



The faces of
Childhood Onset
HSP

Hereditary Spastic Paraplegia Childhood Onset Survey 2022

Public Report



Thank you for accessing the 2022 survey report on Hereditary Spastic Paraplegia (HSP) in children. We are delighted to present you with the key findings from parents of children with HSP and adults who experienced symptoms before turning 18. This report is publicly available, and we urge you to disseminate it among healthcare providers and researchers in your child's care network.

Ece Filiz & Bridget Lassig

Who implemented the Survey?



Ece is mom to Emily who has SPG3A
They live in London.



Bridget is mom to Donovan who has de novo early onset SPG4. They live in Michigan.

Why was the Survey done?

It's been our observation that a great deal of information on childhood HSP is shared through personal experiences on social media. We wanted a means to capture the perspectives of parents, facilitate connections, and communicate trends to researchers to enhance wider recognition.

What are the goals of the Survey?

The goal of the survey is to broaden the number of identified early onset HSP cases with the aim of:

- supporting researchers
- connecting the community
- discovering trends, including shared variants
- informing diagnosis trends for reduction of misdiagnosis

What the Survey is NOT!

It is not a scientific survey; we do not gather personally identifying information and we do not validate responses.

The survey is not a complete picture. The survey was shared through social media and foundations focusing on HSP. Respondents are continuing to complete the survey and we will leave it open for this reason.

The data has not and will not be sold. This initiative is entirely driven by parents who volunteer their time and effort to share self-reported trends and information for the betterment of our children.

How do I complete the Survey?

If you have not seen or completed the Survey, we are leaving it open. You can find it here... [HSP Childhood Onset Survey](#)

We are leaving the original survey “evergreen.” It will remain open for new respondents indefinitely.

What if I already completed the Survey....

Occasionally, we may add new sections to the survey to collect data that is relevant to research or our children's quality of life. We will announce these additions on the Facebook sites and send an email to the addresses provided during the original survey response.

Who responded?



There were **167** entries representing **152** families as of January 19, 2023 (latest entry from January 15, 2023)

