8P FAMILY WELCOME GUIDE

PROJECT 8p FOUNDATION

Welcome to the 8p Community

*From the Project 8p Family & Science Conference

We are so glad you found Project 8p Foundation. You are now part of a caring and supportive community dedicated to advancing understanding, resources, and hope for families affected by Chromosome 8p rearrangements. Our community is made up of families, researchers, healthcare providers, and the individuals we affectionately call 8p heroes, known for their strength, resilience, and courage.

While we recognize that receiving an 8p diagnosis can be a journey filled with a wide range of emotions, we want to assure you that you are not alone in traveling that journey. Families impacted by Chromosome 8p rearrangements are located across the world, and Project 8p, a non-profit organization that consists of a community of Chromosome 8p families, is connected with more than 500 8p heroes and welcomes new families every year.

Chromosome 8p Rearrangements or Disorders are also considered a rare disease, defined in the U.S. as a condition that affects less than 200,000 people. While each disease is individually rare, rare disease are actually quite common. In the U.S., rare disease affects 1 in 10 people. The rare disease collective is a powerful community, filled by the millions across the world that are impacted by a wide variety of conditions.

In short, you are not alone!

This welcome packet is designed to be a resource following a new diagnosis. A new 8p diagnosis not only connects you with our community, but it empowers you and your care team to make more informed decisions about care, management, and next steps. This packet contains content to help inform and navigate those next steps. It will provide context for the underlying genetics of an 8p diagnosis, insight into symptoms and management options, opportunities to connect with resources, and places to find support from others who understand your path.

While this packet contains a wide range of information, we understand that in the early stages of a diagnosis, it may not feel right to take in every detail. This resource is intended to be used for continued referral, and we recognize that not all of the information may be needed or relevant at once. For that reason, the packet offers a table of contents, which allows you to skip to a section that may be most relevant for a specific moment. We encourage you to come back to this packet repeatedly as you encounter a new question, consider new therapies, or meet with new doctors.

It is also important to emphasize that everyone's 8p journey is different. Some 8p Heroes are diagnosed in utero, while others are diagnosed in their 40s. Some heroes will have certain symptoms but not others. While this packet provides a general guide for what you might experience, it does not attempt to grasp the nuances of everyone's individual journey.

A large portion of this packet will walk through some of the main symptoms and medical challenges that of which an 8p diagnosis may consist. While it is intended to provide information on health conditions seen in 8p heroes, it is not a substitute for professional medical care. The information presented in this packet is intended to help families and caregivers better understand these conditions and to facilitate informed discussion with healthcare providers. Always consult with your physician or healthcare provider before making any medical decisions.

If you have any questions regarding the content of the packet or need assistance with its use, please reach out to engagement@project8p.org.

A final note:
The packet largely focuses on the medical concerns and management for 8p heroes, which, while important to learn about, may seem like a daunting list of scariness and uncertainty. For that reason, we want to conclude our welcome by emphasizing the fulfilling lives that many 8p Heroes lead. Each hero is unique and has their own strengths, and the exciting part about your 8p journey is learning what makes your hero special! Project 8p is pleased to accompany your family along that path of discovery.

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I. Our 8p Heroes: Their Stories

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II. What is Chromosome 8p?

Chromosome 8p disorder is a genetic condition that is known to affect 550 individuals worldwide, but has a reported prevalence of 1:10,000 - 1:30,000. Chromosome 8p disorders are caused when there is a rearrangement of genetic information before birth, on the short arm (the p arm) of the 8th chromosome. This genetic rearrangement can be the deletion of information, duplication of information, or inverted duplication and deletion (invdupdel). The chromosomal rearrangement typically arises from spontaneous (de novo) changes early during embryonic development, for reasons that remain unclear. Chromosome 8p disorders have systemic effects, meaning they impact cells and tissues throughout the body, rather than being confined to a single organ. The severity and specific features of 8p disorders can vary significantly based on the amount of genetic information that has changed in addition to other factors that we are still working to understand.

The following section seeks to provide background of the genetics concepts relevant to an 8p rearrangement, explaining many of the terms used above in greater detail.

II.1 Overview of Genetics

The human body is composed of trillions of cells. Cells are the building blocks of each organ in our body, each specialized to work together to allow us to perform daily functions.

Located within every cell is all of a person's genetic information, the code that provides instructions for all of the components needed to build the human body and perform any of its tasks.

The genetic information that is found in a cell's nucleus is organized into 23 pairs of chromosomes (46 total). Chromosomes are organized, compact structures that are made up of DNA (deoxyribose nucleic acid), a molecule that holds our genetic code. Within each of the long stretches of DNA on a chromosome are discrete segments called genes. A gene is a segment of DNA that codes for one specific component (protein) in the cells of our body. The genetic information that makes up the genes contained on each chromosome is called DNA (deoxyribose nucleic acid), a specific molecule that holds our genetic code.

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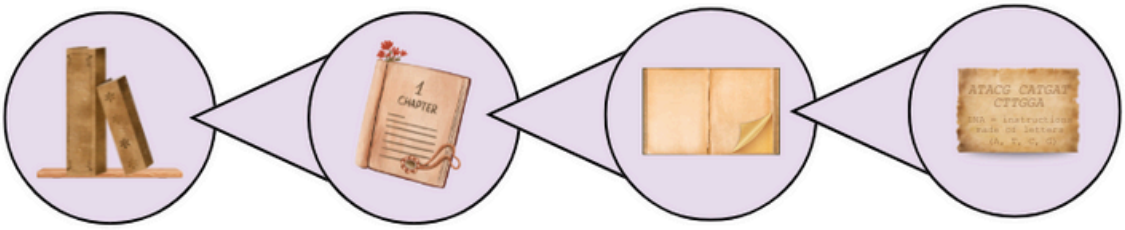

Two Books
Complete Genome

Book Chapter
Chromosome

Page of the book
Gene

Words on the page
DNA

It might be helpful to think of an analogy. The human genome can be thought of as an instruction manual describing exactly how to build our body. Each person has two instruction books, with 23 chapters in each book. Each of these 23 chapters is a chromosome. Within each chapter are hundreds of pages. A single page, like a gene, is a discrete unit that provides instructions for just one of the thousands of components in our body. These pages are composed of words. These words can be thought of as the DNA language, composed of letters of ATGC. One can imagine that if any of these words, pages, or chapters are lost, duplicated, or rearranged in order, some of the instruction's meaning may be lost or confused.

Check it out!: A Useful Video Resource

Project 8p has a three-part series published on Youtube titled "Family Friendly Introduction." This series explains some of the research in the 8p world in family-friendly language. The first part of the video series includes a talk on the basics of 8p biology, which can serve as another format to learn more about these topics.

*An exception: Red blood cell are the only cell type in our body that do not have a nucleus.

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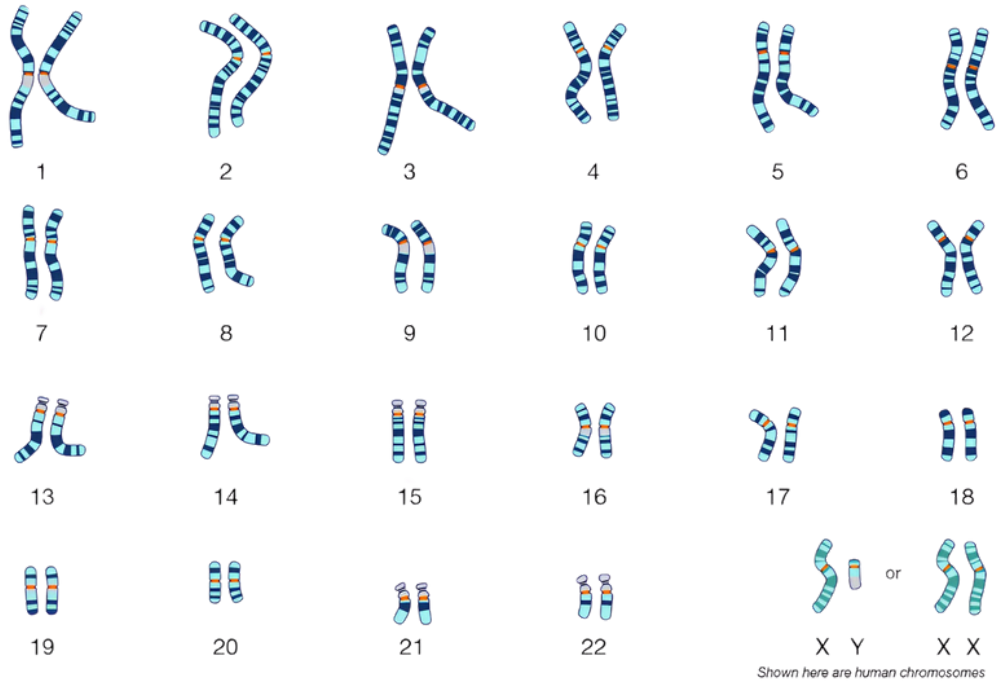
II.2 A Closer Look at Chromosomes

Chromosomes are a structure made up of DNA.

A chromosome is "named" with either a number (1-22) , or in the case of the 2 sex chromosomes, with an X or Y. Chromosomes 1-22 are called autosomes, and they contain the majority of instructions for our body.

For each chromosome, an individual inherits one copy from each parent. From our analogy, one book comes from each parent. Because of this, every individual will have 2 copies of chromosome 1 , 2 copies of chromosome 2, etc. (including 2 copies of chromosome 8!). The chromosome pair will not be exactly identical because, with one coming from each parent, they each will have small differences that create the variation we see in people.

This is a "picture" of a cell's chromosomes, called a karyotype. Notice in this karyotype how the chromosomes are arranged into pairs. Each pair is a set of chromosomes. Humans have 23 pairs, which means there are 46 chromosomes in total.



Shown here are human chromosomes

Let's take a closer look at chromosome 8 to understand more about the general chromosomal structure and terminology.

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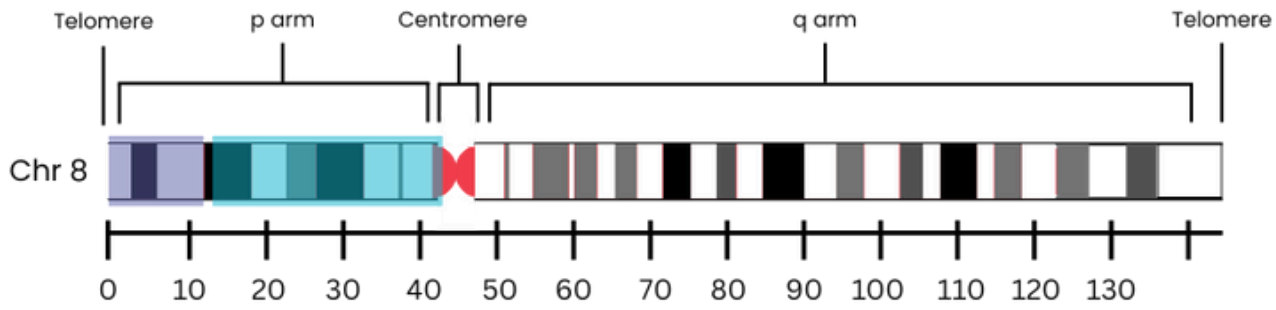

INSERT GRAPHIC – SOMETHING SIMILAR TO "ANATOMY OF A CHROMOSOMES"

Every chromosome has a central structure, called the centromere. The centromere divides the chromosome into two sections, called arms. The smaller arm is called the p arm. The larger arm is called the q arm. Therefore, the term chromosome 8p rearrangements refer to changes that occur at the short arm of chromosome 8.

