HypoPARAthyroidism
Association, Inc.

Hypoparathyroidism Voice of the Patient Report

From the

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

Meeting Date: Tuesday, 5 March 2024

10 a.m. – 3 p.m. U.S. Eastern Time

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Hypoparathyroidism Voice of the Patient Report

The HypoPARAthyroidism Association mission is to improve the lives of people impacted by hypoparathyroidism through education, support, research, and advocacy. This Voice of the Patient report was prepared on behalf of the HypoPARAthyroidism Association as a summary of the input shared by patients and caregivers living with hypoparathyroidism during an Externally Led Patient Focused Drug Development (EL-PFDD) meeting conducted on March 5th, 2024.

Authors and Collaborators: This report was prepared and submitted on behalf of the HypoPARAthyroidism Association by Patty Keating, Executive Director; Michele Rayes, Associate Director; and by Hajar Abu Alrob, medical writer.

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Point of Contact: Please contact Michele Rayes, Associate Director (https://www.hypopara.org), for questions related to this report.

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Anna Garcia, Jaclyn Faestel, Annie Faestel, Julia Richardson, Kim Shade and Mirranda McVay. We would like to thank Dr. Naomi Lowy for presenting an overview on hypoparathyroidism.

Key points

- Patients with hypoparathyroidism experience severe and persistent symptoms such as muscle spasms, fatigue, and cognitive dysfunction. These symptoms disrupt daily activities, from routine tasks to significant life events, and can range from mildly inconvenient to severely debilitating.

- Patients often face a demanding regimen of up to 70 pills a day, which adds a substantial burden to their daily lives. The relentless schedule of medication and the need for regular blood tests create a constant struggle to manage their condition effectively.

- The unpredictability of symptoms causes significant anxiety. Patients live with a pervasive fear of sudden health crises and complications, which often leads to heightened stress and feelings of helplessness.

- The persistent physical discomfort and management challenges contribute to depression, anxiety, and a sense of isolation. Individuals often feel alienated from their peers and unable to participate fully in social or family activities.

- The unpredictable nature of the disease requires frequent accommodations in the workplace and school, affecting career progression and job stability.

- Current treatments for hypoparathyroidism, primarily calcium and active vitamin D, elevate serum calcium but do not replicate the multifaceted functions of parathyroid hormone (PTH). This results in persistent issues like unstable calcium levels, kidney stones, and other complications.

- There is a strong call for therapies that directly address the underlying endocrine disorder rather than just managing calcium levels. Participants emphasize the need for hormone replacement options that more accurately mimic natural PTH functions.

- Patients express a need for personalized treatment plans and better tools for home monitoring of calcium levels, akin to diabetes management.

- There are substantial barriers in accessing knowledgeable healthcare providers and timely treatment adjustments. Patients often face difficulty finding appropriate care and managing their condition effectively due to a lack of specialized options.

- Patients are frequently excluded from clinical trials due to rigorous requirements, such as washout periods or placebo arms, which jeopardize their health and stability.

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Introduction

On March 5th, 2024, the HypoPARAthyroidism Association held an Externally-Led Patient Focused Drug Development (EL-PFDD) meeting. The meeting provided patients, caregivers, and family members the opportunity to directly share their perspectives on the symptoms and burdens associated with hypoparathyroidism in their daily lives, as well as the unmet treatment needs experienced by patients and family members. The panelists were selectively chosen to represent the hypoparathyroidism population with a comprehensive range of causes for the disease. Individuals with postsurgical and nonsurgical hypoparathyroidism (genetic variant, autoimmune, idiopathic) as well as family members and caregivers participated to share their experiences. The meeting was held in person to foster an interactive environment and greater personal interactions to better convey experiences while also incorporating comments from online participants.

This EL-PFDD meeting was conducted as a parallel effort of the Patient Focused Drug Development (PFDD) initiative. The PFDD meetings are a systematic way of gathering patient perspectives on their condition and treatment options available.
The HypoPARAthyroidism EL-PFDD meeting objectives were to provide a platform for patients, caregivers, and family members to share with key stakeholders and the public their perspective on the:

- Health effects, symptoms, and daily impact of hypoparathyroidism
- Impact of current standard of care on participants daily life
- Treatment and management goals
- Discussion on thoughts for future treatment approaches for hypoparathyroidism

This *Voice of the Patient* report provides a high-level summary of the perspectives shared by patients, families, and caregivers of individuals with hypoparathyroidism during the meeting. The report also includes selected comments received through an online portal to provide further depth to the insights shared.

The information in this *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 hypoparathyroidism. It is anticipated that this information will serve as a catalyst for the advancement of treatment options and, ultimately, pave the way towards finding a cure for all those affected by hypoparathyroidism.

Overview of Hypoparathyroidism

The following information was provided by Dr. Mishaela Rubin, who offered a comprehensive overview of hypoparathyroidism, highlighting the challenges faced by patients despite current treatment options.

Hypoparathyroidism is a rare endocrine disorder characterized by low serum calcium levels and high phosphate levels, with inappropriately low or absent, parathyroid hormone (PTH) levels. The most common cause of hypoparathyroidism is surgery to the neck (approximately 75% of cases) resulting in injury to the parathyroid glands or their blood supply. Non-surgical causes of hypoparathyroidism include genetic predispositions, autoimmune conditions, or idiopathic. Despite its rarity, the disease burden is considerable, affecting an estimated 77,000 to 115,000 individuals in the United States alone.

Current treatment of hypoparathyroidism involves a heavy pill burden of calcium, vitamin D, and other supplements, and despite adherence to conventional therapy, patients continue to experience symptoms and poor quality of life in addition to adverse effects of conventional therapy. Patients commonly experience physical symptoms like muscle issues and tingling, cognitive symptoms including memory loss and difficulty concentrating, and emotional challenges such as anxiety and depression. These symptoms persist despite achieving normal serum calcium levels with conventional therapy, leading to significant impairment in daily functioning and overall well-being.

Meeting Overview

This in-person meeting provided patients, family members, and caregivers the opportunity to directly share their experiences living with hypoparathyroidism. Participants were encouraged to engage in the facilitated discussion during the meeting by submitting comments via the meeting site. The discussion revolved around two key topics, including: 1) The health effects and daily impacts of hypoparathyroidism and 2) Patients' perspectives on current approaches to treating hypoparathyroidism. The questions for the meeting discussion were pre-published on https://www.hypopara.org/el-pfdd to inform participants about the focus areas. Throughout the meeting, a diverse panel of participants, encompassing various causes of hypoparathyroidism and different severity of the condition, shared their insights to initiate dialogue. Panelists represented different demographic profiles, ensuring a broad representation of experiences.

For each topic, panelists included individuals living with hypoparathyroidism, along with family members and caregivers. The panel discussions were followed by facilitated large group discussions, where other participants were invited to contribute their perspectives through both written comments and live contributions. The panel for Topic 1 included individuals who have hypoparathyroidism and family members impacted by the disease. The panel for Topic 2 included individuals on various treatment options for hypoparathyroidism including standard of care (SoC) and clinical trial interventions. Panelists were diverse in age, gender, and race.

Panel comments were followed by large group facilitated discussions inviting other participants and family members to submit written comments through https://www.hypopara.org/el-pfdd. Periodic polling questions provided insight into the demographic of participants and the prevalence of certain perspectives within the group.

Approximately 85 people attended in person and 252 people logged in online with approximately 44 of those identifying themselves as healthcare, industry, government or other patient/advocacy organizations. Registration for the meeting was recommended but not required, therefore the characteristics of meeting registrants may differ from those of meeting attendees.

Meeting participants varied in gender, race, age, etiology of hypoparathyroidism, and experiences with hypoparathyroidism. They also varied in their overarching perspectives on hypoparathyroidism and treatment. The input received reflected a range of experiences and perspectives on the effects of hypoparathyroidism and its management approaches.

All meeting attendees were invited to answer the polling questions on demographics shown in the **Appendix 3**. The majority of meeting attendees (72%) were individuals living with hypoparathyroidism, while 28% were caregivers for someone with hypoparathyroidism. Most meeting attendees (48%) resided in the US Eastern time zone. Most individuals living with hypoparathyroidism at the meeting were female (88%). The largest age group represented was 36-55 years (44%), followed by 33% in the 55+ age group, 13% aged 11-18 years, and 10% aged 19-35 years. The majority (55%) of individuals received a hypoparathyroidism diagnosis between the ages of 36-55 years, 9% were diagnosed between 11-18 years, 9% between 19-35 years, and 27% at age 55+.

In preparation of the EL-PFDD the HypoPARAthyroidism Association conducted a survey of 227 patients to show a broader perspective of patient experiences in addition to those of the 13 panelists. This is a brief sample, the full results can be viewed at https://www.hypopara.org/el-pfdd.

HypoPARAthyroidism Association Survey v2.0 reflection: Majority of participants were female (92%) and white/Caucasian (93%). 87% of participants had hypoparathyroidism due to neck surgery with only 11% of respondents fully understanding their risk prior to surgery. 66% of respondents had at least one or multiple hospitalizations before getting diagnosed with hypoparathyroidism which took between 6month to 20+ years for most patients. Hypoparathyroidism negatively impacted 49% of participant's level of employment and only 10% said they were happy with their treatment options.

The meeting agenda is in **Appendix 1** the meeting panelists in **Appendix 2** and the questions provided for the meeting discussions can also be found in **Appendix 3.** The online polling results from Topics 1 and 2 are included in **Appendix 4.**

The online comment portal was open 30 days prior to the meeting and 30 days after the meeting to capture as many patient voices as possible. All submitted comments are included in a separate PDF document, with selected comments included in the body of this report.

The HypoPARAthyroidism Association Voice of the Patient Report

This Voice of the Patient report is provided to all stakeholders including the US FDA, other government agencies, regulatory authorities, medical products developers, academics, clinicians, and any other interested individuals. The input received from the March 5th, 2024, EL-PFDD meeting encompass a broad spectrum of patients experience with hypoparathyroidism, many captured in this report.

The final report along with the submitted comments and a video recording of the meeting can be accessed on the HypoPARAthyroidism website at https://www.hypopara.org/el-pfdd.

