CHILDREN'S TUMOR FOUNDATION
ENDING NF THROUGH RESEARCH

DIAGNOSED WITH SCHWANNOMATOSIS

INCLUDING:

- *SMARCB1*-related schwannomatosis
- *LZTR1*-related schwannomatosis
- 22q-related schwannomatosis
- Schwannomatosis NOS
- Schwannomatosis NEC

with an *NF2*-related schwannomatosis introduction

This brochure is a companion to Diagnosed with NF2-related Schwannomatosis, a separate brochure from the Children's Tumor Foundation.

A MESSAGE FROM THE
Children's Tumor Foundation

This booklet is designed to help you on your journey living with schwannomatosis (SWN). Whether this is a recent diagnosis or a previous one, you will find information and support here to help you and your loved ones.

The Children's Tumor Foundation (CTF) hopes this guide will answer some of the most common questions that people living with SWN may have about coping with a diagnosis, understanding how these genetic conditions occur, recognizing common and less common symptoms, and managing care while living a full life.

This brochure specifically covers the types of SWN in which pain is the most frequently occurring symptom. While the symptoms of *NF2*-related schwannomatosis (*NF2*-SWN) are briefly introduced in this brochure, we encourage patients with a possible diagnosis to also obtain our companion brochure, Diagnosed with *NF2*-related Schwannomatosis, which contains more specific information about that type of SWN. That brochure, along with this one, can be read or downloaded at **ctf.org/education**. You can also request a print copy which we will mail to you free of charge.

Thank you for reading and sharing this resource. We hope to help you connect with other people living with SWN and their families through the active and vibrant CTF community around the world.

Eric, who lives with SWN.

On the Cover:
Joel, who lives with SWN

Contents

A DIAGNOSIS OF SCHWANNOMATOSIS

Newly diagnosed? You Are Not Alone

At the Children's Tumor Foundation (CTF) we want you to know that you are not alone on your journey with schwannomatosis (SWN). A lot of questions and concerns usually arise after receiving a diagnosis. You may need support as you learn about the condition, how to navigate it, and how to live your best possible life. This brochure is designed to give you essential information and provide resources and advice for you, your family, and friends.

There is a lot of information to absorb at one time. You probably want to know how your diagnosis will impact your life. It can be helpful to remember that everyone deals with health-related news in different ways. While some prefer to receive small pieces of information at a time, others like to get as much information as possible. Either of these approaches is perfectly normal.

CTF has many resources available for individuals diagnosed with any type of SWN. These resources include information on specialized clinics around the world, local events to help you meet others affected by SWN, and online opportunities.

Previously diagnosed with SWN

Coping with a diagnosis of a genetic condition can be difficult at any stage of life. Individuals and families must continually learn new things and adjust their coping strategies as challenges come up. Challenges, concerns, and considerations can change over time, especially if new symptoms develop. Also, how you feel emotionally may be different based on the specific symptoms you are experiencing. CTF is here to help you navigate these changes at every point in your life.

Additionally, a greater understanding of SWN is constantly being uncovered. Because of these new discoveries, in 2022, a group of experts published updated guidelines for the diagnosis of (what was then referred to as) neurofibromatosis type 2 and schwannomatosis. This included the renaming of the various types of SWN, which we will discuss in this booklet.

These changes may be hard to accept for some patients or cause fear or uncertainty. The Children's Tumor Foundation, along with your healthcare providers, is here to help you navigate your feelings and your understanding of SWN throughout this evolving landscape.

Rebecca, who lives with SWN.

SCHWANNOMATOSIS: GET THE FACTS

What is NF?

The term NF refers to a group of distinct genetic conditions, which include neurofibromatosis type 1 (NF1), and all types of schwannomatosis (SWN), including *NF2*-related schwannomatosis (*NF2*-SWN), previously known as NF2. They each have different genetic causes, so one type of NF cannot change into another type.

did you know?

One type of NF cannot change into another type.

These are lifelong conditions that affect all populations equally, regardless of gender, race, or ethnicity. NF is not caused by anything you or your parent did or did not do, and NF is not contagious. People who have NF can lead productive lives, but they often require specialized medical care.

Introduction to Schwannomatosis

Schwannomatosis is a type of NF that causes tumors, called **schwannomas**, to grow on nerves in the **central nervous system** (brain and spine) and on **peripheral nerves** (the nerves throughout the rest of the body). Schwannomas are **benign**, meaning they are not cancer. However, sometimes they press on nerves, blood vessels, or other nearby organs, which can cause pain or other symptoms.

