use protocols? Particularly if there is hope in slowing degeneration of the Dravet syndrome patient who has reached adult age but still retains physical function.

### **Michele W. – One comment**

- Some concerns are trials not involving adults.
- Adult Dravet syndrome patients having underlying issues (gastrointestinal, genitourinary, ortho) dismissed as “just Dravet syndrome” when even the experts don't really know what Dravet syndrome looks like as adults.
- Adult doctors not partnering with parent as our pediatric docs did.
- I am concerned we do not have enough doctors who truly understand adults with disabilities, let alone Dravet syndrome.
- Of course, I have done alternate conservatorship and advanced directives if I am no longer around for my son, but I worry about that person trying to navigate a world where disabled adults are minimized.



- I want to know more about the long-term effects of the AEDs on our adult kids.
- I want to know how to distinguish “Dravet syndrome” from things other than Dravet syndrome so I can advocate for him.

### **Matthew J. - Two comments**

#### Comment 1

From my perspective, Dravet syndrome is pretty unique in terms of how it impacts the quality of life. As it does with our son, it includes a severe mental disability (e.g., nonverbal), physical disability (e.g., primarily wheelchair bound), and medical fragility (e.g., photosensitivity can trigger life-threatening seizures in almost any environment). There are strategies to address and improve quality of life as against each of these challenges separately, but addressing all three is extremely difficult.

#### Comment 2

The VNS really was a game changer for my son. Before the VNS, nearly every seizure was a status seizure (10+ minutes that would stop only with rescue medication). With the VNS, status seizures are much more rare. We still have to use multiple other antiepileptic drugs for reasonable seizure control, but the VNS offers significant protection against the more severe seizures.

### **Mandee O. - One comment**

We watched in excitement and waited patiently to try the three newly approved seizure meds for Dravet syndrome (Diacomit, Fintepla, and Epidiolex). Unfortunately, all we saw was side effects and no help. Later I realized they each contained an ingredient that my son had a sensitivity to- methylparaben, sesame seed oil, and aspartame. My child is very sensitive to added ingredients and we need "clean" treatments without chemicals and preservatives that exclude them for his use.

Secondly, diet therapy, homeopathics, vitamins, and herbal supplements have been the most helpful treatments for my son, all of which are not covered by insurance. It would be helpful to get some financial help towards these most effective treatments that are out-of-pocket expenses.

Lastly, drug trials and new treatments usually require lots of extra medical tests and travel, both of which are nearly impossible for my son and our family to comply with. We need quick access to therapies without requiring excessive tests.

### **Darien W. - One comment**

When thinking of my daughter’s current treatment regimen, I often wonder what exactly is control when it comes to Dravet syndrome? Is this as good as it gets? Could it be better? In my opinion it could, but at what cost? We’re running out of options, much less, good options, and



for what? What we see isn't complete control in my mind. When we try one treatment, it may "help" one seizure type, but it increases the frequency or severity of another seizure type. We try another treatment and see improvement in one area, but then another area declines. It's a constant battle between good and bad, yet no outcome yields the most optimal results.

#### **Amy D. – One comment**

Medications and something disease-modifying is obviously the hope/goal. But in the meantime, it's super frustrating not to have an all-in-one device to help monitor our kids at night. Sleep is so important for the whole family and one device that monitors and records and alarms for irregular movements, something that tracks not just pulse/ox, but the quality and type of sleep (deep/REM/light) and can graph it would be so helpful. The technology is available but unfortunately no one is putting it all together for parents like us.

#### **Jenny – One comment**

Also, besides medications and monitoring equipment, treatments like IVIG need to become more accessible, so not only we increase seizure threshold, but also reduce this common seizure trigger.

#### **Jeannette M. – One comment**

For my son Mateo, an eight-year-old child with Dravet syndrome, treatment includes: Medication of divalproex, clobazam, Epidiolex, and Fintepla. Although, all medications work at some level to lessen his seizure frequency it was not until starting Fintepla that we noticed the most change. Mateo began to have more alertness to his surroundings, and - as a non-verbal child - trying to sound words for the first time.

Also, physical activity has helped my child to sleep longer at night. A walk around the neighborhood of one or two blocks in the evening helps to reduce the number of times he wakes up at night and helps him sleep longer than his usual. However, also careful not to exhaust him because that has a countereffect which will bring on seizures while he sleeps.

#### **Kate H. – One comment**

We have seen success reducing seizures using IVIG treatments. IVIG infusions have helped keep our daughter's immunity high and inflammatory response low. Common colds and flu no longer become major seizure events for us. Unfortunately, IVIG is considered an off-label use for intractable epilepsy and is hard to get covered by insurance.

#### **Suellen C. – One comment**

Fintepla, clobazam, stiripentol: Onfi seems to be the only med with positive control and limited side effects. We are trying to wean off Fintepla and stiripentol which is proving to be very



challenging. Depakote caused liver injury unfortunately since it was a game changer. Aiden is seven years old with myoclonics all day long, every day. If these are not interrupted after three seconds they will evolve into a tonic-clonic seizure.

