



Hermansky-Pudlak Syndrome (HPS)

# VOICE OF THE PATIENT REPORT



Externally Led  
Patient-Focused  
Drug Development  
Meeting



This report is dedicated to the individuals who  
courageously shared their stories.



**Hermansky-Pudlak Syndrome**  
**Externally Led Patient-Focused Drug Development**  
**Voice of the Patient Report**

Meeting Date: 10 June 2022

**Meeting hosted by:** Hermansky-Pudlak Syndrome Network, Inc.

**Submitted to:** The U.S. Food and Drug Administration (FDA)

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## Hermansky-Pudlak Syndrome Voice of the Patient Report

The mission of the Hermansky-Pudlak Syndrome Network, Inc., (HPS Network) is to provide education and vital support programs to individuals and families with Hermansky-Pudlak syndrome (HPS) while striving for improved care and innovative research on our journey to cure. This *Voice of the Patient* report was prepared by the Hermansky-Pudlak Syndrome Network, Inc. as a summary of the input shared by people and families living with Hermansky-Pudlak Syndrome during an Externally-Led Patient Focused Drug Development Meeting (EL-PFDD). This meeting was hosted virtually on June 10, 2022.

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*This report is dedicated to Juleiny and all of the cherished members of our community who have passed. We were looking forward to hearing Juleiny speak at the June 10 HPS EL-PFDD meeting, but she passed away shortly before, at the age of 28, as a result of HPS-related pulmonary fibrosis.*

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## Executive Summary and Key Meeting Insights

The Hermansky-Pudlak Syndrome Network, Inc. (HPS Network) hosted the Hermansky-Pudlak Syndrome (HPS) Externally-Led Patient Focused Drug Development (EL-PFDD) meeting on June 10, 2022. This meeting was held to provide a patient and caregiver perspective of the symptoms and burdens associated with HPS in daily life, as well as the massive unmet treatment needs experienced by those who live with HPS every day. 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 patients and caregivers of individuals living with HPS, who participated in the June 10, 2022, EL-PFDD meeting. The report also includes selected comments that were submitted through an online portal.

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 HPS. The hope is that this information will catalyze better treatments and ultimately a cure for those affected by HPS.

The HPS Network 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 HPS community, including the HPS Network's partners and advocacy organizations. Note that the input received from the June 10, 2022, EL-PFDD meeting reflects a wide range of HPS experiences, however not all symptoms and impacts may be captured in this report.

### Key meeting themes and insights:

1. **Hermansky-Pudlak Syndrome (HPS) is extremely rare and in certain gene types, fatal (including the most common gene type).** Patients and caregivers must often educate their health care providers about this disease. Symptoms and their impacts are often minimized, dismissed or misdiagnosed. Many patients are not diagnosed until after experiencing a medical emergency that often could have been avoided.
2. **The combination of HPS symptoms can be deadly.** Blood clotting issues mean that even minor surgeries can be high risk. The inflammatory bowel disease can cause hemorrhaging due to the bleeding disorder and pulmonary fibrosis is fatal.
3. **People living with HPS have many worries and live with a great deal of uncertainty about their future.** For many, their biggest worries are related to developing pulmonary fibrosis, needing a lung transplant and premature death.
4. **HPS is a diverse disease with a variety of clinical manifestations.** Most individuals living with HPS experience multiple HPS-related manifestations. HPS symptoms and severity can vary from one patient to the next and range from severe to life threatening.

5. **All people living with HPS experience albinism (legal blindness, photophobia and nystagmus) and blood clotting issues.** Other symptoms exist based on subtype. Blood clotting issues and visual impairment are the two most common HPS-related health concerns with pulmonary fibrosis as the most lethal.
6. **HPS impacts activities of daily living and profoundly affects quality of life.** Maintaining independence **is difficult when unable to drive.** Visual impairment can lead to injuries and bruising.
7. **There are no FDA approved treatments for any HPS disease manifestations.** People living with HPS instead try to use medications approved for other indications, which only work somewhat.
8. **Treatment for one HPS symptom can affect other outcomes.** For example, the receipt of platelets to treat hemorrhaging can jeopardize future lung transplants because of antibody production. Lung transplant and pulmonary fibrosis medications can increase cancer risk. Medications for the bowel disease can increase infection. Additionally, all of these medications can lead to chronic kidney and liver disease.
9. **Many living with HPS do not have access to even the most basic medications and treatments.** People living with HPS in Puerto Rico are particularly disadvantaged, with no opportunity for life-saving transplants.
10. **Better treatments for patients living with HPS are urgently and desperately needed, particularly to prevent or treat pulmonary fibrosis, bleeding issues and colitis.**

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## Introduction and Meeting Overview

### Clinical Overview of HPS<sup>1</sup>

Hermansky-Pudlak Syndrome (HPS) is rare, hereditary disorder which affects all genders equally. HPS is an autosomal recessive disorder, so both parents must carry a gene variant for a child to have the disorder. Due to a founder effect, HPS impacts one of every 1,800 individuals of Puerto Rican descent, and one in every 21 individuals of northwestern Puerto Rican heritage are believed to be carriers of the HPS type 1 gene variant. HPS 3 is common in the central region of the island.

The syndrome was first described in Czechoslovakia in 1959, in two patients cared for by Dr. Hermansky and Dr. Pudlak and the causative gene for HPS type 1 was identified in 1996. Since then, ten additional HPS-associated genes were identified, each corresponding to one of the known HPS subtypes, ranging from mild disease with few symptoms to very severe and disabling disease and even death. Additional HPS genes may be discovered in the future.

Individuals living with HPS display features of albinism, including hypopigmentation of the skin and hair which are often noticed shortly after birth. Some HPS individuals have more pigment than others and therefore, go undiagnosed. Albinism results in light sensitivity of both skin and eyes, abnormal eye movements (nystagmus) and visual impairment. The first disturbing HPS symptoms usually appear in childhood, as a blood platelet dysfunction results in bruising or prolonged bleeding after an injury, which can be life-threatening. Histological examination of platelet structure and molecular testing for a causative gene variant confirms the diagnosis.

Other HPS symptoms depend on the specific HPS subtype.

- Patients with HPS types 1, 2 or 4 develop pulmonary fibrosis, usually starting in the late twenties or early thirties. This slowly progresses to complete lung failure requiring a lung transplant.
- About 15% of individuals living with HPS experience granulomatous colitis or an inflammation of the colon, which is very similar to Crohn's disease. This occurs in patients of all subtypes.
- Additional manifestations can include kidney disease and storage of a fatty-like substance (ceroid lipofuscin) in various tissues of the body including the lungs, colon, heart and kidneys.

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<sup>1</sup> This information was from the presentations of: (1) William A. Gahl, MD, PhD, Senior Investigator, National Human Genome Research Institute; Head, Section on Human Biochemical Genetics, Medical Genetics Branch; Director, Undiagnosed Diseases Program, National Institutes of Health; and (2) Dr. Bernadette Gochuico, Attending Pulmonologist at the National Human Genome Research Institute, National Institutes of Health.

Variants in HPS-causing genes create defects in the formation or movement of intracellular vesicles or compartments. This means that while essential proteins are present, they are not located where they are required to be functional. For example, the lack of melanosomes in melanocytes (i.e. pigment cells) impairs pigmentation throughout the body and the lack of dense bodies in platelets impedes blood clotting.

The proteins encoded by the different HPS-associated genes interact together in Adaptor Protein Complexes (APCs) or Biogenesis of Lysosome-related Organelles Complexes (BLOCs), leading to phenotypic similarities in interacting subtypes.

- **HPS type 1** (caused by variants in the *HPS1* gene). This is the most common HPS subtype and is present in many individuals of Puerto Rican descent. This subtype manifests with albinism, the bleeding disorder, and pulmonary fibrosis. About 15% of these individuals also have colitis. HPS type 1 and type 4 proteins interact in a complex called BLOC-3.
- **HPS type 2** (caused by variants in the *AP3B1* gene). This subtype is very rare, with only 12 patients identified to date. It features mild albinism and the bleeding disorder. Patients with HPS type 2 also have neutropenia, i.e., a low white blood cell count, which can lead to childhood infections. HPS type 2 and type 10 proteins interact in a complex called APC 3.
- **HPS type 3** (caused by variants in the *HPS3* gene). This subtype is associated with very mild albinism and a bleeding disorder, but these individuals do not experience pulmonary fibrosis. HPS type 3, type 5 and type 6 proteins interact in a complex called BLOC-2.
- **HPS type 4** (caused by variants in the *HPS4* gene). This subtype includes albinism, the bleeding disorder, and pulmonary fibrosis. HPS type 1 and type 4 proteins interact in BLOC-3.
- **HPS type 5** and **HPS type 6** (caused by variants in the *HPS5* and *HPS6* genes, respectively) are both characterized by albinism and the bleeding disorder. At this time, these subtypes are not known to cause pulmonary fibrosis. HPS type 3, type 5 and type 6 proteins interact in a complex called BLOC-2.
- **HPS type 7** (caused by variants in the *DTNBP1* gene). This is a very rare subtype with only three individuals diagnosed to date. This subtype is characterized by albinism and the bleeding disorder, but it is unknown if these patients will experience pulmonary fibrosis. HPS type 7, 8, 9 and 11 proteins interact in a complex called BLOC-1.
- **HPS type 8** (caused by variants in the *BLOC1S3* gene). Only one individual was diagnosed with this HPS subtype to date. This subtype is characterized by albinism and the bleeding disorder. HPS type 7, 8, 9 and 11 proteins interact in the BLOC-1 complex.
- **HPS type 9** (caused by variants in the *BLOC1S6* gene). Only two individuals are diagnosed to date. Patients have albinism, but there is no evidence of bruising and both patients are still too young to determine if they will develop pulmonary fibrosis. HPS type 7, 8, 9 and 11 proteins interact in the BLOC-1 complex.

- **HPS type 10** (caused by variants in the *AP3D1* gene). Only one individual who died at the age of 3.5 years, has been diagnosed to date. This individual experienced seizures, dysmorphisms, microcephaly, developmental delays, poor myelination, and neutropenia. HPS type 2 and type 10 proteins interact in the APC 3 complex.
- **HPS type 11** (caused by variants in the *BLOC1S5* gene). Only two individuals have been diagnosed to date, both with a mild phenotype. HPS type 7, 8, 9 and 11 proteins interact in the BLOC-1 complex.

Genetic counseling is recommended for individuals living with HPS and their families. Each of the different HPS manifestations require specific management by specialists. As there are no medications specifically approved for HPS treatment, therapy is symptom based and supportive only, and often includes medications approved for different indications. In addition, most individuals living with HPS require many tools and adaptations for daily living and are described more fully in this report.

### Meeting summary

The Hermansky-Pudlak Syndrome (HPS) Externally-Led Patient Focused Drug Development (EL-PFDD) meeting was held virtually on June 10, 2022. The meeting represented an important opportunity for the HPS community to come together to support one another and share the patient perspectives on the challenges and unmet treatment needs of those living with HPS with FDA staff and others. To ensure that as many of our HPS community could participate as possible, a live stream of the meeting was simultaneously available in both English and Spanish on the day of the event (in real time).

The HPS EL-PFDD meeting was co-moderated by Larry Bauer, RN, MA and by James Valentine, JD, MHS. Donna Appell, the Executive Director and Founder of the HPS Network, welcomed all HPS community members and guests to the meeting and provided a brief introduction to the disorder. Dr. Wilson Bryan, Director of the Office of Tissues and Advanced Therapies, from the FDA Center for Biologics Evaluation and Research (CBER) provided his perspectives on patient-focused drug development and its importance to the FDA. He emphasized how HPS is a truly rare disorder and encouraged all meeting attendees to provide input about HPS to expand the FDA's understanding of the disorder and to inform drug development and review. William A. Gahl, MD, PhD, Senior Investigator, National Human Genome Research Institute; Head, Section on Human Biochemical Genetics, Medical Genetics Branch; Director, Undiagnosed Diseases Program, National Institutes of Health, provided an overview of HPS disease epidemiology, describing the subtypes and the symptomatology. Key points from Dr. Gahl's presentation are summarized in the clinical overview on the previous page.

Online polling was used to determine the demographics of the meeting attendees and are in **Appendix 1**. Almost half of the meeting participants who participated in polling live in the US on the Eastern time zone, with representation from US Central, Pacific and Mountain time zones. Puerto Rico was well represented as was Canada and Europe. More than two-thirds of the individuals living with HPS were female, almost a third were male and 4% identified as non-binary or other. Meeting attendees spanned all age ranges, with most falling in the 31-to-50-year age range, followed by similar numbers in the 19 to 30 years, the 0–5-year and 51 year and over age ranges. Only small numbers of participants fell in the 6–18-year age range or were over the age of 71 years. Almost three-quarters of individuals living with HPS represented by the polls have a diagnosis of HPS type 1 or 4, and almost a quarter have HPS types 2, 3, 5 or 6. A small proportion of those represented have a clinical diagnosis of HPS, but no genetic diagnosis. Individuals living with HPS types 7,8, 9, 10 or 11 were not represented in the online polling.

James Valentine provided an overview of the meeting structure and encouraged individuals living with HPS to contribute to the dialogue via online polling, calling in by phone, and contributing written comments using the online portal. The HPS EL-PFDD meeting was structured around two key topics. Session 1 was *Living with HPS: Symptoms and Daily Impacts*, and session 2 was *HPS Current and Future Approaches to Treatment*. The meeting agenda is in **Appendix 2**, and questions provided for meeting discussion are in **Appendix 3**.

The morning session continued with presentations from patients who were selected to represent a range of individuals living with HPS. James Valentine moderated a discussion between several people living with HPS who served on a live Zoom panel as well as several individuals who dialed in by phone. As so many of the individuals living with this disorder are from Puerto Rico, their voices and perspectives were specifically included via video recordings from individuals on the island of Puerto Rico living with HPS, who described their experiences and challenges. In addition, Hilda Cardona moderated a live Participation Event in Aguadilla, Puerto Rico concurrently with the live EL-PFDD event. Relevant comments entered through an online submission portal were read by Larry Bauer. This was done to allow HPS members with limited internet connectivity on the island to participate. The names of all panelists and callers are listed in **Appendix 4**.

The afternoon session opened with a presentation from Dr. Bernadette Gochuico, an attending pulmonologist at the National Human Genome Research Institute, NIH. She provided a description of current treatment approaches and an overview of the future treatment pipeline. This was followed by a pre-recorded panel of patients who described different medical therapies and non-medical approaches they have used to address their HPS symptoms. After more online polling, James Valentine moderated a discussion including a live Zoom panel and people who dialed in by phone. Again, Hilda Cardona provided feedback from the live

Participation Event in Aguadilla, Puerto Rico. At the end of the meeting, Becky Nieves provided a reflective summary of the key meeting messages and Donna Appell concluded the meeting by thanking all the participants and attendees.

Online polling results from Session 1 and 2 are included in **Appendices 5** and **6**, respectively. To include as many voices as possible, the 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 an accompanying PDF, which is available with the report.

This *Voice of the Patient* report is provided to all HPS 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, the submitted comments, and a video of the meeting can be found at <https://www.hpsnetwork.org/el-pfdd/>. According to YouTube statistics, the meeting has been viewed over 500 times in English and Spanish, as of January 12, 2023.

## Session 1: HPS Symptoms & Daily Impacts

### Key messages from Session 1

#### **HPS symptoms are often minimized, dismissed or misdiagnosed.**

*“You must have bled so much because of stress.”* Patrice’s symptoms and experiences were dismissed by acquaintances, teachers, family, friends, and even physicians. *“After I got diagnosed, it became, ‘What’s that? How do you spell it? You’re not an albino.’”* – Patrice, 56 years old, living with HPS type 3

*“I went to my primary care physician, told them that I possibly have [HPS], and they said, ‘No, no. You don’t have that,’ and I let it go.”* - Noel, 48 years old, living with HPS-1

When Donna’s daughter was first diagnosed, *“We felt so alone being told over and over again that **they never saw anything like her and never heard of HPS.** If they had, she would’ve been promptly receiving the treatment that she needed.”* - Donna, parent and caregiver of individual living with HPS type 1

**Diagnoses are often delayed.** Access to care can delay a diagnosis of HPS. Some individuals have difficulty obtaining genetic testing and counseling in a timely fashion. Also, comprehensive care can be affected by the fact that some patients are not followed by a single attending physician and instead are seen in clinics by multiple physicians including residents and fellows.

*“We were told that it would be a mild bleeding disorder and not too much to be concerned about. 14 months later, **my baby hemorrhaged so severely** from a GI bleed that she sustained a **hypoxic traumatic brain injury.** She was two. Many of her developmental milestones were lost.”* - Donna, parent and caregiver of individual living with HPS type 1

#### **Many physicians don’t know about the disease, creating diagnostic and treatment barriers.**

*“I have a lot of doctors who I see only annually and for some reason they seem to not remember every single year what my condition is. I have to go through the whole HPS 101, which, if you’re feeling well, is fine but if **you’re in a position where you really need to advocate for yourself,** it can be really challenging. Especially if you’re unable to, if you’re incapacitated or something along those lines.”* Kelly’s partner had to communicate on her behalf when she went into anaphylaxis. - Kelly, 32 years old, living with HPS type 1

*“**I’m educating the doctor** on a condition that I know more of than they do and then telling them or explaining how the fibrosis is different for an HPS patient than maybe someone else that they have dealt with.”* - Noel, 48 years old, living with HPS-1

*“We have problems with doctors that **many do not know our condition well and our life is in their hands**. A misdiagnosis or misprescribed medicine can be fatal for us.” – Marilett (Puerto Rico), comment submitted online*

*“The **lack of knowledge among the medical community** when you mention you have HPS Syndrome, some physicians just start reading about it in front of you.” - Oscar A, comment submitted online*

**While each HPS-related manifestation is challenging, the combination of symptoms can be life-threatening.** Because of blood clotting issues, any minor surgery becomes a major surgery. When patients receive platelets to stop bleeding, they increase the risk of developing antibodies that may exclude them from lung transplantation later.