The centromere is often used as a point of reference to describe where genes are located within the chromosome. If a gene or region is located close to the centromere, it is referred to as proximal. If a gene or region is further away from the centromere, it is referred to as distal. A region at the end of a chromosome is often referred to as terminal. Some deletions and duplications can be described using this language. For example, a deletion of the genetic material at the end of a chromosome arm is often described as a terminal deletion, whereas a deletion close to the centromere is described as a proximal deletion.

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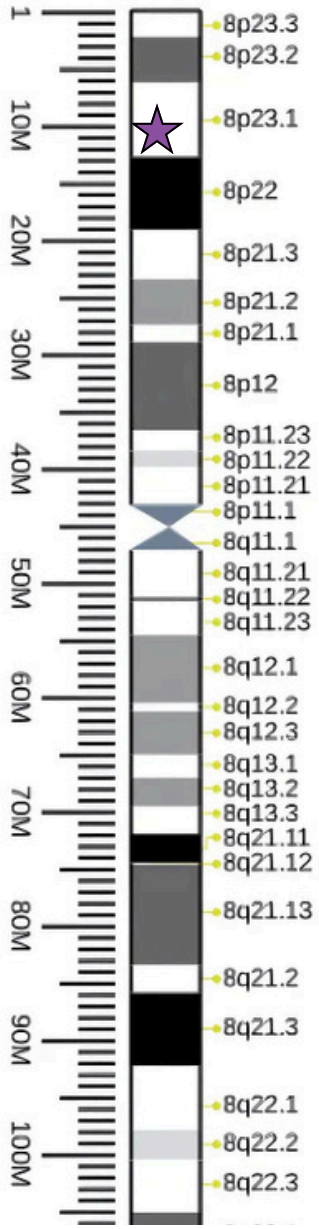
When the lab looks at chromosomes, they use particular staining techniques that create the black and white stripes you can observe in the diagram. These black and white stripes are known as a "banding pattern," and every chromosome will have a distinct banding paper that makes it identifiable. The lab will analyze this banding pattern to determine if all of the information on a chromosome is present and if it is in the correct order. If bands are missing, duplicated, or rearranged, this is called a chromosomal rearrangement.

The following is a picture of a chromosome with its banding pattern labeled.



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A specific position on a chromosome can be described in two different ways. It can be identified by its banding pattern location or by the base pair position. For example, if we were trying to describe the location of the purple star on the chromosome above, we could either:

1. Use the chromosome banding pattern (8p23.1). See the "What is on my genetic report?" section to learn more about what the term 8p23.1 means.
2. Use the base pair position (base pair 10 million)

Both terms are referring to the same general location on the chromosome. However, the banding pattern tends to describe a large general region, whereas the base pair position can describe a more precise point within that region. For this reason, the base pair position tends to be thought of as a more specific "address" than the banding pattern description.

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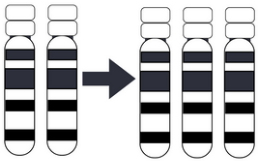
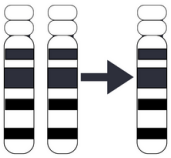
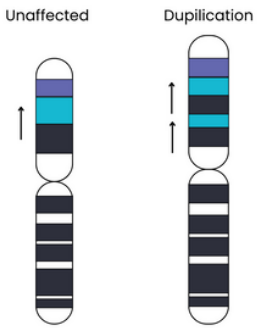
II.3 Chromosomal Rearrangements: Definitions

Chromosomes can vary according to their structure (structural variant) or according to the amount of information they contain (copy number variant). The following includes a table of useful terms used to describe a variety of chromosomal rearrangements.

Chromosomal Rearrangements Glossary

Term	Definition	Useful Picture
Trisomy	An entire extra chromosome is present.	
Monosomy	An entire chromosome is absent or missing.	
Duplication	A piece of a chromosome is repeated, so that there is extra information present. This can also be called partial trisomy. You can think of a duplication as being "extra" pages in our book analogy. You can imagine how adding new pages may confuse how the initial instructions are written, especially depending on where those extra pages are inserted.	 There is an extra blue band and an extra black band, which represent the duplicated material.

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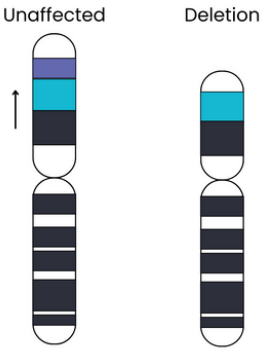
Term	Definition	Useful Picture
Deletion	A piece of a chromosome is missing. This can also be called partial monosomy. You can think of a deletion as "missing' pages in our book analogy. You can imagine how losing pages in the book may confuse some of the initial instructions in the books because it means that some of the instructions in our book are missing.	 The purple band is missing, representing the deleted portion.

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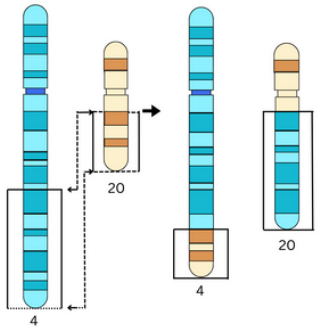
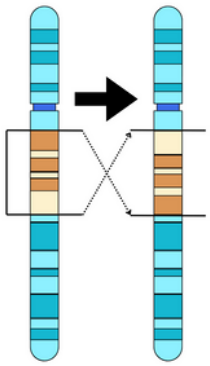
Term	Definition	Useful Picture
Translocation	A segment from one chromosome breaks off and is reattached to another chromosome.	
Inversion	A segment from one chromosome breaks off, flips 180 degrees to reverse orientation, and reattaches to the same chromosome. The result is a chromosome that contains the same genetic material, but with genes in the reverse order. There are two types of inversions: 1) Paracentric - both breaks occur in one chromosome arm 2) Pericentric - the inverted region includes the centromere and there is one break in each arm	 Note how the light orange band is now in a different position. That section has been “flipped” in order, or inverted.

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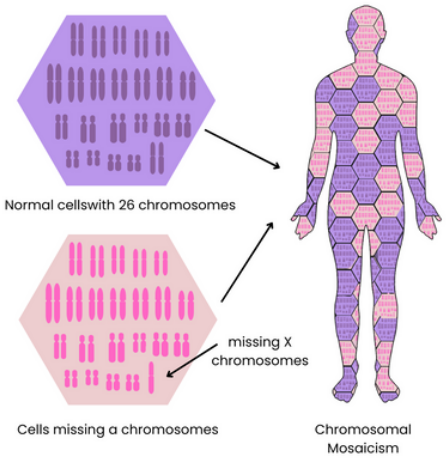
Term	Definition	Useful Picture
Mosaicism	Most of the time, all of the genetic material each of our cells contain is the same. However, mosaicism occurs when a portion of a person's cells have a genetic change that another portion of a person's cells do not have. For example, mosaic trisomy 8 is when some percentage of cells contains an extra chromosome 8 (3 total), while another portion of cells have the normal pair (2) of chromosome 8s.	

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II.4 What is on my genetic report?

Knowing exactly how to interpret a genetic report can be challenging. This section is designed to provide some tools to help you learn more about what may be written on your genetic report. This is not intended to replace the advice of the genetic professionals who have counseled you on your actual report, but rather is supplementary information for context

The first thing to know when you are looking at a genetic report is what genetic test was performed. There are several genetic tests that can be performed on your 8p hero's blood sample in order to diagnose an 8p Chromosomal rearrangement, and each varies in what it is able to detect and how it reports out information.

Some of the common genetic tests used to diagnose 8p heroes include:

- ***Karyotype***

  This technology essentially "takes a picture" of the chromosomes in a cell. An analyst will look through a microscope to look at the banding patterns of the chromosomes and determine if there is any missing, added, or rearranged information. A karyotype is useful for detecting structural variations, like an inversion for example. However, karyotypes are limited by only being able to detect copy number variations that are large enough to see (so they miss smaller deletions or duplications), and they are unable to provide genomic breakpoints.

- ***Microarray***

  This technology uses molecular techniques that take a closer look at chromosomes in order to detect smaller deletions or duplications that a karyotype would not be able to see. However, because this test does not look directly at a picture of the chromosome, it is unable to determine the order or arrangement of the genetic information. Therefore, this test can only determine whether information is lost or gained, but it cannot detect structural differences (like inversions). Microarrays are able to provide genomic breakpoints, numbers that tell us at which base pair in the genome the change begins and ends. Genomic breakpoints provide a more exact estimate of the size and location of the rearrangement compared to a karyotype.

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- ***Next Generation Sequencing (Exome or Genome sequencing)***

  This technology uses molecular techniques that generate the sequence, or exact spelling, of an individual's genome. Little pieces of an individual's DNA are sequenced, and then those sequences are compared back to a human genome reference in order to piece the fragments of sequences back together in order. By doing this, the lab would be able to notice that the sequences that are associated with the 8p arm are either missing or duplicated. Again, because this test does not look directly at a picture of chromosomes, it is unable to detect the order or arrangement of the genetic information. For this reason, it can detect deletions and duplications, but it cannot pick up structural differences (like inversions). Exome and Genome sequencing are also capable of providing genomic breakpoints.

Most genetic reports will identify what the chromosomal rearrangement is (is it a deletion, duplication, inversion, etc.) and where it occurs (the chromosome, the exact chromosomal bands that are affected, and the genomic breakpoints). In order to report this information, genetic reports use a standard nomenclature. While a useful strategy to ensure consistency, it can often look like alphabet soup at first glance.

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Below is a table of commonly used nomenclature in 8p Hero reports that may help you better understand your report:

Genetic Report Nomenclature Glossary

Nomenclature	Meaning	Test Type that Uses this Term
arr[GRCh38/hg38] OR arr[GRCh37/hg19] OR seq[GRCh37/hg19]	Arr stands for array. This indicates that a chromosomal microarray was the testing technology used. To note, some sequencing reports (like certain exome tests) may also use arr on their reports, depending on the technology the lab used for detecting copy number variants. Seq stands for sequencing. This indicates that sequencing was the testing technology used. GRCh38 or GRCh37 refers to the human genome reference sequence that was used to analyze the results. The human genome reference sequence is a standard sequence used for comparison to know what information is typically present in a healthy individual's genome. The genome reference also provides the standard numbering system that is used to describe the genomic breakpoints of a rearrangement.	Microarray Next Generation Sequencing
46, XX or 46, XY	Indicates that 46 chromosomes were counted, including XX sex chromosomes (typically assigned female at birth) or an XY (typically assigned male at birth). Starting with 46, XX or 46, XY is always how a karyotype will be reported, so this is a good clue that you are reading a karyotype report.	Karyotype

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Nomenclature	Meaning	Test Type that Uses this Term
del	deletion	Karyotype
[ ]x1	deletion	Microarray Next Generation Sequencing
dup	duplication	Karyotype
[ ]x3	duplication	Microarray Next Generation Sequencing
inv	inversion	Karyotype
pter	Terminal (end) of the p arm. Often used to describe a deletion that extends to the end of the p arm.	Karyotype
8p23.1	This describes the chromosomal location. To break it down: 8 - The Chromosome number p - The chromosome arm 2 - The chromosomal region, defined by landmarks 3.1 - The band number within the region	Microarray Next Generation Sequencing

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Nomenclature	Meaning	Test Type that Uses this Term
(8) (p23.1)	This describes the chromosomal location. It includes the same information as above, but for a karyotype is written with the inclusion of parenthesis. The order of information remains the same: 8 - Chromosome number P - Chromosome arm 2 - Chromosomal region 3.1 - The band number with the region	Karyotype

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The following are some examples of how this information may be combined in a report to describe an 8p hero's genetic finding:

8p inversion duplication deletion

46, XX, del(8)(p23.1p23.2) inv dup(8)(p21.3p23.1):

- 46 This indicates a karyotype has shown an individual with 23 pairs of chromosomes
- XX is a biological female
- del(8)(p23.1p23.2) The individual has one chromosome 8 with a deletion extending from the 23.1 region to the 23.2 region of the p arm
- invdup(8)(p21.3p23.1) The individual also had a duplication on chromosome 8 extending from 21.3 to 23.1 on the p arm, and this information is inverted.