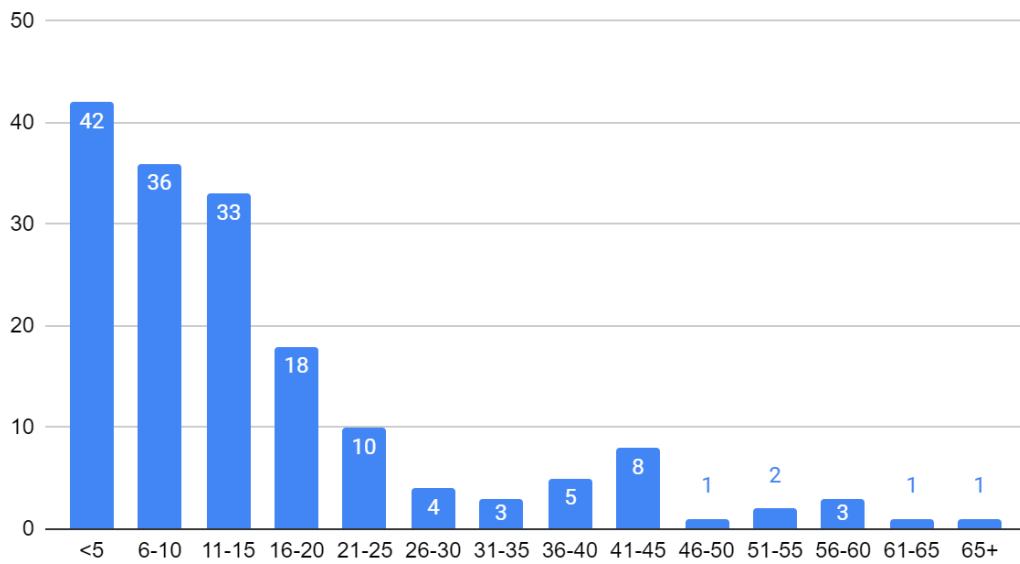
- 53% male
- 47% female

Current age of participants

- 67% of participants are younger than 16 years old



Current age of participants

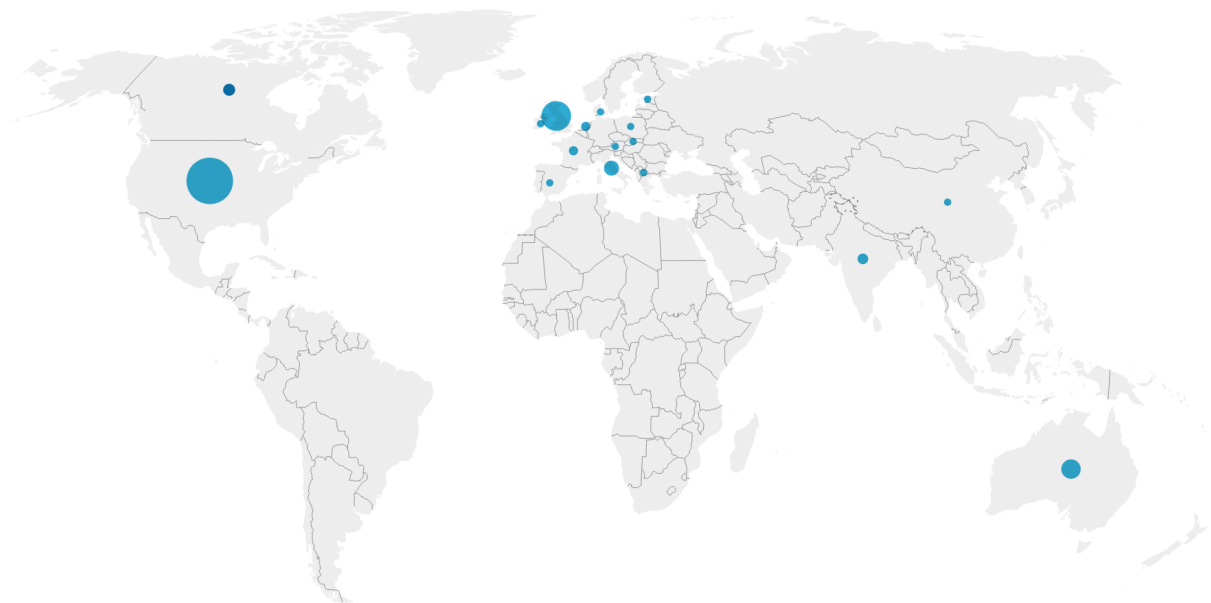
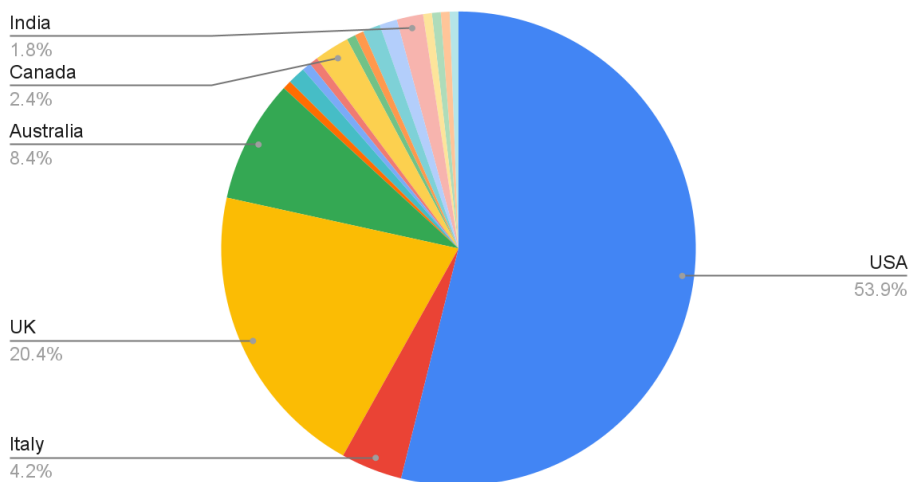


What parts of the world are represented?

The survey respondents are located in 18 different countries, ranging from large nations such as the US and China to smaller ones like Iceland and Estonia.

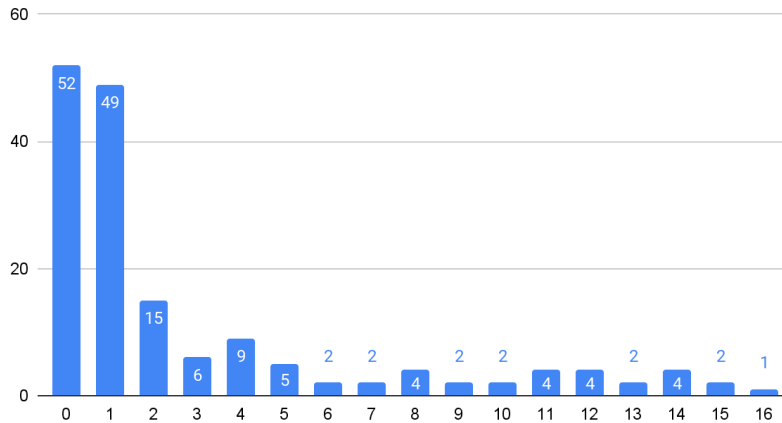
Countries where English is the main language (USA, UK, Australia and Canada) contributed 85% of the participants.

Participant countries



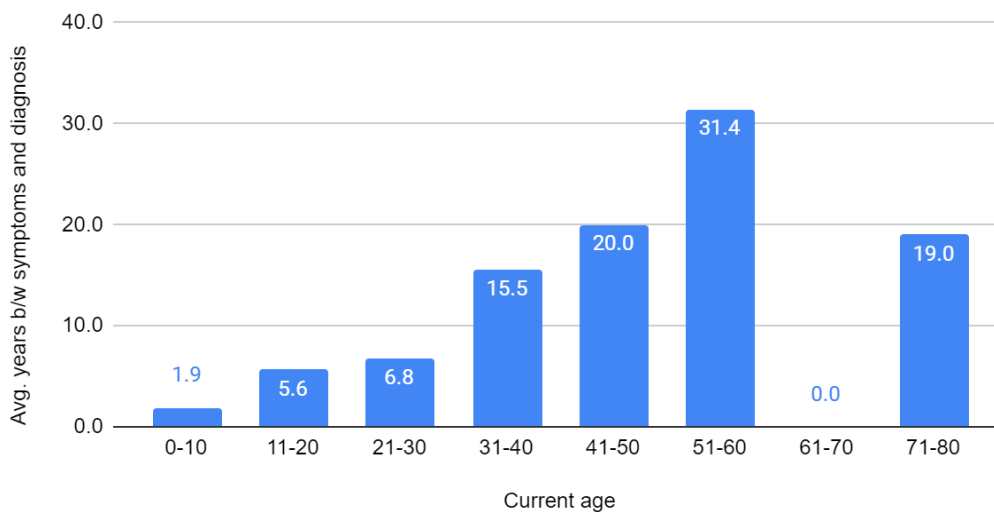
What are we hearing about symptoms & diagnosis?