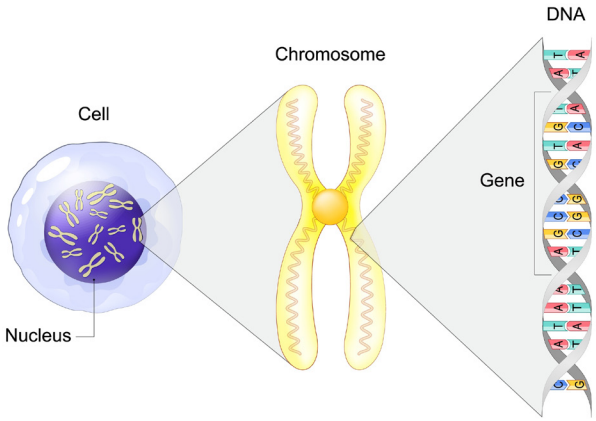
Types of Schwannomatosis

The term schwannomatosis is an umbrella term for several genetic conditions that lead to a risk for multiple schwannomas to grow on nerves.

did you know?

Chromosomes are made up of long strands of DNA, and a gene is a small part of DNA. Think of a chromosome as a recipe book and a gene as a single recipe.

All of the known types of schwannomatosis are a result of a change in a **gene** (a sequence of DNA) located on **chromosome 22**. When a gene change causes the gene to stop working correctly, it is called a **pathogenic variant** (formerly called a genetic mutation) or disease-causing variant.



Before 2022, schwannomatosis and "NF2" were classified as two distinct conditions. However, researchers and doctors have learned that they are very similar, and it is more accurate to group them together under the umbrella term of schwannomatosis.

Recently, there has been a movement to change the way we name genetic conditions. This includes a combination of the name of the gene that is affected (has a pathogenic variant), and a main symptom or feature of the diagnosis. Therefore, we now refer to the types of schwannomatosis according to the gene affected if it is known. *Gene names are always in italics.*

GENE-related schwannomatosis

For example, *NF2*-related schwannomatosis is caused by a pathogenic variant in the *NF2* gene. Likewise, if the *SMARCB1* gene is involved, the condition is instead called *SMARCB1*-related schwannomatosis.

All of the known genes that cause schwannomatosis cause tumors called schwannomas. However, there are some differences in other health issues with each type of schwannomatosis, and researchers are continuing to learn more about these and how this impacts someone's health.

The table below includes the names of the different types of schwannomatosis that are currently known. Researchers believe there are more genes to be discovered that cause schwannomatosis. As researchers continue to study these conditions, their findings will further inform healthcare professionals about the types of schwannomatosis and how to better care for their unique patients.

Type of Schwannomatosis	Causative Gene	Estimated Incidence
NF2-related schwannomatosis	*NF2*	1 in 25,000 births
SMARCB1-related schwannomatosis	*SMARCB1*	1 in 280,000 births
LZTR1-related schwannomatosis	*LZTR1*	1 in 500,000 births
22q-related schwannomatosis	Unknown – genetic testing of blood/saliva is negative, and tumor testing localizes the disease-causing variant on chromosome 22q	Unknown
Schwannomatosis-NOS (not otherwise specified)	Unknown – genetic testing is not available or not performed	Unknown
Schwannomatosis-NEC (not elsewhere classified)	Unknown – genetic testing of blood/saliva and tumors is performed but does not identify any disease-causing variants	Unknown

NF2-related Schwannomatosis

NF2-related schwannomatosis (*NF2*-SWN) affects about 1 in 25,000 births, and is caused by a change, or pathogenic variant, in the *NF2* gene. *NF2* carries the instructions for making a protein called merlin, which prevents cells from continuing to divide. Without merlin, cells continue to multiply, causing tumors.

NF2-SWN is characterized by the development of tumors called vestibular schwannomas on the nerve that carries sound and balance information from the inner ear to the brain. These tumors often affect both ears and may lead to partial or complete hearing loss. *NF2*-SWN can also cause schwannomas to develop on other brain or peripheral nerves.