*“Living with HPS is overwhelming. **I live under the shadow of uncertainty**. I don't know if the doctors will be able to control the bleeding during thyroid surgery, or if they will find a compatible donor for lung transplant before I stop breathing. And I still doubt I will be able to wake up from such a complicated procedure. **HPS is a multi-organ disease and needs to be attacked on several fronts**.” - Leslie (Puerto Rico), living with HPS type 1*

*“I had a heart attack ...and on the way to the hospital, I wasn't thinking, ‘Will I survive the heart attack?’ I was thinking, ‘**Will I bleed to death** if they don't know that I have HPS and don't get the platelets?’” - Jill, living with HPS type 5*

Individuals living with HPS experience many worries. Top worries are related to developing pulmonary fibrosis, HPS progression, bleeding issues, and premature death. Poll respondents used online polling to select their top three worries about their or their loved ones condition in the future. Poll results are presented in **Appendix 5, Q1** and illustrated with patient comments below.

### ***Developing pulmonary fibrosis***

Developing pulmonary fibrosis was the top worry, selected by 59% of poll respondents. This percentage would likely be higher if only adults with HPS were polled. There are no medications or treatments to pulmonary fibrosis. Worries about developing pulmonary fibrosis include many other worries: **the need of a lung transplant** was the second top worry, selected by 50% of poll respondents; **premature death from pulmonary fibrosis** was the third top worry, selected by 46% of poll respondents; **developing antibodies that could complicate future transplants** was selected by 19% of poll respondents as one of their top three worries.

*“The most significant concern is **predicting and preparing for pulmonary fibrosis onset**.” – Richard, comment submitted online*

*“On my worst days its thinking about my future **knowing pulmonary fibrosis very well might be in my future** and the anxiety, fear, and guilt that comes with it, especially*

*being 36 years old and about to get married and hoping to one day have children.” – Eric, comment submitted online*

*“**Developing pulmonary fibrosis is one of my greatest fears.** Not being able to pursue my passion of singing as well as my goals for the future.” - Crystal, identical twin living with HPS type 4*

*“We know that **HPS type one leads to pulmonary fibrosis a hundred percent of the time** and that's my gene. As I am getting older, I think about it all the time and I'm afraid of what's coming next. - Ashley, 35 years old, living with HPS type 1*

*“As a parent I have to think about two of my children develop... they both have HPS 1, which is **guaranteed to develop the pulmonary fibrosis.** ... You just don't know when. So you feel like it's a little bit of a ticking time bomb. We don't know when these things are going to happen. That's very scary for our family to think about what their picture looks like.” - Kristen, parent of 15- and 5-year-old daughters, both living with HPS type 1*

*“Knowing that my beautiful, loving, full of sunshine 7-year-old daughter will develop pulmonary fibrosis and that **a lung transplant is in her future** is our biggest concern. Better treatment options are needed TODAY to save her!” – Briana, comment submitted online*

*“We have to think about their lung health all the time and being aware what they're around. If there's smoke around, ... especially with COVID, we had to keep them very safe because we did not know what that would do to their lungs. So there's a whole other level of worry, even though it's in the future, we have to think about **every move we make today could impact the onset of the pulmonary fibrosis.**” - Kristen, parent of 15- and 5-year-old daughters, both living with HPS type 1*

### **Need of a lung transplant.**

*Carmen is, “Living with the fear that **a lung match might never come** and that **I am running out of time.** The frustration of knowing that transplant is simply re-switching one health condition for another. For me, **transplant is a temporary band-aid** and it's not enough. **I need a cure.**” - Carmen, 57 years old, living with HPS type 1*

*“Being a candidate for a **bilateral transplant** is a constant concern because it implies **moving from our country.**” – Jose (Puerto Rico), caregiver, comment submitted online*

*There are even more worries after receiving a lung transplant. “My latest fear is the **possibility of chronic rejection**, which I will forever be on medication in hopes of preventing. I think I've handled life's curve balls pretty well. However, as I age, I find myself more anxious with each medical blow I endure and wonder if I have the stamina to jump the next hurdle.” - Karen, 58 years old, living with HPS type 1, lung transplant recipient*



## Premature death.

*“The possibility of having pulmonary fibrosis in the future, it's a big concern. It's on the top of my head recently because **we recently lost a girl that's just my age**. And she lost her battle with the fibrosis recently. And she wasn't a candidate for a transplant. ... The possibility of that happening is terrifying.”* – Angeliz (Puerto Rico), 30 years old, living with HPS type 1

*“Not only I have to deal with the intensity of the symptoms of the fibrosis of HPS, but I have to deal with the losses that come with having this syndrome. Since I started volunteering for the HPS Network, **I have seen over 25 of my fellow HPS [community members] who have passed away**. Some acquaintances, some good friends. 10 over the span of one year, sometimes is hard to keep hope.”* - Carmen, 57 years old, living with HPS type 1

## Developing antibodies that could complicate future transplants.

*“The most significant downside to treating the bleeding disorder with platelet transfusions is the **risk of adding antibodies that will prevent a double lung transplant later on**. We have been told HLA matched platelets are too hard to find and have had to fight to convince blood doctors that they are a necessity, unless in emergency situations.”* – Bethany, comment submitted online

## *The stress of not knowing how HPS will progress*

The stress of not knowing how or when HPS will progress was selected by 38% of poll respondents as one of their top three worries.

*“My biggest worries are **my symptoms are getting worse** because I'm only 30 years old and I already really feel like I'm in a very strict diet, my bones are starting to hurt, I almost feel like I'm an old man and I'm only 30 so I don't know what's going to happen in the future.”* - Abdiel (Puerto Rico), 30 years old, living with HPS type 1

*“One of the hardest things for me is me being 15 and not knowing where my future holds and **how fast things will progress and when I will need a lung transplant** and when to expect it's coming.”* – Kylee, 15 years old, living with HPS type 1

*“My top worry is just the **unknown around how the disease would progress**.”* – Kelly, 32 years old, living with HPS type 1

*“It's an unknown how fast it will happen or how slow it will happen. We just don't know.”* – Jill, living with HPS type 5

## Individuals with HPS also worry about whether the treatment for one symptom will impact eligibility for future therapies.

*"Since this is a multisystem disorder, different things are being treated. With the bowel disease and ... the bleeding issues, there's treatments that we might be choosing to do now, because that's at the forefront, the main issue. But we also have to worry, **is that going to impact their eligibility in the future to get a treatment or get a lung transplant?** So it weighs on you very heavy."* - Kristen, parent of 15- and 5-year-old daughters, both living with HPS type 1

*"I also learned that I should only receive HLA platelets so as not to accumulate antibodies, that could make it **difficult to find a donor**. This causes me great concern as I have received several platelet transfusions throughout my life. Most were single donor transfusions as **obtaining an HLA match in Puerto Rico has been impossible.**"* - Leslie (Puerto Rico), living with HPS type 1

### **Parents of children living with HPS expressed worries about their children especially.**

Hilda Cardona reported that parents of children living with HPS in Puerto Rico, *"Would love to have **a normal life for their children**. At home, at school, and to out with friends."*

*"Our two-year-old son was diagnosed with HPS when he was four months old. With this diagnosis came many fears: The fear that **our child might be legally blind**, the fear that his platelet dysfunction would put him at a much higher risk when doing daily activities. The fear of him being bullied for his glasses, his pale skin, his differences. The fear that **he might face pain and hospitalization** due to debilitating colitis. The fear that **his lungs might eventually give out on him**, and he will need a life-saving double transplant. This fear is too scary to dwell on for too long."* - Beth, comment submitted online

*"It is a **constant state of worry and preventive measures** -- as a parent you persistently question if you are doing or have done enough for your children's health."* – Rick, comment submitted online

### **Bleeding issues**

Bleeding issues were selected by 26% of poll respondents as one of their top three worries.

*"It's a challenge when you need to have surgery or any medical procedure because doctors are afraid of any bleeding that might occur. In reality, **you don't know if heavy bleeding may happen**. It's kind of a box of surprise."* – Christina (Puerto Rico), comment submitted online

*"I want to get pregnant. I want to have a baby in the near future, but I'm very worried about having bleeding complications upon giving birth. So that's scary knowing that if you decide to go through that process, **you can lose your life or get treated by people that not necessarily know how to treat our disorder.**"* - Angeliz (Puerto Rico), 30 years old, living with HPS type 1

### **Getting skin cancer**

Getting skin cancer was selected by 18% of poll respondents as one of their top three worries. This is particularly worrisome as having skin cancer will exclude people with HPS from qualifying for a lung transplant in the future.

*“It would be nice to be able to be outside without worrying about the sun exposure as much the **risk of skin cancer** and that sort of thing.”* - Kelly, 32 years old, living with HPS type 1

*“We have a double whammy, we have albinism so we don't have the pigmentation protection from the sun but we're also on immunosuppressants which makes us even **more susceptible to skin cancers and other cancers**, by the way.”* - Nancy, 63 years old, living with HPS type 1, double lung transplant recipient

### **Legal blindness**

Legal blindness was selected by 18% of poll respondents as one of their top three worries and was related to losing their independence.

*“I fear **losing more eyesight** and becoming even more dependent on others. I'm afraid of the next time I need a procedure or surgery, who will do it? Will they be able to stop the bleeding? Will they hurt me in the process of stopping the bleeding? I pray one day for a treatment or a cure.”* - Patrice, 56 years old, living with HPS type 3

### **Developing colitis, need of an ostomy and/or surgical removal of part of your colon**

Developing colitis or Inflammatory Bowel Disease was selected by 9% of poll respondents as one of their top three worries. Need of an ostomy and/or surgical removal of part of your colon was selected by 7% of poll respondents as one of their top three worries.

*“We worry about limitations and bigger problems in the future. Everyone time she complains of stomach pain, we worry. **Is it the start of HPS-related colitis?** We worry about what it will be like when she gets her period. But most of all, **we worry about her lungs.**”* – Jessica and Alex, parents of a nine-year-old with HPS type 1, comment submitted online

### **Other worries**

Although other worries were only selected by 3% of poll respondents as one of their top three worries, individuals living with HPS and their caregivers expressed many other worries during the meeting and in the written comments.

**Worries about safety.** These worries were mostly related to challenges with visual impairment and caring for those living with HPS.

*“I just wanted to add to the point about **safety concerns around food and the visual impairment**. I actually have a very severe tree nut and shellfish allergy. So I have a lot of concerns around especially things like buffets and that sort of thing. I can navigate labels decently well, but food that I don't know how it's been prepared or if **I can't read the menu or see what's going on with the food**. I actually went into anaphylaxis and almost died in February because I didn't have the proper knowledge of what was in the dressing of a salad that I'd had.”* - Kelly, 32 years old, living with HPS type 1

*“As a grandparent and sometimes caregiver to two young, active, daredevil grandchildren with HPS1 it's always a little concerning when **accidents happen with bleeding**.”* – Stephanie, comment submitted online

Beth's son is only two years old, so she worries that caregivers or emergency personnel will have the information that they need. She is, *“Trying to act precautionary and [by] making sure his daycare providers have an idea of **what to do if the bleeding happens** or making sure they're **putting sunscreen on him** every time they go outside. ... The fears of getting in a car accident and not being able to communicate that he has HPS. So trying to put tags on his car seat or trying to put things so people could maybe... To **flag that he has a medical disorder so they could treat him if they needed to for that platelet dysfunction**.”*- Beth (caller), parent of a child with HPS type 1

**Worries about obtaining medical treatment.** Many individuals living with HPS worry about their inability to access treatments. There are no treatments available for pulmonary fibrosis.

*“What frustrates me most is the **difficulty in getting treatment for bleeding and gastrointestinal problems**, but what worries me most is the **lack of treatment for pulmonary fibrosis**.”* – Milagros (Puerto Rico), 56 years old, living with HPS type 1

*“It is worrying for a patient with HPS to go to a doctor and that doctor does not know anything about what the syndrome is. Your health and your life depend on the special treatment you need and **what will happen if the doctor doesn't know?**”* – Leida (Puerto Rico), comment submitted online

Kelly worries about, *“Receiving the right medical care at the right time. And **having doctors that care enough to find out about the condition** and remember the condition. That sort of thing that in my experience, it's been relatively rare.”* – Kelly, 32 years old, living with HPS type 1

*“I also worry about **getting rides to medical appointments** should something happen to my husband.”* – Karen, 58 years old, living with HPS type 1, lung transplant recipient

**Worries about how HPS will impact other family members.**

*“The one future worries question option that wasn't there is the fear of the **impact on your kids of your premature dying will have**. I think of not just my kids but my friend*

*Matt's kids since he passed away from the lung fibrosis in 2016.” – Ryan, comment submitted online*

*“The hardest part of living with HPS is the legal blindness. I have two children and being divorced, I live with the fact that **my kids couldn't participate in events because I wasn't able to get them to places.** I will live with this guilt all my life. There have been many times that my kids resented me. As they get older they understand more but it is still a hard issue to deal with.” – Caryn, comment submitted online*

### ***For those with HPS type 2 - Getting recurring infections***

Getting recurring infections (HPS 2) was selected by 1% of poll respondents as one of their top three worries.

Although symptoms manifest differently from one person to the next, most individuals living with HPS experience multiple HPS-related manifestations, the three most troublesome being blood clotting, legal blindness, and pulmonary fibrosis.

Meeting attendees used online polling to first select all of the HPS-related manifestations that they or their loved ones ever had, and then were asked to select the three most troublesome. Poll results are presented in **Appendix 5, Q2 & Q3** and described in the sections below. HPS is characterized by a very high number of health concerns, with poll respondents each selecting 7.4 symptoms on average. Albinism, visual sensitivity to light, skin sensitivity to sunlight and blood clotting issues, low vision and involuntary eye movements were all selected by the majority of meeting participants. However, symptoms can be heterogeneous, as illustrated by the differing symptoms of Candice and Crystal, identical twins living with HPS type 4. Blood clotting issues and legal blindness were selected as the two most troublesome HPS-related health concerns, followed by pulmonary fibrosis.

### ***Blood clotting issues***

Blood clotting issues, including bruising and prolonged bleeding, is experienced by 90% of poll respondents, and were selected as a top health concern by 66% of poll respondents. Meeting participants experienced horrible bleeding episodes and hemorrhaging as a result of menstruation, nosebleeds, surgery, and colitis. For some, excessive bleeding impacted their mental health.

#### **Many experienced bruising.**

*“My parents began to notice many **bruises**, but they thought since I was legally blind, I just ran into things, and my doctor agreed.” – Karen, 58 years old, living with HPS type 1, lung transplant recipient*

### Menstrual bleeding is severe.

*“At the age of 10, I had my first menstruation. ... **My bleeding each day became more intense.** After days and weeks, I had not finished my period, every day I felt my body more exhausted than normal. I filled my pad (Kotex) every 30 minutes. The time came when **I passed out in my mom's arms.**” - Chrisyeily (Puerto Rico), living with HPS type 1, comment submitted online*

*“At 12 years old, I started my period and **I bled for a year straight, soaking pads every hour.**” After being given excessive amounts of hormonal birth control pills, “**My bleeding didn't stop or slow down. It took a huge toll on my body. I was always extra tired,** missing out on school days and wrapped up in weeks' worth of make-up work to get through middle school. **This was one of the hardest times of my life.**” - Christina, 21 years old, living with HPS type 3*

### Post-surgical bleeding can be uncontrollable.

*“When I was 16, **I couldn't stop bleeding after having my wisdom tooth out,** and I wound up in the hospital for eight days and needed a **blood transfusion.** That stopped the bleeding, but nobody knew why. ... I couldn't stop bleeding after a dental cleaning. The dentist assumed I had to have the tooth pulled. The oral surgeon who pulled my tooth, told me something wasn't right, **I was bleeding through my stitches.** I went back to the emergency room, this time the hematologist put it together. He saw my eyes and told me I must have Hermansky-Pudlak syndrome. That night **I woke up with blood all over me,** I looked like I got shot. My doctor put me back in the hospital, and I was there for **five days before they could stop the bleeding.**” - Patrice, 56 years old, living with HPS type 3*

### Bleeding can potentially be catastrophic.

*“At two years old, my parents heard me whimper in my crib and they found that **I was hemorrhaging from a GI bleed** that was very severe. They rushed me to the emergency room. The bleeding was not stopped fast enough and due to oxygen deprivation in the brain, **I developed a traumatic brain injury.** I was in the hospital for three months.” - Ashley, 35 years old, living with HPS type 1*

### Legal blindness

Low vision is experienced by 90% of the poll respondents and was selected by 66% of poll respondents as one of their top three most troublesome health concerns. Most individuals living with HPS are legally blind. Low vision impacts driving and independence and can be disastrous when trying to read gauges on oxygen tanks.

*“Visual issues of HPS create other issues like **reading the gauges on oxygen tanks that are using the last century technology.** I'm always trying to read the gauge, to see if*

*there's **enough oxygen in my tank** for me to get to the next tank. It causes a lot of anxiety.”* - Heather K., 49 years old, living with HPS type 1, single lung transplant recipient

### **Pulmonary fibrosis**

Pulmonary fibrosis is one of the top three most troublesome HPS-related health concerns, as selected by 39% of respondents. Pulmonary fibrosis is experienced by 29% of those represented by the poll results. Some community members coughed and visibly struggled to breathe during the meeting, but still found it important enough to attend to provide their testimony.