Age at which symptoms started



- 52% of patients received their diagnosis before the age of 6

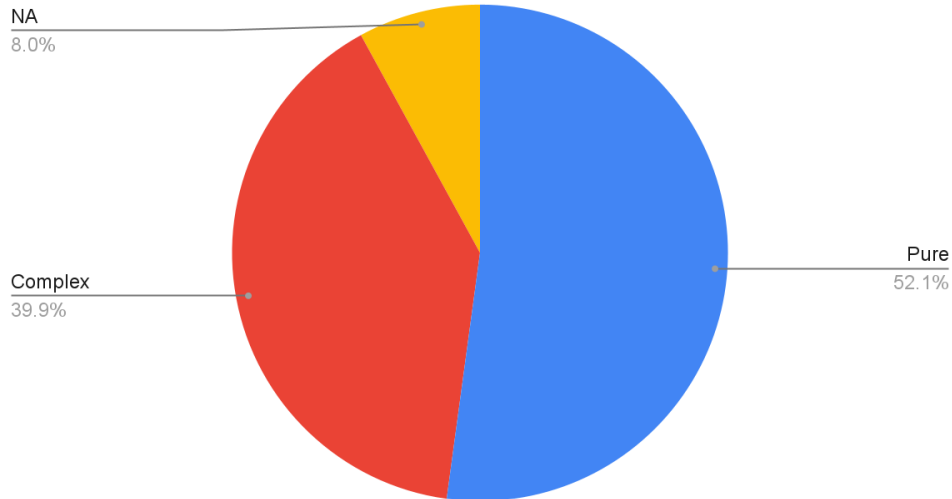
Average years between symptoms and diagnosis by current age



- The average time difference between first sign of symptoms and diagnosis is 6 years
- As shown by the graph on the right, patients are receiving a much faster diagnosis in the last 10 years

What kinds of symptoms are being reported?

Pure vs complex HSP



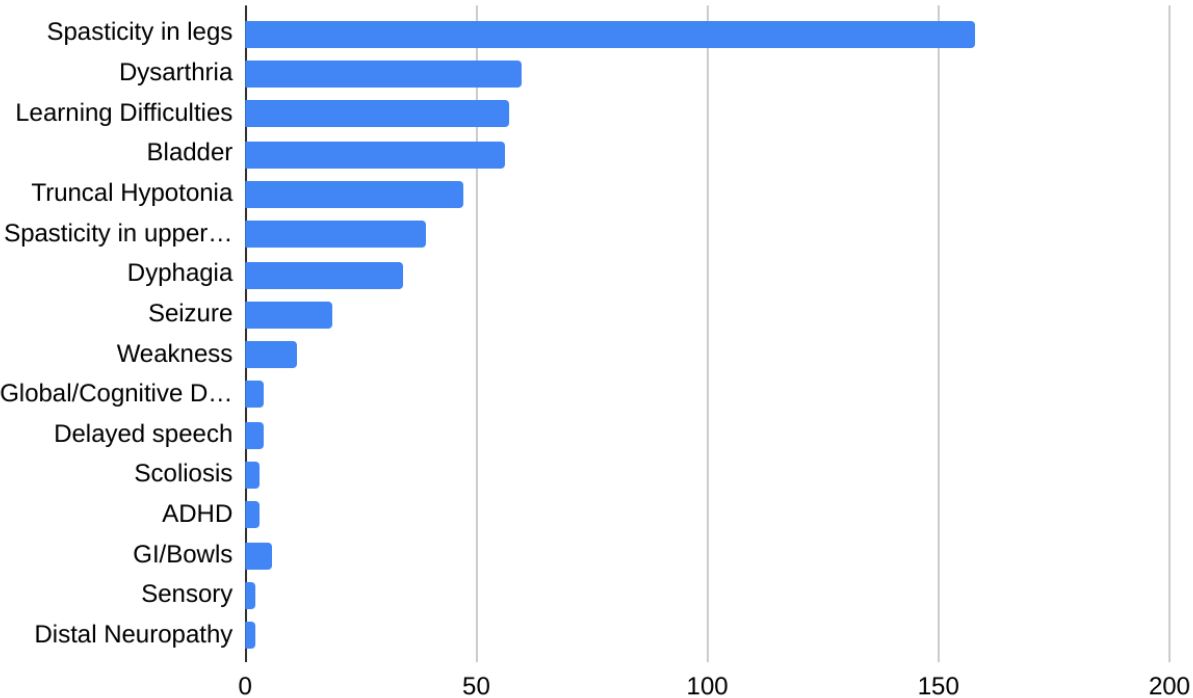
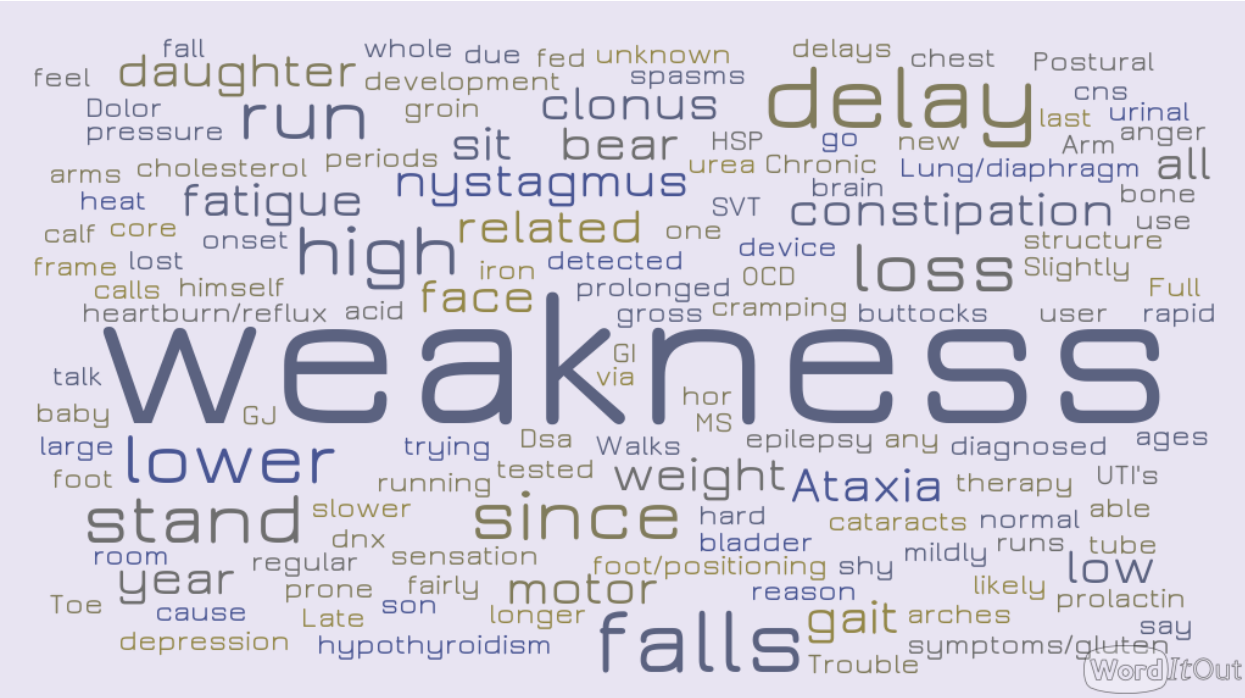
Symptoms