A reminder that an array or sequencing will not be able to definitively detect an inversion. An array or sequencing can report the deletion and duplication associated with a invdupdel, and the report will often suggest that the findings may be consistent with the inversion duplication deletion rearrangement. However, these two tests will not be able to confirm the inversion. A karyotype may be ordered as a follow-up test to confirm the structural arrangement of information.

8p Deletion Heroes

46, XY, del(8)(p23.1pter):

- 46 This indicates a karyotype has shown an individual with 23 pairs of chromosomes.
- XY is a biological male
- del(8)(p23.1pter): The karyotype indicates that one chromosome 8 has a starting at the region p23.1 and extending to the end of the p arm.

arr[GRCh38]8p23.1(8,093,168_9,039,703)x1 :

- arr[GRCh38] This indicates a microarray that used GRCh38 as their reference sequence
- 8p23.1 (.....)x1 This indicates that there is a deletion on the p arm of chromosome 8 at the region 23.1.
- (8,093,168_9,039,703) These numbers are the genomic breakpoints. They indicate that the deletion begins at base pair 8,093,168 and ends at base pair 9,038,703.

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8p Duplication Heroes

46, XY, dup(8)(p23.1_p23.2):

- 46 This indicates a karyotpye has shown an individual with 23 pairs of chromosomes
- XY is a biological male
- dup(8)(p23.1_23.2) This indicates a duplication on chromosome 8 that includes regions 23.1-23.2

arr[GRCh38]8p23.1(9,040,038_11,881,742)x3:

- arr[GRCh38] This indicates a microarray that used GRCh38 as their reference sequence
- 8p23.1(.....)x3 This indicates the 23.1 region on the p arm of chromosome 8 has been duplication
- (9,040,038_11,881,742) These numbers are the genomic breakpoints. They indicate that the duplication begins at the base pair 9,040,038 and ends at the base pair 11,881,742.

In addition to the information on what and where the chromosomal rearrangement is, the genetic report will list the classification of the chromosomal rearrangement. All of us have variation in our genetic information: some of this variation has no significance for our health, while other variation may be contributing to a health condition. The variant classification is a standardized way of reporting whether a genetic change is thought to be clinically significant or contributing to a health condition. The following is a glossary of the 5 standardized terms that are used by genetic laboratories for their variant classification.

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Variant Classification Glossary

Classification Term	Definition
Benign	The variant is not the cause of disease. The evidence is strong and well-established that the variant does not contribute to disease.
Likely Benign	The variant is not likely to be the cause of disease. There may be less evidence than for a benign classification, however there is sufficient evidence to conclude that the variant is not causing a condition
Variant of Uncertain Significance (VUS or VOUS	It is unclear what the variant's impact on disease is. The variant may have some characteristics of a disease-causing variant, however the evidence is either lacking to prove pathogenicity, or there is conflicting evidence. The variant may have some characteristics of a non-disease-causing variant, however the evidence is either lacking to prove it is benign, or there is conflicting evidence.
Likely Pathogenic	The variant is considered to be the probable cause of the patient's health condition. There may be less evidence available than a well-established pathogenic variant to establish a causal relationship, however correlation between the genetic variant and the disease is strong.
Pathogenic	The variant is considered to be the cause of the patient's health condition. It is well-established as disease-causing in the literature and there is a wide consensus on the variant's pathogenicity

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It is important to recognize that both genetic testing technologies and variant classification are limited by the current scientific knowledge available at the time of the test. As genetic testing evolves, newer technologies can more precisely define the breakpoints of a rearrangement or identify genetic variants that were unidentifiable on previous testing. Further, as new knowledge evolves and more variant evidence arises, variant classifications may be changed or updated. This is especially true for VUS classifications, and VUS classifications are often updated as new information is gained. For these reasons, 8p families are encouraged to seek updated genetic testing or variant reanalysis every few years.

There may be some additional terminology on your report that provide additional details. The following is a table summarizing what some of those terms mean.

Other Genetic Report Terms Glossary

Term	Definition
Heterozygous	Heterozygous means that an individual has two different copies of a particular region or gene. In the context of 8p, a heterozygous individual will have one copy of chromosome 8 with the rearrangement and one copy of chromosome 8 that doesn't have the rearrangement.
Homozygous	Homozygous means that an individual has two copies of a particular region or gene that are the *same*. It might be helpful to think of zygosity like a pair of socks. Socks, like chromosomes, come in pairs. If the socks are two different colors, they can be said to be heterozygous. If the socks in a pair are the same color, they can be said to be homozygous.

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Term	Definition
Autosomal Dominant	Autosomal Dominant describes the inheritance pattern of certain genetic conditions. An autosomal dominant condition means that only one copy of the chromosome pair needs to have the genetic change in order to cause disease. In other words, an individual who is heterozygous for the genetic change will develop the condition in an autosomal dominant pattern of inheritance. In most cases of 8p rearrangements, they are autosomal dominant conditions. In contrast, some conditions are described as autosomal recessive, which requires that both copies of the chromosome have the genetic change to cause disease. This means that only individuals who are homozygous for the genetic change will develop the condition
De novo	A de novo genetic change is one that is new in an individual. This means that it was not inherited from either parent, but rather arose spontaneously in the individual.

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II.5 How do chromosomal rearrangements occur?

Chromosomal rearrangements most often occur when the egg and sperm cells are forming. The egg and the sperm are unique cells that contain only half of the genetic material the rest of our cells contain. In other words, instead of 46 total chromosomes, the egg cell has 23 chromosomes and the sperm cell has 23 chromosomes. When they combine during fertilization, typically they create a cell (zygote) which again has 46 chromosomes and which will go on to become an individual with a full number of 46 chromosomes.

In order for an egg and a sperm cell to have 23 chromosomes instead of 46, they go through a division process called meiosis. A key part of this process is called homologous recombination. In this process, the two chromosomes find their pair using matching areas to line up next to each other, and then they exchange DNA segments. This means that children do not inherit the exact copies of their parent's chromosomes, but rather the chromosomes they inherit are a mixture of the genetic information from their parent's chromosome pairs.

[Graphics]

If you think back to the book analogy from earlier: we have two books, each with the same 23 chapters, representing our 23 chromosomes. While they contain the same chapters, the two books are written with a different color ink. You can think of the process of homologous recombination as turning to the same page within the chapter "Chromosome 1" in each book, ripping those pages out, and pasting them in the opposite book. Because the chapters contained the same instructions, this exchange of pages would still make the instruction manual understandable to read, but now the chapters would have a combination of ink colors.

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The Books: A Useful Takeaway

Our book analogy provides a useful tool to think about how your 8p hero's rearrangement fits into the context of their "genetic library."

Most of our attention is spent on their Chromosome 8 book that has missing, extra, or rearranged pages. However, like our analogy points to, there are two copies of every book in the library. That means they also have a Chromosome 8 book that has all of the necessary pages in the correct order

This exchange of material is a normal process. However, it also can be vulnerable to random errors. Sometimes, an unequal amount of information is exchanged, creating chromosomes that have information missing or added. This unequal exchange results in chromosomes with deletions, duplications, and inversions. Put in the context of our analogy, this would be like accidentally grabbing a few extra pages from one book when making the exchange: one book would be left with extra, duplicated pages, while the other book would have missing, deleted pages.

Chromosome 8p is a chromosomal region that contains a particular genetic pattern that makes it more susceptible to these unequal exchanges of information in the division process during meiosis. This is why Chromosome 8p rearrangements are said to be "recurrent," meaning that similar rearrangements happen in multiple unrelated individuals.

A natural follow-up question to this explanation is to wonder whether there was anything that parents could have done to cause or prevent these rearrangements:

The answer is a resounding no. The genes we inherit (along with any of the errors we inherit) are beyond our control and subject to the randomness of biology. There is nothing anyone can do to change or predict the combination of genetic information that will be passed to a child.

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II.6 What makes Chromosome 8p Rearrangements Different from other Neurodevelopmental Diagnoses?

Some of the features of Chromosome 8p conditions resemble other neurodevelopmental disorders that may sound familiar, like Down Syndrome or Autism. We have heard from some 8p families that a common question asked is what makes Chromosome 8p rearrangements different from these other conditions. The following is a section that provides some brief insight into some of the key differences. This section can be a good starting point for developing language to communicate what makes 8p special to those wondering.

For example, Down Syndrome is a common neurodevelopmental disorder that has some similarities with Chromosome 8p Rearrangements and some differences. Both are chromosomal conditions, with Down Syndrome being caused by an extra copy of chromosome 21 (Trisomy 21) and Chromosome 8p conditions being caused by extra, missing, or structural difference with the p-arm segment of Chromosome 8. Additionally, both typically result in neurodevelopmental symptoms like developmental delay and can also have a range of impacts across the body. A key difference between the two is the degree of individual variation in their genetic causes. In the case of Down Syndrome, the genetic cause is largely consistent across individuals, as most people with Down Syndrome have an extra copy of chromosome 21 (Trisomy 21). Meanwhile, Chromosome 8p conditions is a broad category that encompasses an incredibly varied range of rearrangements. Some 8p heroes have deleted 8p material, others have duplicated 8p material, and the breakpoints and exact size of every genetic change is generally unique to the individual. This variation in genetic rearrangement often means that the features of 8p heroes are widely varied, making it hard to describe (or predict) exactly the symptoms a hero may experience.

Another neurodevelopmental condition that some may be familiar with is Autism Spectrum Disorder. Autism Spectrum Disorder is a clinical diagnosis that refers to a neurodevelopmental difference that impacts how individuals socialize and interact with others. On its own, Autism is thought to be largely multifactorial, relying on the interaction of a variety of genetic factors. However, Autism is also a feature that can be a part of the expected presentation of a wide range of genetic diseases that impact neurodevelopment. For Chromosome 8p rearrangements, Autism is a feature that can arise in some individuals. Therefore, while Autism Spectrum Disorder is a clinical diagnosis that can be found on its own without any underlying genetic cause or syndrome, it is also a diagnosis that is known to be associated with genetic disorders, including the spectrum of symptoms known to present for Chromosome 8p Rearrangements.

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II.7 Introduction to the Patient Passport

While this portion of the packet provided some background to generally guide how to interpret a genetic report, it is by no means comprehensive. Every 8p Hero has slightly different rearrangements and breakpoints, which means each hero will have a unique genetic report. For that reason, we have designed a resource dedicated to individualizing the interpretation of an 8p hero's genetic report: the **Patient Passport**. This can be very helpful to have at doctor appointments, other provider encounters (like occupational therapy, for example), and education planning discussions.

A hero's patient passport incorporates information from their genetic report to provide a personalized interpretation. It also provides additional information to support your family through understanding what this diagnosis could mean for you and your hero, based on their exact genetic change.