A first symptom is often a shortness of breath, which is sometimes misdiagnosed as allergies. Some develop a continuous cough. Symptoms eventually progress, and individuals eventually require oxygen supplementation, then continual oxygen. They can do less and less until their only option is a lung transplant. Lung transplant creates another set of chronic health concerns.

*“My **pulmonary fibrosis** is in a really early stage, so right now, it doesn't prevent me from teaching, singing in a choir, commuting, cooking, and doing my daily activities but my pulmonologist recommended the treatment to maintain that quality of life that I have.”* - Mariel, 26 years old, living with HPS type 1

*“Right now [pulmonary fibrosis has] affected me quite a bit. ...You might see that as I speak in this meeting, I'll start coughing because **the pulmonary function has decreased to 46%**.”* - Wilson (Puerto Rico), living with HPS type 1

*“Another symptom I have developed is **shortness of breath. I choke at night, tiredness, fatigue, and severe coughing fits with phlegm.**”* — Milagros (Puerto Rico), 56 years old, living with HPS type 1

*“The **cough from the fibrosis has affected the quality of our sleep** for both of us. The worst day is when **she chokes on a cough** when drinking water or eating.”*— Jose (Puerto Rico), caregiver, comment submitted online

*“The worst days **I can barely breathe, leave my bed and need medication to calm down the coughing fits.**”* – Lenis (Puerto Rico), comment submitted online

*“**Living with pulmonary fibrosis is very difficult.** It affects our family life, our social life, our work lives, we deteriorate to the point that **there's not a whole lot we can do.** But if we're lucky, move from one room to the other within our homes before **we really can't do anything at all.**”* - Nancy, 63 years old, living with HPS type 1, double lung transplant recipient

### **Colitis or inflammatory bowel disease**

Colitis or inflammatory bowel disease (IBD) or HPS Crohn's-like colitis is experienced by 30% of those represented by the poll results and was selected by 26% of respondents as one of their top three most troublesome. Many individuals living with HPS experience this symptom in

childhood and described abdominal pain, nausea, and bloody diarrhea. Symptoms can be extreme, requiring hospitalization.

Hilda Cardona summarized the feedback from individuals attending the Participation Event in Puerto Rico. *“The daily difficulties: most of them have reported colitis. The biggest problem is **bleeding and diarrhea** they have all the time. ... Several of them have been **hospitalized for a long time due to the colitis.**”* Hilda Cardona expressed how hard life is for parents whose young children have HPS, as their children are unable to participate in life because of the colitis-related bleeding.

*“Suffering with IBD can be very debilitating and painful. I have **anal fistulas and fissures** and there are days when they swell up so much that just sitting or standing causes me a great deal of **discomfort and pain.**”* During a recent GI flare, Candice experienced, *“Running high fevers three times a day, very tired, **struggling with severe stomach pain and diarrhea as well as bleeding from my colon.**”* – Candice, identical twin living with HPS type 4

*“From the age of five, I started having gastrointestinal symptoms with bleeding. One day, suddenly, I started **vomiting and bloody diarrhea**, which was treated as a virus, but I was not getting better and I lost weight. Finally, after three weeks, I was diagnosed.”* – Milagros (Puerto Rico), 56 years old, living with HPS type 1

*“A worst day would be not being able to go to school or to dance because the **crampiness is so bad.** And I just need to be in bed with like a heating pad.”* - Kylee, 15 years old, living with HPS type 1

### **Nausea and GI flareups lead to appetite loss resulting in weakness and weight loss.**

*“I often do not feel like eating during these GI flareups and so my weight takes a dip. This causes my body to be **very weak, which prolongs my recovery.**”* - Candice, identical twin living with HPS type 4

Blood loss and GI flareups led to weakness and weight loss for Kristen’s daughter. *“She got so **weak because of [the blood loss] from the low iron**, but also her **lack of interest in eating** because she knew if she would eat, she would feel sick. She just declined so quickly, **she lost almost 20 pounds.** It was pretty scary.”* - Kristen, parent of 15- and 5-year-old daughters, both living with HPS type 1

*“Because of [IBD], I have **struggled with weight gain** as long as I can remember, ... I've been admitted to the hospital because I've been **underweight.**”* Samantha’s IBD sometimes flares up and she experiences severe appetite loss. *“It gets frustrating sometimes. ... My doctors don't want me to lose weight because it's never a good thing, but sometimes **it's out of my control.**”* - Samantha (caller), 21 years old, living with HPS type 1



**Some experience the daily horror of seeing blood in the toilet bowl.**

*“Even though I bled often and had many blood transfusions, I have never gotten used to seeing **blood in the toilet, it’s a sight that has always frightened us.** It makes me wonder if it can be stopped in time before something bad happens again.” - Ashley, 35 years old, living with HPS type 1*

**Many suffer with secondary symptoms of colitis including joint and skin inflammation, including hidradenitis suppurativa, a chronic inflammatory skin disease.**

*Kristen’s daughter’s inflammation, “Was very unexpected. We knew the bowel disease was a possibility but these parts of it were shocking to us. ... Her **legs would swell and cause her a lot of pain.** So, that was part of the reason that she wouldn't want to get up and move around. It was just this inflammation. So, it's **not just in the bowel, it affected her whole body, and she even lost a bunch of hair** and everything because of it.” - Kristen, parent of 15- and 5-year-old daughters, both living with HPS type 1*

*“I have extra-intestinal manifestations of the IBD unfortunately in my vulva. It is **very painful, and I get sores and lesions** and it was very difficult to diagnose.” Cassandra hoped that having her colon removed would resolve the issue. “It flared right back up a few years after my total colectomy.” - Cassandra, 24 years old, living with HPS type 1*

*Before Kelly’s HPS-related Crohn’s disease was treated, “I had really **bad joint pains, especially in the knees and in the ankles.**” - Kelly, 32 years old, living with HPS type 1*

### **Albinism**

Albinism is a manifestation of the disease that is associated with low vision, photophobia, and skin sensitivity to sunlight. Albinism is the most frequent HPS-related health concern experienced, selected by 96% of poll respondents. Albinism was selected by 26% of respondents as their top three most troublesome, but there were few comments about albinism specifically.

### **Visual sensitivity to light or photophobia**

Visual sensitivity to light is the second most frequent HPS-related health concern, experienced by 94% of poll respondents and was selected by 19% of poll respondents as one of the three most troublesome HPS-related health concerns.

*Despite having darker, brownish hazel eyes, Casey said, “**I can barely open my eyes at all.** Even with sunglasses, they're completely closed usually when I'm outside. ...I know it's nothing compared to lung disease or Crohn's but [light sensitivity] does really affect my life and **I get very bad headaches and fatigue** and I have a hard time being outside. And even when I go outside just to walk my dog, the **sunlight basically completely blinds***

*me where I can't see anything that I'm doing and so even with sunglasses, it's really hard for me to function.” - Casey (caller), living with HPS type 3*

*“**She can't go outside** for walks in the stroller without a full canopy coverage, in addition to a sun hat and sunglasses, because **she just cannot open her eyes to the light.**” – Christine, parent of a daughter, age one with HPS, comment submitted online*

### **Anxiety or depression**

Anxiety or depression is experienced by 41% of those represented by the poll results and was selected by 12% of respondents as one of their top three most troublesome. Anxiety can be a daily occurrence as individuals living with HPS navigate a life of uncertainty. Some experience a life of isolation and mental health challenges.

Heather’s visual impairment causes her anxiety and impacts her ability to socialize.

*“Having those anxieties and having it lead to **depression related to the visual impairment and the isolation.**” - Heather W., age 31, living with HPS type 4*

*“I need a double lung transplant. When it comes to coping, I don’t know if I cope or not. **This is the only life I know, and I can’t give up.** I am really stubborn like that. I rather keep going. At some point I know I will need a lot of therapy to come to terms with all this trauma, but **until then I just keep going.**” – Lenis (Puerto Rico), comment submitted online*

*“For years, I suffered from **serious mental illness.** Because of the amount of bleeding and hormones I was given to stop it, **my teenage years were extremely negative.** I missed so much school and always felt myself in a battle with a choice to use hormonal birth controls, such as an IUD that would give my body a break from the bleeding or to let myself be more centered and not so depressed all the time. This was a serious battle to face as a young teenage girl. ... The older I have gotten the more of these things have caused me **emotional and physical pain and hardship.**” - Christina, 21 years old, living with HPS type 3*

**HPS-related mental health challenges can be extreme.** At the meeting we learned that one of the HPS community members who was scheduled to present at the meeting, had tried to take her own life several weeks prior to the event, but was recovering.

*“Although I love myself for who I am and I wake up and I try to do my best every day, I do know for a fact that **if I did not have this condition, many things would've been so much easier on me, both mentally and physically throughout my 21 years of life.**” - Christina, 21 years old, living with HPS type 3*

### **Skin sensitivity to sunlight and skin cancer**

Skin sensitivity to sunlight results from hypopigmentation and is the third most frequent HPS-related health concern, experienced by 94% of poll respondent. This was selected by 16% of

respondents as their top three most troublesome. Skin sensitivity can lead to skin cancer, which is experienced by 24% of those represented by the poll results and was selected by 8% of respondents as one of their top three most troublesome.

### ***Compromised immune system in those with HPS type 2***

A compromised immune system is a distinct characteristic of HPS type 2, resulting in profound neutropenia and infections and illnesses. Many with lung transplants also experience immune suppression because of the side effects of anti-rejection medications, as do those who are receiving biologics for colitis. During the polling, 17% of those represented by the poll results selected this health concern and 5% of respondents selected this as one of their top three most troublesome.

### ***Additional HPS-related health concerns included in the polls***

Involuntary eye movements (nystagmus), heart and kidney problems and crossed eyes (strabismus) are experienced by many individuals, as indicated in the polling results.

**Involuntary eye movements** are experienced by 86% of those represented by the poll results and was selected by 8% of respondents as one of their top three most troublesome.

**Crossed eyes** are experienced by 20% of those represented by the poll results and was selected by 1% of respondents as one of their top three most troublesome.

**Heart problems** are experienced by 10% of those represented by the poll results and was selected by 3% of respondents as one of their top three most troublesome.

**Kidney problems** are experienced by 10% of those represented by the poll results and was selected by 3% of respondents as one of their top three most troublesome.

*“My kidneys have to be monitored because of the beginnings of **chronic kidney disease**. When I was young, I went into **total renal failure**, which resolved, but I always have blood and protein in my urine. At age 15, HPS even complicated **kidney stones**. Because of the bleeding issues lithotripsy couldn't be done and I had to have a ureter laser to get the stone out because I was bleeding so much.” - Ashley, 35 years old, living with HPS type 1*

### ***Other HPS-related health concerns not represented in the polls***

A total of 14% of those represented by the poll results experienced other HPS-related health concerns not listed as one of the poll response options, and 1% of poll respondents indicated that these are one of their top three most troublesome. These include traumatic injuries, hospitalizations, fatigue, other digestive issues and asthma, described below. Meeting participants also experience cataracts, multiple hospitalizations from GI flareups, infections and asthma. Many HPS-related health concerns including osteoporosis, adrenal insufficiency and dizziness occur as side effect of medications used to treat the symptoms of HPS.

### Traumatic injuries from uncontrolled bleeding.

*“Traumatic brain injuries are not typically associated with HPS, but it was a direct result of the lack of HPS information and because the disease is so rare. ...I have **trouble managing time** and have **trouble with memory and executive functioning.**” - Ashley, 35 years old, living with HPS type 1*

*“I am legally blind. When I was 14 years old. I accidentally fell face first to the ground and had **severe bleeding from my nose and mouth.** I ended up so weak that I **lost consciousness several times.**” - Leslie (Puerto Rico), living with HPS type 1*

**Hospitalizations.** Individuals living with HPS are frequently hospitalized for prolonged periods.

*“I’ve been on a **vent in the ICU three times in the last 12 months.**” – Heather K., 49 years old, living with HPS type 1, single lung transplant recipient*

**Fatigue.** Many different things contribute to HPS-related fatigue.

*“A bad day is when I have episodes of GI, cough, fatigue, tiredness, pain, **they don't let me do my daily activities.**” – Milagros (Puerto Rico), 56 years old, living with HPS type 1*

*“On my worst days it's a challenge because it's **extremely hard to have energy when you're anemic** from heavy bleeding from menstruation.” – Amber, comment submitted online*

**Other digestive issues.** This includes difficulty eating, choking and acid reflex.

*“My **acid reflux** has been severe and has **affected my vocal chords** to the point of having laryngitis. It is an ongoing battle and makes it challenging, especially because I am a vocalist. - Crystal, identical twin living with HPS type 4*

**Asthma.**

*“**My breathing is affected.** I have asthma. When I was little I was also in the hospital a lot because of asthma.” - Abdiel (Puerto Rico), 30 years old, living with HPS type 1*

*“Living with asthma can be difficult on some days. I experience **wheezing and shortness of breath** that comes and goes accompanied by a **dry cough.** It can make it hard to accomplish activities such as talking, singing, and working out. Certain chemicals and scents such as cleaning agents, colognes and perfumes trigger that **tight feeling in my chest.**” - Crystal, identical twin living with HPS type 4*

*“There are days when my **chest feels so tight** that I can't draw in a complete breath. It limits my ability to do physical exercise or practice my music because **I have to stop and take breaths periodically** or stop and take breaks periodically. I also feel at times as*

*though I am **gasping for air and cannot fully complete sentences** while speaking with family and friends.” – Candice, identical twin living with HPS type 4*

Driving was selected as the top specific activity of daily life that individuals living with HPS are unable to do.

*“Specific activities impacted by HPS on a daily basis: **not able to drive, read small print, enjoy a normal beach or camping day and the need for medication preparation, platelet administration, for certain medical procedures or surgeries.** Even dental procedures.” – Oscar A, comment submitted online*

Poll respondents used online polling to select their top three activities of daily life that are most important to them or their loved one struggles with due to HPS. Poll results are presented in **Appendix 5, Q4** and illustrated with patient comments below.

### **Driving**

Driving was the top specific activity of daily life impacted by HPS, selected by 78% of the individuals represented by the poll results. The inability to drive severely impacts their independence, ability to attend medical appointments and manage their medications. It also impacts their ability to work and socialize. Many have fought to retain their driver’s licenses and have very limited conditions under which they can drive.

#### **The inability to drive impacts independence.**

*“Most of my daily activities are impacted by driving most significantly due to the **inability to get to and from doctor's appointments or feeling as though I'm a burden on the person who will be providing transportation for me to those activities.**” - Heather W., age 31, living with HPS type*

*“**Not being able to drive** in Puerto Rico makes you **dependent on other people** due to the limitation of public transportation in the Island. Many people with HPS move to the states just to gain some level of independence.” – Leslie (Puerto Rico), comment submitted online*

#### **Inability to drive prevents individuals living with HPS from attending medical appointments and managing medications**

*“The number one thing that **I wish I could do is drive.** For me this is a matter of **independence**, and it would mean that I could **complete simple errands and get to medical appointments** myself.” – Esdi, comment submitted online*

### **Pulmonary fibrosis and bleeding interferes with recreational activities or exercise**

Participating in sports, recreational activities or exercise was the second most frequently selected activity of daily life they are unable to do or struggle with due to HPS. This was selected by 39% of the individuals represented by the poll results and generated many comments as pulmonary fibrosis, asthma, the risk of bleeding, and joint pain and swelling,

vision impairment and sun sensitivity all impact movement and exercise. Many have had to modify their activities as symptoms progressed.

*“The fibrosis **does not allow me to exercise, limits my breathing** to the extent that many things are happening.”* When Wilson was first diagnosed, the symptoms were minimal. *“As time has been going by, it has been **getting worse** in a sense where I have **less endurance** when I exercise, when I walk, when I do my tasks at work.”* - Wilson (Puerto Rico), living with HPS type 1

*“I have always been an active person, love swimming, dancing and being active. Because of HPS I **never could play sports with my friends** at school, I currently **can’t move without oxygen assistance** and can’t really leave the house anymore.”* – Lenis (Puerto Rico), comment submitted

*Due to her asthma, “Oftentimes I had to **leave my dance class to use my inhaler. Wheezing, chest tightness, and feeling short of breath** were a constant struggle. Any involvement in sports and dance seemed to result in wheezing.”* - Crystal, identical twin living with HPS type 4

Kelly’s activities are limited due to Crohn’s-related joint pain. *“I’m very active. I like to run and hike ... but I’ve noticed over the last couple of years, especially that my **knees and ankles aren’t recovering** the way that they used to.”* - Kelly, 32 years old, living with HPS type 1

*“She’s expressed an interest in learning karate, but **she can’t do contact sports** due to her platelet disorder. She wants to learn how to ice skate and ride horses, but the **risk of falling and getting injured** concerns us greatly. She is incredibly independent and looks forward to driving one day, but we don’t know if that can be a reality for her.”* – Jessica and Alex, parents of a nine-year-old with HPS type 1, comment submitted online

### *Spending time outdoors*

Spending time outdoors was selected by 36% of the individuals represented by the poll results, as a specific activity of daily life that is important, but they are not able to do or struggle with due to HPS. Sun sensitivity and photophobia severely limit outdoor activities, as does environmental factors like mould and dust.

*“The **sensitivity to sunlight** and the **lung disease** prevents us from doing outdoor activities. Environmental factors like the **high levels of mold and the dusts** coming from the Sahara Desert also prevent people with PF from enjoying the outdoors.”* – Leslie (Puerto Rico), comment submitted online

### *Attending school or having a job*

Attending school or having a job was selected by 33% of the individuals represented by the poll results, as a specific activity of daily life that is important, but they are not able to do or struggle

with due to HPS. Individuals living with HPS require accommodation for low vision and other eyesight-related issues, and some were even mistakenly classified as learning impaired. Several experience severe bleeding or colitis that prevented them from attending school or work.