- Of 167 participants, 71 (43%) had at least one of the three “core” HSP symptoms (spasticity in legs, truncal hypotonia and bladder dysfunction) and had none of the other symptoms.
- This can be a better presentation of pure vs. complex types of HSP.

Pure = Symptoms involving the lower extremities.

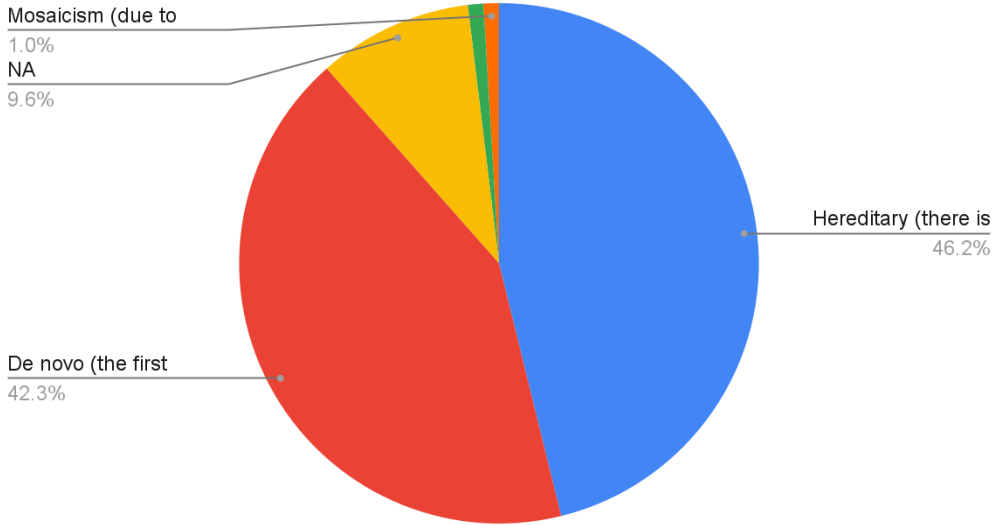
Complex = Pure symptoms plus other system involvement

24 categories of symptoms were identified by the parents. This word-cloud shows the emphasis. The chart shows the top symptoms listed



What are the inheritance patterns?

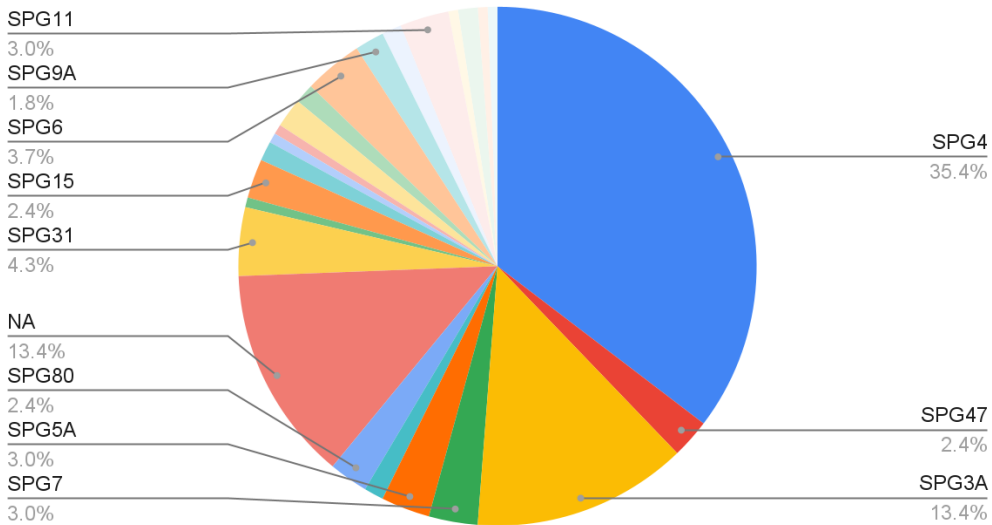
Hereditary vs de novo



Which HSP types are represented?