**Marla A. - One comment**

My daughter is currently receiving Keppra, Topamax, clobazam, and Epidiolex. She has had the best seizure control so far since Epidiolex was added. We are currently weaning off Topamax which seemed to affect her appetite and most meals were stressful, trying to get her to eat anything without screaming through meals and throwing food on the floor. She lost weight over the past summer because of her poor appetite and a dietician provided counseling to me to add calories to the bites of food she would eat. We have not been completely sure if this was a side effect of medications, her personality, or being a toddler. Now that she is almost completely weaned off Topamax this week, her appetite has drastically improved, and it is a relief to watch her eat all the food served to her without fussing.

**Clare C. - One comment**

As the number of adults with Dravet syndrome is increasing, it can feel like a whole new syndrome as new co-morbidities appear, and little research to understand the best course of action. The development of Parkinsonian-like symptoms is one example, with changes in gait, behavior, posture. So should we be looking at adding Parkinson medications? Obtundation status [defined as a dulled or reduced level of alertness or consciousness] is another area that, for us, is far more difficult to manage than typical seizures. There doesn't seem to be much consensus on how to treat obtundation status, or even a well-defined definition of what it is.

**Nichelle D. - Two comments**

Comment 1

Sleep is a major challenge for my 7-year-old son with Dravet syndrome. It always takes him at least 1-2 hours to fall asleep and he often wakes up multiple times throughout the night. We use several monitoring devices (pulse ox, seizure monitors, and video monitors) which also equates to poor, fragmented sleep for myself and my husband as the alarms sound an average of 10-20 times per night which affects our jobs, our marriage and our other family members.

Comment 2

Short of a cure, a reduction in risk for SUDEP would be very important for my son and our family. My son has very good seizure control, but we have a fear every day that even when he is not having seizures, he is not protected from SUDEP.

**Jennifer W. - Two comments**

Comment 1

How do we pick just three? Honestly. How just three? There are just two - prevent seizures



WITHOUT all the crazy other side effects in a method my child will take (some with Dravet syndrome have issues with the method of meds) and "consider a tube to make med management easier" just isn't realistic.

#### Comment 2

I can accept that there will be seizures so long as we have a rescue med that works. In drug development, my main focus would be day-to-day quality of life. So please consider side effects - organs that can be affected and their development, behavioral, and bodily control. Giving our son daily meds at such a young age (where he fights us and really doesn't/can't understand) is extremely difficult.

#### **Kristen R. - One comment**

My son Jaxton is extremely photosensitive. His neurologist at CHOP and I have been discussing medication options but unfortunately there isn't a medication proven very effective. We try to get sunglasses, but I wish there was either an effective medication or effective prescription lens that would help him be a kid and go outside. We have been in a dark home for months on end.

#### **Aimee B. - One comment**

Of course, getting rid of the seizures would be the top goal for our 12-year-old, but it would also be wonderful for him to be able to communicate with us...be able to tell us what he is feeling or needing. Developmentally, we would love to get him to a state where we could transition him from diapers to being able to use the toilet.

#### **Cara N. - One comment**

Our son, Rylan, 8-years-old, is currently going through an "easier season" with Dravet syndrome. He is currently 14 months seizure-free and of course we are so grateful for this time. However, we are not blind to the reality that this can change at any point. A top treatment goal at this point would be directed at comorbidities. Something that would allow the body and mind to continue to develop and grow (even when seizure freedom isn't happening). I think this would help behavior significantly and quality of life in general for all Dravet syndrome patients and their families.

#### **Rachel D. - One comment**

The next Dravet syndrome drug needs to be disease-modifying and improve cognition. Developmental delay and risk for early death do not appear to correlate with seizure control. Seizure control (just masking a symptom) isn't enough. I would even accept living with some level of "manageable" seizures that do not significantly impact quality of life, if my son could have significant cognitive gains. I agree with others that it would be amazing if this disease-modifying treatment could eliminate all of the other medications and treatments we need to use to manage our son's quality of life.

**Zaheen I. – One comment**

Living with Dravet syndrome is hard because no one knows about this syndrome, even doctors. When your kid is diagnosed with this and doctor said to you “unfortunately there is no proper treatment for this” and we try our best. And when you go for treatment options there are a long list of side effects with every treatment and parents always confused. Shall we have to go for treatment or no? When your first seizure is long and under 1 year it could be Dravet syndrome. Doctors can do testing during pregnancy.

When seizures start, most of your time is spent in the hospital. No family time even so many birthdays, festivals are spent in the hospital. So many times, fever came for no reason but kids still have high fever and seizures even you start Tylenol and ibuprofen round the clock but fever doesn't go fever still there. And goes up so quickly even when I was in the hospital, all nurses and doctors confused how quickly her fever goes up. I remembered then I put cold clothes on her forehead and under legs and under arms then fever goes down, but you have to do this all day. Now someone told me put some alcohol on a towel pad and put this towel in the underarms the fever come down in 20-30 mins now. I used the method - it's really working for me.