Topic 1: Health Effects and Daily Impacts

Topic 1 centered on drawing insights into the effects of hypoparathyroidism on individuals' health and daily functioning. The discussion aimed to allow patients and caregivers to share their perspective on the health effects and daily challenges associated with hypoparathyroidism in addition to the extent to which hypoparathyroidism impedes their ability to engage in routine activities.

To initiate the discussion, a panel of six individuals shared their perspectives. The panelists comprised of:

1. A woman with post-surgical hypoparathyroidism, once a fiercely independent and high-achieving healthcare executive, saw her life unravel just days after her thyroidectomy. A medical emergency three days post-surgery left her young children, aged five and seven, watching in terror as their strong mother was wheeled out on a stretcher, nearly unconscious. This marked the start of an unrelenting battle that transformed her from self-sufficient to frail, insecure, and dependent. The physical toll was devastating, but the mental anguish was even more profound—constant fear of dying, a descent into addiction as she struggled to manage overwhelming anxiety, and the loss of her former self. Her children only 5 and 7 years, became caregivers, a heartbreaking role reversal. Managing her condition is a relentless burden: 29 pills daily, alarms disrupting her sleep at 1 AM and 3 AM daily, and the ever-present fear of a sudden health crisis, even during routine activities like traveling, where she must share her condition with strangers to avoid a potential crash, as she experienced during a flight. Her survival depends on meticulous consistency in her diet and daily activities, knowing any deviation could be life-threatening. Her story is a powerful testament to the profound and lasting impact hypoparathyroidism has on patients and their families, far beyond physical symptoms (presentation can be found at https://youtu.be/rJTHU7DesEE).

2. The devoted mother of a young girl diagnosed with idiopathic hypoparathyroidism at age 10, shared the profound challenges they have faced. The girl's first seizure, initially misdiagnosed as epilepsy, led to unnecessary anti-seizure medication before her true condition was recognized. The mother felt dismissed by doctors who downplayed the severity of her daughter's condition, advising only Vitamin D, Calcitriol, and Tums, but the reality has been far more complex. The costs of frequent ER visits, medications, and numerous specialist appointments—including endocrinologists, nephrologists, pediatricians, gastroenterologists, foot doctors, nutritionists, therapists, and psychiatrists—are overwhelming. Her daughter's health struggles have severely impacted her life, causing her to miss school, experience fatigue, and feel isolated from friends. The family has even faced legal challenges due to her absences. Every aspect of their lives, including vacations and social events, revolves around her daughter's medical needs,

requiring meticulous planning around doctor's appointments and lab tests. The mother worries constantly about her daughter's calcium levels, fatigue, and future, all while hoping for better treatment options as her daughter grows up (presentation can be found at https://youtu.be/MwJXDMresc4).

3. A soon-to-be 15-year-old has been battling hypoparathyroidism since she was 10. Her suffering began with a seizure that not only shocked her but also traumatized her younger sister. Despite her dangerously low calcium levels, she was initially misdiagnosed and placed on epilepsy medication, leading to frequent ER visits and painful lab draws that left her covered in bruises. The physical and emotional toll has been immense. She feels isolated and burdensome to her family and friends, who struggle to understand her condition. Unable to live a normal childhood, her life has been overshadowed by constant fear of severe symptoms, including the anxiety of a potential crash during a sleepover and a panic attack in the school bathroom that required her friend to call her mom. These experiences have left her feeling alienated and, at times, hopeless. Her mental health has deteriorated, marked by severe anxiety and depression, and at times, she has questioned her will to live (presentation can be found at https://youtu.be/mFwgHskKOao).

4. A female with hypoparathyroidism diagnosed at 12 years old when a surgical procedure to remove a goiter led to unexpected and severe complications. Unaware of the long-term consequences of the surgery and pressured by a lack of time and understanding, her mother was rushed into a life-altering decision for a full thyroid removal, which included the risk of developing hypoparathyroidism. Post-surgery, she faced a traumatic experience of confusion, vocal cord damage, and severe symptoms that led to an ICU stay. The lack of proper documentation and understanding of her condition prolonged her suffering. She struggled academically and was placed in special education classes due to brain fog and concentration issues and developed an eating disorder as a coping mechanism. The high cost of specialized calcium for absorption and numerous IV infusions, especially during pregnancy, strained her family financially, leading to bankruptcy. Despite enduring over 150 IVs and home health care, she had to quit nursing her children due to the inability to stabilize their calcium levels and her own. Her condition has made her feel invisible and misunderstood, with every change in her life—stress, sleep, or exercise—causing detrimental effects on her calcium levels. At 31, she continues to feel constrained by her condition, which has significantly impacted her relationships, career, and overall health (presentation can be found at https://youtu.be/kreLnajZTpo).

5. A female with APS type 1 hypoparathyroidism. Her journey with hypoparathyroidism began at age three when she experienced her first hypocalcemic seizure but was misdiagnosed with epilepsy. By age five, she was correctly diagnosed due to experiencing severe symptoms such as laryngospasms. Despite treatment with calcitriol and calcium, she experienced significant challenges, including being legally blind and needing contacts and glasses to function, and suffering from severe calcium swings of 4.8-13.0, often requiring hospitalization four times a year. The calcium supplements has led to unseen damage such as cataracts, calcifications in the brain, osteoporosis, and calciuria. The advent of Natpara

in 2015 marked a life-changing improvement, reducing severe symptoms and hospitalizations, though she faces the daunting prospect of returning to less effective standard therapies when Natpara is discontinued at the end of 2024. Her experiences highlight the urgent need for advancements in hypoparathyroidism treatment to improve quality of life and manage long-term health impacts (presentation can be found at https://youtu.be/63RzR2dZjDE).

6. A caregiver shared her experience of managing her daughter's idiopathic hypoparathyroidism, diagnosed at age eight. Initially prescribed Tums and calcitriol, the treatment led to severe stomach pain and constant fluctuations in her calcium level. Despite switching to calcium carbonate and later calcium citrate, the ongoing stomach discomfort made it difficult for her daughter to take her medication consistently, leading to additional issues like paresthesia, fatigue, and kidney pain. Throughout their journey, she felt that their concerns were often dismissed by healthcare providers, who failed to recognize the severity of her daughter's pain. The burden of managing the condition, with over 18,000 pills taken in four years, and the relentless stress on their family life were immense. She passionately calls for better treatments that address the root causes of hypoparathyroidism, emphasizing that no child should have to endure such chronic pain and that the current standard of care falls far short (presentation can be found at https://youtu.be/7xzyNQ0cFXA).

The panelists' opening comments provided a range of perspectives on the health effects and daily impacts of hypoparathyroidism. Their stories provided insight into the physical, social, mental, and financial impacts of hypoparathyroidism. During the large group facilitated discussion that followed, panelists and meeting participants discussed additional impacts of the condition.

The remainder of this section summarizes in more depth the input from participants on the topics related to the health effects and impacts of hypoparathyroidism.

Perspectives on health effects of hypoparathyroidism

Participants described their paths and difficulties in receiving an accurate diagnosis, often facing misdiagnosis or delayed diagnosis, with the most common misdiagnosis being epilepsy or seizure disorders. Participants recounted experiences of initially being diagnosed with epilepsy due to presenting symptoms such as seizures, which were later identified as manifestations of severe hypocalcemia associated with hypoparathyroidism. This misdiagnosis or delayed diagnosis led to inappropriate treatment and management strategies, causing further complications and delays in receiving appropriate care for hypoparathyroidism. They also highlighted the lack of awareness among healthcare providers about hypoparathyroidism, leading to misunderstandings and inappropriate treatments.

In a polling question (Appendix 3), 453 participants identified hypoparathyroidism-related health concerns. The most common symptoms reported were paresthesia (numbness/tingling sensation) (14%), fatigue (14%), muscle cramps/tetany (14%), and brain fog or cognitive dysfunction (13%). In the following question about the most troublesome hypoparathyroidism-related health concerns, 24% of participants selected brain fog or cognitive dysfunction, 23% selected muscle cramps/tetany, 19% selected fatigue, and 11% selected paresthesia (numbness/tingling sensation). When asked about their top worries regarding their own or their loved one's condition in the future, the top three concerns were loss of current skills/functioning (26%), symptoms worsening (25%), and needing extended or long-term care (20%).

Throughout the meeting, participants discussed the significant impacts of hypoparathyroidism on their health

- Participants explained the complexity of managing hypoparathyroidism which emerged as a prominent theme. They discussed challenges related to standard of care, finding knowledgeable healthcare providers, and navigating the healthcare system to access appropriate care and support. Patients may need to advocate for themselves and seek out specialists who understand the complexities of the condition

- Patients must regularly monitor their calcium levels through blood tests to ensure they remain within a narrow therapeutic range. Fluctuations in calcium levels can lead to symptoms of hypocalcemia or hypercalcemia, requiring adjustments to medication dosages. Often, accessing timely blood tests can be challenging for some patients. In some cases, patients may not have immediate access to blood tests, leading to delays in monitoring their serum calcium levels. Additionally, there may be instances where blood test results are not available in real-time, making it difficult for healthcare providers to make timely adjustments to medication dosages based on current calcium levels. A caregiver described "*We've been to the ER several times, at least three or four times a year for a calcium level blood check as there are no home devices available or any other reliable means for knowing how low or high her calcium is and if she's too low, will she have a seizure again or have difficulty breathing from going up the stairs at school*?"

- Participants mentioned that hypoparathyroidism can cause a range of symptoms, including muscle spasms, tingling sensations, fatigue, and cognitive difficulties. While patients are on standard of care, calcium and active vitamin D, patients are still experiencing these symptoms.

- Managing hypoparathyroidism requires long-term planning to anticipate and address potential complications, such as kidney stones, soft tissue calcification, cataracts, and neurological symptoms. Patients and caregivers must stay vigilant and proactive in managing the condition to minimize the risk of complications over time.

- Participants shared the emotional and psychological toll of living with hypoparathyroidism, including feelings of frustration, anxiety, isolation, and depression. Coping with chronic pain, uncertainty about the future, and the limitations imposed by the condition contributed to significant psychological distress.

- Despite the challenges they faced, panelists expressed a sense of advocacy and hope for improved treatments and outcomes for individuals with hypoparathyroidism. They emphasized the importance of raising awareness, advocating for better healthcare resources, and supporting research efforts to advance understanding and management of the condition.