### **Transportation to work and school is a major issue.**

*“I was offered a position I really wanted at work, but **I couldn't take it because I wasn't able to drive** to the various school districts.”– Patrice, 56 years old, living with HPS type 3*

### **Visual impairment often interferes with education and employment.**

Angela spoke on behalf of herself and her sister. *“Our school lives or academic lives, to be more general, has been impacted by us having HPS. It impacts us in the way that since **we have low vision**, well, we don't see very far. So, if there is some material from class being presented, well, **we can't see it very well.**” - Angela (Puerto Rico), 21 years old, living with HPS type 1*

*“Growing up with a **visual impairment** was challenging as it did restrict me in my social, physical and educational goals. It **lowered my learning and reading comprehension skills**, as my eyes had to work harder, to focus and fatigued quickly.” – Candice, identical twin living with HPS type 4*

### **Heavy bleeding can be a problem.**

*“I had to **miss many days of school, work and social obligations** because I **was bleeding too heavily** or in too much **pain** to go.” - Patrice, 56 years old, living with HPS type 3*

### **Colitis is also an issue.**

Colitis and pulmonary fibrosis impact Wilson’s employment. *“They both affect me in my daily life, in my normal routine but as well as in my work or my job, because with **colitis**, I literally **have to have a restroom next to me.**” - Wilson (Puerto Rico), living with HPS type 1*

*“My HPS symptoms started when I was nine years old, I had GI symptoms that were accompanied with **stomach pain and diarrhea**, and high fevers of 105. I was in the nurse's office many times due to **toileting accidents** at school.” – Candice, identical twin living with HPS type 4*

### **Reading**

Reading was also selected by 33% of the individuals represented by the poll results, as a specific activity of daily life that is important, but they are not able to do or struggle with due to HPS.

*“I still struggle with **straining my eyes** to read small print and even large print displays on screens. I **take longer to read books and proofread my essays.** I often stay up until*

1:00 AM trying to finish homework and assignments and have **contemplated withdrawing from my classes.**" - Christina, 21 years old, living with HPS type 3

"My low vision is an obstacle for **reading to my children**. I love to read and I want to pass this on to my children, yet it is **very frustrating having to use my magnifier** to do so. It gets in the way, **blocks the words or pictures** on the books and is distracting to my kiddos, all they want to do is hold the magnifier to help me." – Denisse, comment submitted online

### **Participating in social engagements and events**

Participating in social engagements and events was selected by 29% of the individuals represented by the poll results, as a specific activity of daily life that is important, but they are not able to do or struggle with due to HPS. Heather W., who is living with HPS type 4 described all the ways that HPS causes her anxiety in social situations as she tries to navigate an unfamiliar layout and interpret subtle social cues with her low vision and determine if she can eat the food that has been prepared. During the meeting, many described how lonely and isolated they often felt.

#### **Vital social cues are missed because of visual impairment.**

"**In social settings**, I've never realized how much things like **eye contact and certain gestures are so important**. I've always had a hard time with this. I cannot see if someone is looking at me or talking to me unless my name is called out. Many times, I've put my two cents into a conversation that wasn't directly invited to. And I've had to answer questions on why **I haven't looked someone in the eye or answered them** when they waved at me." - Christina, 21 years old, living with HPS type 3

#### **Social isolation is often related to the inability to drive.**

"Not a day goes by that I don't face the challenges from HPS, not only medically but socially. **It's difficult for me to make and maintain friendships** because I can't drive to see people. - Patrice, 56 years old, living with HPS type 3

"**Lack of driving** impacts how close I can travel to work and where I can go socially with friends and family. And also for **dating situations** and circumstances. It provides a **safety concern** when you have to rely on other people for transportation or you're **meeting people** for the first time out in public." - Heather W., age 31, living with HPS type

### **Travel and vacationing**

Travel and vacationing were selected by 14% of the individuals represented by the poll results, as a specific activity of daily life that is important, but they are not able to do or struggle with due to HPS.



Pulmonary fibrosis led Jill to consider her vacation plans. *“My husband retired, we were going to vacation and you stop and think, ‘Should I do that? **Should we be saving money?**’ So all those things come into play now just thinking that through.”* - Jill, living with HPS type 5

### **Self-care or chores**

Self-care or chores were also selected by 14% of the individuals represented by the poll results, as a specific activity of daily life that is important, but they are not able to do or struggle with due to HPS. Both the lack of vision and bleeding were discussed.

*“**Vision limits my ability to go out and run normal errands.** ...Its annoying getting a **small cut** and having to stop what I am doing to wait for it to **stop bleeding**, or have constant subsequent interruptions to re-patch the cut because it **bleeds through the bandage.** (Sometimes I do not take or have the time to do the multistep bandaging process I am supposed to do; ie. when I cut my finger while I am cooking)”* – Denise, comment submitted online

### **Other activities of daily living impacted by HPS – family planning, family time and sleep**

Only 6% of individuals represented by the poll results selected “Other activities” as a poll response option. Many shared comments about how HPS impacts family planning. Low vision and other HPS-related health concerns impact how they spend time with their family and sleep is impacted by coughing.

### **HPS impacts family planning**

*“Before I was diagnosed, we were thinking about **having children**, but was not sure because if they couldn't stop my tooth from bleeding, **how could I carry a child to term?** And how would they **control my bleeding?**”* - Patrice, 56 years old, living with HPS type 3

*“HPS has impacted my husband and I's plans for the **future of our family.** We have turned to IVF for the **genetic screening option** so our next child will not have to face the same health issues or even worse than our son with HPS type 1.”* – Bethany, comment submitted online

*“As most of us in our thirties are starting to get married and have children, I definitely share some of those **concerns about childbirth, labor and delivery.** But even beyond that, even if I choose not to have **biological children**, what do the concerns look like if I choose to **adopt children** and will my visual impairment impact adoption agencies' choices to allow me to that freedom, right? What does that look like? And if I am able to have my own biological children and if we get through the bleeding of labor and delivery will I have signs of fibrosis at that point or not? How does that change my timeline and how quickly I need to start having a future planned and have that discussion. **Pregnancy will decrease your lung function** normally without even a diagnosis of fibrosis.”* - Heather W., age 31, living with HPS type 4

**HPS impacts time spent with family members.**

*“I struggle with my lungs, bleeding and joint pain. Makes it hard to do things I enjoy with my family.”* – Vanesa, comment submitted online

*“I have a hard time with simple things like letting my daughter run off on her own and play in the backyard or a playground on a beautiful sunny day, just because I can't see and I fear I will miss something.”* - Christina, 21 years old, living with HPS type 3

**HPS impacts sleep.**

*“The cough from the fibrosis has affected the quality of our sleep for both of us.”* – Jose (Puerto Rico), caregiver, comment submitted online

## Session 2: Current & Future Approaches to Treatment for HPS

### Key messages from Session 2

**Treatment for one HPS symptom can affect other outcomes.** The receipt of platelets to treat hemorrhaging can jeopardize future lung transplants. Lung transplant medications can increase cancer risk. Most of these medications have side effects.

*“I was going to have **strabismus surgery to straighten one of the eyes** out again, but now we have a **concern with platelets** because you don't want too many antibodies. And so, all that plays into it now with a new diagnosis.”* – Jill, living with HPS type 5

*“Even though I've had a **lung transplant**, I now have to **worry about chronic rejection, and dying** from that. I also have severe bleeding which complicates all surgeries. I wound up having **complications after transplant** which caused me to have a 121 day hospital stay, which has caused a difficult recovery. All the medication I now take cause **skin cancer**, so I have to worry about that.”* – Karen, comment submitted online

*“I was told that I had **adrenal insufficiency**. It was found that it was **caused by the inhalers** that I took for my lungs for many years.”* - Ashley, 35 years old, living with HPS type 1

**Many living with HPS do not have access to even the most basic medications and treatments.** People living with HPS in Puerto Rico are particularly disadvantaged, with no opportunity for life-saving transplants.

Hilda Cardona reported from the live Participation Event in Puerto Rico. *“We would like **more access to the treatment for bleeding, and better equipment to improve vision, better control and treatment for colitis, and they would love more help and access to the lung treatments for pulmonary fibrosis.**”*

*“**Not having accessible treatments and services** to care for my HPS is frustrating. Things have gotten **worse after Hurricane Maria.**”* – Joe (Puerto Rico), comment submitted online

*“I was advised at the NIH that I should move to the United States near a **transplant center, as it is the only treatment that could prolong my life.**”* Leslie explained that she needs to have a thyroid nodule removed, *“But no surgeon in Puerto Rico would perform this surgery because of the **risk of bleeding** and the problems they might face in **removing the breathing tube.** So I need to **travel to the United States** to have this surgery.”* - Leslie (Puerto Rico), living with HPS type

*“**Lack of pulmonary fibrosis treatments, lack of good bleeding control, lack of skin cancer prevention**”* - Y (Puerto Rico), comment submitted online

There are no FDA-approved medications for HPS.

Instead, individuals living with HPS are referred to many specialists to address the different symptoms that they are experiencing. They take medications developed and approved for other indications, including medications for bleeding including platelet and blood product transfusions and hormones and contraceptives. Additional medications are taken for lung or breathing problems as well as medications to manage depression and anxiety. Some rely on surgical interventions including ostomy, hysterectomies and lung transplants.

Poll respondents used online polling to select all medications or medical treatments that they or their loved one have used, currently or previously, to treat symptoms associated with HPS. Respondents each selected an average of 3.5 responses. Poll results are presented in **Appendix 6, Q1** and illustrated with patient comments below.

### **Medications for bleeding**

Medications for bleeding was the top choice, selected by 67% of individuals represented in the poll results as a medication or medical treatment that they had used to treat HPS symptoms. Medications for active bleeding include DDAVP/ desmopressin acetate and Stimate. Tranexamic acid (Lysteda) and Amicar (aminocaproic acid) are antifibrinolytic agents administered prophylactically. Many require multiple approaches to stop bleeding.

*Christina experienced profound menstrual bleeding, “Eventually I was admitted into the hospital and given **IV platelets** along with a **drug called Amicar** and **birth control pills**. This treatment **helped slow the bleeding down**, but my body did not have a true break from the excessive bleeding I endured for over a year since it had first started. I was also given a **nasal spray medication** as a child called Stimate but seemed to have **absolutely no effect** in helping my bleeding. I have also been hospitalized for **IV iron infusions** because my body doesn't respond well to the pill form.” - Christina, 21 years old, living with HPS type 3*

*“I went to see a hematologist to be evaluated and prescribed medication. Medications are **iron, vitamin c, Lysteda** ...During my childhood, whenever I needed a dental procedure, I went to my doctor, (pediatrician) to prescribe **Amicar, to prevent any bleeding event.**” - Chrisyeily (Puerto Rico), living with HPS type 1, comment submitted online*

**Downsides:** some effective medications were recently taken off the market, challenges in determining the correct amount of medication for each bleeding episode, side effects, and some simply do not work.

*“One of the medications that **worked really well for me**, for my bleeding issues was **Stimate, which is an inhaled DDAVP or a nasal**, but unfortunately that was **taken off market**. I had to switch over to **tranexamic acid, which doesn't work as well for me**,*

unfortunately. *I'm still adjusting to that change.*" - Yeida, 44 years old, living with HPS type 1

*"The amount of [tranexamic acid] medication you need to take is different. Heavier episodes need several more days of medication, where smaller episodes may use [less]... It's two pills, three times a day up to several days, depending on the episode. So how many days are you going to be taking it? You never really know. It's still a learning curve for me."* - Yeida, 44 years old, living with HPS type 1

*"I currently use Amicar before going to the dentist for routine cleaning. I am not responsive to Desmopressin or DDAVP."* - Leslie (Puerto Rico), living with HPS type 1.

### **Platelet and blood product transfusions**

Platelet transfusions were selected by 48% of individuals represented in the poll results as a medication or medical treatment that they had used to treat HPS symptoms. Platelet transfusions can be administered to patients with excessive bleeding or to prevent bleeding. Ideally, patients should be administered single donor blood that has been HLA matched through a blood bank as well as irradiated and leuco-reduced, to prevent immunization. Unfortunately, this is not always possible.

*"I have received over 140 units of blood products. I can remember going into the hospital in one season and coming out during an entirely different season."* – Ashley, 35 years old, living with HPS type 1

As a result of prolonged menstruation, *"The time came when I passed out in my mom's arms. Upon arrival at the emergency hospital, I had to be confined in San Lucas de Mayagüez because my hemoglobin was (6). I received blood transfusions."* - Chrisyeily (Puerto Rico), living with HPS type 1, comment submitted online

**Downsides:** Patients with HPS types 1, 2 or 4 must use platelet transfusion sparingly, as multiple transfusions can induce antibodies which will exclude them from receiving a lung transplant later. Another downside mentioned was anaphylaxis.

*"At this time a platelet transfusion is the only alternative I have to getting any invasive procedure. The first time I had a platelet transfusion was for a molar extraction when I was 20 years old. During the transfusion of the first unit, I had an anaphylactic reaction. Since then before any transfusion, I must be premedicated with Benadryl and Solu-Medrol."* - Leslie (Puerto Rico), living with HPS type 1

### **Medications for lung or breathing problems**

Medications for lung or breathing problems were selected by 43% of individuals represented in the poll results as a medical treatment that they had used to treat HPS symptoms. Inhalers are used for asthma, pirfenidone is an anti-fibrotic medication used for the treatment of idiopathic

pulmonary fibrosis and nintedanib has been approved for other fibrotic lung diseases. Some patients were also prescribed steroids for inflammation.

*“I was about 19 years old when I started getting **inhalers** and luckily, taking an inhaler, some **Albuterol and a Symbicort inhaler**, helped with being able to go to choir rehearsal in the middle of Chicago winter.” - Mariel, 26 years old, living with HPS type 1*

*“I take **prednisone** five milligrams to avoid a little bit the excess **inflammation**. I know that it's **not an approved treatment** to help with fibrosis, but in a way it does help to stay stable since it **avoids the excessive inflammation**. I know there are some **side effects** to this medication, but since it's such a low dose, only five milligrams, it hasn't caused any consequences to my health.” - Jose (Puerto Rico), 48 years old, living with HPS type 1*

*“As an adult, I developed **pulmonary fibrosis**, which was initially treated with **prednisone**. I later learned about a **clinical trial** by the NIH to test the efficacy of pirfenidone. So I decided to stop prednisone and participate in this study that could change many people's lives. ...I experienced **dizziness, nausea, and loss of appetite**, but **no progression** of fibrosis until some 30 months into the study. I was using the active drug, but the study has **stopped prematurely** because overall, the data did not show that the drug was beneficial. ... The **fibrosis has slowly progressed** over the years. In 2017, my pulmonologist prescribed **pirfenidone** for use. The side effects are the same as what I experienced during the clinical trial. - Leslie (Puerto Rico), living with HPS type 1*

**Downsides.** Steroids and pirfenidone have many side effects. In addition, some younger patients are reluctant to start pirfenidone as there are no studies on whether it interferes with pregnancy or lactation.

*“I got two different pulmonologists' opinions and opinions from staff at the National Institutes of Health because the question at the forefront of my mind is, **“Is it even worth starting pirfenidone if I might have children in the next five years?”**... It was really at the forefront of my mind when thinking about that treatment.” - Mariel, 26 years old, living with HPS type 1*

### **Hormones and contraceptives**

Hormones and contraceptives were selected by 41% of individuals represented in the poll results as a medication or medical treatment that they had used to treat HPS symptoms. These medications are typically administered to women with excessive menstrual bleeding.

*“To control **menstrual bleeding**, I used **birth control pills** for most of my life. They generally worked well, but I had to live with their **side effects**.” - Leslie (Puerto Rico), living with HPS type 1*

*“With my gynecologist who evaluated me, I began to use **contraceptives** such as: Aviane, then due **to consecutive pain and lack of regularity**, they changed me to **Sprintec**. Now I go regularly to the gynecologist. I always go to my appointments.” - Chrisyeily (Puerto Rico), living with HPS type 1, comment submitted online*

**Downsides:** multiple side effects including mood disorders.

*“My **bleeding** has not only caused **physical setbacks, but also mental**. I was given an **enormous number of hormones** and my body did not take well to them. I had every **side effect** that was deemed rare. I was always **irritable, tired, and depressed**. My body was at war with itself, both physically and mentally. - Christina, 21 years old, living with HPS type 3*

### **Medications for Inflammatory bowel disease**

Medications for inflammatory bowel disease were selected by 31% of individuals represented in the poll results as a medication that they had used to treat HPS symptoms. HPS Crohn’s-like colitis is managed similarly to Crohn’s disease and treatment includes biologics such as Remicade (infliximab), Humira (adalimumab), Entyvio (vedolizumab), Stelara (ustekinumab), antacids for acid reflux, anti-inflammatory drugs such as corticosteroids. For some, biologics alleviate Crohn’s disease-like symptoms as well as related inflammation.

Remicade is helping to reduce Kylee’s colitis symptoms, enabling her to regain her stamina, strength and muscle back. However, *“At least once a week will go late to school or something because in the morning **I just don’t feel as well and my stomach hurts.**” - Kylee, 15 years old, living with HPS type 1*

*“**Joint pain and inflammation** were **debilitating** until I was diagnosed with **bowel disease** and began **treatment**. There are still flares of joint pain, though.” – Monica, comment submitted online*

*“Ever since I’ve had **colitis**, I have **failed nearly every biologic** I’ve tried from Remicade to Entyvio to Humira which caused me to have a reaction. ...And then, I got put on STELARA and it doesn’t fully do the job. It is the best one for now and **I am afraid of switching** because I don’t want to get rid of the thing that has worked slightly the best than anything else.” - Cassandra, 24 years old, living with HPS type 1*

**Downsides:** biologics do not work for all individuals with HPS and even when they do, biologics don’t entirely resolve symptoms. Patients are afraid to switch medications because they fear losing efficacy.