When you are ready to get your patient passport, follow the below steps to receive your hero's personalized passport:

1. Email engagement@project8p.org to sign up for the Chromosome 8p Registry
2. Upload your 8p Hero's Genetic Report
3. Complete surveys about your 8p Hero
4. Receive your passport!

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III. When will symptoms arise and what will they be?

III.1 Overview of 8p Symptoms

A predominant symptom across all 8p rearrangements is an impact on neurodevelopment. A majority of 8p heroes will have developmental delay and/or intellectual disability, and a major area of development that may be difficult for 8p heroes tends to be expressive language. That being said, the neurodevelopmental symptoms exist on a wide spectrum and vary greatly between heroes.

Beyond neurodevelopment, certain features across other body systems are noted to occur more commonly in those with Chromosome 8p rearrangements. Chromosome 8p Rearrangements will have varying effects on each 8p hero, and each hero experiences some features and not others. For example, one 8p hero may have gastroesophageal reflux, while another 8p hero has epilepsy. In these cases, the symptoms will be treated according to standard care practices.

III.2 Introduction to Project 8p's Patient Navigator

We have developed an interactive resource designed to provide families, caregivers, and healthcare providers up-to-date information on the health of 8p heroes. Organized by body system, the resource walks through the symptoms of a Chromosomal 8p rearrangement and recommendations for management, supported by literature, patient data, and research. This resource provides an incredibly useful overview of many of the symptoms, and is a great reference for continual referral.

You can access the Patient Navigator here, or by going to project8p.org and navigating to the Families tab and clicking on Patient Navigator.

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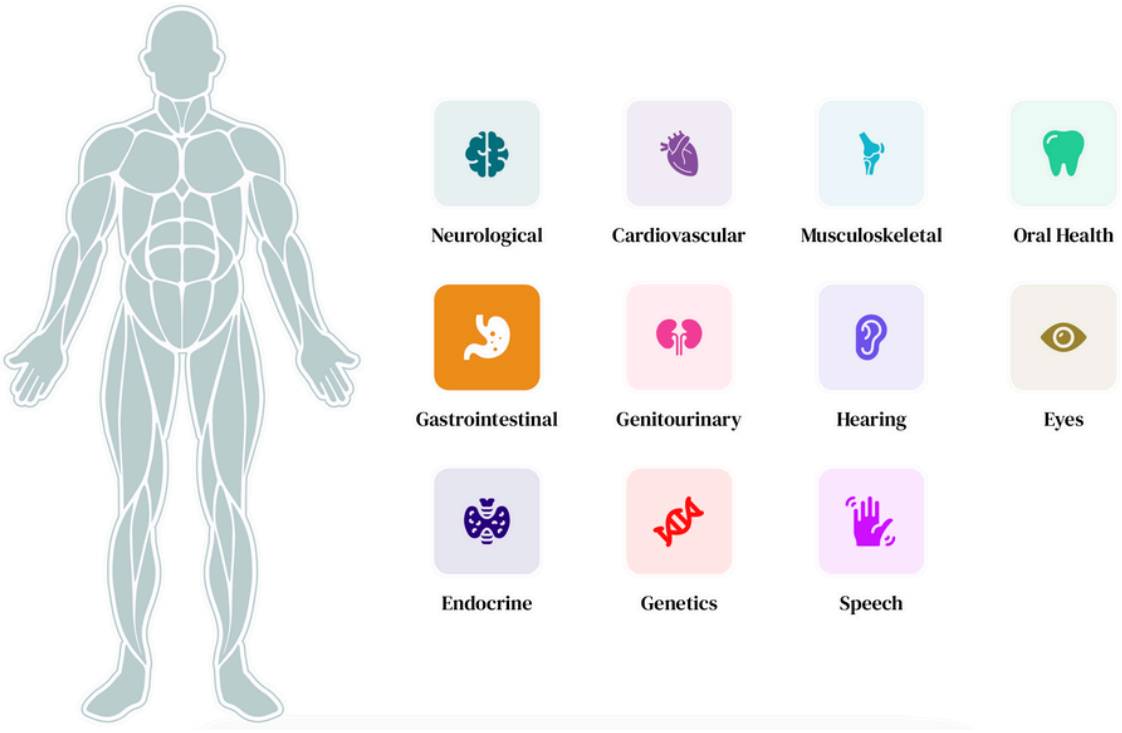

*Patient Navigator

Again, it is important to emphasize the variation in every 8p hero's journey. This image, taken from the Patient Navigator page, is a perfect depiction of how wide the spectrum of symptoms can be between heroes. There are a dozen body systems listed, and each one lists the different features that have been seen in 8p heroes. However, it's important to remember that no 8p hero has all the symptoms. Most only have a few. But by showing all the possible symptoms in one place, this image helps you see just how different each 8p hero's experience can be. The symptoms for 8p exist on a wide spectrum with a large degree of variability between individuals.

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III.3 Timeline of Symptoms (InvDelDup Timeline)

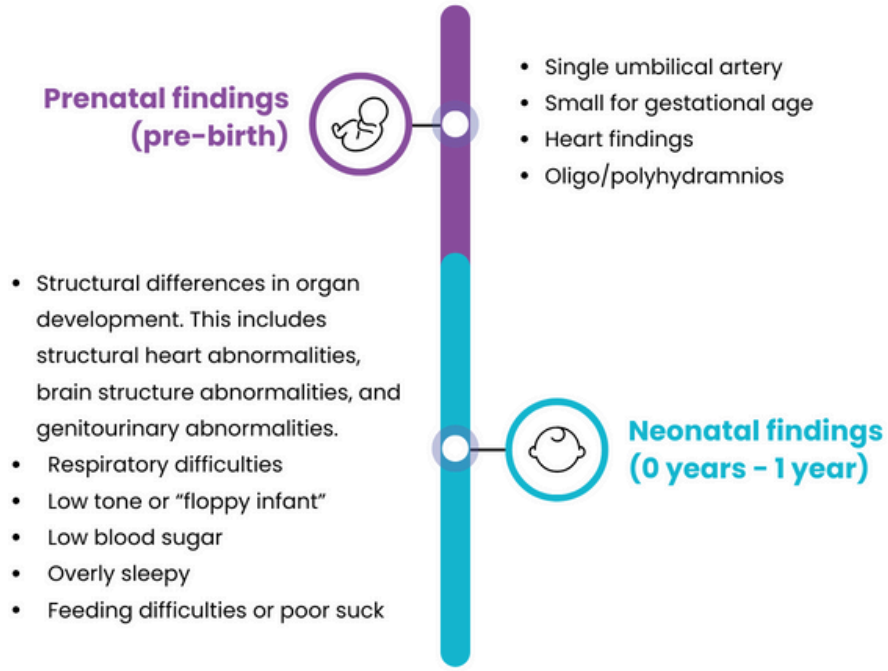
While it is important to refer to the Patient Navigator to have a general overview of what symptoms to expect, it is also useful to know when to expect certain symptoms.

The following is a timeline that lays out the generalized journey that many 8p invdupdel heroes take. The timeline is annotated with particular symptoms that tend to arise at certain times and with the ages that 8p heroes tend to achieve certain developmental milestones. First, it is important to note that this is a guideline and not a rule: your child's symptoms and developmental achievements may arise at different times or may not arise at all. However, this can still be a helpful tool to use to guide what things may be important to look for at which developmental stages and what interventions may be important for your 8p hero at different stages.

The content in this timeline is generated in part through research sponsored by Project 8p and through surveys collected as part of the Chromosome 8p registry. We extend our heartfelt thanks to the families who have participated in these - surveys - your contributions are helping to improve care and knowledge for all 8p heroes.

The information in this timeline is also drawn from the paper titled "Clinical and genomic characterization of 8p Cytogenomic Disorders" from Okur et al., 2021). If you are interested in seeing this paper in more detail, you can access it here, or find it under the publications tab on the Project 8p website.

InvDelDup Timeline



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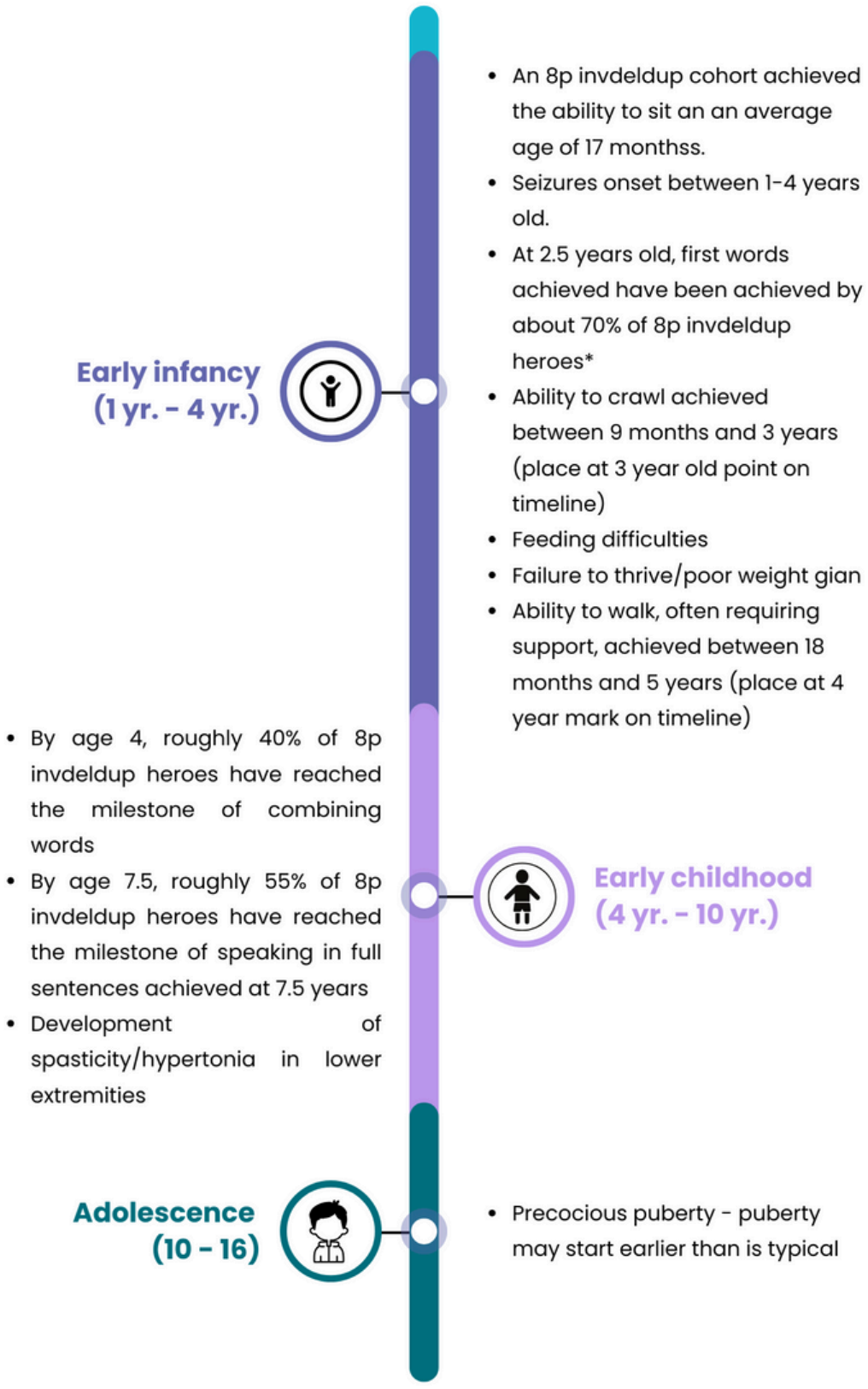

*Data from Project 8p Natural History Study

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Description of prenatal findings:

- ***Single umbilical artery***

  A single umbilical artery is a difference identified by prenatal imaging in the structure of the vessels in the umbilical cord. 16% of 8p invdupdel heroes had a single umbilical artery (Okur et al)

- ***Small for gestational age***

  An ultrasound identified differences in growth trajectory. Has been noted to be present for 14% of 8p invdupdel heroes (Okur et al)

- ***Heart findings***

  Prenatal imaging identified a difference in the structure or function of the heart in 10% of 8p invdupdel heroes (Okur et al). It's important to note that even if a heart finding is not identified prenatally, this doesn't exclude your child from having a heart condition noted once born.