Impacts of hypoparathyroidism on Daily Life

Participants described hypoparathyroidism as having a significant impact on their daily lives. They described difficulties in maintaining stable serum calcium levels and participating fully in work and school. Participants recalled how hypoparathyroidism limited their ability to care for their children and damaged their relationships.

Participants described their symptoms consisting of muscle spasms, tetany, numbness, tingling, and fatigue. These symptoms often disrupt daily activities and can range from mildly uncomfortable to debilitating. Panelists described instances where their hands would spasm shut or their legs would become too weak to climb stairs, highlighting the significant physical limitations imposed by the condition. One participant described "*Every time my calcium fluctuated, my body would go into a fight or flight response. My heart raced and I was sure I was going to die. It was paralyzing, but now is a warning sign that I recognize. I never appreciated how debilitating anxiety was and that people really do not have control over it*." A caregiver described "*we'd find her in bed with severe leg pain, stomach cramps that made her hunch over with pain, tears coming down her eyes, her skin behind her knees was dry and peeling. Her nails were brittle and if she ran too much she would become short of breath and became dependent on an inhaler*"

Meeting participants expressed the burden of managing medication regimens. Patients with hypoparathyroidism are often required to take multiple medications multiple times a day, sometimes in large quantities. One participant shared *"No child should have to take up to 15 pills a day. In a little over four years since diagnosis, she's taken over 18,000 pills*". Another individual expressed that she is taking "*between 60 and 70 pills per day*". Another participant shared "*'Every day feels like a battle, with countless pills to take just to maintain some semblance of normalcy*.'

Participants shared the profound emotional and psychological impact on them and their families. They described feelings of frustration, isolation, and anxiety stemming from the unpredictability of their condition and the challenges of managing symptoms on a daily basis. Caregivers, in turn, expressed feelings of helplessness and guilt as they watched their loved one's struggle with the effects of the disease. One participant shared *"Living with hypoparathyroidism feels like constantly walking on a tightrope, never knowing when I might fall. The anxiety of not being in control of my own body is overwhelming at times*." Other participants stated:

- "*There's this constant fear of the unknown. Will today be a good day or a bad day? It's exhausting always being on edge, never knowing when the next symptom will strike*."
- "*The daily struggle of managing hypoparathyroidism took a toll on my mental health. The relentless cycle of symptoms and medication adjustments left me feeling overwhelmed and hopeless, leading to persistent feelings of anxiety and depression*."

- "*Hypoparathyroidism turned my life into a constant battle against my own body. The physical symptoms, coupled with the fear of complications, robbed me of my sense of security and stability, fueling anxiety and depression*".

Additional Impacts
Participants described in detail the impact that hypoparathyroidism has on daily life, including:

- **Impact on Relationships:** Panelists highlighted feelings of isolation and alienation, often experiencing feelings of frustration, isolation, and anxiety, leading to strained interpersonal connections. Caregivers may also struggle with feelings of helplessness and guil. One participant shared "*I felt so alienated when I realized my classmates didn't have to take a cup of meds every morning just to survive the day. Having to explain to my friends why I had to watch what I ate, take medications with my meals, and why I constantly missed school made me feel like a burden and a charity case*." "*No one around me knew what it was like to miss out on holidays because I'm stuck in bed or leave sleepovers early because my calcium is too low. This disease has not only taken over my physical health but also my mental health. I feel like I'm living in a different world from everyone else*."

- **Impact among adults:**
  "Living half-life, with post-surgical hypopara has affect every facet of my life. I feel alone always. I lost my friends, my husband I have constant PTSD. I try to work 15 hours a week. I work one day then spend 2 days in bed to recover."

  "This is a hugely difficult condition to live with and manage. Doing it alone can be sometimes overwhelming. I live alone and my adult children are far away. It is impossible to expect friends to understand. I have learned that I have to establish and lean on a community of friends, though, for particularly rough days or crises. It's tough."

  "I also never have friends or family over to my house because preparing the house and food is just too much for me anymore. I used to love to travel but now it is generally just too exhausting and we don't do it much. I also feel guilty because I can't keep up with friends and family and always feel like I'm letting them down. This disease has been extremely isolating for me."

- **Impact on Work Life:** Several panelists emphasized the effects of hypoparathyroidism on education and work. Children and adolescents with the condition may face academic challenges due to cognitive impairments, difficulty concentrating, and frequent school absences. Likewise, adults may encounter difficulties in retaining employment or advancing in their careers due to the unpredictable nature of their symptoms and the necessity for frequent medical appointments and accommodations. A caregiver described for her daughter "*She has missed so much school and social events from the fatigue that shows up uninvited at any given moment. Last school year, she was crippled with anxiety that sent her for two weeks to a behavioral hospital. Out of 180 school days, she missed 45 days. We were sent to court for absences and had to put her under a special program*." Another participant

stated “*I spent the next several years fighting my way through school. I was placed in special education classes due to being unable to read or complete simple math. It was almost like my brain was no longer working after my surgery. I could no longer think, could not retain information, and I struggled to concentrate and hold simple conversations*.”
Among adults with hypoparathyroidism, one panelist stated "*As an adult with hypoparathyroidism, I've faced numerous obstacles in my career due to the unpredictable nature of my symptoms. Frequent medical appointments and accommodations have made it difficult to maintain steady employment*." Other participants described:

“Unable to work full time in my management consulting work as worried I have a bad day and I am unable to meet clients requirements. Some days unable to think clear enough to deal with complex problems.”

“I'm unable to work, I'm often very down, and most days I don't have energy to do much beyond taking care of myself through the day and then maybe cooking dinner. It's not the life I'd I thought I'd be living at 43 years old. I really am hopeful that a PTH replacement therapy will help.”

“When I first acquired the disease (post-surgical thyroidectomy) at 21 years old, I was able to carry on with life pretty normally for the first few years, even working full time. Looking back, I can see that after 3-4 years things began to change. I quit working full-time 5 years after my surgery and haven't been able to work that much ever since. I have tried for many years to find a job that I can fit in around my symptoms, but I have finally reached a point where there isn't anything that I can make work and am currently unemployed without feeling the possibility of finding work any time soon. I feel like I used to have a sharp mind and now I struggle to learn new things quickly and comprehend things as well as I used to.”

- **Financial Impacts:** Panelists describing the financial costs associated with managing hypoparathyroidism. From frequent hospitalizations and emergency room visits to the high cost of medications and specialized care, the financial burden of the disease can be overwhelming for patients and their families, often leading to bankruptcy and other financial hardships. One participant shared “*The financial toll of hypoparathyroidism has been staggering for our family. With frequent hospitalizations and emergency room visits, the medical bills have piled up, pushing us to the brink of bankruptcy*."

Several participants mentioned potential interventions or improvements that could address the major concerns associated with living with Hypoparathyroidism. One key suggestion was the need for advancements in treatment options beyond the current standard of care, which typically involves calcium and vitamin D supplementation. Participants expressed a desire for more effective treatments that address the underlying cause of the condition and provide better symptom management, such as direct parathyroid hormone replacement therapy. Additionally, there was an emphasis on the importance of raising awareness among healthcare providers to improve diagnosis and management of the condition, as well as advocating for better access to healthcare services and financial support for patients and their families facing the substantial financial burden associated with managing Hypoparathyroidism.

Topic 2: Perspectives on Current Approaches to Management

The second part of the meeting began with a presentation by Dr. Michael Mannstadt, focusing on the limitations of current treatment options for hypoparathyroidism and the critical physiological roles of parathyroid hormone (PTH) in calcium and bone metabolism. Current standard treatments, primarily involving calcium and active vitamin D supplementation, are effective in elevating serum calcium levels but fail to replicate the comprehensive physiological functions of PTH. These functions include the regulation of bone turnover, renal calcium reabsorption, and phosphate excretion, which are not adequately addressed by conventional therapy. The existing therapeutic regimen, often involving multiple daily doses of supplements, is burdensome and does not prevent long-term complications such as nephrolithiasis and chronic kidney disease. Conventional treatments are inadequate compared to PTH, particularly in achieving stable urinary calcium levels and maintaining consistent serum calcium concentrations throughout the day. Although PTH (1-84) has demonstrated some therapeutic benefits, its discontinuation highlights the need for improved treatment options that more closely mimic the physiological actions of PTH. Such advancements are essential for enhancing disease management and improving patient quality of life.

During the second panel discussion, panelists shared their experiences, not only on the management approaches they used, but also the factors they considered when making decisions about their recovery. Seven panelists (Appendix 2) provided comments to start the dialogue.

The panelists included:

1. A woman with post-surgical hypoparathyroidism shared her challenging journey with the condition. Her story illustrates the severe impact and complexity of managing hypoparathyroidism, emphasizing that no two patients are the same and each requires a personalized approach, as no standard regimen effectively controls the disease. From her experience, she detailed the devastating effects of the Natpara recall, which resulted in over 70% of patients requiring emergency care, 20 being admitted to the ICU, and the tragic loss of three of her friends. The disease's impact extended beyond her health, profoundly affecting her family life as her young child witnessed her ongoing struggles, and the severe limitations imposed by her condition. Her oral health deteriorated dramatically, leading to numerous dental procedures, including crowns and fillings. Additionally, she faced a significant challenge in participating in clinical trials, as the necessary washout periods or the risk of being placed in a placebo group could result in severe health consequences. Her experience highlights the urgent need for continuous and effective treatment options to manage this complex and debilitating condition (presentation can found at https://youtu.be/evxYVjhxswg).

2. A woman with idiopathic hypoparathyroidism shared her journey of being diagnosed with the disease after suddenly losing her eyesight while driving off a freeway ramp one evening. As

her sight gradually returned days later, she began experiencing extreme fatigue, hair loss, and the shocking crumbling of her teeth while eating something as simple as a muffin. These alarming signs of her body deteriorating left her fearful for her life. Her doctor soon called, urging her to get to the emergency room as her calcium levels had dangerously plummeted. Initially, the doctors were uncertain of her condition and questioned her about possible cancer or sickle cell disease. Days later, she was diagnosed with hypoparathyroidism. Although she received calcium through IV treatment during her hospital stay, the relief was only temporary. Weeks later, she experienced an even more severe crash, leading to repeated hospitalizations, debilitating seizures, and painful muscle spasms that made walking nearly impossible. During one hospital stay, after yet another crash, she received seven calcium infusions and went into tachycardia while on the phone with her husband, ultimately requiring a defibrillator. The relentless nature of the disease left her taking between 60 to 70 pills a day, with frequent calcium infusions. Despite these overwhelming challenges, she remains hopeful, to see a day when better treatment options exist and the quality of life for hypoparathyroidism patients is restored (presentation can found at https://youtu.be/uEHm3kV-214).