### **Other medications or procedures not represented in the poll results**

Other medications were selected by 26% of individuals represented in the poll results as a medication or medical treatment that they had used to treat HPS symptoms, including

supplemental oxygen, antirejection medications/photopheresis, supplemental iron, surgeries for skin cancer, cataracts and nystagmus.

**Supplemental oxygen.** Patients who have low oxygen levels because of pulmonary fibrosis require supplemental oxygen. When the disease progresses, they sometimes need a ventilator or even extracorporeal membrane oxygenation (ECMO) for end stage pulmonary fibrosis. A downside is that oxygen needs to be continually monitored and adjusted, which can be challenging for individuals living with visual impairment

*"I've been **on oxygen** since I was 35. **Progressively getting worse**, using it more often. ... It is **helpful in keeping up with daily life** to be on oxygen." Yeida continually adjusts her oxygen levels based on many factors including her levels of physical activity and the weather. When her levels of oxygen saturation are good, "I tend to be very good at **feeling it in my lungs**, I feel it. But I also check it with a **pulse oxygen monitor** to make sure that I'm staying above 92%, which is where you want to be." - Yeida, 44 years old, living with HPS type 1*

Jose has a large constant flow oxygen machine in his bedroom to quickly stabilize his oxygen if his portable oxygen machine is not enough. *"I constantly walk with an **oximeter** because I **monitor myself constantly**, my oxygen levels because I know if this drops too much, the **consequences would be severe**. And I always try to monitor it to keep my health as stable as I can." - Jose (Puerto Rico), 48 years old, living with HPS type 1*

*"Steve's **home oxygen concentrator** couldn't keep up with his needs. We span to the emergency department and Steve was placed on the most oxygen he could receive without being on a ventilator. The emergency medicine team ordered an **inpatient transplant evaluation STAT**." Caren described how Steve was placed on **ECMO (extracorporeal membrane oxygenation)** while waiting for a lung transplant. "At that time, only around 50% of people on ECMO made it to transplant. The 35 turbulent days Steve spent on ECMO were a **scary roller coaster ride** for me as a caregiver. I can only imagine what it was like for Steve." - Caren, caregiver and widow of a husband who died at the age of 43 from complications of HPS type 1*

**Antirejection medications/photopheresis.** Individuals who have had lung transplants rely on these medications, which often have other side effects and increase cancer risk.

*"I've since developed **chronic rejection** and are undergoing **photopheresis treatments** twice a month to treat this. I get, **IVIG infusions** once a month, but they make me sick. I require a **home healthcare nurse** for these infusions that make me often **body aches, chills, fatigue** with really **bad headaches and kidney problems**. Photopheresis appears to be **slowing down the rejection**, but seems to make my **bleeding** worse. I've had two **emergency department visits** because of bleeding post-treatment." - Heather K., 49 years old, living with HPS type 1, single lung transplant recipient*



**Supplemental iron.** This is required because of excessive blood loss. Not all patients tolerate iron supplements.

*“With the **bleeding**, my **iron levels were super low**. And so when I went to the doctor, they **started me on iron**. I would get **lightheaded** sometimes.”* – Kylee, 15 years old, living with HPS type 1

*“I have also been **hospitalized for IV iron infusions** because my body doesn't respond well to the pill form.”* - Christina, 21 years old, living with HPS type 3

**Surgeries for skin cancer, cataracts and nystagmus.** Surgery is often used to address some of the challenges oculocutaneous albinism, but surgery has downsides for individuals with HPS.

*“At the age of five. I underwent **eye surgery to slow down the nystagmus** and the doctor told my mother **I nearly hemorrhaged.**”* - Crystal, identical twin living with HPS type 4

### **Other medications represented in the poll results**

Medications to manage depression or anxiety were selected by 24%, medications to aid with sleep were selected by 22%, and cannabidiol or CBD were selected by 11% of individuals represented in the poll results as a medication or medical treatment that they had used to treat HPS symptoms.

### **I have not used medications or medical treatments recently**

A total of 13% of the individuals represented in the poll results did not use medications or medical treatments recently to treat HPS symptoms.

*“I selected **no medical treatments** as part of the 4% that responded as such because **my daughter is 14 months old** and so she has (luckily) not needed any medical treatments thus far.”* – Kristine, comment submitted online

### **Ostomy or bowel surgery**

Ostomy or bowel surgery were selected by 9% of individuals represented in the poll results as a medication or medical treatment that they had used to treat HPS symptoms. This is a major procedure often undertaken in those who do not respond to medical therapy.

*“Having my **ostomy surgery** was massively helpful back in 2015, I got my **entire large intestine removed** due to **consistent hemorrhaging and inflammation**. And that solved a lot of problems within my intestines themselves. I have gotten frequent scans and for the most part, **things look okay in my intestines**. That doesn't mean that I'm cured though.”* Cassandra's inflammation and lesions, *“Flared right back up a few years after my total colectomy.”* - Cassandra, 24 years old, living with HPS type 1

**Downsides:** While an ostomy or bowel surgery helps to address some HPS-related IBD symptoms, it is not the cure that some hope for and requires daily management.

*“Although my **bowel disease** is pretty much in remission, I still manage an **ielostomy** daily. **Ostomy bags** are not foolproof and tend to **leak** at the most inopportune moments. Embarrassment can be the least of your problems when you're in this situation. I've gotten pretty good at being creative. I've had lots of practice after years of being covered, the **skin breakdown** and **can bleed**. Even modest bleeding makes it moist and makes it **very difficult to keep a bag on**. Try managing this in say an airplane while you're traveling for work or even worse on a date. - Heather K., 49 years old, living with HPS type 1, single lung transplant recipient*

### **Lung transplant**

Lung transplant was also selected by 9% of individuals represented in the poll results as a medication or medical treatment that they had used to treat HPS symptoms. Both single and bilateral lung transplants are used for those with severe end-stage pulmonary fibrosis.

*“10 years ago, I had a **double lung transplant**. ... One of the things we heard earlier is that the **average life expectancy** for a lung transplant patient is **five years**. It's five to six years and I'm **10 years out**. From that regard, it's really been a successful treatment option.” - Nancy, 63 years old, living with HPS type 1, double lung transplant recipient*

*“Steve received the gift of life from an **altruistic donor** named Tommy. Steve's first words in recovery were, **‘It's so easy to breathe!’** Steve was 40 years old when he got **new lungs** that would give him two and a quarter or more years of life. They were treasured years, but they weren't easy ones. Steve now had to take **26 pills a day**. He had to **learn to walk again**. He became **diabetic**, requiring attention to his diet and his blood sugar. His **kidney function declined** and two years after his transplant, we were told he'd soon need to **begin dialysis or have a kidney transplant**.” - Caren, caregiver and widow of a husband who died at the age of 43 from complications of HPS type 1*

*“They tell everyone that receives a **lung transplant** that you're **trading one lung disease for another** and that is so true. ... Lungs are one of the most difficult organs to transplant because they're openly exposed to so much of what's around you. **Maintaining a lung transplant takes a lot of hard work**.” - Heather K., 49 years old, living with HPS type 1, single lung transplant recipient*

*“Transplant comes with many, many, many issues ... **you trade one set of problems for another** and that's certainly true. Even in my case, with the success that I've had, I developed **high blood pressure, high cholesterol**, I have **kidney disease**, I've had **four skin cancers** in the last four years, we're very **prone to infection** so I've had a lot of that which often requires **hospitalizations**. There's a lot of **fear** involved in addition to **not really knowing how long we're going to live** which obviously, not anybody does, but I think our it's a little more in our face in this situation after a transplant. Just a lot of issues that are worrisome.” - Nancy, 63 years old, living with HPS type 1, double lung transplant recipient*

After Karen's had a double lung transplant, "My life will never be the same. **I now wear a mask every time I go outside and hugging isn't allowed**, except for people I know are keenly aware of my situation. Food preparation is carefully orchestrated and my husband helps with that. There are **two things I miss more than anything**. One is **swimming, which I can never do again**. And the other is **singing**. After transplant, I had complications and needed a **tracheostomy, which has affected my voice**." – Karen, 58 years old, living with HPS type 1, lung transplant recipient

**Eligibility for a lung transplant can be compromised by antibody formation from previous transfusions.**

"I was told that it's likely that **my body won't assimilate the transplant** because I've had several surgeries. ...I have **received platelet transplants** and I was informed that there was a great possibility that this could affect how my body would accept the transplant." - Lymaris (Puerto Rico), 45 years old, living with HPS type 3

**Downsides:** surgical complications, the fact that a lung transplant is "only switching one disease for another", and multiple medications are required to ensure that the new organ is not rejected. Lung transplants are expected to only last for five years and ultimately not a cure.

"Steve's story is a reminder that **transplant is a limited treatment and not a cure**. It's also a **difficult treatment that depends on luck, privilege, and sacrifice**. Even after receiving a **rare lung transplant**, Steve's **biggest fear came true**. He didn't get to enjoy the fruits of his life. He didn't get to keep being a father to his children and watch them grow up. Annie was eight and Elliot was six when **they lost their dad**." - Caren, caregiver and widow of a husband who died at the age of 43 from complications of HPS type 1

### **Investigational medicine in a clinical trial**

Investigational medicine in a clinical trial was selected by 7% of individuals represented in the poll results as a medical treatment that they had used to treat HPS symptoms. When enrolling in a clinical trial, there is no guarantee that you will receive the active agent.

"Before my transplant, I was part of a drug study for **esbriet, an antifibrotic drug** to treat, and hopefully **slow down pulmonary fibrosis**. It turned out I was on **placebo**, but that's okay. I know what good science is and I understand why it's important. And I understand that somebody has to be on placebo. I didn't mind that that's how it turned out to be. I didn't mind because even for me, the drug trial helped because **it gave me hope. It gave all of us hope**." - Heather K., 49 years old, living with HPS type 1, single lung transplant recipient

Alternative approaches do nothing to resolve potentially catastrophic bleeding disorders, colitis or pulmonary fibrosis, but instead only address sun protection and visual impairment.

Poll respondents used online polling to select all the approaches, besides medications or treatments that they or their loved one have used, currently or previously, to help manage symptoms associated with HPS. Poll results are presented in **Appendix 6, Q2** and illustrated with patient comments below. Poll respondents selected an average of 6 responses each, and the top two responses, protective clothing and lenses to magnify vision, were tied. Not one single person who responded to this polling question said that they are not doing anything to help manage symptoms.

### ***Sun protection – protective clothing and use of UV sunglasses***

Skin cancer prevention is about protection, surveillance and early intervention. Most individuals living with HPS rely on protective clothing or UV sunglasses which were selected by 91% and 84% of the individuals represented by the poll results, respectively. Many also use sunscreen, sunblock, umbrellas, window shades and other things to block the rays of the sun.

### ***Addressing visual impairment – lenses to magnify vision, magnifying device and/or speech software for computer, closed circuit television, white canes or guide dogs.***

Most of the individuals living with HPS use various methods to address their vision impairment. Lenses to magnify vision, including glasses and magnifiers, are used by 91%, magnifying device and/or speech software for computer are used by 85%, closed circuit television is used by 36%, and white canes or guide dogs are used by 24% of the individuals represented by the poll results. While these are effective, they don't fully resolve all low vision issues.

### ***School, work or home modifications***

School or work modifications are used by 75% of the individuals represented by the poll results. In addition, meeting attendees described the home modifications that they used to make life easier.

### ***Self-Help Activities/Yoga, exercise, meditation***

Self-Help Activities/Yoga, exercise, meditation, other are used by 45% of the individuals represented by the poll results to help them address HPS-related health concerns. Several also mentioned the value of support groups.

### ***Therapies including psychotherapy***

Psychotherapy is used by 29% of the individuals represented by the poll results. Individuals living with HPS also mentioned other kinds of therapy including physical therapy, occupational therapy, and speech therapy.

***“Frequent infections and hospitalizations have caused me to have muscle atrophy. I'm undergoing physical therapy and occupational therapy, but I need an electric***

**wheelchair to go any distance.**” - Heather K., 49 years old, living with HPS type 1, single lung transplant recipient

*“From my **brain injury**, I needed to catch up cognitively and developmentally. I didn't talk until I was about five and developed **oral apraxia** and had **lots of speech therapy** to work on **chewing**.”* - Ashley, 35 years old, living with HPS type 1

### **Naturopathic approaches, supplements or herbals**

Naturopathic approaches, supplements or herbals are used by 20% of the individuals represented by the poll results. Jose reported using mint spray to prevent coughing.

*“**[Mint spray]** has helped a lot because it helps to control the **itchiness in the throat**. And by **not coughing**, my oxygen levels stay stable. When I cough that I have the cough fits, my **oxygen levels drop a lot**.”* - Jose (Puerto Rico), 48 years old, living with HPS type 1

### **Other approaches**

Other approaches are used by 16% of the individuals represented by the poll results. These include preventative approaches to preserve lung health, modified transportation and transportation alternatives, and following a strict diet.

**Preventative approaches for lung health.** Many individuals discussed how they are protecting their and their loved ones lungs from smoke, environmental pathogens or from infections like COVID-19.

*“We have been doing everything possible to keep her lungs as healthy as possibly, from **improving and monitoring the air quality in our home**, to keeping Alora **out of school during the pandemic**. She was a remote student up until this past January when she was finally vaccinated and when the first Omicron wave subsided.”* – Jessica and Alex, parents of a nine-year-old girl with HPS type 1, comment submitted online

*“Daily actions to **preserve the lungs of our children** -- we buy **air purifiers & filters** for multiple rooms in the home, **do not light candles or use perfume/cologne etc.**, **distance ourselves from family members that smoke**, and intend to nudge our children to **become swimmers or participate in other activities** to help lung health (but are also realistic with the blood clotting disorder). Every time my son gets a cold we cannot help but be concerned about his overall lung health.”* – Rick, comment submitted online

**Modified transportation and transportation alternatives including paratransit, Uber/Lyft, cabs, wheelchairs.**

Current HPS treatment approaches come with devastating side effects, are not available or accessible to many of those with HPS and are not very effective.

Poll respondents used online polling to select the top three biggest drawbacks of current approaches to managing HPS. Poll results are presented in **Appendix 6, Q4** and illustrated with

patient comments below. Many drawbacks were described in the section describing medications.

### **Side effects**

Side effects was the top drawback of current approaches and was selected by 44% of the individuals represented in the poll results. Often individuals living with HPS are forced to make hard choices to select treatments for symptoms that are often contraindicated. Delayed diagnosis often make these choices even harder. Surprisingly, individuals living with HPS expressed an unexpected optimism and hope about treatments that caused devastating secondary side effects including osteoporosis, adrenal insufficiency, dizziness, migraines and difficulty concentrating, skin cancer, liver and kidney toxicity.

*“I am dealing with the **side effects** from all my medications, **nausea, tiredness, reflux, sun sensitivity.** I'm also dealing with the **blindness, pain, oxygen issues and my RA symptoms.** ... “I was diagnosed with rheumatoid arthritis about four years ago. The **pain and inflammation** are constant reminder that **RA can also affect my lungs.** There are treatments for RA that may affect my pulmonary fibrosis conditions, so **I struggle finding a medication that helps me with pain and do not affect the progression of my fibrosis.** At this time, I must find the less of two evils, live with pain, but not accelerate the progression of the lung disease or leave pain free knowing that the progression of the PF can make my life shorter. Why do I have to choose? It's not fair.” - Carmen, 57 years old, living with HPS type 1*

*“I have fractured my back three times from **osteoporosis** which is due to the **medications I take for the bowel disease of HPS.** Throughout the years I have had **dizzy spells** and developed **adrenal insufficiencies from the lung inhalers.** I have **passed out** in a treatment room, in an elevator, at a dance class, and on a plane needing oxygen.” - Ashley, 35 years old, living with HPS type 1*

*“I have a lot of **fatigue** and now I've got **migraines** from the medication.” - Maryanne (caller), living with HPS, lung transplant recipient*

*“The medications that I take since **lung transplant** can make me **sleepy, shaky hands, and sometimes forgetfulness.** This makes it difficult to concentrate and take care of tasks such as writing checks or even typing on computer or phone. With lung transplant I have also developed **kidney issues,** which makes me fear the **possibility of dialysis.** Also with being so fair skinned I worry about skin cancers as the **transplant medications also causes skin cancer.**” – Karen, comment submitted online*

*“Currently, most of the medical interventions I am using are to treat the **side effects of other medical decisions.** ... **I don't regret any of those decisions.** Four years ago, I underwent a **single lung transplant.** ...I fought on **multiple infections** from the first day and never completely cleared two of them. ... **My hands shake** because of the*

**antirejection medications.** *It's made doing everyday tasks harder from doing the dishes without breaking them to typing.*" - Heather K., 49 years old, living with HPS type 1, single lung transplant recipient

**Maintaining a lung transplant takes a lot of hard work.** *Many of the medications have their own **side effects** such as **kidney and liver toxicity**. ...For me, one of the hardest things to cope with my disease is how **ditzy** it's made me. Too often, I've had to cancel plans or back out of projects I care a lot about it at the last minute. The old me would have never done those things.*" - Heather K., 49 years old, living with HPS type 1, single lung transplant recipient

*"I have **kidney disease** and that scares me to a great degree because it continues to decline and I see a **kidney transplant sometime in my future**."* - Nancy, 63 years old, living with HPS type 1, double lung transplant recipient

Many of those with lung transplants also experience a compromised immune system because of the side effects of anti-rejection medications.