- ***Oligo/polyhydramnios***

  Prenatal imaging identified a difference in the amount of amniotic fluid for 8p invdupdel heroes in 8% of case. Oligohydramnios refers to a smaller amount of amniotic fluid than normal and polyhydramnios is a larger amount of amniotic fluid than normal.

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Description of neonatal findings:

- Any structural differences in how certain organs formed will be present from birth. **It is important to note that while these differences will be present from birth, they may not be identified until later, depending on what type of imaging or symptoms your 8p hero has.

  - ✓ Structural heart abnormalities - 65% of invdupdel heroes noted a variety of different structural and functional heart abnormalities (Okur et al.)

  - ✓ Brain structure abnormalities - Most often for 8p invdupdel heroes (67%), the brain structure abnormality that is noted on MRI is a difference in the formation of the corpus callosum, a structure that connects the left and right hemisphere of the brain. Other brain imaging abnormalities have also been reported, like ventriculomegaly (a difference in the amount of cerebral spinal fluid contained in the ventricles) or cerebral//cerebellar atrophy, a shrinking of a certain part of the brain.

  - ✓ Genitourinary anomalies - Some invdupdel heroes have been noted to have differences in the structure of their kidney. Additionally, some males are noted to have cryptoorchidism, a condition where the testes do not descend into the scrotum, or hypospadias, a condition where the opening of the urethra is on the underside of the penis instead of the tip.

- ***Respiratory difficulties***

  18% of 8p invdupdel heroes are noted to have breathing distress at birth (Okur et al)

- ***Low tone- "floppy infant"***

  1% of 8p invdupdel heroes are noted to have low muscle tone (hypotonia) when they are born. An infant with hypotonia is often described as "floppy" and it means that their muscles don't have the normal resistance when at rest.

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- ***Low blood sugar***

  18% invdupdel heroes are noted to have hypoglycemia or low blood sugar at birth (Okur et al)

- ***Overly sleepy***

  43% invdupdel heroes are noted to be overly sleepy or are described to have challenges with alertness as a baby (Okur et al)

- ***Feeding difficulties or poor suck***

  63% of invdupdel heroes are noted to have feeding challenges in early infancy and 57% are noted to have poor suck when breastfeeding (Okur et al)

Description of Early infancy:

- ***Seizure***

  8p invdupdel heroes can have a range of seizure experiences. Some may never have a seizure, while others may have many in their lifetime. For those who do experience seizures, the average age of onset was 1-4 years in a invdupdel cohort. Most commonly, the seizures experiences by invdupdel 8p heroes are absence seizures.

- ***Feeding difficulties***

  Feeding difficulties can often continue in this age phase, beyond breastfeeding. Many children find it difficult to chew hard foods and may require food mashed or pureed.

- The developmental milestones placed in this section are what have been noted to be average ages for achievement in an invdupdel 8p cohort, however it is important to note that development is highly variable and these estimates are unlikely to be accurate for your child.

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Description of Early childhood:

- ***Continued feeding difficulties***

  Most children find chewing difficult and may require soft foods

- ***Spasticity/hypertonia***

  Many families report that their children experience muscle tightness, especially in the lower limbs, that often develops as their children age. This tightness may result in spasms and reduced mobility.

- The developmental milestones placed in this section are what have been noted to be average ages for achievement in an invdupdel 8p cohort, however it is important to note that development is highly variable and these estimates may not be accurate for your child.

Description of Adolescence:

- ***Precocious puberty***

  Puberty may start earlier than is typical.

There also is a bucket of symptoms that we have established to occur more frequently in individuals with Chromosome 8p invdupdel but for which we don't have a complete understanding of the time frame, which are listed beneath the timeline. You can also read more about these symptoms in the Patient Navigator. For some, there may be reason to believe that they have age-related onset, but for now, those time frames are not fully understood. This is one of the things that Project 8p's Natural History Study hopes to address (see "Introduction to Project 8p section), and we hope that with research, more of these symptoms can be placed on the timeline.

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- Neurobehavioral symptoms - Families have reported ADHD, autism, and other mental health concerns for their children.
- GI symptoms - 8p heroes often have gastrointestinal symptoms that can included constipation, GERD (Gastroesophageal Reflux Disease), and diarrhea
- Sleep disturbance
- Frequent infections
- Short stature/growth issues
- Dental problems
- Joint laxity - joints may be hypermobile or extra flexible, resulting in greater range of motion than normal.
- Scoliosis - an abnormal curvature of the spine
- Cortical vision impairment - a condition that impacts the brain's ability to process visual information, resulting in vision loss.

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III.3 Timeline of Symptoms (Deletion Timeline)

While it is important to refer to the Patient Navigator to have a general overview of what symptoms to expect, it is also useful to know when to expect certain symptoms.

The following is a timeline that lays out the generalized journey that many 8p heroes with a deletion may take. The timeline is annotated with particular symptoms that tend to arise at certain times and with the ages that 8p heroes tend to achieve certain developmental milestones. First, it is important to note that this is a guideline and not a rule: your child's symptoms and developmental achievements may arise at different times or may not arise at all. However, this can still be a helpful tool to use to guide what things may be important to look for at which developmental stages and what interventions may be important for your 8p heroes at different stages.

The content in this timeline is generated in part through research sponsored by Project 8p and through surveys collected as part of the Chromosome 8p registry. We extend our heartfelt thanks to the families who have participated in these - surveys - your contributions are helping to improve care and knowledge for all 8p heroes.

The information in this timeline is also drawn from the paper titled "Clinical and genomic characterization of 8p Cytogenomic Disorders" from Okur et al., 2021). If you are interested in seeing this paper in more detail, you can access it here, or find it under the publications tab on the Project 8p website.

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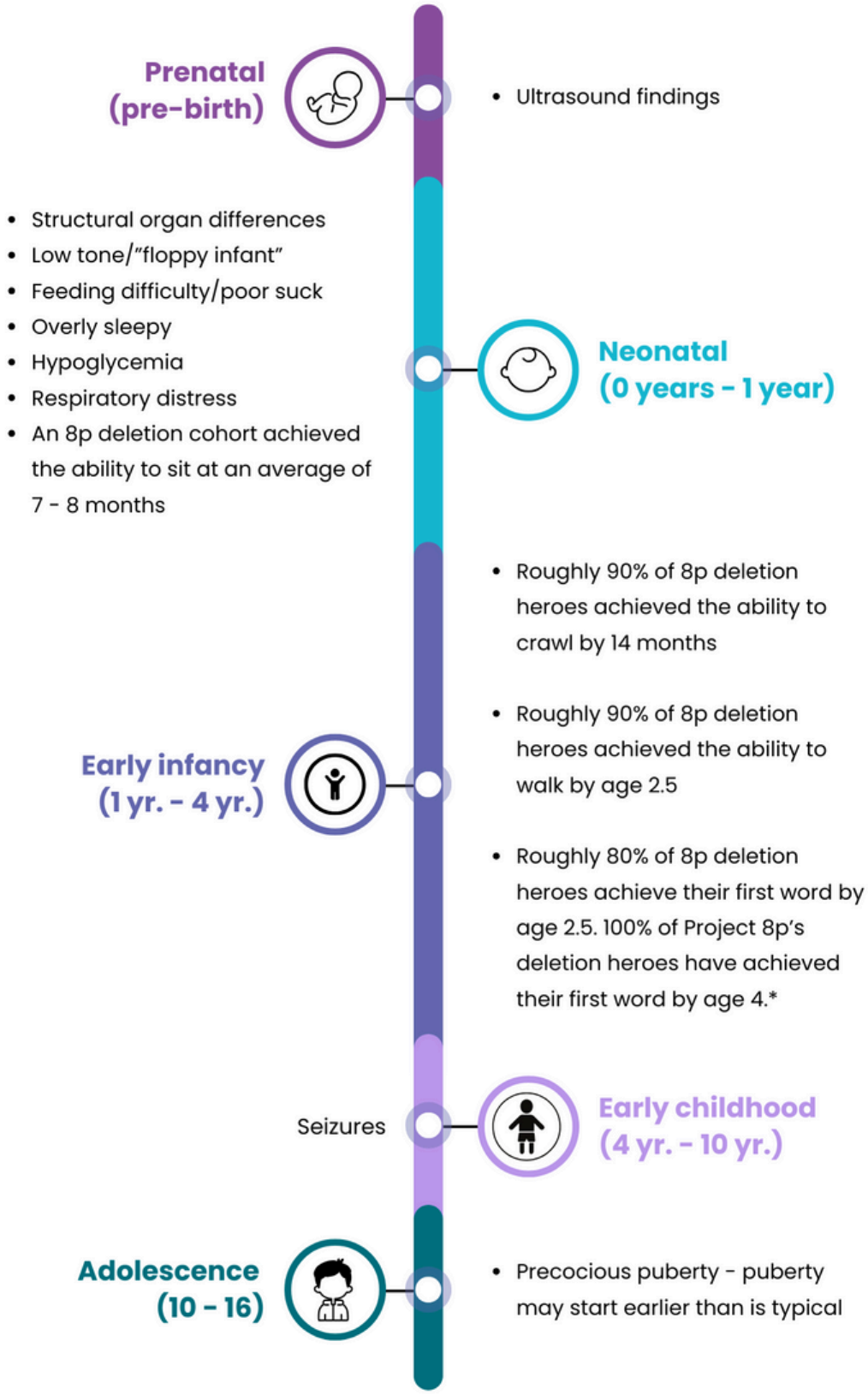
Deletion Timeline



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Description of prenatal:

- 8p heroes with a deletion can sometimes be noted to have abnormal ultrasound findings during pregnancy. Depending on the location and size of the deletion, findings include things like a single umbilical artery (a structural difference in the vessels of the umbilical cord), small for gestational age (a difference in fetal growth trajectory), heart findings, or a difference in how much amniotic fluid is present.

Description of neonatal:

- ***Structural organ differences***

  Many 8p heroes with a deletion will be noted to have findings that result from a difference in the formation of certain organ systems. For example, many 8p heroes with a deletion will be born with a difference in the structure of their heart, often called a congenital heart defect. Other structural differences include kidney differences, genitourinary differences (male heroes may have hypospadias or cryptorchidism), and brain structure differences like absence of the corpus callosum or ventriculomegaly. It is important to note that while all of these structural differences will be present at birth, they may not be things that are fully appreciated immediately. Depending on the evaluations you receive, you may not be aware that certain structures are abnormal until later in life. However, these differences are also not things that will develop with time. For example, if your hero does not have a congenital heart defect, they will not go on to develop one later (important to note that this does not refer to the function of the heart - it is possible for your hero to develop arrhythmias or other concerns with the function of the heart).