- 22 HSP types are represented
- SPG3A & SPG4 make up 49% of all survey participants, with SPG31 as the next largest sample

HSP types



- Types with less than 1% represented:
- ALS
 - SPG18
 - SPG2
 - SPG30
 - SPG46
 - SPG49
 - SPG50
 - SPG52
 - SPG54
 - SPG56
 - SPG84

SPG4

58 participants

Pure v complex

Pure: 39

Complex: 15

Hereditary v de novo

Hereditary: 24

De novo: 31

SPG3A

22 participants

Pure v complex

Pure: 14

Complex: 8

Hereditary v de novo

Hereditary: 8

De novo: 14

SPG31

7 participants

Pure v complex

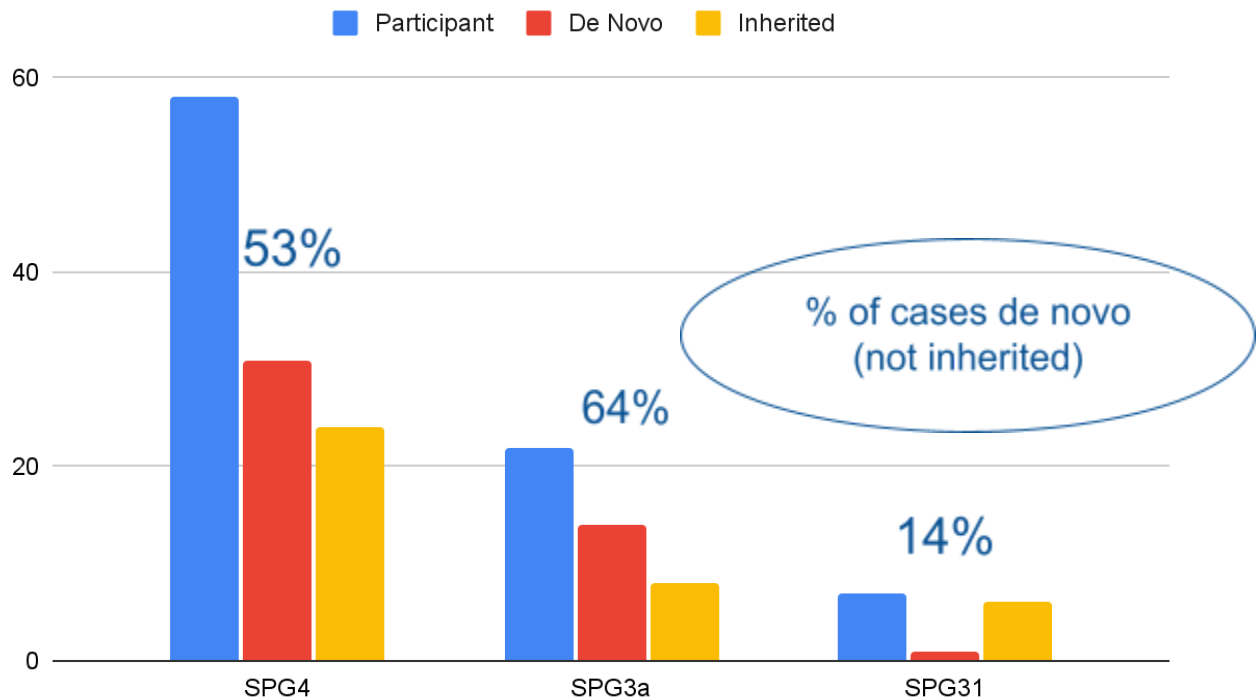
Pure: 5

Complex: 2

Hereditary v de novo

Hereditary: 6

De novo: 1



Were there any shared variants?

What is a variant? A **variant** tells the researcher where on the gene the error is. A goal of the survey is to identify **shared variants**; two or more unrelated individuals that share the exact same variant.

The 2022 responses show three variants that are shared by unrelated individuals. Interestingly, they are all de novo mutations.

Within SPG4:

p.Arg499His	c.1496G>A	De novo
p.Arg499His	c.1496G>A	De novo
p.Arg499His	c.1496G>A	De novo
p.Arg499His	c.1496G>A	De novo

p.Met390Val	c.1168A>G	De novo
p.Met390Val	c.1168A>G	De novo
p.Met390Val	c.1168A>G	De novo

Within SPG3A:

p.Lys407del	c.1220_1222del	De novo
p.Lys407del	c.1220_1222del	De novo

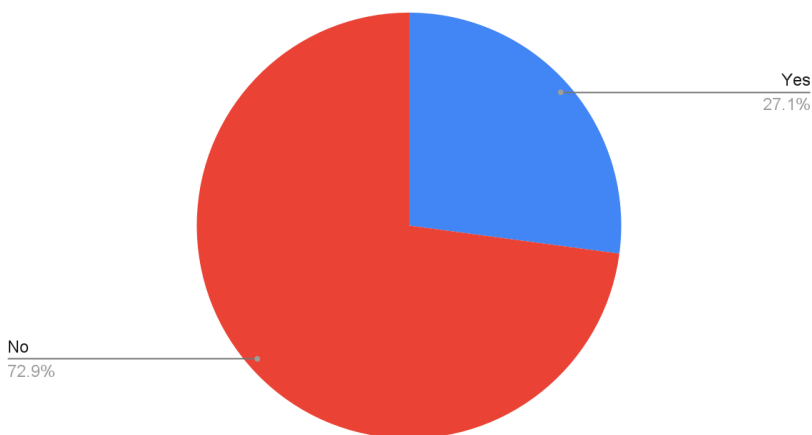
How are we informing research?