Living with Dravet syndrome is not only hard for the patient, also for the family too. You can't go outside in summer because of heat (trigger). You can't go outside in winter. If the weather is good, you are good and you plan go to outside - maybe that day is seizure day. So many times, with me we couldn't go because my daughters start seizures that day. Treatment options didn't help in my case. I think we have to do more research in keto diet or any other diets because diets are safer than meds. And also research patient outcomes both with and without any treatment. Because when my twins are little and they a had long seizure, some day if I used rectal med - they are really sleepy. When I didn't use the medication they had long seizures but they are normal playing and all. I met two people in my life they had long, long seizure their parents didn't use any meds and any testing and their last seizure was at the age of 12 now they are 21 and both are good. Hopefully we together find the best treatment for this syndrome.

**Laura S. – One comment**

My daughter was given the diagnosis of having Dravet syndrome in July of 2021 when she was 10 - 1/2 months old. After numerous additions to medications and increases in doses, she still has breakthrough tonic clonic seizures. I do not have the help of a pediatric dietitian, so I'm doing an adapted version of the keto diet. I have seen a significant decrease in the amount of myoclonic seizures. I was astounded to see the amounts of sugar that are in foods that are targeted and "made" for infants and toddlers. There really needs to be a keto-friendly formula for infants and toddlers, that is more easily and more cost efficient available, not only for Dravet patients, but children with epilepsy in general.



### Alexis S. – Three comments

#### Comment 1

What worries me most about Sawyer's condition as he gets older are the risks of SUDEP and what will happen to him as he gets older. I worry that one morning I'll get up and find him passed away in his sleep. That's a real fear. I worry about who will care for him when we get old or die. Will his older brother have to carry that burden? Will Sawyer be lonely? Will he be safe? Is he going to be able to be at all independent? I worry about what will happen to him when he is out of high school, and we don't have the supports he has now while in school. So many things. I am frustrated constantly by the issues we encounter because Sawyer is currently stable enough that he does not have seizures regularly, but he does of course still have them. So he is not able to get private nursing care through insurance because he is too stable, but he also cannot access many activities or camps because it is not safe for him without a nurse. We are so grateful that he is stable right now, but unfortunately that doesn't make having Dravet syndrome any easier because there is still always a great risk of seizures and schools, camps, facilities are afraid of that and don't know what to do. It's still a constant battle. Our other most frustrating thing we grapple with is balancing medication amounts to keep seizures at bay, but trying to gain cognitive improvement and better independence. We are stuck right now at a place where we know lowering one of his meds will help increase cognition and help him make strides towards better independence and academic ability, but if we lower any more then his seizures will increase dramatically. Finding that balance is basically impossible and extremely frustrating because we know he can do more and improve if not for the cognitive toll of the medications.

#### Comment 2

Currently Sawyer is taking Epidiolex (CBD) and Onfi. He also takes Prozac. He's been on that regimen since about age 5 and he's 11 now. It's been very successful for him in treating his seizures and he has gone long stretches without seizures over these last 6-7 years. He does still have seizures when he gets overexcited or when he is sick, but he's been remarkably stable overall. His seizures when he does have them do not go into status and are usually pretty short and don't need rescue. The Onfi has been good for that. The major problem we have is that Onfi has been really impactful on his cognition. Although we do not attribute all of Sawyer's intellectual disability to him taking Onfi, he has been on that drug since the age of 2. What we have noticed is that when we lower it, his seizures increase but his cognition skyrockets. With each time we have lowered by even a tiny amount he improves with cognition, academics and across all of his abilities. We know he can do more and it's very frustrating that we are stuck where we are. We know if we go any lower his seizures will be out of control again.

An ideal treatment for Dravet syndrome would be something he doesn't have to take daily if possible, that improves seizures dramatically without the need for multiple drugs and without the side effects we currently have to contend with. Treatments that do not impact cognition and behavior. A treatment that would allow us to remove his other AEDs and hopefully improve his ability to learn, improve his daily independence to maybe help him access even somewhat of an independent life. A life where we don't worry day-to-day who will watch and care for him, and eliminating the worry of SUDEP.



Comment 3

The three symptoms that impact Sawyer's life the most are behavior issues, cognitive impairment, and unexpected seizures. Behavior is a constant challenge. It's been by far the hardest to deal with over time, something we have gotten a handle on with the help of Prozac beginning at age 5, but it's an issue that impacts and influences his life every single day both at school and at home. Similarly, the impacts of his intellectual disability/cognitive impairment, autism, and OCD also influence his daily life and present daily challenges for him. We don't know what the future holds for him with those challenges. And finally, seizures even while mostly under decent control still are a huge challenge because we don't know when they will happen and they often happen when Sawyer is in the midst of something he loves to do. He tends to have them when he is having fun and playing and excited. It's a shadow that is always looming. SUDEP is also a very real and scary concern.