- ***Feeding difficulty/poor suck***

  Many babies with an 8p deletion will have difficulty coordinating sucking with swallowing or may have a poor suck that impedes breastfeeding. Some may experience other difficulties that make feeding difficult.

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- ***Low tone/"floppy infant"***

  Some 8p heroes with a deletion will be described as having hypotonia or low tone. This is often referred to as a "floppy infant," meaning that the muscles do not have normal resistance against gravity at rest.

- ***Overly sleepy***

  Some 8p heroes with a deletion are described as being overly sleepy in the neonatal period or having difficulties with alertness.

- ***Low blood sugar***

  Some 8p deletion heroes are noted to have hypoglycemia or low blood sugar at birth.

- ***Respiratory distress***

  Some 8p deletion heroes have difficulty breathing adequately right at birth.

Description of Early childhood :

- ***Seizure***

  Some 8p deletion heroes are reported to experience seizures. The average age of onset for seizure activity is 2-5 years old.

- ***T***he developmental milestones placed in this section are what have been noted to be average ages for achievement in our 8p deletion hero cohort, however it is important to note that development is highly variable and these estimates may not be accurate for your child.

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There also is a bucket of symptoms that we have established to occur more frequently in individuals with Chromosome 8p deletions but for which we don't have a complete understanding of the time frame. You can also read more about these symptoms in the Patient Navigator. For some, there may be reason to believe that they have age-related onset, but for now, those time frames are not fully understood. This is one of the things that Project 8p's Natural History Study hopes to address (see "Introduction to Project 8p section), and we hope that with research, more of these symptoms can be placed on the timeline.

- Neurobehavioral symptoms - symptoms such as short attention span, ADHD, autism, stereotypic behavior, anxiety, and depression are noted to be frequent in an 8p deletion cohort.
- Developmental delay or learning disability - most 8p deletion heroes have developmental delay or some mild cognitive or learning disability. A stream of development that seems to be more difficult for 8p heroes is expressive language, with speech capabilities often developing later than other milestones. The range of delay or disability varies greatly amongst different deletion sizes and locations.
- Learning disability or intellectual disability - the potential cognitive impact of an 8p deletion is quite varied and broad. Many 8p deletion heroes will have some degree of learning disability, ranging from mild to severe, but the degree of impact varies greatly and often relates to the size of the deletion.
- Heart arrhythmia - some 8p deletion heroes are noted to have differences in the rhythm of their heart that require management.
- Gastrointestinal symptoms - some 8p deletion heroes are noted to have some GI concerns including constipation, diarrhea, Gastroesophageal reflux disease (GERD).
- Flat feet
- Short stature
- Obesity
- Difficulty walking/clumsiness
- Frequent infections
- Sleep problems
- Dental problems

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III.3 Timeline of symptoms (Duplication Timeline)

While it is important to refer to the Patient Navigator to have a general overview of what symptoms to expect, it is also useful to know when to expect certain symptoms.

The following is a timeline that lays out the generalized journey that many 8p heroes take. The timeline is annotated with particular symptoms that tend to arise at certain times and with the ages that 8p heroes tend to achieve certain developmental milestones. First, it is important to note that this is a guideline and not a rule: your child's symptoms and developmental achievements may arise at different times or may not arise at all. However, this can still be a helpful tool to use to guide what things may be important to look for at which developmental stages and what interventions may be important for your 8p hero at different stages.

The content in this timeline is generated in part through research sponsored by Project 8p and through surveys collected as part of the Chromosome 8p registry. We extend our heartfelt thanks to the families who have participated in these - surveys - your contributions are helping to improve care and knowledge for all 8p heroes.

The information in this timeline is also drawn from the Unique packet titled "Duplication of 8p."

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Duplication Timeline

Prenatal (pre-birth)

- Structural organ differences
- Low tone/"floppy infant"
- Feeding difficulty/poor suck

- By age 1, over 50% of 8p duplication heroes have achieved the ability to crawl.*

Neonatal (0 years - 1 year)

- Developmental delay

- About 75% of 8p duplication heroes speak in syllables by 14 months

- About 60% of 8p duplication heroes have spoken their first word by age 2.5.

Childhood (1-12)

- By age 5, 50% of 8p duplication heroes have reach the language milestone of combined words.

- By age 5, roughly 80% of duplication heroes have achieved the ability to walk.

- At age 9, 50% of 8p duplication heroes have achieved speaking in sentences.

Adolescence (10 - 16)

*Data from Project 8p Natural History Study

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Description of neonatal:

- ***Structural organ differences***

  Many 8p heroes with a duplication will be noted to have findings that result from a difference in the formation of certain organ systems. For example, many 8p heroes with a duplication will be born with a difference in the structure of their heart, called a congenital heart defect. Other structural differences are often found in brain imaging. Most commonly, a thinning or absence of a structure called the corpus callosum, a structure that connects the two hemispheres of the brain, is identified. Another feature more common in 8p duplication heroes is cleft lip or palate, which is caused by a difference in formation in the lip and palate structures.

  While all of these structural differences will be present at birth, they may not be things that are fully appreciated immediately. Depending on the evaluations you receive, you may not be aware that certain structures are abnormal until later in life. However, these differences are also not things that will develop with time. For example, if your hero does not have a congenital heart defect, they will not go on to develop one later (important to note that this does not refer to the function of the heart - it is possible for your hero to develop arrhythmias or other concerns with the function of the heart).

- ***Low tone/"floppy infant"***

  Some 8p heroes with a deletion will be described as having hypotonia or low tone. This is often referred to as a "floppy infant," meaning that the muscles do not have normal resistance against gravity at rest.

- ***Feeding difficulty/poor suck***

  Many babies with an 8p deletion will have difficulty coordinating sucking with swallowing or may have a poor suck that impedes breastfeeding. Some may experience other difficulties that make feeding difficult.

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Description of Childhood:

- ***Developmental delay***

  Most 8p duplication heroes experience delay in acquiring certain developmental milestones. A stream of development that seems to be more difficult for 8p heroes is expressive language, with speech capabilities often developing later than other milestones.

Description of Adolescence:

There also is a bucket of symptoms that we have established to occur more frequently in individuals with Chromosome 8p conditions but for which we don't have a complete understanding of the time frame. You can also read more about these symptoms in the Patient Navigator. For some, there may be reason to believe that they have age-related onset, but for now, those time frames are not fully understood. This is one of the things that Project 8p's Natural History Study hopes to address (see "Introduction to Project 8p section), and we hope that with research, more of these symptoms can be placed on the timeline.

- Neurobehavioral symptoms - symptoms such as short attention span, ADHD, autism, stereotypic behavior, problematic behavior, anxiety, and depression are noted to be frequent in an 8p deletion cohort.
- Learning disability or intellectual disability - the potential cognitive impact of an 8p duplication is quite varied and broad. Many 8p duplication heroes will have some degree of learning disability, ranging from mild to severe.
- Dental Problems
- Sleep disturbance
- Scoliosis - some children with an 8p duplication experience a curvature of their spine, called scoliosis.
- Joint stiffness - some 8p duplication heroes experience stiffening of their joints, which may make mobility more challenging and necessitate physical therapy or bracing to maintain mobility.

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IV. Who do I go to for medical care?

IV.1 Which Specialists Should I Visit and When?

Because Chromosome 8p rearrangements can affect many families often find themselves working with a team of healthcare providers to support their 8p heroes' health and development.

Each 8p hero may face different health and development concerns. While every hero's healthcare team may look different, the list below offers a general guide to the types of specialists many families connect with throughout their care journey. If something specific is on your mind, your pediatrician or primary care provider is a great place to start. They can help you decide if a referral to a specialist is the next best step.

An important consideration when building your health care team is that, because 8p rearrangements are a rare condition, many local healthcare providers may not have direct experience treating an 8p hero. While these providers can still provide excellent care, it's often recommended to connect with a provider who has knowledge and expertise in complex chromosomal rearrangements, if not 8p rearrangements. They will be able to anticipate potential challenges, understand what to expect at different stages, and help guide your overall care journey. You can think of this expert as the "orchestra conductor" of your care team, someone who coordinates the different healthcare providers involved and can ensure everything is moving harmoniously in the right direction.

We understand that not every family may have regular access to a provider with expertise in chromosome 8p conditions. However, there are still meaningful ways to include such clinicians in your care team. One option is to suggest provider-to-provider consultations, encouraging your regular healthcare provider to connect with an 8p expert for guidance in managing care. In the following sections, you'll find a few highlighted clinics that may be able to assist with coordinating this type of support. Additionally, we host a Family and Science Conference, a gathering that brings together families and 8p experts. This event offers an excellent opportunity to meet researchers and clinicians with knowledge of 8p conditions. Even if they are not your primary provider, these experts can still offer valuable insights and guidance to your care team. If you'd like to learn more about providers with 8p expertise or get connected to potential resources, please reach out to us at **engagement@project8p.org**.

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Over time, you'll become an expert in your hero's medical needs. Don't hesitate to ask questions, trust your instincts, and seek a second opinion when something doesn't sit right. You are your child's greatest advocate, and Project 8p here to support you every step of the way.

Note:
This table is adapted from the National French Protocol and Guidelines to Care for 8p invdupdel and Santucci et al. 2024 Management Guidelines. While a general list of who to think about and when to think about them, this is by no means comprehensive nor directive of the exact schedule families should follow. Please defer to your healthcare provider for advice directly related to your 8p hero.

Health Care Providers Frequently Involved in 8p Hero's Care

Specialist	Purpose	How often to follow	What questions to ask?
Geneticist or Provider with knowledge of 8p Chromosomal Rearrangements	Performs regular comprehensive clinical exam and evaluates for additional symptoms related to the condition. Able to inform family about evolving knowledge. Identification of key specialists to follow with. Provides family with access to genetic counseling, depending on evolving needs of family.	Annual follow-up*	

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Specialist	Purpose	How often to follow	What questions to ask?
Pediatric neurologist/ neurologist	Evaluation of psychomotor development. Evaluation of seizure concerns, and MRI brain imaging upon any seizure suspicion. Evaluation of sleep concerns. Evaluation for spasticity. Can provide therapy, testing, and other specialist recommendations to address any of the above.	Annual follow-up* Follow-up may be reduced upon transition to adult care.	What are the signs/symptoms of seizures to be aware of? What would be the course of action if a seizure were to occur?
Pediatric cardiologist/ cardiologist	Evaluate for a heart malformation or arrhythmia. If a cardiac concern is present, monitor and treat concern.	If there is a cardiac condition, the follow-up care should be adapted based on the symptoms.	What are the interventions necessary to manage my child's specific heart condition?

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Specialist	Purpose	How often to follow	What questions to ask?
Pediatric gastroenterologist	Monitoring of growth and weight development, with evaluation of nutritional intake. Assess safety of feeds clinically. Evaluation for GERD. Evaluation for constipation.	If there are difficulties with feeding, growth deceleration or faltering, constipation, or gastroesophageal reflux, a referral may be appropriate to establish care and follow as needed In adulthood, if there is weight loss, gastroesophageal reflux, or constipation, it is important to assess the underlying causes and provide appropriate management.	
Physical therapy	Evaluation, management, and prevention of various physical and orthopedic symptoms.	Per therapist recommendation.	

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Specialist	Purpose	How often to follow	What questions to ask?
Occupational therapy	Evaluation, management, and assistance with self-care and daily living tasks, such as feeding, fine motor coordination, and toileting.	Per therapist recommendation.	
Speech therapy	Evaluation and management of expressive language difficulties. Evaluation and management of language difficulties, and implementation of alternative and augmentative communication.	Per therapist recommendation.	
Pediatric Endocrinologist	Assessment and treatment for short stature.	As needed.	
Pediatric Behavioral/ Developmental Specialist	Evaluate for neurobehavioral concerns.	As needed.	How do we access early intervention services?