3. A male patient shared his personal story of growing up in a family where genetic hypoparathyroidism was all he knew—a disease so ingrained in his family that it became their "normal," affecting entire generations and whole families. As the youngest of five boys, all diagnosed with the condition, he lived in a world where monitoring symptoms like low calcium levels and tetany was a constant necessity, not just for himself but for his brothers. The disease's impact became even more profound when his youngest daughter suffered a severe calcium crash at age 12, leading to a traumatic ER visit where doctors refused to administer the necessary treatment despite his pleas. The emotional toll was immense as he watched his daughter writhe in pain, helpless against the medical system's indifference. This experience echoed the frustration his father had felt decades earlier when doctors dismissed his symptoms. His story illustrates the unique struggles faced by those with hypoparathyroidism, emphasizing that each patient is like a snowflake—unique in their symptoms and experiences, as panelist 1 also noted. He passionately argued that the standard care approach is fundamentally flawed and inadequate. It fails to address the underlying endocrine disorder, reducing treatment to merely managing calcium levels however low calcium is only one symptom of hypoparathyroidism, not the root cause. This flawed treatment paradigm leaves patients at risk of life-altering complications, despite their resilience and determination to lead normal lives (presentation can found at https://youtu.be/9u0e7eFoz1k).

4. A woman with post-surgical hypoparathyroidism, shares her journey with the disease after a surgery to treat papillary thyroid carcinoma inadvertently damaged her parathyroid glands. At just 24 years, her life became dominated by labs, ER visits, and a constant struggle with cognitive decline, fatigue, and kidney dysfunction. Standard care treatments not only failed to help her but actively harmed her. Determined to find a solution, she entered a Phase 3 clinical trial for TransCon PTH. The results were life-changing: her cognitive function improved almost immediately, and her kidney function, bone turnover, and calcium levels

stabilized. While her condition is not perfect, the treatment has vastly expanded her capacity to live a full life. She no longer battles daily symptoms but now enjoys a quality of life where her medical issues are just one facet of her existence. She expressed profound gratitude for the chance to reclaim her life, emphasizing that the right treatment can transform a patient's experience from mere survival to truly living (presentation can found at https://youtu.be/ZkMnLYwcPng).

5. A woman with postsurgical hypoparathyroidism, marking her nine-year battle with the disease, shared how she never imagined that the cancer diagnosis would be the easy part of her medical journey. Living with this poorly understood disease, has been a nightmare, as she was required to endure the standard treatment of calcium and calcitriol. Despite consulting five endocrinologists, she felt abandoned when none could offer solutions beyond the ineffective and harmful standard care, which left her bedridden with severe anxiety, debilitating pain, and depression, leading to hospitalization. The constant burden of managing her condition required 10 alarms a day to take 18 calcium pills, turning her life into a tightrope walk where one misstep could trigger a medical emergency. However, her life changed dramatically after switching to PTH therapies like Natpara and TransCon. She now feels liberated, able to enjoy life again with her family, and looks forward to the future with optimism, as her mental health has significantly improved, and her anxiety is now manageable (presentation can found at https://youtu.be/XrcX9yleUII).

6. A 16-year-old female with ADH1 diagnosed since the age 10, she struggled with understanding what symptoms were normal due to her lifelong experience with the condition. As an athlete, she faced unique challenges, constantly comparing her reactions to those of her peers and questioning if her symptoms were "normal" by asking her friends if they too had similar experiences. The standard care of calcium supplements and Vitamin D failed to provide consistent relief, leaving her in a constant state of guesswork with her medication timing and dosage, impacting her daily life. Despite being an active participant in a medical trial, she still endures symptoms and worries about potential kidney failure and stones. Her frequent blood draws, essential for monitoring her condition, result in noticeable bruises that prompt questions from friends and logistical challenges, such as carrying a backpack with urine samples for 24-hour tests during vacations or at school. She feels that the current approach to hypoparathyroidism does not adequately address the complexities of the disease (presentation can found at https://youtu.be/0s1rcd6RMPc).

7. A woman diagnosed with ADH1 at 40, spent most of her life untreated, enduring severe muscle pain, exhaustion, and an extreme heart rate, which led to misdiagnoses of depression and anxiety. Despite being offered a Division 1 soccer scholarship, she turned it down, knowing she couldn't keep up due to her physical limitations. Interestingly, she felt her best during pregnancy, wishing she could be pregnant all the time to escape her symptoms. Managing her condition has been a constant struggle, as balancing calcium intake with urine calcium levels is so difficult that she never truly feels good. Even with treatments like NATPARA, her quality of life remained compromised. Driven to improve both her life and the lives of others, she pursued medical trials, ultimately improving

her condition and advocating for better treatment options for the hypoparathyroidism community (presentation can found at https://youtu.be/Lo1mmivg3ac).

In the facilitated discussion that followed, individuals with hypoparathyroidism and caregivers discussed experiences with current treatment options/standard of care, clinical trials, therapy options, and effects of treatments. Many participants voiced concerns that the current standard of care is inadequate in addressing the condition, as it primarily focuses on managing low calcium levels—a symptom of hypoparathyroidism—without directly addressing the underlying endocrine disorder, characterized by low to no parathyroid hormone in the blood. They highlighted the need for tailored approaches to treatment, recognizing the uniqueness of each individual's symptoms and severity levels.

In a polling question (Appendix 3, Question), participants were asked what medications or medical treatments they have currently or previously used to treat symptoms associated with hypoPARA. Majority of participants were on calcium supplements (18%), calcitriol (18%), and magnesium (15%). Nine percent of participants were on Natpara, 5% were on Forteo, and 4% were on clinical trial medication. Majority of participants (52%) also described that the current treatment regiment only somewhat treats their hypoparathyroidism symptoms, and that the biggest drawback of their current treatments is that they only treat some but not all of the symptoms in addition to having side effects from the medication, and not being very effective at treating target symptom. Throughout the discussion, participants shared the perspectives on current treatment options and the resources and community support systems that were available to them. Several participants stressed that their comments represent the management approaches which worked best for them personally and may not be applicable to all individuals with hypoparathyroidism.

Perspectives on Approaches to Management:

Participants provided insights into various treatment approaches used to manage the condition. Many emphasized the importance of addressing the underlying causes of their condition, highlighting that current treatment options, such as calcium and vitamin D supplementation, do not effectively address these root issues. Several participants voiced their desire for medication specifically targeting low parathyroid hormone (PTH) levels, recognizing it as a crucial aspect of effective condition management. They also stressed the importance of being able to frequently test their serum calcium levels at home and the necessity of tailored interventions for each individual.

Obstacles and barriers for management of hypoparathyroidism

Participants described the obstacles and barriers to current therapy options for hypoparathyroidism, including struggling to stabilize on standard of care and concern about long-term complications such as kidney failure and soft tissue calcification and the lack of access and lack of awareness of healthcare providers. Examples of treatment barriers they encountered are captured in the statements below:

- *“If I tell my doctors that I'm not feeling well and I want to know what my calcium is, they tell me to go get my labs in the morning, but that doesn't fix the problem because it won't be the same level in the morning and it won't work. I want to know what it is now. Like diabetics, they're able to check their sugar levels instantly, almost, and we just aren't able to.”*

- *“I started taking calcium at 7:00 AM, 9:00 AM, 11:00 AM, 1:00 PM, 3:00 PM, 5:00 PM, 7:00 PM, 9:00 PM, 11:00 PM for a total of 18 pills, or 5,994 milligrams of calcium or more a day. Taking my calcium perfectly every day did not guarantee that my calcium was stable. Every day was a guessing game. You never know what you're going to get. I took my levothyroxine at 3:00 AM for a total of 10 alarms daily, preventing me from getting a solid night's sleep.”*

- *“Although there are trials for molecules that might be a better fit [than Forteo], I can't consider joining the trials. I would be hospitalized long before the required 30 to 90 days without PTH was completed. I also can't risk being placed in a placebo arm. I would lose my job if that happened, possibly my life. I don't stabilize anymore on orals. When I searched through the FDA's clinical trial site, I'm unable to find a single insulin trial that requires diabetics to stop using insulin for any period of time, and I can't find one that uses a placebo arm with no insulin provided to them.”*

- *“One day while in a hospital, after yet another crash, I received seven calcium infusions. I went into tachycardia of the heart while on FaceTime with my husband. I knew for sure I wasn't going to make it home to him, but the grace of God was on my side. I made it through. I now have a heart defibrillator.”*

- One caregiver who had his daughter experience very low serum calcium levels and ended up in the ER described his experience in the ER *“As suspected, her serum calcium levels came back extremely low. Her symptoms continued to worsen, and she was now experiencing severe tetany, fatigue and brain fog. She didn't know where she was or what was happening. I told the doctors that if they started her on IV calcium, the symptoms would subside. They did not listen to me, no matter how much knowledge and experience I had, but they disregarded the low calcium and instead focused on treating the multitude of symptoms that were related to low calcium. Unfortunately, this experience has echoed throughout the community of hypopara.”*

  “I visited a doctor who was an expert in this condition, and knowing the disease burden and the limitations of treatment options at the time, he told me to "limp along" until better options became available.”

  “My endocrinologist, a series of five in the past four years, had zero options for me. All of them promised they could help me, but every one of them could only prescribe the standard of care, calcium and calcitriol. When they figured out that the standard of care didn't work for me, they gave up on me. I tried to explain to these endocrinologists the side effects I was having from calcitriol. Their response was, "Take it anyway" and I honestly tried.”

“Today, March 5th, it's my nine-year anniversary of living with postsurgical hypothyroidism. We don't celebrate this day. I never would've imagined that a cancer diagnosis would be the easy part of my medical journey. I am a person living with a rare disease that is poorly understood by the medical professionals that we must rely on to keep us healthy”

- *“The hard thing about having a genetic condition is knowing no different. Having it your whole life, you don't know what is normal or what is not.”*

- *“Hypopara is a very unpredictable condition and hard to cure. Every day I have to figure out the best time to take my medication and where it can benefit me the best that day. If I take it too early, then I'll crash earlier in the day, but if I take it too late, then I won't feel my best the whole day”*

Current Treatment

Throughout the discussion, panelists shared their desires for more effective treatments for hypoparathyroidism, drawing from their own experiences and challenges with current management options. They emphasized the importance of addressing the underlying cause of hypoparathyroidism and the need for individualized care.