We work closely with Boston Children's Hospital's two studies; [Registry and Natural History Study of Early Onset Hereditary Spastic Paraplegia \(Natural History Study\)](#) and [Hereditary Spastic Paraplegia Genomic Sequencing Initiative \(HSPseq\)](#) to help families connect with the research.

The Natural History Study plays a critical role in establishing a comprehensive database of individuals affected by Childhood Onset Hereditary Spastic Paraplegia (HSP), which will serve as the foundation for future clinical trials. Since therapeutic research often has lengthy development cycles, the team at Boston Children's Hospital, along with their partners and committed researchers, are working tirelessly to create a comprehensive and substantial dataset. Our survey was conducted with the intention of supporting this essential initiative.

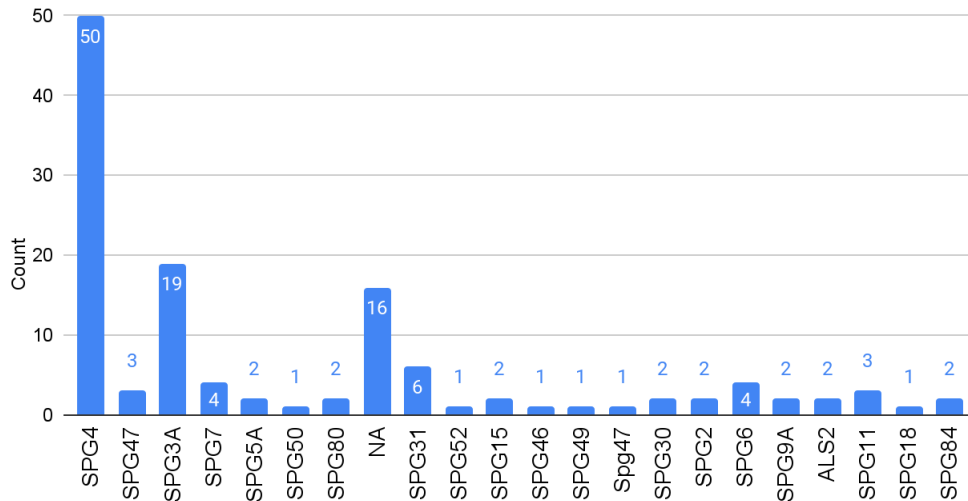
At the time of completing their surveys, 73% of respondents had not enrolled their child in the Natural History Study. 108 individuals were sent letters personally introducing each of them with the Research Coordinator, who is now [Amy Tam](#). This resulted in approximately 70 people initiating enrollment in the Study

Registered with the Natural History Study?



Of those referred to the Study, the following graph shows the representation of the HSP Types.

Potential new participants in the Natural History Study



What is the status of the Natural History Study?

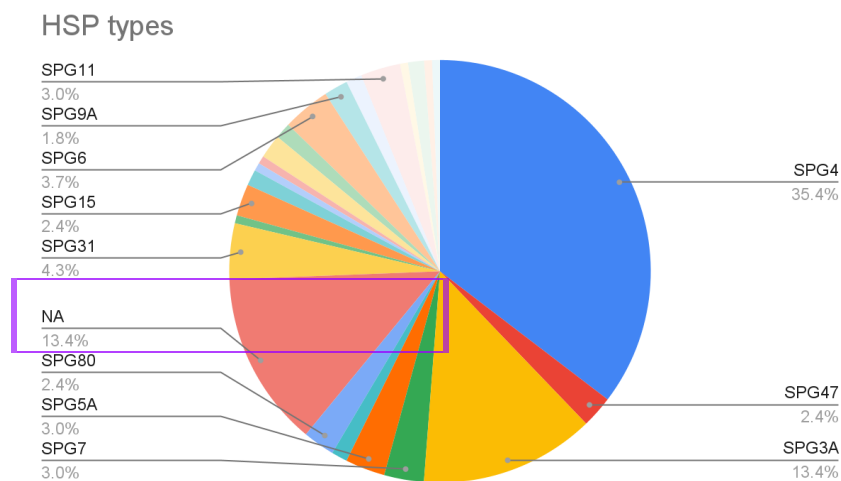
As of January, 2023 the following was shared:

- **421 participants** are enrolled in the Natural History Study
- As the Study originally focused on AP-4 subtypes, there are many families representing SPG47, SPG 50, SPG51, and SPG52. However, there are **25 gene types** represented overall
- The majority of participants are from Europe and North America, followed by the Middle East and North Africa. [Every continent is represented.](#)
- Enrolling in the study **can be virtual** or in person and involves: an initial interview, two questionnaires, an MRI and other optional steps such as blood sample for biomarkers and there are follow-up appointments every 6-9 months which, again, can be virtual.
- Challenges the research team is facing: Getting patients questionnaires filled and scheduling follow-up visits.