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Specialist	Purpose	How often to follow	What questions to ask?
Pediatric Behavioral/ Developmental Specialist (con...)	Evaluate for development and refer to developmental therapies.	Neuropsychological evaluation is recommended serially to guide therapies at points of transition (preschool, Kindergarten, 2nd grade, 6th grade, 9th grade, 11/12th grade and in the 6months before the child turns 21).	What developmental therapies would be useful?
Rehabilitative Medicine Specialist or Orthopedic specialist	Evaluate for concerns of joint laxity, hypertonia, spasticity and/or scoliosis. May assess for scoliosis via X-ray.	As needed.	
Dentist	Evaluation for dental abnormalities and provision of routine dental care.	Routine dental care every 3-6 months	

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Specialist	Purpose	How often to follow	What questions to ask?
Opthmalogist	Ophthalmological evaluation annually, specifically for Cortical Visual Impairment	Annually	Ensure vision assessment includes an evaluation for cortical visual impairment. If visual impairment is present, what are the supports that are present through school? Ensure receive necessary documentation to receive IEP that includes Teacher for the Visually impaired.
Otolaryngologist (ENT)/Hearing Specialist	Assess for hearing impairment. Rates of hearing loss is not elevated in this population, but hearing should be assessed with speech delay or clinical concerns.	As needed.	
Nephrologist/ urologist	Evaluate for kidney malformations or hypospadias (location of urethral opening is misplaced) and/or cryptorchidism (testicles fails to descend in the scrotum before birth).	Initial assessment and as needed.	

*Recommendations for follow-up are based on the French National Guidelines for care, however clinical guidance should be provided by healthcare providers and patient families should always defer to the advice they receive from their healthcare providers.

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IV.2 Children's Hospital of Colorado Multidisciplinary Clinic

For U.S.-based families, the Children's Hospital of Colorado hosts a multidisciplinary neurogenetic pediatric clinic that specializes in knowledge of 8p chromosomal rearrangements. Their clinic includes care from a variety of healthcare providers with the goal of addressing the multisystemic needs of 8p patients.

While receiving care exclusively at this clinic is by no means a necessity (let alone a realistic possibility for many families), knowing about this clinic as a resource for care may be useful for families as they begin their 8p journey. It might be possible for doctors and therapies from outside the U.S. to confer with the Children's Hospital team if they are seeking advice. Please be sure to consider your country's specific medical guidelines and regulations when determining the feasibility of receiving guidance from an international provider.

Visit this link to learn more about the Children's Hospital of Colorado's clinic.

IV.3 UTHealth Houston Telehealth Genetic Counseling

UTHealth Houston hosts a telehealth genetic counseling clinic for epilepsy and neurodevelopmental disorders. They have clinical genetic counselors available for a virtual consult to provide an up-to-date explanation of chromosome 8p conditions, help explain your family's genetic report, and provide recommendations on whether updated testing is necessary.

While based in Texas, this group is able to consult to families living in other states. Visit their website to learn more about their genetic counseling services.

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V. Who do I go to for support?

V.1 Introduction to Project 8p

At Project 8p, we are a non-profit group dedicated to creating support and community for 8p families and to driving research efforts to discover treatments. Visit project8p.org to learn more about us, our mission, and our resources.

Some of the our initiatives and/or resources that may help you and your hero include:

Project 8p Initiatives

Initiative	Definition	Where to learn more
Patient Navigator	An online interactive tool that outlines 8p medical concerns and management strategies	In this packet - Under "When will Symptoms Arise?" Online Link
Patient Passport	A personalized document provided to 8p Families interpreting their hero's genetic report and providing information tailored to their hero's development.	In this packet - under "What is Chromosome 8p." See that section for instructions on receiving your patient passport.
Patient Registry	A multisystem data collection initiative that consists of a series of caregiver surveys. It is used to inform researchers and physicians working in 8p and to drive the work done by Project 8p	In this packet - under "How can we make progress in 8p" Online Link

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Initiative	Definition	Where to learn more
Patient Biorepository	A collection of blood, skin, and saliva samples from both 8p heroes and their families, which are critical to driving research.	In this packet - under "How can we make progress in 8p" Online Link
A Global Retrospective and Prospective Study of Affected Individuals with Chromosome 8p Rearrangements - Natural history study	Project 8p is leading a longitudinal natural history study to learn more about the life course of individuals living with 8p rearrangements and understand how chromosome 8p conditions unfold over time. The natural history study helps identify patterns in development, medical challenges, and responses to care, so we can improve outcomes for all 8p heroes. Part of this work consists of the data collected from the Patient Registry and Patient Biorepository. You can also provide ongoing updates about your child's development, care, and experiences through optional surveys and interviews. This research lays the foundation for better diagnostics, treatments, and clinical care guidelines tailored to 8p, and it is one of the most powerful tools to accelerating progress.	

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Initiative	Definition	Where to learn more
Project 8p Leadership	The individuals on Project 8p Leadership are dedicated to serving the 8p community. Many of them are inspired by their own 8p hero's story. They remain available as a resource for your family for any needs that arise along your journey.	Read more about Project 8p's Leadership at project8p.org/leadership-team-management

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V.2 Introduction to Project 8p's Peer Support Network

Our organization strives to provide connections to those 8p Hero families seeking community. An initiative that hopes to meet those needs is the Project 8p Peer Support Network. Patient families can work with our Patient Engagement Manager to be connected with another 8p family with whom they can connect, talk, and share their journey.

If you have an interest in being connected with another 8p family, follow this link to fill out a request form.

V.3 Introduction to Rare Disease Support Resources

Both the rare disease community and neurodevelopmental disorders community have a seemingly never-ending list of useful resources aimed at benefiting the broad rare disease collective. The following are resources that the 8p community has suggested as being helpful in their journey.

Once Upon a Gene Podcast	A podcast that explores the stories of families navigating a rare genetic diagnosis.
Child Neurology Foundation	An organization dedicated to supporting families diagnosed with a neurological condition.
Global Gene	An organization dedicated to providing support, advocacy, and education to all rare disease families.
Kids' Waiver	United States–based source for information on children's Medicaid Waivers, Katie Beckett programs, and other Medicaid programs.
Medical Grant Database	United States–based collection of grants to fund families with financial needs of all sizes.
8p Community Authors	There are three books that have been written and published by 8p mothers. If you are interested in reading these books or learning more about them, you can follow this link to Project 8p's website, where there are links to each.

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VI. How do I care for my child?

VI.1 Overview of How to Care for your Child

To date, there is no pharmacological treatment for Chromosome 8p rearrangements. Clinical care for any 8p hero will be oriented towards symptom management. See "Who do I go to for management" to learn more about the symptom-based care and an overview of the healthcare providers that would provide symptom-based management.

Outside of the clinic, there are some other resources that may be helpful to utilize to support your child's developmental needs and access educational resources*:

*Note that the following information applies to U.S.-based families.

Early Intervention are state-based programs that provide support and services to children 3-years-old and younger who have any kind of developmental delay. These services in many cases provide access to physical therapy, occupational therapy, and speech therapy to support your child's development. Requirements and programs differ by state. Visit the CDC's website on Early Intervention to learn more about your state's program.

After age 3, developmental support is transferred to school-based Special Education interventions. The Individuals with Disabilites Education Act (IDEA) is a federal law that requires that schools provide individuals with a disability related supports and the necessary accommodations for their education. This will most often entail building an Individualized Education plan (IEP) outlining what supports and therapies your child may require. Visit the U.S. Department of Education to learn more about special education services policy. Implementation will likely vary by state and school district.

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VI.2 What are other therapies that 8p Families have used?

[Add info on this]

Glossary: Therapy Types

Therapy Types	Definition
Physical Therapy	Physical therapy involves using exercise, massage, electrical stimulation, and other techniques to maximize strength and movement, with the overall goal of promoting physical functionality.
Occupational Therapy	Occupational therapy involves using exercises, adaptive tools, and techniques to help individuals improve their ability to independently perform daily tasks like feeding, self-care, or work-related tasks.
Speech Therapy	Speech therapy utilizes techniques aimed at treating speech challenges, communication difficulties, and swallowing problems.
Music Therapy	Music therapy is the clinical-use of music that aims to address physical, emotional, cognitive, and social needs of an individual. Treatment includes creating, singing, moving to, and/or listening to a song. It can be used for goals like reducing stress or improving quality of life.

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Therapy Types	Definition
Massage Therapy	Clinical massage therapy can be used to address orthopedic issues. Its overall goals are to reduce pain, improving overall function and restoring movement.
Feeding Therapy	Feeding therapy uses techniques that help children develop chewing skills, improve sensory tolerances to certain food types, teach self-feeding skills, and develop healthy eating patterns.
Hippotherapy (also may be referred to as Equine Therapy)	Hippotherapy is a treatment tool that uses the movement of a horse to improve functional outcomes. It can be provided as a part of standard physical, speech, or occupational therapy care plans.
ABA (Applied Behavioral Analysis) Therapy	ABA therapy uses behavioral therapy tools to help individuals with autism or other developmental disorders to increase positive skills and lessen challenging behavior. It is focused on teaching individuals effective social skills, self-care skills, and learning/academic skills.

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VI.3 Navigating Financial Assistance

Navigating the medical costs of a rare disease diagnosis can often be a challenge for many families.

There are a variety of rare disease organizations that have helpful collections of resources and guides to support families navigating these difficulties.

Our organization has developed a Project 8p Local Assistance program through a partnership with Unite Us. The Unite Us program aids in searching for local organizations to assist with needs, referring other families to connect, and tracking the outcome of those referrals. Other benefits that may be offered through Unite Us include benefits eligibility screening, insurance assistance, medical bills assistance, and more. Follow this link or go to the Local Assistance Program tab under the Families header at Project 8p's website to learn more.

Additionally, The EveryLife Foundation for Rare Diseases has a web page that references a large variety of nonprofit groups and grant funding opportunities that are designed to support families navigating a rare disease diagnosis. Ranging from support with medical costs to groups that provide airline funding and accommodations, the resources covered on this page are varied.

Global Genes has created a guide to understanding Medicare/Medicaid services*. They also have a toolkit series that provides detailed information on the Medicare/Medicaid process.

Additionally, KidsWaivers.org is a resource providing information on Medicaid programs* and other programs for children with disabilities and medical needs. They can direct families to their state's programs and policies and they house a list of states that have programs for paid parent caregiving.

*Note that this information applies only for U.S.-based families

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VII. What does this mean for the future?

VII.1 Family Planning Genetic Considerations

The following section describes the inheritance considerations for an Chromosome 8p rearrangement that might impact future family planning. A genetic counselor is a healthcare provider who, based on your family's specific situation, can provide guidance on what the important next steps are for your family when thinking about recurrence risk. While this section provides an overview, it is not intended to replace a discussion with a certified genetic counselor. Please seek the advice of a genetic counselor or a similar healthcare provider before making any decisions about reproductive risk or family planning.

In general, there are three scenarios to think about when considering inheritance implications.

01. The first possibility is that the chromosomal rearrangement was a new change in your 8p hero. This means that this was not something that was inherited but rather was a result of a sporadic, random error in meiosis that most likely has no relation to either parent's genetic make-up. This is called a de novo change. If your 8p hero's rearrangement is de novo, it is generally cited to be a ~1% risk for having another child impacted with the same rearrangement. This risk is not zero due to the possibility that a percentage of either the eggs or the sperm contain the same rearrangement (a concept called gonadal mosaicism), which can't be assessed by any form of genetic test.