*"We have a double whammy, we have **albinism** so we don't have the **pigmentation protection from the sun** but we're also on **immunosuppressants** which makes us even more susceptible to **skin cancers** and **other cancers**, by the way."* - Nancy, 63 years old, living with HPS type 1, double lung transplant recipient

*"In early 2019, Steve contracted the **flu**. He was hospitalized and placed on the **ventilator** that his **lungs ended up as a burnt battlefield**. Steve could not overcome the infection and he **passed away** February 4th, 2019."* - Caren, caregiver and widow of a husband who died at the age of 43 from complications of HPS type 1

### **Limited availability or accessibility**

Limited availability or accessibility was selected by 25% of the individuals represented by the poll results. This downside generated so many comments that it was moved up in the polls. Some live far from a transplant facility, most are unable to drive. Those living in Puerto Rico are especially affected and some moved to the US to obtain care as transplant is not available on the island.

*"Our preferred transplant facility, Mayo clinic was in Minnesota, a **four-and-a-half-hour drive** from our home in Iowa. Distance wasn't the only problem, Steve's job **didn't provide health insurance** out of state. Steve pleaded for a **job transfer** to Minnesota, we called in favors and in July left our home a tight knit community and **moved into my parents' basement**."* - Caren, caregiver and widow of a husband who died at the age of 43 from complications of HPS type 1

*"We don't have a transplant center in Connecticut. Being **legally blind, I don't drive**. The closest center to me is in Boston, **two hours away**. That's very **difficult for me to manage**." - Yeida, 44 years old, living with HPS type 1*

*"My **condition was worsening** and my **quality of life was getting to be so bad** I had no choice but **move from Puerto Rico to the US** so I can get the treatment and care I needed; even in the US my condition is so rare that **I have a hard time finding care**." – Yaritza, comment submitted online*

*"My symptoms, it's **fibrosis and stomach bleeding**. I would like to face HPS but **access to healthcare is difficult**." – Vanessa (Puerto Rico), comment submitted online*

### **Current HPS treatment approaches only treat some, not all of the symptoms and are not very effective at treating the target symptoms.**

Only treats some, not all of the symptoms was selected by 42% of the individuals represented by the poll results, and not very effective at treating the target symptom was selected by 40% of the individuals represented by the poll results. This is consistent with the results of a poll question where poll respondents were asked to indicate how well their current regimen control your or your loved one's disease overall. Poll results are presented in **Appendix 6, Q3** and illustrated with patient comments below. The greatest response was "somewhat", selected by 60% of poll respondents. "Very little" was selected by 20%, "To a great extent" was selected by 20%. "Not at all" was selected by 2% of poll respondents and "Not applicable because not using anything" was not selected at all.

*"I want to start by just saying that **I've never been on a treatment that has ever fully worked**. I've never reached remission in any part of my journey with HPS. - Cassandra, 24 years old, living with HPS type 1*

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

High cost or co-pay, not covered by insurance was selected by 33% of the individuals represented by the poll results.

*"Living with this condition is difficult. We have **constant expenses on sun creams that we use daily**." – Marilett (Puerto Rico), comment submitted online*

*"I have to deal with the **frustration** of seeing the **numbers of my PFT decline** and having to **stay at work** so I can get my medical and care covered by my **health insurance**." - Carmen, 57 years old, living with HPS type 1*

*Steve's job **didn't provide health insurance out of state**." - Caren, caregiver and widow of a husband who died at the age of 43 from complications of HPS type 1*



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

Requires too much effort and/or time commitment was selected by 22% of the individuals represented by the poll results.

Caren's husband had a lung transplant. *"During those **final years**, outpatient **appointments were a full-time job**. There were **appointments with his transplant teams, the nephrologist, a dermatologist**. Steve had **numerous hospitalizations** during this time too. Our post transplant life revolved around **balancing exposure and infection risk while living a full life**." - Caren, caregiver and widow of a husband who died at the age of 43 from complications of HPS type 1*

*"In the past 7 months since our 14-month-old daughter's diagnosis for HPS, we have been seen at a **low vision clinic**, have had **multiple appointments** with an **ophthalmologist, optometrist, an orientation and mobility specialist, a social worker, and an occupational therapist**. We have had appointments with **dermatologists** to get her skin screened and a **hematologist** to do blood work and confirm the disfunction of her platelets. We have had multiple appointments with our **genetics counsellor** to further understand her HPS diagnosis." – Kristine, comment submitted online*

### **Route of administration (IV, pills or injection)**

Route of administration, by IV, pills or injection was selected by 42% of the individuals represented by the poll results.

*"Some of my **infusions can take hours** and I have to put wash out days on my calendar because after them, I know I'm going to be **excessively tired** and/or **not feel well**." - Heather K., 49 years old, living with HPS type 1, single lung transplant recipient*

### **Not applicable/not using any treatments/Other**

Not applicable/not using any treatments was selected by 11% of the individuals represented by the poll results and only 4% of the individuals represented by the poll results selected other reasons.

Pirfenidone, *"does come with the drawback that based on the **limited research** we have on this drug, there's **no studies on how this drug could interact with pregnancy or lactating**."* -Mariel, 26 years old, living with HPS type 1

Preventing/treating pulmonary fibrosis, resolving bleeding issues and preventing or treating IBD were ranked as the most important for a possible new drug today.

*"I think a lot of people with HPS could really empathize with that idea of **wanting to maintain a high quality of life** for as long as we possibly can." - Mariel, 26 years old, living with HPS type 1*

Hilda Cardona reported from the live Participation Event in Puerto Rico. *“They really, really, **really want a cure for HPS** and some of them are **willing to enter in any clinical trials** and in therapy and maybe **treatments or help for skin cancer**. Most of them want the cure ASAP or as fast as possible and they are putting all of these on the people who are listening on this presentation in their hands and they wish that cure fast.”*

Poll respondents used online polling to select the top three aspects of their condition that they would rank as most important for a possible new drug today. The results of this poll were a poignant reminder that many who are living with HPS, particularly those in Puerto Rico, do not have access to existing treatments or therapies. Poll results are presented in **Appendix 6, Q5** and illustrated with patient comments.

### ***Preventing and/or treating pulmonary fibrosis and breathing difficulties***

Preventing and/or treating pulmonary fibrosis and breathing difficulties was the option selected most frequently. A total of 80% the individuals represented by the poll results selected this option.

*“As a provider, the fact, after 25 years of study, that **there is no FDA-approved treatment for HPS-Pulmonary Fibrosis** (nor any of the other significant manifestations of HPS) makes **management of these patients very challenging**.”* – Samuel, comment submitted online

*“I believe the **ideal treatment** for HPS is a **gene therapy** that would delete the possibility that HPS patients would experience life-long fibrosis, **no one should ever have to suffer like Steve did, fighting until their last breath**.”* - Caren, caregiver and widow of a husband who died at the age of 43 from complications of HPS type 1

*“You **can't undo the fibrosis**. And so if we could halt that or completely keep it from occurring in the first place, that would be ideal.... The other conditions that I happen to have vision and the skin and things like that are things that are not completely life threatening.”* – Noel, 48 years old, living with HPS-1

*“Ever since I was a teenager, I lived with the threat of knowing I'm going to have **pulmonary fibrosis** someday and that has framed my entire worldview and my life and career and relationships. That would be **something that I would be wanting to not have to go through** if it's possible.”* - Cassandra, 24 years old, living with HPS type 1

**Individuals living with HPS would like to include nonsurgical options to address pulmonary fibrosis.**

*“The biggest concern with this condition is the **pulmonary fibrosis**. [We need] some sort of treatment to exist, that it **doesn't have to do with surgery**. And that large problem that we have with the **bleeding** and that **every surgery** that we go through, it's a **threat to our life**. So if we could find some other method to treat this condition, it would be*

*fantastic. **Something less invasive.***” - Lymaris (Puerto Rico), 45 years old, living with HPS type 3

*“We need a drug that will allow the continuation of normal lung processes that **prevent fibroses.**”* – Mary Ann, comment submitted online

*“Find a way for the **fibrosis not to develop.** Secondary to that would be, **the need for transplant would be eliminated.** Those are my dreams for our community for the future.”* - Nancy, 63 years old, living with HPS type 1, double lung transplant recipient

### **Resolving bleeding issues**

Resolving bleeding issues was selected by 70% of the individuals represented by the poll results selected this option.

*“Finding a **treatment for platelet dysfunction** is crucial.”* - Leslie (Puerto Rico), living with HPS type 1

*“Even **improvements in hormone contraceptives,** because sometimes taking those treatments for a long time can be contra-indicative and bring up other issues. - Mariel, 26 years old, living with HPS type 1*

### **Preventing or treating the Inflammatory Bowel Disease**

Preventing or treating the inflammatory bowel disease was selected by 54% of the individuals represented by the poll results. This includes addressing inflammatory skin issues.

*“At this point in my current life with HPS, **I would love to get rid of these skin issues especially in intimate areas.** It's painful, it's embarrassing. Really, I would love to get rid of that.”* - Cassandra, 24 years old, living with HPS type 1

### **Improving visual acuity**

Improving visual acuity was selected by 48% of the individuals represented by the poll results.

*“My biggest issue that I would like to see addressed, are the **vision issues for more independence,** a way to treat the lung disease so it doesn't develop, and of course the bleeding issues, which are always an issue when you're talking about something like having to get a transplant. - Yeida, 44 years old, living with HPS type 1*

### **Preventing skin cancer**

Preventing skin cancer was selected by 17% of the individuals represented by the poll results.

*“It would be nice to be able to **be outside without worrying about the sun exposure** as much the risk of **skin cancer.** It would be nice to be able to do that without the same level of concern.”* - Kelly, 32 years old, living with HPS type 1

### ***Eliminate persistent coughing and improving photophobia***

Eliminate persistent coughing and improving photophobia were each selected by 7% of the individuals represented by the poll results.

### ***For those with HPS type 2 - Correcting immune deficiency***

Correcting immune deficiency (HPS2) was selected by 4% of the individuals represented by the poll results selected this option.

### ***Maintaining normal kidney function***

Maintaining normal kidney function was selected by 4% of the individuals represented by the poll results.

### ***Other***

Other aspects were selected by 4% of the individuals represented by the poll results. These include finding a cure and creating a greater awareness of HPS among medical professionals.

*“I have a lot to complain about with these treatments, but I'm thankful to have them. I'm thankful to have something as an option. But **what we need are better options. We need better therapies. We need therapies targeted to the problems of HPS specifically, not just general public. We need therapies that have better results and ultimately what we need, what we really need is a cure.**”* - Heather K., 49 years old, living with HPS type 1, single lung transplant recipient

*“Please **recognize HPS in the recommended use literature for medications to control bleeding and improve symptoms of HPS colitis.**”* – Monica, comment submitted online

### ***Increasing skin pigmentation***

Increasing skin pigmentation was not selected by any of the individuals represented by the poll results.

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

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 challenges of living with HPS. 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 HPS. The data resulting from this meeting may help inform the development of HPS-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 patients living with HPS presented at the June 10, 2022, meeting. It 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 HPS Benefit-Risk Table**

|  | EVIDENCE AND UNCERTAINTIES   | CONCLUSIONS AND REASONS   |
|--|--|---|
| ANALYSIS OF CONDITION/ IMPACTS ON ACTIVITIES OF DAILY LIVING | <p><b>Hermansky-Pudlak Syndrome (HPS) is extremely rare and in certain gene types, fatal (including the most common gene type).</b> Many patients are not diagnosed until after experiencing a medical emergency that often could have been avoided.</p> <p><b>HPS is a diverse disease with a variety of clinical manifestations.</b> Most individuals living with HPS experience multiple HPS-related symptoms which can vary from mild to life threatening.</p> <p><b>All people living with HPS experience albinism (legal blindness, photophobia and nystagmus) and blood clotting issues.</b> Other symptoms exist based on subtype. Blood clotting issues and visual impairment are the two most common HPS-related health concerns with pulmonary fibrosis as the most lethal.</p> | <p><b>People living with HPS have many worries and live with a great deal of uncertainty about their future.</b> For many, their biggest worries are related to developing pulmonary fibrosis, needing a lung transplant and premature death.</p> <p><b>The combination of HPS symptoms can be deadly.</b> Blood clotting issues mean that even minor surgeries can be high risk. The inflammatory bowel disease can cause hemorrhaging due to the bleeding disorder and pulmonary fibrosis is fatal.</p> <p><b>HPS impacts activities of daily living and profoundly affects quality of life.</b> Maintaining independence is difficult when unable to drive. Visual impairment can lead to injuries and bruising.</p> |
| CURRENT TREATMENT OPTIONS/ PROSPECTS FOR FUTURE TREATMENTS   | <p><b>There are no FDA approved treatments for any HPS disease manifestations.</b> People living with HPS instead try to use medications approved for other indications, which only work somewhat.</p> <p><b>Treatment for one HPS symptom can affect other outcomes.</b> Receipt of platelets to treat hemorrhaging can jeopardize future lung transplants because of antibody production. Lung transplant and pulmonary fibrosis medications can increase cancer risk. Medications for the bowel disease can increase infection. Additionally, all of these medications can lead to chronic kidney and liver disease.</p>  | <p><b>Many living with HPS do not have access to even the most basic medications and treatments.</b> People living with HPS in Puerto Rico are particularly disadvantaged, with no opportunity for life-saving transplants.</p> <p><b>Better treatments for patients living with HPS are urgently and desperately needed, particularly to prevent or treat pulmonary fibrosis, bleeding issues and colitis.</b></p>   |
|  | <b><i>See the Voice of the Patient report for a more detailed narrative.</i></b>   |   |

## Conclusion & Acknowledgements

*"The streets of heaven are populated by too many of my friends with HPS. I will probably join them before the next treatment, or the cure, is found. I want to leave a legacy for the next generation. I want them to never know what it is like to think the thoughts I've thought or have to face the decisions I've faced. My hope is that the research/medical community can help me, and the rest of my generation. We've shared our wisdom, but it is your wisdom that is our future." - Heather K., 49 years old, living with HPS type 1, single lung transplant recipient*

The Hermansky-Pudlak Syndrome community is strong and supports one another. This came through powerfully at the June 10, 2022, HPS EL-PFDD meeting. We heard many stories, impactful statements and we experienced a lot of emotion. We are hopeful that the information gathered at this meeting and captured in this report will encourage future research and successful new product development for people living with Hermansky-Pudlak Syndrome, who urgently need safe and efficacious treatment options.

The HPS Network wishes to thank all those living with Hermansky-Pudlak Syndrome and their loved ones who attended the June 10, 2022 meeting. Thank you for sharing your experiences and insights about living with HPS. Thank you also to those who contributed by phoning in or submitting comments online. We thank you for your courage in representing in your own stories, and for being the voices of those who are no longer with us.

Thank you to the US Food and Drug Administration for attending our EL-PFDD meeting, we are incredibly grateful for this opportunity to share our experiences with you. Special thanks to both Shannon Sparklin from the FDA's Patient Focused Drug Development staff, and Karen Jackler from the Center for Biologics Evaluation and Research, who together guided us through this process.

Thank you also to our generous supporters who have financially sponsored this meeting, including the Chan Zuckerberg Initiative, *Rare As One* and the EveryLife Foundation for Rare Diseases. Thank you to the many representatives from advocacy and professional organizations, drug companies, federal agencies, and universities from around the world who were in attendance.

Thank you to Dr. Wilson Bryan from the FDA for your perspectives on the importance of externally led patient focused drug development meetings, and to our Dr. William Gahl for a very interesting clinical overview of HPS, and to Bernadette Gochuico for her overview of clinical treatments.