One participant explained that treating hypoparathyroidism is not only about treating serum calcium levels, stating that “*hypoparathyroidism is the only endocrine disorder that does not have an FDA-approved hormone replacement option available, and our health reflects this*.” Another participant stated that “*For years, hypoparathyroidism has been associated with low serum calcium levels, and the standard of care is just to treat low calcium with more calcium. This treatment is false. Low calcium is only a symptom of hypoparathyroidism. It is the low to no parathyroid hormone in the blood. That is what needs to be treated. hypoparathyroidism is an endocrine disorder first and foremost and must be treated as such, and I compare it to telling a person with diabetes to manage their blood sugar by just watching what they eat and nothing else*.”

SoC treatment:

- *“I have seen how standard of care is inefficient and leads to long-term complications from kidney failure to calcifications of soft tissues, brain fog, kidneys stones, fatigue, tetany, the list goes on and on. I could testify that each person diagnosed with hypopara is different. Indeed, we are like snowflakes, each unique in symptoms and severities”*

  “Hypoparathyroidism is often viewed to be a low calcium disease. The inability of patients to stabilize on oral medications is a stark reminder that this is an endocrine disorder, most similar to diabetes type one in terms of severity, blood level volatility, and complexity of treatment.”

  “For years, hypoparathyroidism has been associated with low serum calcium levels, and the standard of care is just to treat low calcium with more calcium. This treatment is false. Low

> *calcium is only a symptom of hypopara. It is the low to no parathyroid hormone in the blood. That is what needs to be treated. Hypopara is an endocrine disorder first and foremost and must be treated as such, and I compare it to telling a person with diabetes to manage their blood sugar by just watching what they eat and nothing else."*
>
> *"Diabetes without insulin. That is hypopara without parathyroid hormone."*

Participants described that not being able to test their serum calcium levels at home limits their ability to monitor their condition effectively. One participant stated that "*If we could get a kit where we can test our calcium at home and not have to wait for the labs to come back. While we're in the wait, we're becoming extremely critical, which is ending us up in a hospital.*"

Meeting participants identified barriers to care that impacted their ability to manage their hypoparathyroidism, which included challenges in in finding healthcare providers knowledgeable about hypoparathyroidism and its management, difficulty accessing timely and comprehensive calcium testing and monitoring their symptoms, and overall access to alternative treatment options.

Meeting participants shared their experiences with using other therapies, beyond calcium and active vitamin D. They emphasized the importance of recognizing individual differences and providing tailored treatment plans to improve each person's condition. Participants highlighted how characteristics such as etiology (genetic, idiopathic, post-surgical), activity level, diet, and stress levels, can impact experiences of hypoparathyroidism and stressed the need for a more intersectional approach to care. One patient mentioned that "*As a genetic patient, I guess, for me, numb might be a way of saying how I feel a lot of the times.*" Additionally, participants discussed specific therapies they are undergoing, with further details provided below categorized by treatment types.

Standard of care (calcium, active D supplements, diuretic, magnesium): several participants described their experiences with standard of care to manage their hypoparathyroidism. Many focused on how standard of care is inadequate in managing their symptoms, as they still experience chronic symptoms including brain fog, fatigue, tetany, calcium crashes and poor quality of life. Participants shared:

- *"At 24 years old, my life consisted of labs, 24-hour urine tests, ER visits, and going to the pharmacy multiple times per week. My cognitive function, energy levels and kidney function suffered. My inability to retain and process information became a source of immense frustration. Standard of care treatment was not only not helping me, it was harming me."*

- *"Calcitriol causes me to have severe headaches, bone and joint pain, severe anxiety, heart palpitations, unstable calcium, panic attacks, and many days that I just did not get out of bed. Three years ago, I decided to wean myself off of calcitriol. I had to choose between my quality of life and my kidneys. I chose my quality of life"*

- *"I got prescribed standard of care, which was calcium supplements and Vitamin D. Standard of care was not being effective. I'd feel good in the morning, but once it became the afternoon,* *I'd immediately fall asleep right after school and even on the weekends. Standard of care isn't an accurate cure, because it works differently on every person and differently and different everyday"*

- *"The standard of care, calcitriol and calcium. I was hospitalized on average four times a year, weekly hospitalizations due to critically low calcium. This oral medication regimen was not ideal. It continues to miss the mark, but it was all I had. It was my only option."*

- A caregiver *"But I cannot help but wonder what the standard of care is doing to her body. While she has significant calcification of soft tissues, cataracts, kidney failures, she's only 17 with a lifetime ahead of her, and I can only pray that she can maintain a high quality of life."*

- *"I have seen how standard of care is inefficient and leads to long-term complications from kidney failure to calcifications of soft tissues, brain fog, kidneys stones, fatigue, tetany, the list goes on and on."*

- While sharing their experiences on standard of care, patients commented on the need to choose between kidney complications and quality of life, one patient mentioned *"for a long time. I've had recurring kidney stones, a lot of tetany, and it's like that balance between stones and tetany, I'm always on."*

- One patient described the struggle of management with standard of care stating *"I was prescribed the standard of care of oral calcium, active vitamin D, and also hydrochlorothiazide in hopes to keep my urine calcium lower. I was told, to preserve my kidneys, I had to keep my calcium levels as low as possible in the normal range. I was taking calcium supplements around the clock. I was taking up to 5,000 milligrams of calcium. My urine turned cloudy, and my symptoms still were there"*.

  "*The current standard of care does not get me anywhere near having a reasonable quality of life. My life revolves around taking pills, blood draws, without my symptoms improving. My mind revolves around determining what I ate, how I slept, what activity possibly caused some of my symptoms. Exercising exhausted me. Brain fog. I have anxiety, mood changes throughout the day, headaches, paresthesia. I was unable to work, and I was actually feeling ill from the calcium supplements*."

Natpara: Some participants shared their experiences using Natpara to manage their hypoparathyroidism.

- *"I got into the Natpara Phase 4 trial investigating twice daily use. In the first hour of injection, my calcium went up from 7.8 to 8.7 with no orals on board. My urine concentration dropped by 75%, and my heart arrhythmia disappeared. The brain fog lifted, the tetany in my feet dissipated. I started Natpara, moved up to the 100-microgram dose, and was able to stop orals altogether."*

- *“When I began using Natpara in 2015, it was life-changing for me. Life-changing for my family. I know what my quality of life can be like now. The wide fluctuations have ceased. The symptoms are not as severe. My quality of life is drastically improved.”*

- *“My symptoms are minimal while on Natpara. Natpara gave me my life back. I lead a very happy, active life now. My urine calcium is in a normal range prior to Natpara I was in stage 3 renal failure. Off of Natpara I am bed or sofa bound within a day or two. The symptoms come back and hit hard and it takes twice plus the pills I was on prior to starting Natpara.”*

- *“Best day Natpara PTH 1-84 in a pump. I feel absolutely normal all my labs a in great shape including 24 hr urine. Lots of energy can drive. Motorhome, do martial arts, workout in gym, 10 mile hikes, no brain fog very articulate, no issues.”*

Impact of Natpara Recall

The section below details the severe physical, emotional, and socioeconomic challenges patients faced due to the Natpara Recall, including recurrent emergency visits and significant disruptions to their quality of life. The first-hand accounts highlight the need for effective and reliable treatment options to address this gap in care.

While other patients discussed the impact of the Natpara recall including:

- *“In one of the Natpara support groups I'm part of, from September to mid-December 2019, more than 70% of us ended up in the emergency room with critically low calcium. About 60% of these ER visits resulted in admissions, and at least 20 people were moved to the ICU. More than half of us were in the ER more than once in those three months. Personally, three of my friends died as a result of this recall.”*

- *“NATPARA worked lovely for about four to six hours a day. Each afternoon my symptoms would reappear and I would just take my calcium. In 2019, the recall of NATPARA. I was back to popping pills every three to four hours, waking up in the middle of the night and being told not to take more calcium because my urine calcium was so high. I have to protect my kidneys. The current standard of care does not get me anywhere near having a reasonable quality of life. "*

- *“After losing access to Natrpara, I lost my job and had to switch careers, but even now, I can feel my strength and Quality of life draining away.*

- *“September 5th, 2019, my life was shattered again with the recall of Natpara. As patients, we found out when we couldn't get our prescriptions filled. My endo found out when I emailed her. The recall was the equivalent of removing all forms of insulin from the market via a note in the news section of one manufacturer's website. The flood of patients being hospitalized after the recall and the subsequent initiation of the special use program just 19 days later demonstrates the significant and severe patient harm that is experienced when patients don't have access to PTH.”*

Forteo: Some participants shared their journey on Forteo. One patient mentioned "*My endo move me to Forteo, but with a 90-minute half-life, Forteo just wasn't the same [as Natpara]. My urine levels were high, so we had hydrochlorothiazide, then potassium magnesium. I woke up daily between 2:00 and 3:00 AM in severe pain due to calcium crashes. I added in calcitriol, calcium, calcium patches. I could now get to 4:00 AM before I woke up with the pain. My teeth started decalcifying again, and since 2019, I've had six crowns and twice that number of fillings. I started having kidney stones formed for the first time. My vision deteriorated dramatically*." She found that Forteo in an Omnipod worked better. "*I asked my endo about putting Forteo in the Omnipod. This has been a miracle for me. I have found that I functioned best with calcium levels between 9.2 and 9.6. My urine levels are back under 250. I haven't grown any new kidney stones. I spent a year in physical therapy, and now I can work out again*." Another patient mentioned that her current treatment is using Forteo, delivered every hour, through an insulin pump, she states that "*it's the best decision I've ever made for myself. It was a little bit of time and effort to get things dialed in, but I can go do a CrossFit workout, I can take care of a severe calcium crash at home without an emergency room or IV calcium*." However, as Forteo and the pump are off label there is a challenge of getting approval from her insurance company "*I spend about a hundred to 150 hours a year fighting with my insurance company to keep this, but the medication itself and the delivery system is glorious*." Another patient mentioned that "*My request to be admitted to some of the Forteo and other options was declined by my insurance company on the grounds that my symptoms were being managed relatively well within the normal levels with calcium and calcium trial*". Participants also discussed:

- *"I'm on Forteo, on a pump, but I'm still not able to work or do daily chores so it's not optimal for me."*

- *"When I was on Forteo, prior to the NATPARA, I was needing up to nine injections a day of Forteo. So, I was using nine full Forteo pens, and it still wasn't enough to last my body throughout an entire 24-hour period."*

- *"Before starting Forteo, I struggled with basic activity like walking down stairs or going to the mailbox. Initially, it seemed inevitable that I'd be in a wheelchair full time. While using Forteo in a pump has kept me out of a wheelchair, my daily function remains limited. I can't help out around the house, work or exercise, as my muscles lack the necessary calcium and electrolytes for proper repair after activity. Even a single repetition of anything that resembles exercise leaves my muscles sore and weak for days, hindering any progress in maintaining or improving my overall physical condition, despite my efforts working with a physical therapist."*

Desire for treatment

TransCon PTH: One patient described her journey with TransCon PTH as nothing short of transformative. After years of suffering from hypoparathyroidism, which felt trapped in a body burdened by severe cognitive impairment, constant ER visits, and overwhelming fear. TransCon PTH restored her kidney function, stabilized her calcium levels, and cleared her brain fog. Today, she has reclaimed her life, going from merely surviving to thriving, and is once again able to fully participate in her career, relationships, and daily activities. Other patients described their experience as follows:

- "*My kidney function has been 100% restored. My bone turnover is normal. My calcium levels are stable. My brain fog is gone. It is not perfect all the time. I still get symptoms when my body has had enough, but my capacity to tackle life's challenges has vastly expanded. Symptoms are now a cause for alarm rather than a daily burden. My quality of life has returned because of quality treatment.*"

- *"I started taking TransCon through the EAP program on April 4th, 2023. I have not been in an emergency room since January 13th, 2023. I'm able to go for walks, ride my bike again, play with my grandchildren, go to the grocery store. Basically, I can participate in life again. I am no longer a spectator. Instead of having 10 alarms set, I now have two. One at 9:00 AM for my TransCon injection and one at 11:30 PM for my Tirosint. My mental health has improved, I'm no longer battling depression. My anxiety is manageable by going for walks or doing yoga. I can look at my future with optimism.*"

Participants expressed a strong desire for treatments that target the core issue of hypoparathyroidism: low or absent parathyroid hormone (PTH). They indicated that ideal treatments should not only manage symptoms like low calcium levels but also directly address the underlying hormonal imbalance to improve overall health and quality of life.

Topic 3: Risk-Benefit Assessment

	EVIDENCE AND UNCERTAINTIES	**CONCLUSIONS AND REASONS**

ANALYSIS OF CONDITION / IMPACTS ON ACTIVITIES OF DAILY LIVING	For many, hypoparathyroidism is **misdiagnosed**, and very little information is available about this disorder to patients. Patients and family members diagnosed with hypoparathyroidism expressed that at the time of their diagnosis they were horrified to know that the only standard care available consists of calcium and vitamin D supplements, rather than a parathyroid hormone (PTH) replacement therapy. Individuals living with hypoparathyroidism experience many **health concerns**. The condition significantly impacts their daily lives, leading to challenges in managing routine activities. Patients often report symptoms such as fatigue, muscle cramps, seizures, and cognitive impairments, which can severely limit their ability to work, study, and engage in social activities. The lack of effective treatments exacerbates these challenges, leading to a diminished quality of life.	Hypoparathyroidism imposes **significant disease burden** on patients and their families. The condition impacts all aspects of daily life, affecting both physical and mental well-being. **Key impacts include:** • Compromised independence due to unpredictable symptoms and frequent medical interventions • Challenges with maintaining consistent calcium levels, leading to fatigue, muscle cramps, and cognitive issues • Difficulties in work, study, and social activities due to symptom fluctuations • Burden of complex medication regimens and dietary restrictions • Emotional toll, including anxiety and depression related to managing a chronic condition • Financial strain from ongoing medical care and potential loss of work productivity Concerns for the future include: • Long-term health complications, such as kidney problems or soft tissue calcifications • Potential for worsening symptoms over time • Availability and access to effective treatments • Physical and mental health of both patients and caregivers These factors collectively underscore the profound and multifaceted impact of hypoparathyroidism on patients' quality of life and the urgent need for improved

		management strategies and support systems.
CURRENT TREATMENT OPTIONS/ PROSPECTS FOR FUTURE TREATMENTS	**There are no FDA approved treatments for hypoparathyroidism.** Currently all individuals living with hypoparathyroidism require large number of pills to try to stabilize calcium levels. However, standard of care can potentially inflict more harm than good, leading to severe long-term consequences and falling short in managing the debilitating symptoms patients face daily.	**Individuals living with hypoparathyroidism have an urgent unmet need for effective treatments. Existing treatments are not always effective and are enormously difficult to get access to.** All hypoparathyroidism patients are in need of therapies to manage symptoms, prevent further deterioration and improve quality of life. Access to parathyroid hormone therapies and developing effective treatment options that address the complex needs of individuals with hypoparathyroidism are essential. There is a critical need to enhance medical knowledge of the condition to improve diagnosis and management of hypoparathyroidism.

Conclusion

The insights shared by participants during this meeting underscored the profound impact of hypoparathyroidism on daily life and the significant challenges faced in seeking effective treatment and management strategies. The HypoPARAthyroidism Association’s endpoint is the recognition that hypoparathyroidism is fundamentally a parathyroid hormone (PTH) disorder, rather than merely a calcium disorder. The association acknowledges the invaluable contributions of individuals living with hypoparathyroidism, as well as their caregivers and family members, in enhancing our understanding of this condition and its management.

We extend our gratitude to all participants for their willingness to share their experiences navigating the complexities of hypoparathyroidism, including the limitations of current treatment options such as calcium and active vitamin D supplementation. This Externally Led Patient-Focused Drug Development meeting has provided key stakeholders with firsthand insights into the lived experiences of those affected by hypoparathyroidism.

The HypoPARAthyroidism Association's mission is to improve the lives of people impacted by hypoparathyroidism through education, support, research, and advocacy. This Voice of the Patient report serves as a vital step in advancing that mission by summarizing the input shared by patients and caregivers during this meeting. The insights gathered here not only underscore the urgent need for more effective treatments but also reinforce our commitment to driving research and advocating for better management strategies for those living with hypoparathyroidism.

We are deeply appreciative of the courage and openness demonstrated by individuals and their families in sharing their personal journeys with hypoparathyroidism. Their voices will continue to guide our efforts in improving the quality of life for those impacted by this condition.

Appendix 1 Meeting Agenda

Externally Led Patient Focused Drug Development (PFDD) Meeting on Hypoparathyroidism

Date: Tuesday March 5th, 2024
Time: 10:00 am – 3:30 pm EST

AGENDA

10:00 am- 10:05 am	**Welcome** Michele Rayes, *Associate Director - HypoPARAthyroidism Association*
10:05 am-10:15 am	**FDA Opening remarks** Dr Naomi Lowy, M.D. *Deputy Director, Division of General Endocrinology at FDA*
10:15 am-10:20 am	**Overview of discussion format** Patty Keating, *Executive director - HypoPARAthyroidism Association*
10:20 am-10:35 am	**Hypoparathyroidism clinical overview** Dr. Mishaela R Rubin, M.D. *Division of Endocrinology, Columbia University*
10:35 am-11:15 am	**Panel #1: Health Effects & Daily Impacts of Hypoparathyroidism**
11:15 am-12:30 pm	**Facilitated Group Discussion Health Effects & Daily Impacts** Patty Keating
12:30 pm-1:15 pm	**Lunch Break**
1:15 pm-1:30 pm	**Hypoparathyroidism treatment overview** Dr Mannstadt
1:30 pm-2:00 pm	**Panel #2: Current Approaches to Treatment**
2:00 pm-3:15 pm	**Facilitated Group Discussion Treatments** Patty Keating
3:15 pm-3:35 pm	**Closing Remarks** Patty Keating

Appendix 2: Patient and FDA Panel participants

Patient Panel Topic 1,

1. Andrea Ligler
2. Anna Garcia
3. Emilia Garcia
4. Mirranda McVay
5. Julia Richardson
6. Kimberly Shade

Patient Panel Topic 2,

1. Tisha Horton
2. Caroline Warmkessel
3. Bob Sanders
4. Katie Gillick
5. Lynette McGregor
6. Annie Faestel
7. Jackie Faestel

FDA Panel: Dr. Naomi Lowy, Lena Merzoug, and Ethan Gabbour

Appendix 3: Meeting Polling Questions

Demographic questions

1. **Are you:**
    a. Someone living with HypoPARA
    b. A caregiver of someone with HypoPARA

2. **Where do you currently reside?**
    a. US Pacific time zone
    b. US Mountain time zone
    c. US Central time zone
    d. US Eastern time zone
    e. US Alaska time zone
    f. US Hawaii time zone
    g. Europe
    h. Middle East
    i. Asia
    j. Canada
    k. Mexico
    l. Central or South America

3. **Is the person living with hypoPARA:**
    a. Female
    b. Male
    c. Other

4. **How old is the person living with hypoPARA?**
    a. 0-10 years of age
    b. 10-18 years of age
    c. 19-35 years of age
    d. 35-55 years of age
    e. 55+ years of age

5. **At what age was the person diagnosed with hypoPARA?**
    a. 0-10 years of age
    b. 10-18 years of age
    c. 19-35 years of age
    d. 35-55 years of age
    e. 55+ years of age
    f. 35 years of age or older

Topic 1 - LIVING WITH HypoPARA: SYMPTOMS AND DAILY IMPACT

6. **Which of the following HypoPARA-related health concerns have you or your loved one ever had? Select ALL that apply**
    a. Brain Fog or Cognitive dysfunction
    b. Paresthesia (numbness/tingling sensation)
    c. Seizures
    d. Muscle Cramps/Tetany
    e. Fatigue
    f. Kidney Stones
    g. Chronic Kidney Disease
    h. Heart Arrhythmias
    i. Laryngospasms
    j. Calcium Related Cataracts
    k. Dental issues
    l. Other