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02. The second possibility is that the chromosomal rearrangement was inherited from a parental chromosomal rearrangement. In some cases, a parent may have the same chromosomal rearrangement as their child, but have milder symptoms that may not have warranted clinical suspicion. In these cases, a family would have a 1 in 2 (50%) chance of having another child impacted by the same rearrangement. In other cases, a parent may be mosaic for the same chromosomal rearrangement as their child. This means that a portion of the parent's cells contain the 8p rearrangement, while another portion of their cells do not contain the rearrangement. In the case of parental mosaicism, a family would have up to a 1 in 2 or 50% chance of having another child impacted by the same rearrangement, however depending on which cells contain the rearrangement, the risk may be lower than 50%.

03. A third possibility is that a parent carries a chromosomal rearrangement on 8p that is different from their child's but that may partly explain why their child has an 8p rearrangement. Because Chromosome 8p has regions that make it more susceptible to rearrangement, a portion of the population carries a structural variant on chromosome 8p. This change is benign, meaning that the person carrying this change would not experience any symptoms and would be healthy. Some can be a relatively common change with 25% of certain ancestral populations carrying an 8p inversion. In very rare cases, the structural variant could undergo recombination events that may result in a child with a Chromosome 8p rearrangement. This recombination event is quite rare. For this reason, it is difficult to provide an exact percentage for how likely it is that a parent with an inversion would have another affected child. However, the likelihood is thought to be low such that the risk is clinically insignificant, meaning no additional recommendations would be provided to change the care of these families.

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Because these various possibilities exist, it may be recommended after a child's 8p diagnosis that parents undergo parental karyotyping or genetic testing to investigate whether the rearrangement in their child was de novo or inherited from a parent's rearrangement. Even for individuals where a de novo change is highly suspected, undergoing parental testing gives the genetics providers the best ability to counsel families on what to expect for future children.

In either case of inheritance, it is possible for families who are wanting to have more children to undergo prenatal genetic testing for the chromosomal rearrangement to determine whether a pregnancy is affected.

If your family has more questions on the inheritance of chromosomal rearrangements and what they may mean for future children, we encourage you to consult your genetic counselor or genetics provider, as they can provide guidance tailored for your family's situation. You can visit the National Society of Genetic Counselors (NSGC)'s online "Find a Genetic Counselor" tool to locate a genetic counselor near you (https://findageneticcounselor.nsgc.org/).

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VII.2 The Future of Research in 8p: A Shared Vision for Progress

Receiving a diagnosis of a chromosome 8p rearrangement often comes with uncertainty—families are left searching for answers, and many providers have never encountered 8p before. That's exactly why research matters so much. Together, we are changing the outlook for individuals with 8p and the families who love them.

We are now entering a new era—one where data, lived experience, and science are working hand in hand to transform how 8p is understood, diagnosed, and treated.

Where We Are

The 8p community has made incredible strides in recent years. Thanks to the dedication of researchers, clinicians, and families like yours:

- ✓ A patient registry and biorepository are collecting essential data across ages and experiences.
- ✓ Our multidisciplinary clinic team has developed the first **clinical guidelines** specific to 8p—a valuable stepping stone toward consistent, informed care.
- ✓ New tools like the **Patient Passport** and the **Patient Navigator** are helping providers understand each individual's genetic diagnosis in the context of the broader 8p community.

Where We're Going

Looking ahead, our goals are ambitious—but achievable with continued family participation and scientific collaboration:

- ✓ **Build a complete picture** of how 8p affects individuals over time, through natural history studies and real-world data.

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- ✓ **Predict symptoms before they emerge** using individual-level data and shared trends.
- ✓ **Identify biomarkers and treatment targets** to guide care and lay the groundwork for future therapies.
- ✓ **Create clinical tools and resources** that give families and providers confidence, clarity, and connection.

This work takes time—but every family who joins the registry, contributes data, or shares their story moves us closer to the future we envision: one where 8p is recognized, understood, and treated with care tailored to each child's needs.

Together, We're Shaping the Future of 8p

Today:

- First-ever clinical guidelines for 8p
- Growing global patient registry
- Personalized Patient Passports for families and providers

Tomorrow:

- Predictive tools to anticipate symptoms
- Biomarkers to guide treatment and care
- New therapies, grounded in real-world data

You can drive progress:

Every survey, biosample, and story brings us closer to a world where 8p is recognized, understood, and treated with precision.

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Your Tools for the Journey

The Patient Navigator

Your starting point for understanding 8p and accessing support.
This guide walks you through what to expect after diagnosis, common symptoms, medical terms, therapy options, and how to talk to your providers. It's designed with input from families and experts to give you clear, actionable information—right when you need it.
❗Access it anytime: project8p.org/patient-navigator

The Patient Passport

Your personalized care summary, built from your child's genetic and clinical data.

This easy-to-understand document helps doctors quickly grasp your child's unique diagnosis, medical history, and how their experience compares to the broader 8p community. It's a powerful tool for improving care coordination across specialists.

✉️ To join the registry and request a Patient Passport, email: **engagement@project8p.org**

Together, these tools help reduce uncertainty, improve communication with providers, and give you confidence as you navigate the care journey ahead.

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VIII. How can we help make progress in 8p?

VIII.1 The Project 8p Registry

Our Patient Registry is a data collection initiative that seeks to collect a variety of information about 8p heroes and their clinical journey in order to better inform care guidelines and research projects.

The registry consists of a series of patient and caregiver surveys to collect data across a variety of fields. The registry also requires an upload of your 8p hero's genetic testing report.

The Project 8p Patient Registry is a crucial piece of ensuring that both clinical care and research efforts reflect the true spectrum of 8p Chromosomal conditions. By having data that speaks to what the symptoms are that 8p heroes experience, how often they experience those symptoms, and how those symptoms compare to the larger 8p community, researchers and clinicians can gain a better understanding of an 8p phenotype. This means that clinical care guidelines can be better tailored to fit your hero. This also means that researchers have data to pull from when designing their studies and when trying to better understand how a chromosome 8p rearrangement results in symptoms.

In other words: completing the Project 8p Registry is part of what drives research efforts to finding a treatment!

By completing the Patient Registry, there are also direct, immediate benefits that you can gain as a patient family. Completing the registry is the first step to receiving your patient passport, a useful tool to understanding your child's exact genetic change and a resource to provide to your healthcare providers to inform your child's care (see section titled "Introduction to Patient Passport"). The registry also informs the Patient Navigator, another important resource that providers can use to tailor your child's care (See section titled "Introduction to Patient Navigator").

Follow this link to learn more about how to participate in the Patient Registry.

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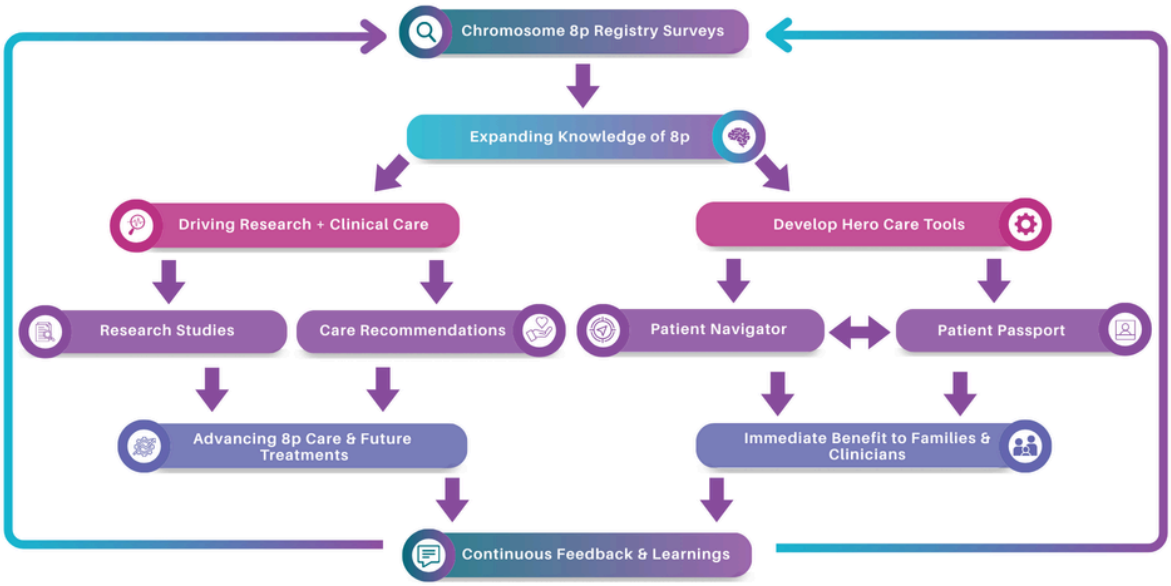

VIII.2 The Project 8p Biorepository

Our biorepository is a centralized location that stores a collection of biospecimens from both 8p heroes and their family members, including both tissue and blood samples.

These samples may be used for genetic testing or to inform research efforts. Having these samples is incredibly helpful for researchers who are trying to identify treatments for patients with 8p, as it allows them to use patient's genetic information to inform animal models and replicate patient genetic changes in their cell lines.

In other words: participating in the Project 8p Biorepository is a part of what drives research efforts to find a treatment!

Follow this link to learn more about how to participate in the biorepository.

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VIII.3 Other Ways to Join Project 8p

We're a growing community united by the belief that change is possible—when families, researchers, and advocates work together. Project 8p offers multiple ways to get involved, make a difference, and stay connected.

Ways to join the movement:

✓ ***Volunteer with Project 8p***

Whether you're great with organization, outreach, design, or just want to help, we'd love to have you. Volunteers support social media, scientific materials, events, and more.

✓ ***Participate in 8,000 Steps for 8p***

This is our annual community-building and fundraising event. Families create or join teams and walk 8,000 steps a day for 8 days in honor of the chromosome. The event funds research, clinical tools like the Patient Passport, and family support efforts. It's fun, meaningful, and a great way to invite your community to rally around your hero.

✓ ***Fundraise or host an event***

From birthdays to fun runs to bake sales, many families have raised funds in creative and heartfelt ways. We can provide support, templates, and promotion.

✓ ***Stay informed and connected***

Subscribe to our newsletter, attend virtual roundtables, and join our private Facebook community to stay up-to-date on resources and opportunities.

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VIII.4 Increase Awareness: Your Voice Creates Ripples

When more people know about Chromosome 8p disorders, more resources follow—more scientists become interested, more clinicians recognize symptoms, and more funding becomes available for research and support.

As a rare disease community, we must build that awareness together. Every story, every conversation, and every share helps move 8p from unknown to understood.

The more people who know, the closer we get to better care and real answers.

Ways to raise awareness:

Share your hero's story

We can help you share your child's story on our website or in our newsletters. These stories help others feel less alone and draw attention to the need for better care and research.

Engage your community

Let your local school, clinic, or community center know about 8p. We can support you with flyers, brochures, and talking points.

Awareness Days

Participate in Rare Disease Day, 8p-specific campaigns, and more. These shared moments help amplify our collective voice.

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PROJECT 8p FOUNDATION

Join Project 8p for family links, information and support.
Project 8p is a charity without government funding, existing entirely on donations and grants. If you can, please make a donation via our website at www.project8p.org. Please help us to help you!

Project 8p Foundation is a registered 501(c)(3) charitable organization with EIN 83-2545342. All contributions are deemed tax-deductible