What is the status of the HSP Genomic Sequencing Initiative?

This HSPseq [study](#), which enrolls individuals with early onset HSP clinical symptoms but have not had genetic confirmation began in April 2022.

- There are **35 probands** (a person who is a starting point of a genetic study) enrolled
- DNA samples are gathered from the child and both parents.
- At the time of this report, there have been **100 samples collected**.
- These are mostly from within the US but starting to reach international community and collaborators

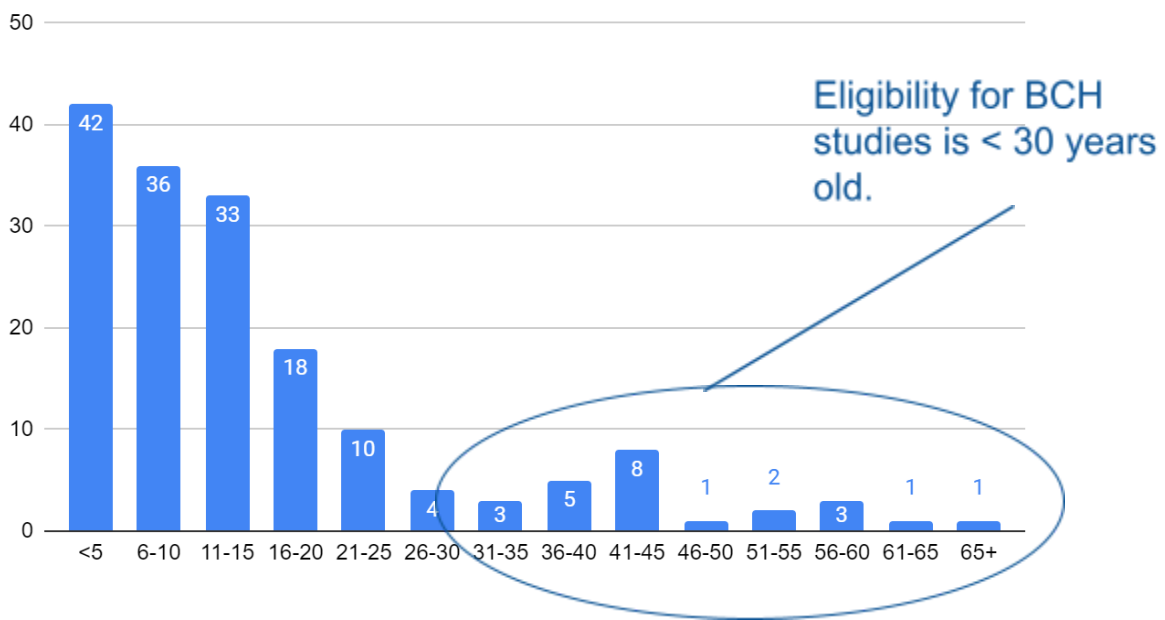


These 14 participants without a genetic test confirmation have been referred to the HSPSeq Study

What about the adults who completed the survey?

There were 47 adults (participants age 18 and above) who experienced childhood onset of symptoms that completed the survey. Of those, 24 do not meet enrollment criteria for the BCH Natural History Study of being under 30 years of age. We are working to contact researchers to determine how these adults can also enroll in research.

Current age of participants



How are we sharing this information?

We are pleased to announce that, in addition to making this public report available to all survey participants and on social media, a more detailed report is being made available to numerous researchers who are devoted to advancing their understanding and developing treatments for Hereditary Spastic Paraplegia (HSP). This list of recipients includes, but is not limited to:

Australia

- Griffith University, Queensland
- Murdoch Children's Research Institute, RDNOW Program
- National Hospital for Neurology & Neurosurgery, Queen Square,
- University of Sydney, Concord Clinical School, ANZAC Research Ins.

Estonia

- Tartu ülikooli kliinikum (Tartu University Hospital)

France

- SPATAX in Paris

Germany

- Tuebingen University- Schüle Lab

Italy

- Stella Maris Foundation

United Kingdom

- 100,000 genome project, University college hospital
- National Hospital for Neurology & Neurosurgery
- Sheffield Children's Hospital
- University of Exeter

United States

- Albert Einstein College of Medicine, Brain Study
- Applied Therapeutics
- Atlantic Health Systems; Pediatric Neurology
- Baylor College of Medicine
- Boston Children's Hospital, Natural History Study/Genomic Sequencing
- Columbia University

- Drexel University
- Invitae
- Massachusetts General Hospital, Movement Disorder Clinic
- NIH: Undiagnosed Disease Program & Rare Disease, and NIA
- NINDS: Ultra-Rare Gene-Based Therapy (URGent) Network
- Northwestern University
- Scottish Rite Hospital
- St Louis University Hospital
- Texas Scottish Rite Children's Hospital
- University of Florida, Clinical and Translational Science Institute
- University of Florida, Movement Disorders
- University of Illinois
- University of Kansas-SEALS
- University of Michigan Medicine, Adult Neurology
- University of Massachusetts
- ANZAC Research Institute"
- Valley Children's Hospital
- Washington University in St. Louis, "Answer ALS"

**On average, it takes 6 years to
get diagnosed after showing
first symptoms. Let's spread
awareness and diagnose earlier!**

We encourage you to [share this report with your child's provider\(s\) to help increase awareness of Childhood Onset HSP.](#)

Attachments

1. Where to Find/Who to contact?
2. Meet just a Few of the Kids
3. What is Hereditary Spastic Paraplegia
4. Questions from the Survey

Many thanks to outgoing Boston Children's Hospital Research Coordinator, Catherine Jordan whose compassion and attention to details has cared for many of our children! Catherine's email address will be active for the month of March.
Welcome to Amy Tan

Where to Find/Who to contact?