7. **Select the TOP 3 most troublesome HypoPARA-related health concerns that you or your loved one has ever had. Select up to 3**
    a. Brain Fog or Cognitive dysfunction
    b. paresthesia (numbness/tingling sensation)
    c. Seizures
    d. Muscle Cramps/Tetany
    e. Fatigue
    f. Kidney Stones
    g. Chronic Kidney Disease
    h. Heart Arrhythmias
    i. Laryngospasms
    j. Calcium Related Cataracts
    k. Dental issues
    l. Other

8. **What specific activities of daily life that are important to you or your loved one, do you feel they are NOT able to do or struggle with due to hypoPARA? Select TOP 3**

    a. Regular sleep
    b. Social Interaction
    c. Walking
    d. Attending school or having a job
    e. Household chores
    f. Other

9. **What worries you most about you or your loved one's condition in the future? Select TOP 3**
    a. Seizure activity
    b. Symptoms will get worse
    c. Not knowing what is causing pain

d. Loss of current skills/functioning
e. Social isolation
f. Needing extended or long-term care
g. Who will care for my child if I'm not able
h. Other

Topic 2 - PERSPECTIVE ON CURRENT AND FUTURE APPROACHES TO TREATMENT

10. What medications or medical treatments has you or your loved one used (currently or previously) to treat symptoms associated with hypoPARA? Select ALL that apply

a. Calcium supplements
b. Calcitriol/Rocaltrol
c. Forteo
d. Natpara
e. Clinical Trial medication
f. Magnesium
g. Potassium
h. Vitamin D2
i. Hydrochlorathiazide (HCTZ)
j. Other
k. Not used medications/medical treatments recently

11. How well does your current treatment regimen treat the most significant symptoms of hypoPARA?

a. Not at all
b. Very little
c. Somewhat
d. To a great extent
e. Not applicable; not using anything

12. What are the biggest drawbacks of you or your loved one's current treatments? Select up to 3

f. Not very effective at treating target symptom
g. Only treats some but not all symptom(s)
h. Limited availability or accessibility
i. Side effects
j. Route of administration (how it's taken)
k. Requires too much effort and/or time commitment
l. Other
m. Not applicable; not using any treatments

13. Short of a complete cure, what TOP 3 specific things would you look for in an ideal treatment for hypoPARA? Select up TOP 3

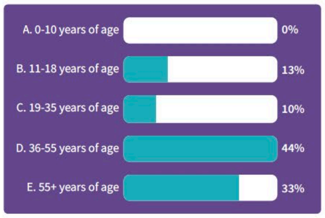
a. Improved cognition (brain fog)

b. Improved stamina/ability to do daily activities
c. Less muscle and joint pain
d. Improved ability for self-care
e. Improved sleep
f. Reduction in urine calcium levels
g. Reduction in kidney stones
h. Other

Appendix 4: Polling Results

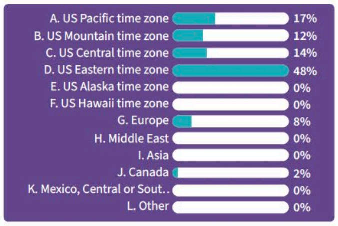
Demographic polling results

04. How old is the person living with hypoPARA?



Response options	Count	Percentage
A. 0-10 years of age	0	0%
B. 11-18 years of age	8	13%
C. 19-35 years of age	6	10%
D. 36-55 years of age	**28**	**44%**
E. 55+ years of age	21	33%

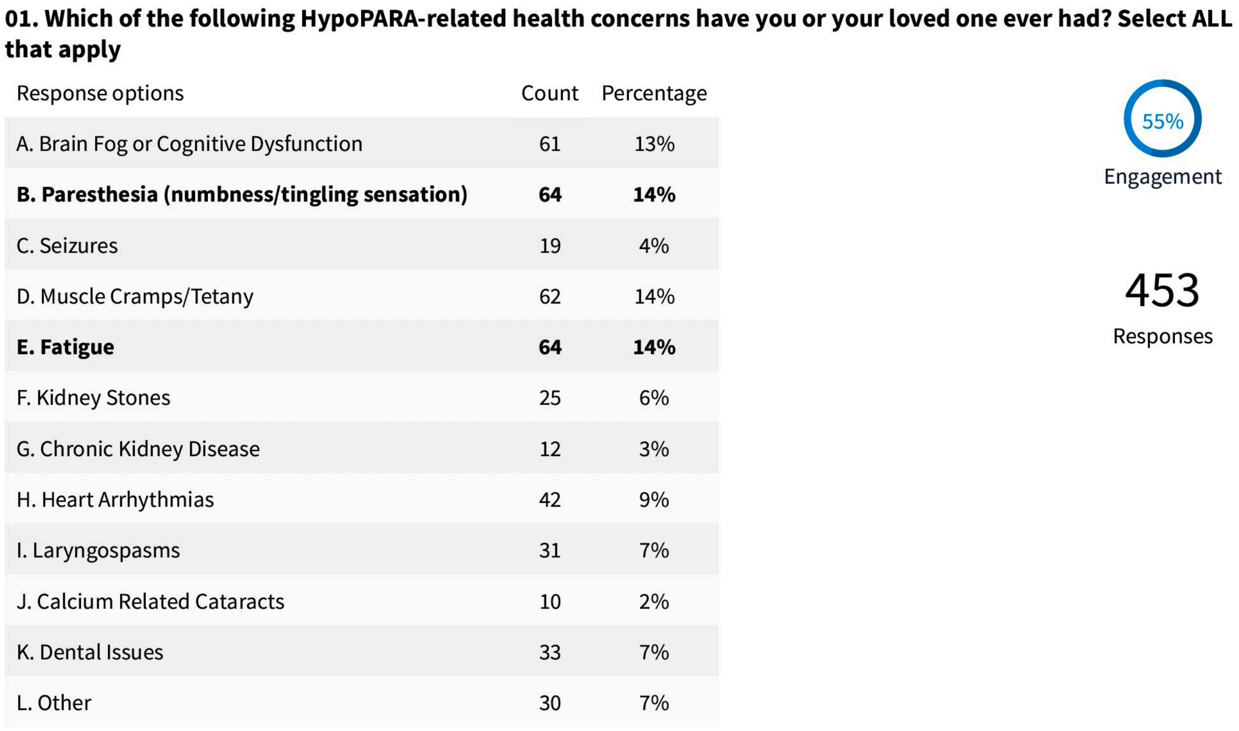
02. Where do you currently reside?



Response options	Count	Percentage
A. US Pacific time zone	11	17%
B. US Mountain time zone	8	12%
C. US Central time zone	9	14%
D. US Eastern time zone	**31**	**48%**
E. US Alaska time zone	0	0%
F. US Hawaii time zone	0	0%
G. Europe	5	8%
H. Middle East	0	0%
I. Asia	0	0%
J. Canada	1	2%
K. Mexico, Central or South America	0	0%
L. Other	0	0%

03. Is the person living with hypoPARA:

Response options	Count	Percentage
A. Male	7	12%
B. Female	**53**	**88%**
C. Other	0	0%



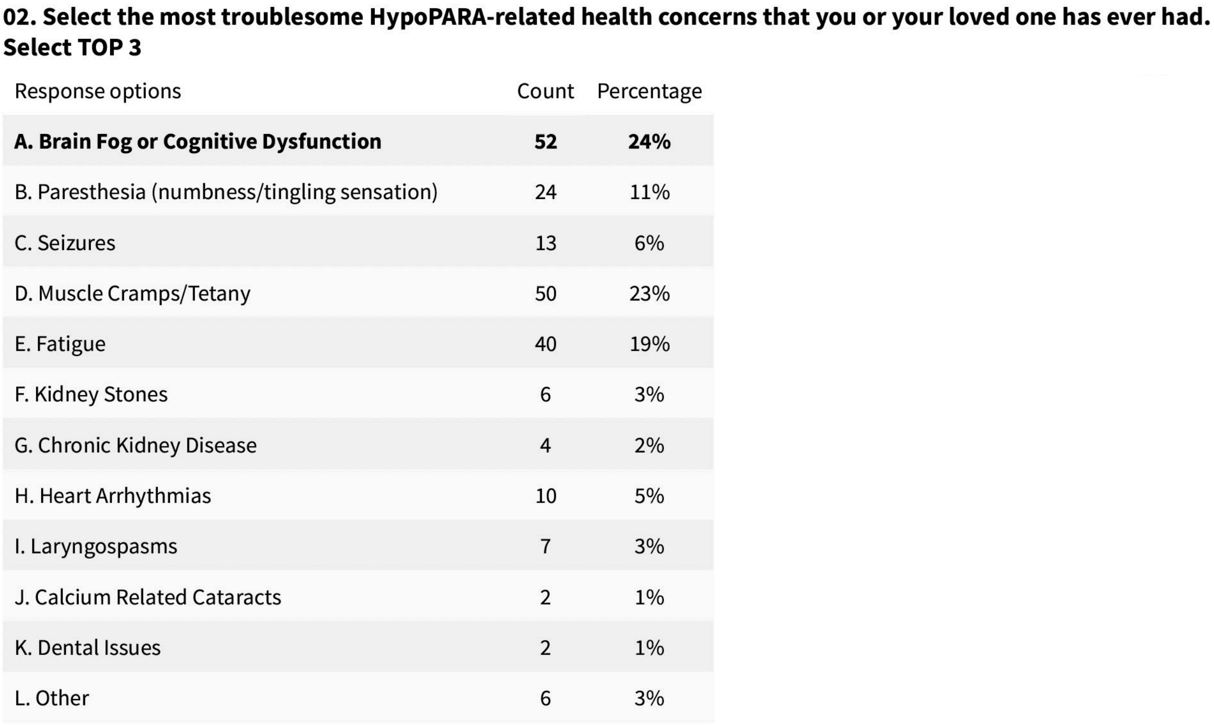
01. Which of the following HypoPARA-related health concerns have you or your loved one ever had? Select ALL that apply

Response options	Count	Percentage
A. Brain Fog or Cognitive Dysfunction	61	13%
B. Paresthesia (numbness/tingling sensation)	**64**	**14%**
C. Seizures	19	4%
D. Muscle Cramps/Tetany	62	14%
E. Fatigue	**64**	**14%**
F. Kidney Stones	25	6%
G. Chronic Kidney Disease	12	3%
H. Heart Arrhythmias	42	9%
I. Laryngospasms	31	7%
J. Calcium Related Cataracts	10	2%
K. Dental Issues	33	7%
L. Other	30	7%