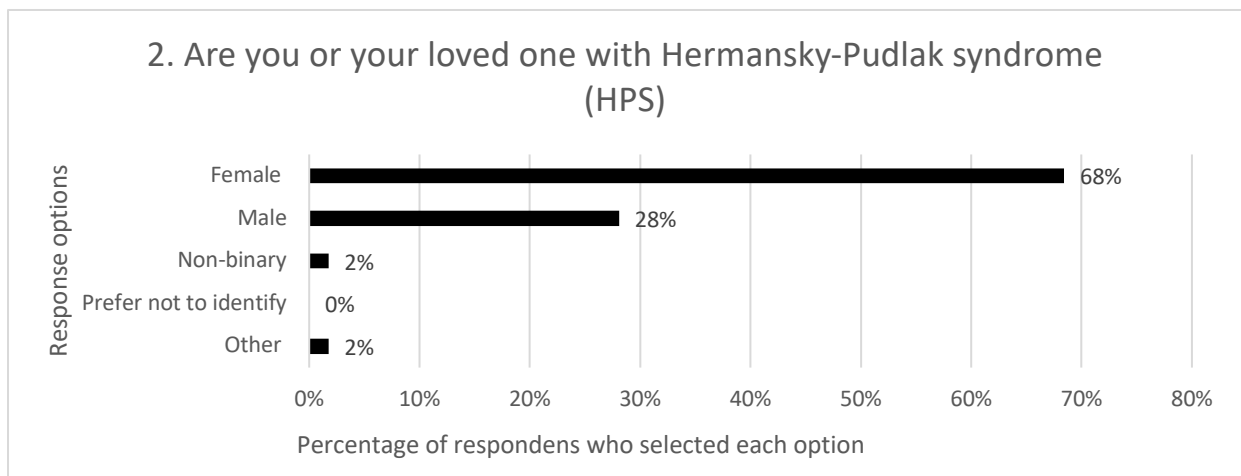
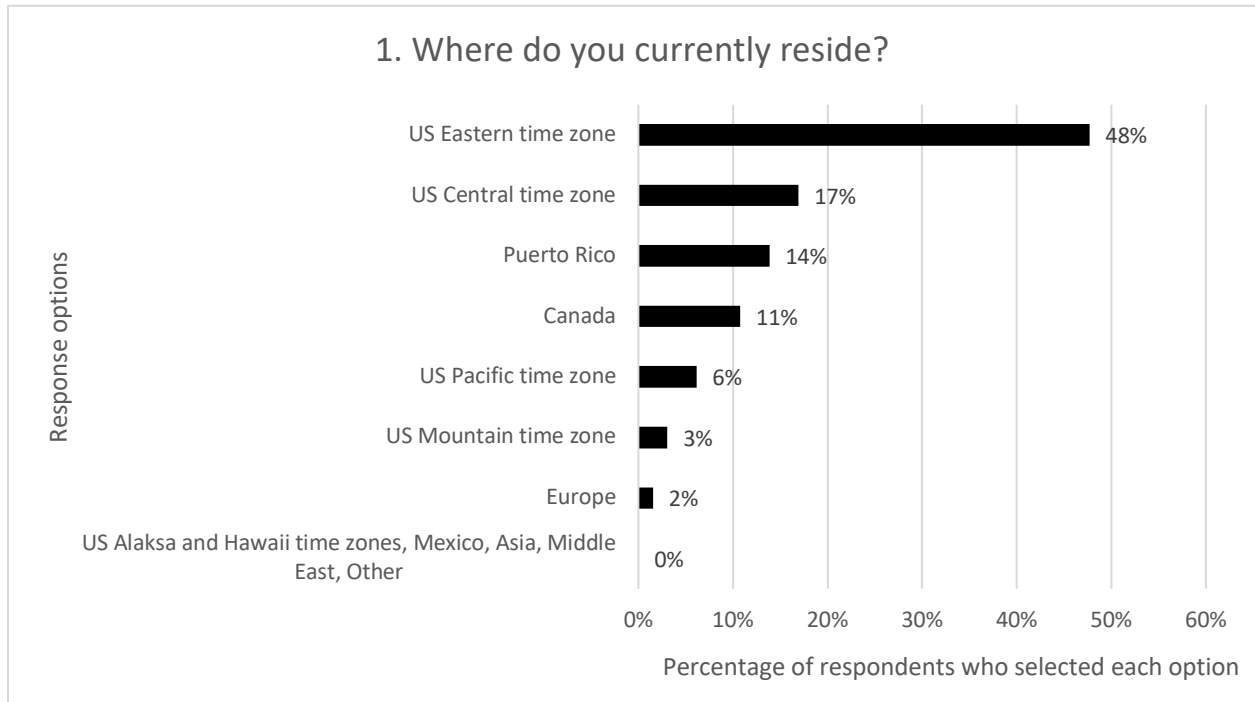
Thank you to wonderful James Valentine and Larry Bauer from Hyman, Phelps, and McNamara and to the HPS staff and leadership team. A special thanks to Michelle, O'Connor who worked so hard to help plan and execute our meeting and report.

Thank you to Hilda Cardona and Aleshka Ortiz Rojas from the HPS Network who helped with our speakers and hosted our live Participation Event in Puerto Rico, and Carmen Camacho and Frankie Feliciano for their help with translators and translations. In addition, thank you to our translators here who provided live translation for the meeting and for this report.

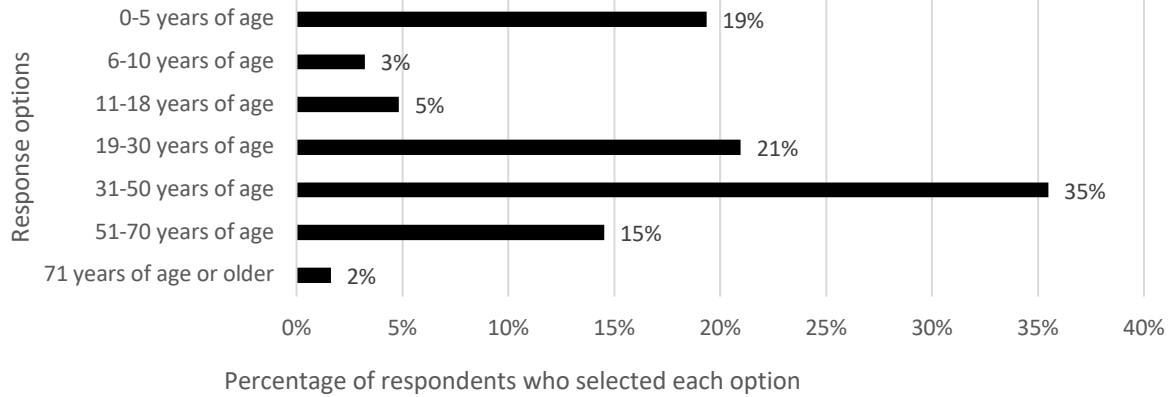


## Appendix 1: Demographics

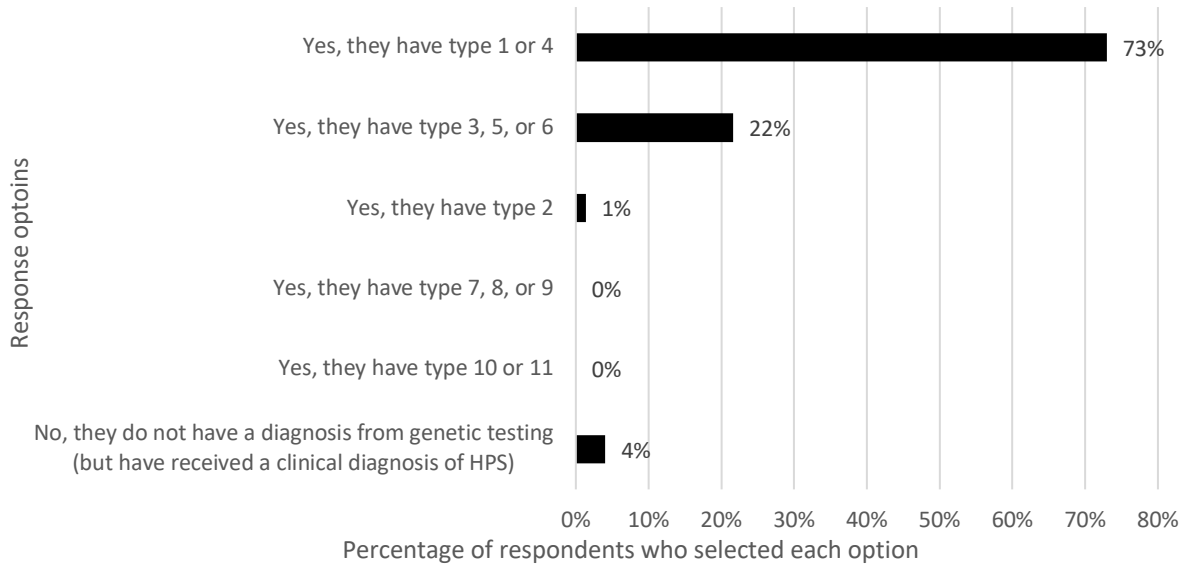
The graphs below include all attendees who chose to participate in online voting. While the response rates for these polling questions is not considered scientific data, it provides a snapshot of those who participated in the HPS EL-PFDD meeting and is intended to complement the live and pre-recorded comments throughout the meeting.



### 3. How old are you or your loved one?



### 4. Do you or your loved one have a genetic diagnosis or subtype identified?



## Appendix 2: EL-PFDD for HPS Meeting Agenda – 7 June 2022

*All times are Eastern Daylight Time*

|                   |  |
|-------------------|--|
| 10am – 10:05am    | <b>Welcome and Opening Remarks</b><br><i>Donna Appell, RN Executive Director &amp; Founder</i>   |
| 10:05am – 10:15am | <b>FDA Introduction to PFDD</b><br><i>Wilson Bryan, MD, Dir., Office of Tissues &amp; Advanced Therapies, CBER, FDA</i>  |
| 10:15am – 10:30am | <b>Disease Epidemiology Overview</b><br><i>William A. Gahl, MD, PhD, Director, Undiagnosed Diseases Program, NIH</i>   |
| 10:30am – 10:40am | <b>Discussion Format Overview &amp; Demographic Polling</b><br><i>James Valentine, JD, MHS, Meeting Moderato</i>   |
| 10:40am – 11:05am | <b>Patient Testimonials</b><br><i>Patrice Wein, Living with HPS</i><br><i>Milagros Santiago, Living with HPS</i><br><i>Candice and Crystal Sipe, Living with HPS</i><br><i>Karen Tillman, Living with HPS</i><br><i>Ashley Appell, Living with HPS</i> |
| 11:05 – 12:30pm   | <b>Discussion of Symptoms and Daily Impacts</b>  |
| 12:30pm – 1:00pm  | Break  |
| 1:00pm – 1:10pm   | <b>HPS Standard of Care &amp; Treatment Options</b><br><i>Dr. Bernadette Gochuico, MD, Attending Pulmonologist, NHGRI, NIH</i>   |
| 1:10pm – 1:35pm   | <b>Patient Testimonials</b><br><i>Christina Cislak, Living with HPS</i><br><i>Leslie Rojas, Living with HPS</i><br><i>Carmen Camacho, Living with HPS</i><br><i>Heather Kirkwood, Living with HPS</i><br><i>Caren Shank, Former Caregiver</i>          |
| 1:35pm – 2:55pm   | <b>Discussion of Current and Future Treatments</b>   |
| 2:55pm – 3:05pm   | <b>Meeting Summary</b><br><i>Becky Nieves, Board Member</i>  |

## Appendix 3: Meeting Discussion Questions

### **Session 1: Living with HPS: Symptoms and Daily Impacts**

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

### **Session 2: HPS Current and Future Approaches to Treatment**

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

## Appendix 4: Panel Participants, Discussion Starters and Callers

### Session 1: Living with HPS: Symptoms and Daily Impacts

#### Patient/caregiver testimonials

- Patrice, 56 years old, living with HPS type 3
- Milagros (Puerto Rico), 56 years old, living with HPS type 1
- Candice and Crystal, identical twins living with HPS type 4
- Karen, 58 years old, living with HPS type 1, lung transplant recipient
- Ashley, 35 years old, living with HPS type 1

#### Zoom discussion starters

- Jill, living with HPS type 5
- Kylee, 15 years old, living with HPS type 1
- Kristen, parent of 15- and 5-year-old daughters, both living with HPS type 1
- Heather W., age 31, living with HPS type 4
- Kelly, 32 years old, living with HPS type 1

#### Voices from Puerto Rico - individuals living with HPS

- Wilson (Puerto Rico), living with HPS type 1
- Angela (Puerto Rico), 21 years old, living with HPS type 1
- Angeliz (Puerto Rico), 30 years old, living with HPS type 1
- Hilda Cardona, gave a voice to all in attendance at the live Participation Event in Aguadilla, Puerto Rico

#### Callers

- Casey (caller), living with HPS type 3
- Maryanne (caller), living with HPS, lung transplant recipient
- Beth (caller), parent of a child with HPS type 1

### Session 2: Current & Future Approaches to Treatment for HPS

#### Patient/caregiver testimonials

- Christina, 21 years old, living with HPS type 3. Her story was read by Casey, also living with HPS type 3
- Leslie (Puerto Rico), living with HPS type 1
- Carmen, 57 years old, living with HPS type 1
- Heather K., 49 years old, living with HPS type 1, single lung transplant recipient
- Caren, caregiver and widow of a husband who died at the age of 43 from complications of HPS type 1

**Zoom discussion starters**

- Cassandra, 24 years old, living with HPS type 1
- Yeida, 44 years old, living with HPS type 1
- Nancy, 63 years old, living with HPS type 1, double lung transplant recipient
- Mariel, 26 years old, living with HPS type 1
- Noel, 48 years old, living with HPS-1

**Voices from Puerto Rico - individuals living with HPS**

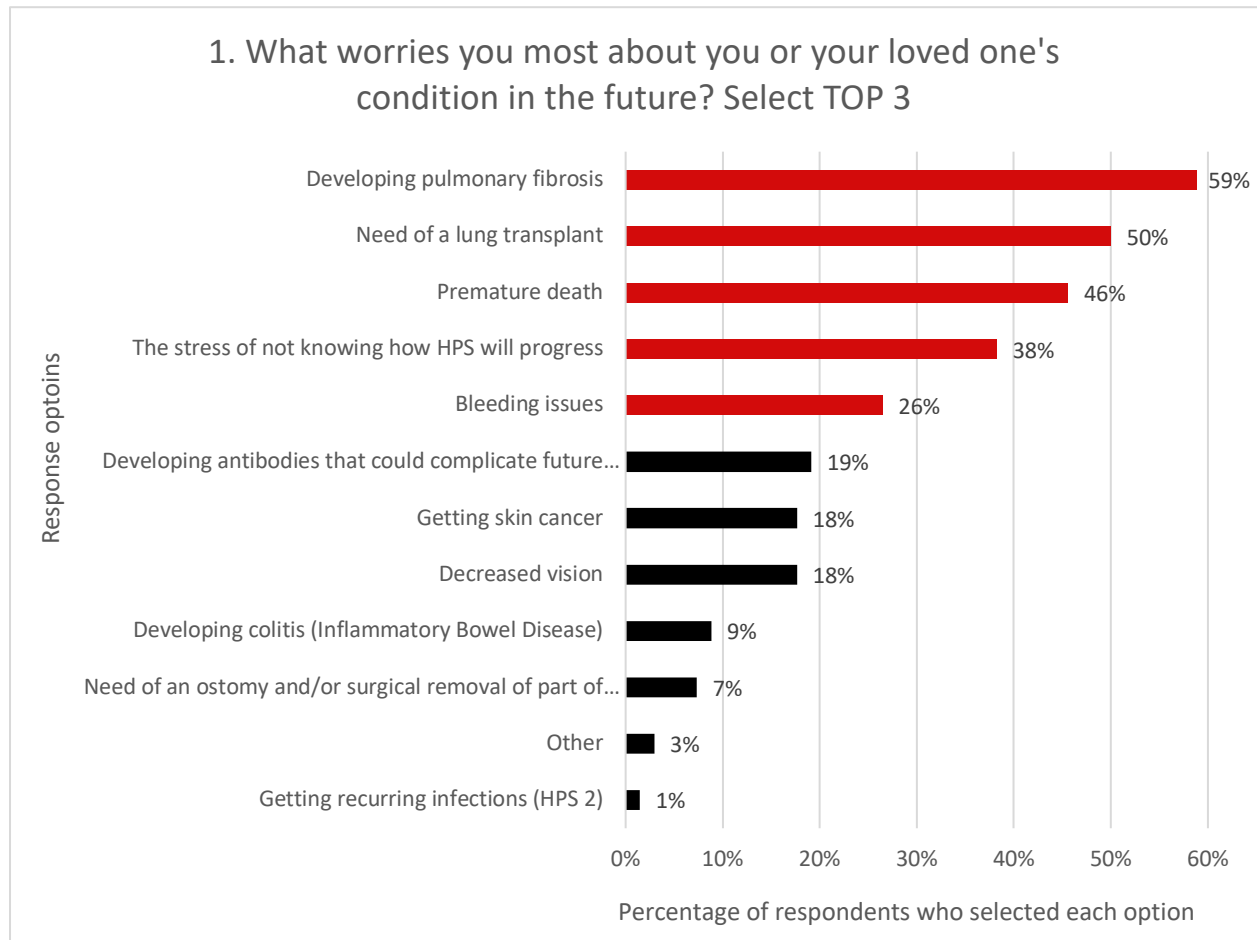
- Jose (Puerto Rico), 48 years old, living with HPS type 1
- Abdiel (Puerto Rico), 30 years old, living with HPS type 1
- Lymaris (Puerto Rico), 45 years old, living with HPS type 3
- Hilda Cardona, gave a voice to all in attendance at the live Participation Event in Aguadilla, Puerto Rico

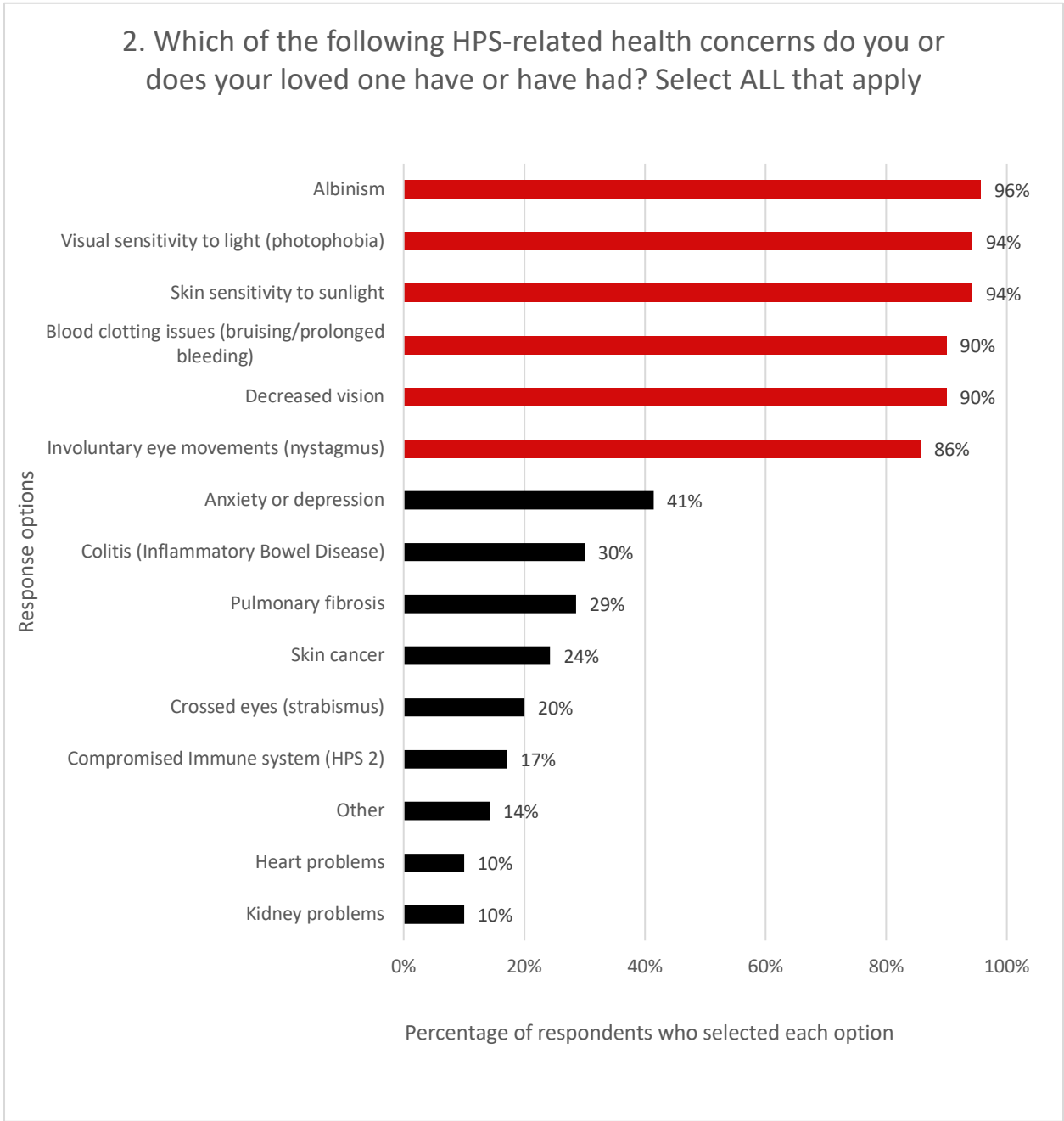
**Callers**

- Samantha (caller), 21 years old, living with HPS type 1

## Appendix 5: Session 1 Polling Results

The graphs include those attendees who chose to participate in online voting. For most questions, poll respondents could select more than one response. While the response rate data for these polling questions is not considered scientific data, it provides a snapshot of who participated in the HPS EL-PFDD meeting and is intended to complement the live and pre-recorded comments throughout the meeting.