Survey:

<https://forms.gle/wBWXw8QfzJrAYvUY7>

Survey Contacts:

Ece Filiz efiliz@gmail.com

Bridget Lassig bridget.lassig@gmail.com

Boston Children's Hospital Contacts:

Dr. Darius Ebrahimi-Fakhari darius.ebrahimi-fakhari@childrens.harvard.edu

Amy Tam Amy.Tam@childrens.harvard.edu

Studies:

[*Registry and Natural History Study of Early Onset Hereditary Spastic Paraplegia \(Natural History Study\)*](#)

[*Hereditary Spastic Paraplegia Genomic Sequencing Initiative \(HSPseq\)*](#)

HSP Cure and Support Foundations:

[Cure AP-4 \(SPG 47, SPG 50, and SPG 51\)- US](#)

[Cure SPG4 - US](#)

[Cure SPG50- Canada](#)

[Enorev \(Gwenaëlle Airdon- France\)](#)

[HSP Research Foundation - Australia](#)

[Kids with SPG3a](#)

[Our Moon's Mission- SPG 56 - Australia](#)

[Saving Jordan Foundation - SPG49](#)

[Team Leni Foundation - SPG49](#)

[The Hereditary Spastic Paraplegia Support Group- UK](#)

[The Lily & Blair Foundation- De Novo HSP - US](#)

[The Maddi Foundation-England SPG 15](#)

[The HSP & PLS Foundation - US](#)

[The Tom Wahlig Foundation- Germany](#)

Meet Just a Few of the Kids and the Types we are fighting....

What is Hereditary Spastic Paraplegia (HSP)?

-a simple explanation by two moms; Ece Filiz & Bridget Lassig (2023)

HSP is a progressive rare genetic disorder. A mutation in any one of up to 80+ genes discovered to date can result in a range of symptoms. The primary symptom is changes to the legs, including spasticity, weakness, and sometimes cramping. This is caused by the degeneration of upper motor neurons that travel from the brain to the legs. The severity of symptoms ranges from minor balance issues to complete dependence on a wheelchair for mobility.

HSP can manifest as **Pure**, with symptoms affecting only the lower extremities. In other cases, it can be **Complex** (or sometimes referred to as “complicated”), affecting, in addition to the lower extremities, other systems such as speech and fine motor skills.

HSP symptoms can begin at any age. New research is suggesting that the age at which symptoms begin might have to do with the specific mutation a person has within each **Type** or gene involved (i.e. SPG4). The severity of symptoms for each variant can range widely; an area of active research is looking to understand how an individual may have protective factors that reduce the intensity of the symptoms.

HSP, as the “hereditary” in the name suggests, is most often inherited from parents. On the other hand, there seems to be increasing awareness of de novo cases, i.e. cases that occur due to a spontaneous mutation in an individual.

At present, there are no cures for HSP, and treatment is focused on managing the symptoms. However, there is a growing field of passionate and dedicated researchers actively exploring therapeutic options and working towards clinical trials. Their areas of research include gene editing (CRiSPR), gene replacement, ASO, mRNA and drug repurposing.

Identifying and engaging families affected by HSP can provide valuable data for developing and testing new treatments. When it comes to finding a cure for a rare disease such as HSP, there is strength in numbers.

2022 Childhood Onset HSP Survey

Source Questions

Questions:

Has your child been diagnosed with Hereditary Spastic Paraplegia (HSP)?

Section 2 of 6

Demographics

- Is your child male or female?
- What year was your child born?
- How old is your child now?
- At what age did your child begin to show symptoms?
- How old was your child when he/she was diagnosed with HSP?
- Where do you live (Country, State, Province, etc)?

Section 3 of 6

Diagnosis

- Has your child had a genetic test to confirm their HSP diagnosis?
- Was the test positive for an HSP diagnosis?
- If you answered "yes" to the previous question, what type of HSP does your child have (SPG3, SPG4, etc)?
- What is your child's gene variant (for example: c.1168A>G MetVal 390 on exon 8)? This may be found on the genetic test report.
- Is your child's gene variant hereditary or de novo?
- If you answered yes to Hereditary, is the gene Recessive or Dominant?

Section 4 of 6

Symptoms

- Does your child exhibit pure or complex symptoms?
- What are your child's symptoms? Please select all that apply.
- Are there other symptoms you would like to mention or describe?

Section 5 of 6

Research

- Have you registered your child with the Natural History Study for Early Onset HSP managed by the Boston Children's Hospital (<https://clinicaltrials.gov/ct2/show/NCT04712812>)?
- If you answered "no" to the previous question, would you like the research coordinator from Boston Children's Hospital to reach out to you?
- Does your child participate in any other research studies?
- If you answered "yes" to the previous question, can you please share which researcher and/or institution you work with?

Section 6 of 6

Further Communication

- Can the survey organizers contact you to ask further questions or ask you to participate in future surveys?
- Can the researchers, with whom the results of this survey will be shared, reach out to you with questions?
- Are there any other researchers with whom you would like us to share the results of this survey? If yes, can you please share their name, institution and contact details?
- If another survey participant has the same gene variant as your child, would you like to be informed and contacted?