55%
Engagement

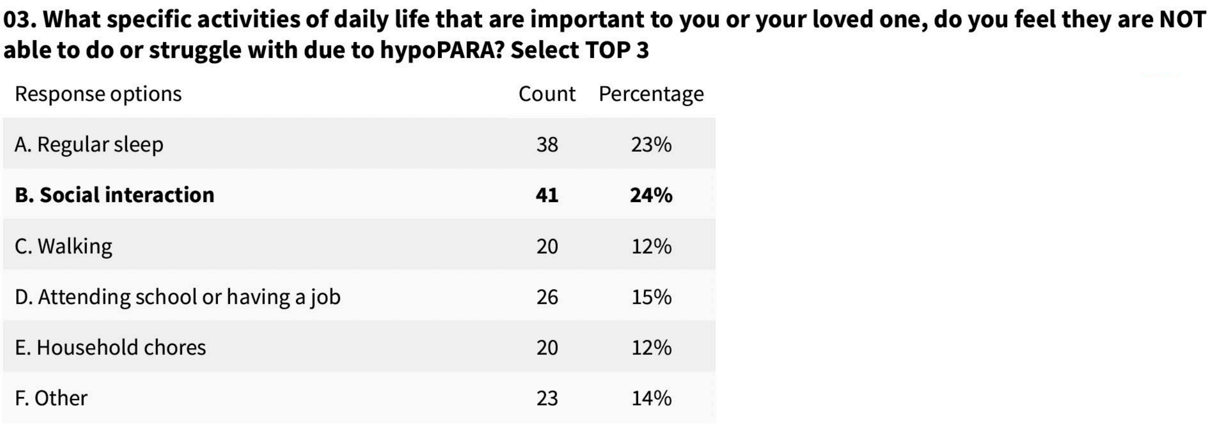
453
Responses

Topic 1 polling results



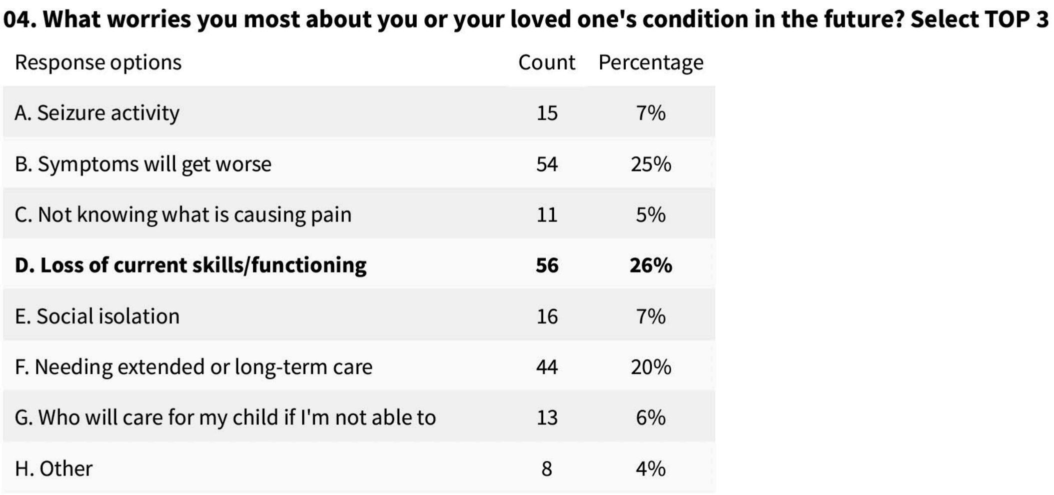
02. Select the most troublesome HypoPARA-related health concerns that you or your loved one has ever had. Select TOP 3

Response options	Count	Percentage
A. Brain Fog or Cognitive Dysfunction	**52**	**24%**
B. Paresthesia (numbness/tingling sensation)	24	11%
C. Seizures	13	6%
D. Muscle Cramps/Tetany	50	23%
E. Fatigue	40	19%
F. Kidney Stones	6	3%
G. Chronic Kidney Disease	4	2%
H. Heart Arrhythmias	10	5%
I. Laryngospasms	7	3%
J. Calcium Related Cataracts	2	1%
K. Dental Issues	2	1%
L. Other	6	3%



03. What specific activities of daily life that are important to you or your loved one, do you feel they are NOT able to do or struggle with due to hypoPARA? Select TOP 3

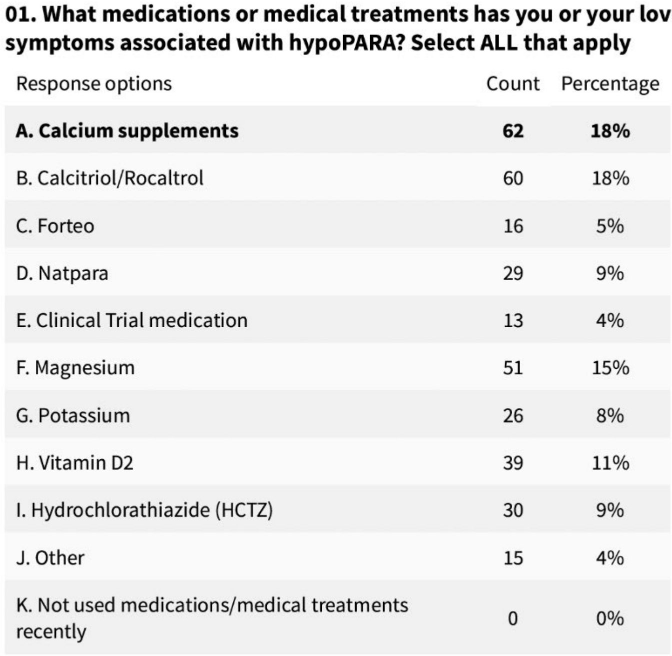
Response options	Count	Percentage
A. Regular sleep	38	23%
B. Social interaction	**41**	**24%**
C. Walking	20	12%
D. Attending school or having a job	26	15%
E. Household chores	20	12%
F. Other	23	14%



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

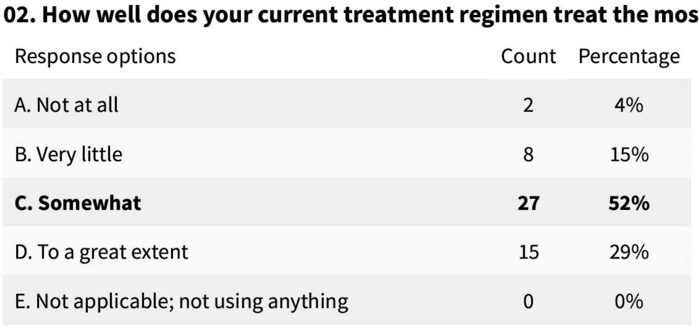
Response options	Count	Percentage
A. Seizure activity	15	7%
B. Symptoms will get worse	54	25%
C. Not knowing what is causing pain	11	5%
D. Loss of current skills/functioning	**56**	**26%**
E. Social isolation	16	7%
F. Needing extended or long-term care	44	20%
G. Who will care for my child if I'm not able to	13	6%
H. Other	8	4%

Topic 2 polling results



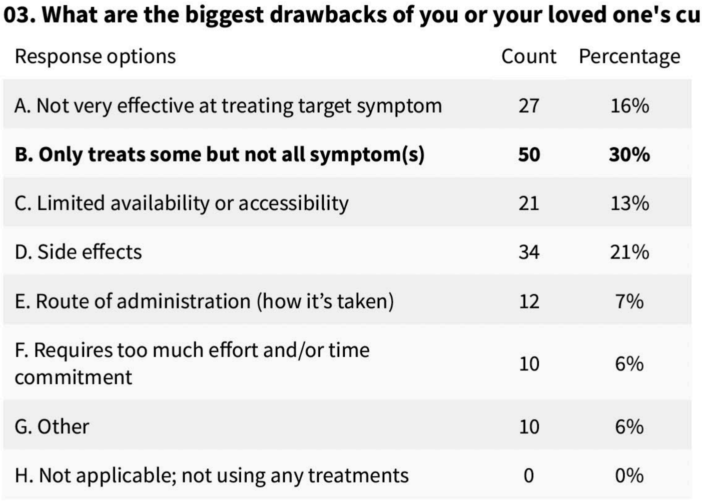
01. What medications or medical treatments has you or your loved one used (currently or previously) to treat symptoms associated with hypoPARA? Select ALL that apply

Response options	Count	Percentage
A. Calcium supplements	**62**	**18%**
B. Calcitriol/Rocaltrol	60	18%
C. Forteo	16	5%
D. Natpara	29	9%
E. Clinical Trial medication	13	4%
F. Magnesium	51	15%
G. Potassium	26	8%
H. Vitamin D2	39	11%
I. Hydrochlorathiazide (HCTZ)	30	9%
J. Other	15	4%
K. Not used medications/medical treatments recently	0	0%



02. How well does your current treatment regimen treat the most significant symptoms of hypoPARA?

Response options	Count	Percentage
A. Not at all	2	4%
B. Very little	8	15%
C. Somewhat	**27**	**52%**
D. To a great extent	15	29%
E. Not applicable; not using anything	0	0%



03. What are the biggest drawbacks of you or your loved one's current treatments? Select up to 3

Response options	Count	Percentage
A. Not very effective at treating target symptom	27	16%
B. Only treats some but not all symptom(s)	**50**	**30%**
C. Limited availability or accessibility	21	13%
D. Side effects	34	21%
E. Route of administration (how it's taken)	12	7%
F. Requires too much effort and/or time commitment	10	6%
G. Other	10	6%
H. Not applicable; not using any treatments	0	0%

04. Short of a complete cure, what specific things would you look for in an ideal treatment for hypoPARA? Select up TOP 3

Response options	Count	Percentage
A. Improved cognition (brain fog)	44	24%
B. Improved stamina/ability to do daily activities	**50**	**27%**
C. Less muscle and joint pain	36	20%
D. Improved ability for self-care	7	4%
E. Improved sleep	15	8%
F. Reduction in urine calcium levels	18	10%
G. Reduction in kidney stones	10	5%
H. Other	4	2%