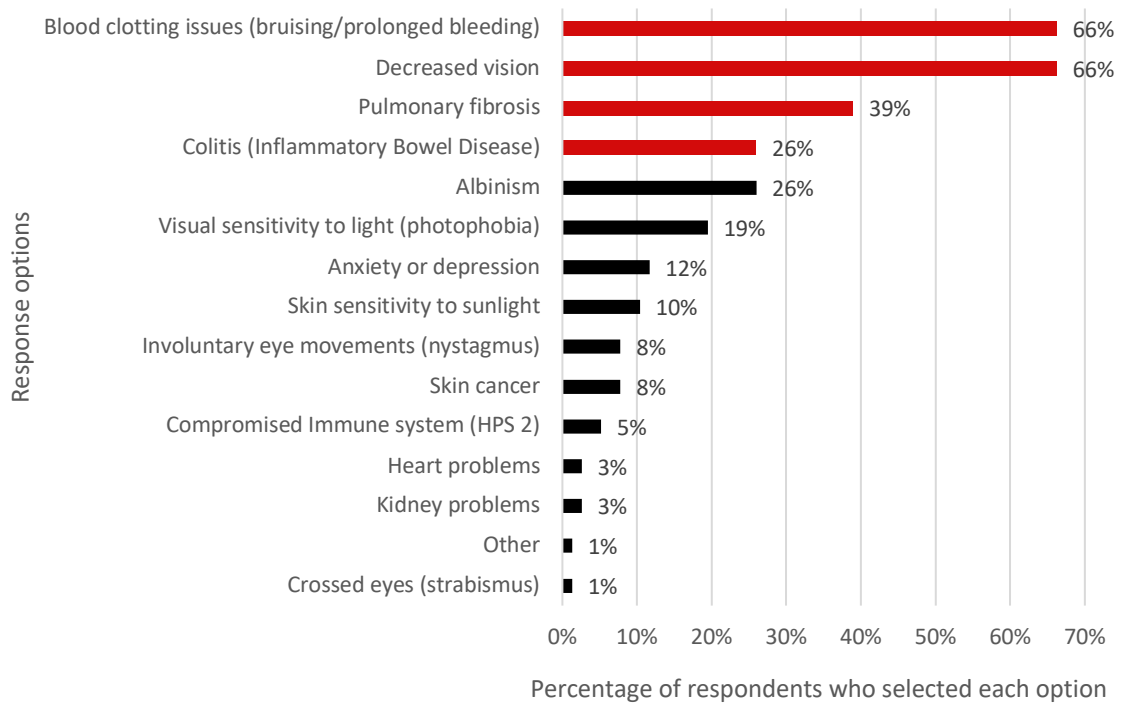




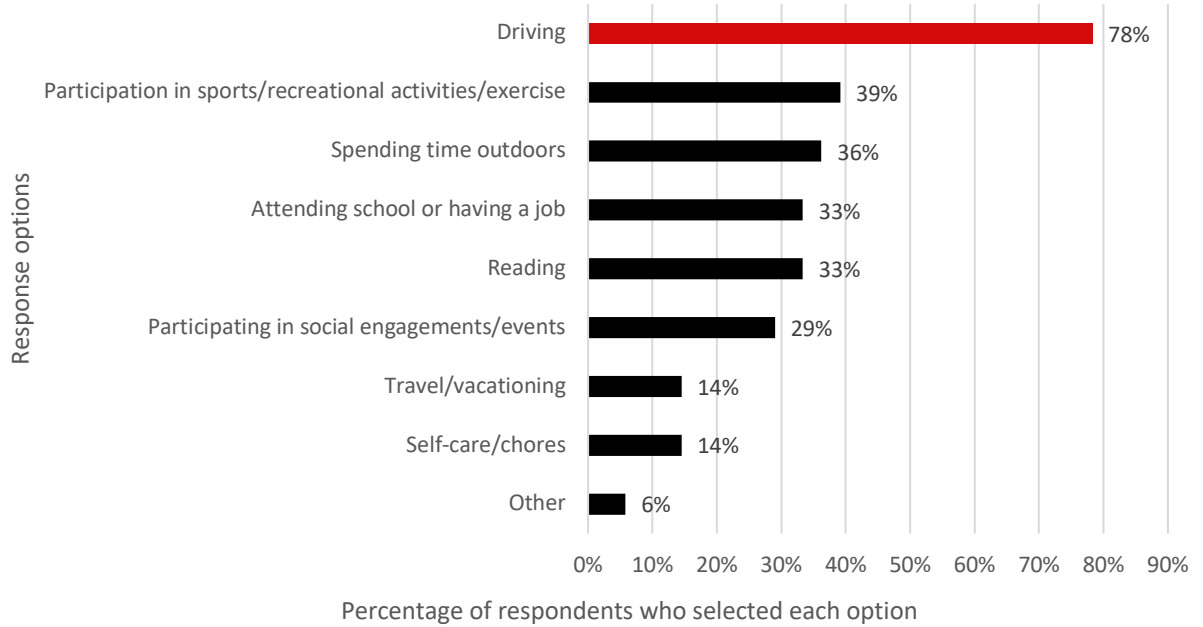
Respondents each selected an average of 7.4 responses to this poll question.



### 3. Select the TOP 3 most troublesome HPS-related health concerns that you or your loved one have or have had

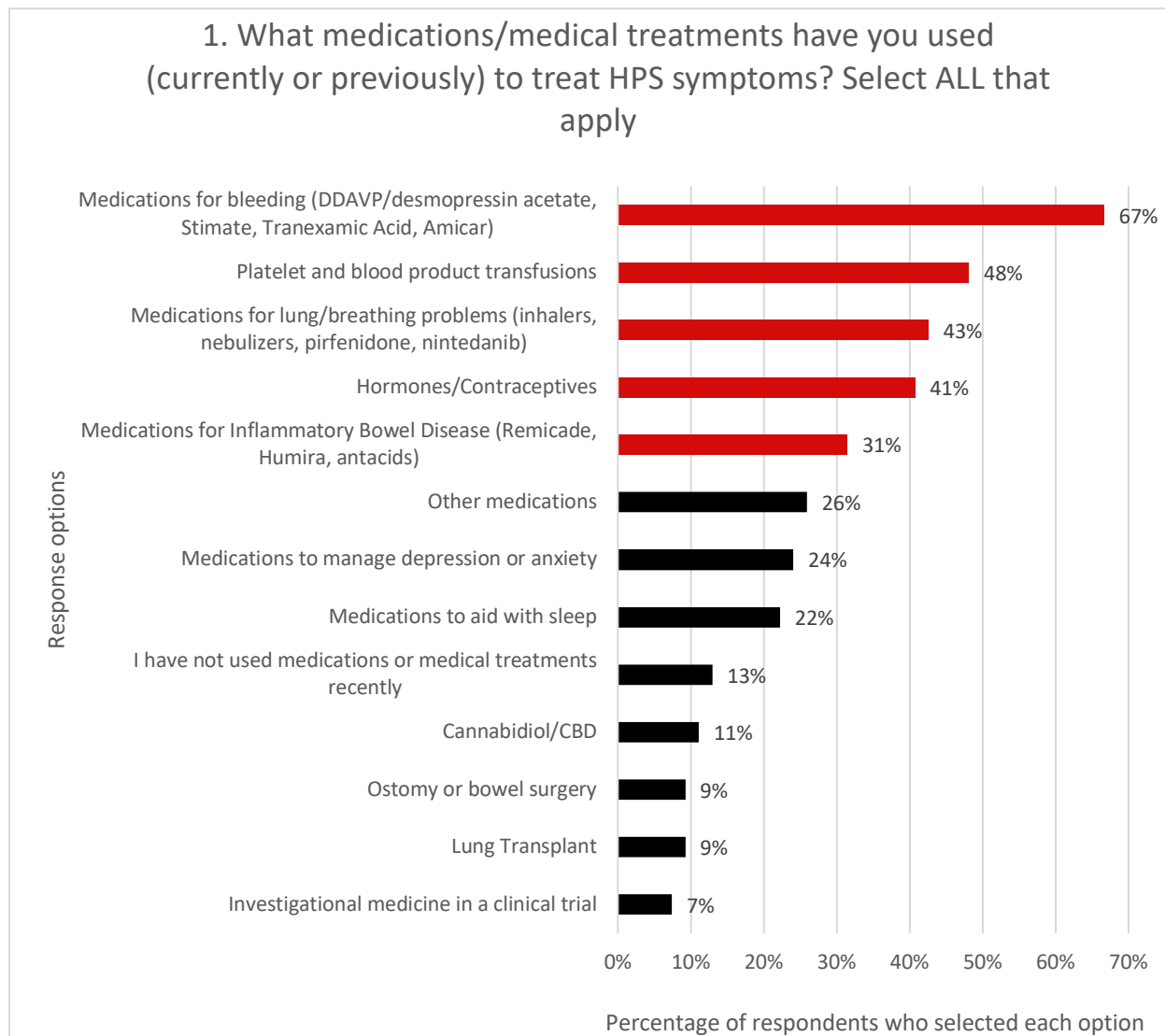


4. What specific activities of daily life are most important to you that you or your loved one is NOT able to do or struggles with due to HPS? Select TOP 3



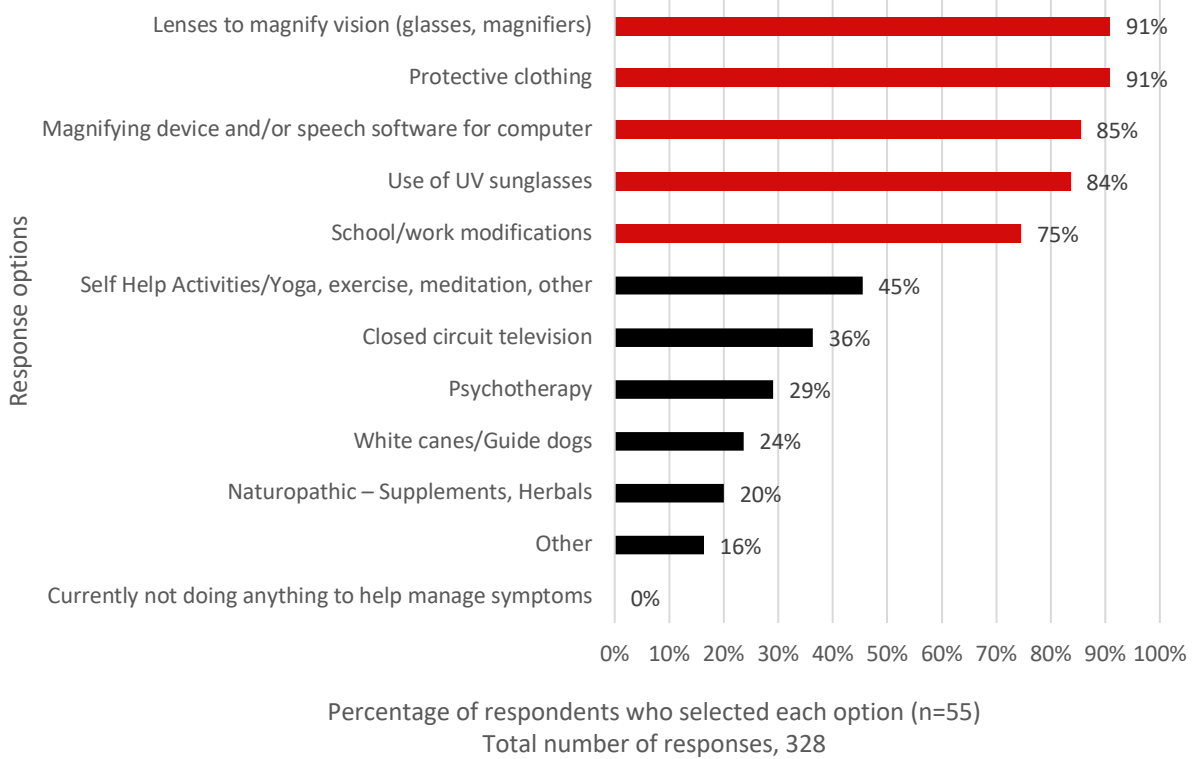
## Appendix 6: Session 2 Polling Results

The graphs include those attendees who chose to participate in online voting. For most questions, poll respondents could select more than one response. While the response rate data for these polling questions is not considered scientific data, it provides a snapshot of who participated in the HPS EL-PFDD meeting and is intended to complement the live and pre-recorded comments throughout the meeting.



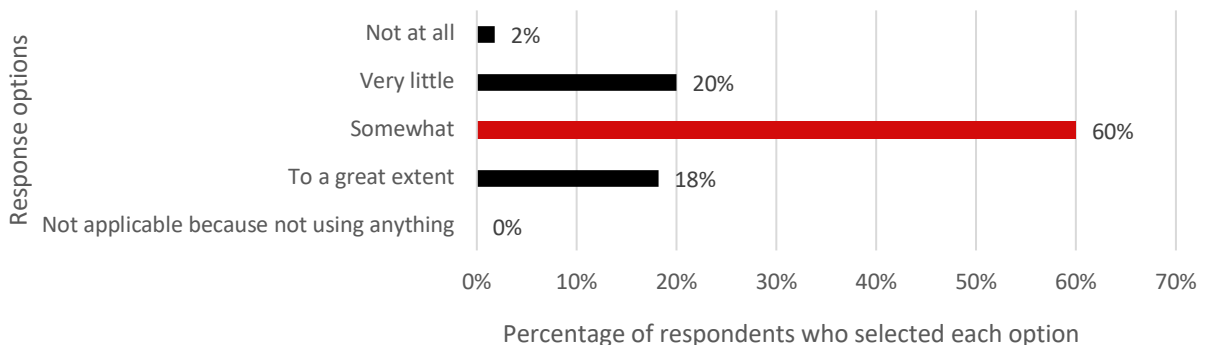
Respondents each selected an average of 3.5 responses to this poll question.

2. Besides medications/medical treatments (currently or previously), what have you used to help manage the HPS symptoms? Select ALL that apply

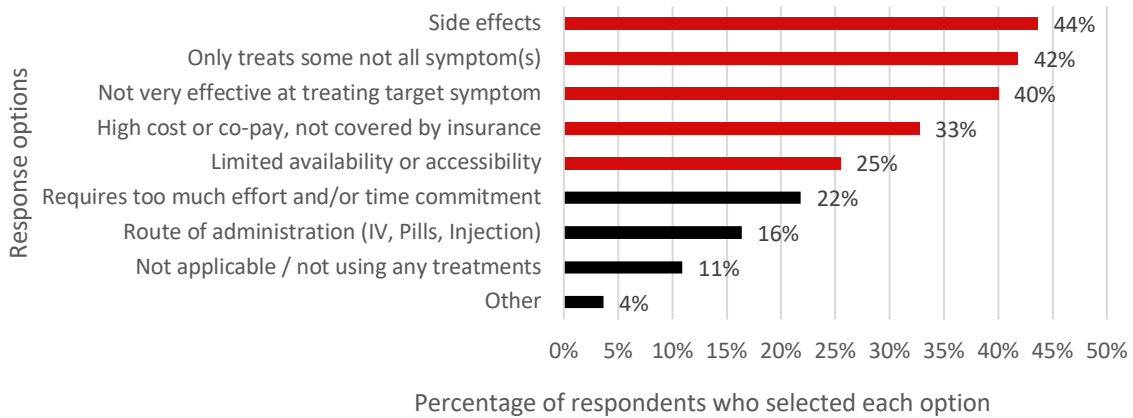


Respondents each selected an average of 6 responses to this poll question.

3. How well does your current regimen control you or your loved one's disease overall?



#### 4. What are the biggest drawbacks of your current approaches? Select TOP 3



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