People with *NF2*-SWN may also develop other tumors called **meningiomas** (tumors of the membranes surrounding the brain and spinal cord) and **ependymomas** (tumors that develop from cells lining the ventricles of the brain and center of the spinal cord). The condition can also cause the development of juvenile cataracts, potentially compromising vision. Most people develop symptoms in the late teen and early adult years, although about 10% of people develop symptoms during late childhood. The most common symptoms of *NF2*-SWN include ringing in the ears (tinnitus), gradual hearing loss, and balance issues.

The remainder of this brochure will cover information about the types of non-*NF2*-related schwannomatosis. However, this brief introduction to *NF2*-SWN might be important, especially if you are currently in the process of being diagnosed.

Because the symptoms of *NF2*-related schwannomatosis differ somewhat from the other types of schwannomatosis, we have created a separate brochure with further information. ***Diagnosed with NF2-related Schwannomatosis*** can be read and downloaded at **ctf.org/education.**

SMARCB1-related Schwannomatosis
LZTR1-related Schwannomatosis
22q-related Schwannomatosis
Schwannomatosis-NOS
Schwannomatosis-NEC

These types of schwannomatosis are rare conditions that collectively affect about 1 in 70,000 people. In each of these types of schwannomatosis, the most common symptom is pain, which will be discussed further on pages 12-13.

Schwannomatosis is characterized by the development of benign tumors called schwannomas. These tumors develop when the Schwann cells that form the nerve sheath (the insulating cover around nerve fibers) grow abnormally. Schwannoma tumors stay on the outside of the nerve but may push against it, causing pain and damage.

Schwannoma development is caused by a change, or variant, in a gene. The variant prevents the gene from making the protein (merlin) that normally controls cell proliferation, or cell growth and division. Without the needed protein, cells can multiply more than they normally do and form tumors.

As their names suggest, *SMARCB1*-related schwannomatosis (*SMARCB1*-SWN) is due to a change, or pathogenic variant, in the *SMARCB1* gene. *LZTR1*-related schwannomatosis (*LZTR1*-SWN) is due to a pathogenic variant in *LZTR1*. A patient is diagnosed with 22q-related schwannomatosis (22q-SWN) when a genetic test using blood or saliva shows no variants in the *NF2*, *LZTR1*, or *SMARCB1* genes, but the testing of two of their tumors (removed by surgery) shows other genetic variations on chromosome 22.

A diagnosis of schwannomatosis NOS (SWN-NOS), which stands for "Not Otherwise Specified," is given to patients who develop schwannomas but who have not had genetic testing.

A diagnosis of schwannomatosis NEC (SWN-NEC), which means "not elsewhere classified," is given to patients in whom genetic testing did not find a pathogenic variant in a gene known to cause schwannomatosis. It is possible some of these patients may have a variant in a different gene, one that has not yet been identified as a gene that causes schwannomatosis, while others may have mosaicism (see below).

Segmental or Mosaic Schwannomatosis

For some individuals with schwannomatosis, not all of a person's cells carry the genetic changes that cause the condition. Mosaicism for schwannomatosis may present with a less widespread or uneven distribution of tumors, often affecting one part of the body more than others. Mosaicism happens when a variation in the gene associated with schwannomatosis, such as *SMARCB1* or *LZTR1*, occurs after fertilization, leading to a mix of cells in the body—some with the variation and some without. This can result in a milder or more localized form of the condition compared to someone with the variation in every cell. The implications of being mosaic for schwannomatosis can vary, but it often means potentially less severe symptoms. For family planning, the risk of passing the condition to biological children may be lower for those with mosaicism than if the variation were present in all cells, but genetic counseling is important to understand specific risks, as some forms of mosaicism do carry a chance of transmission.

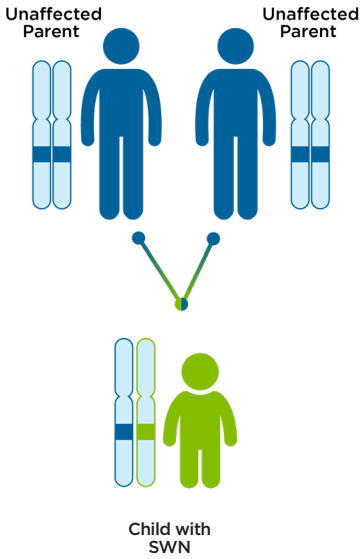
What Causes Schwannomatosis?

Inherited Schwannomatosis

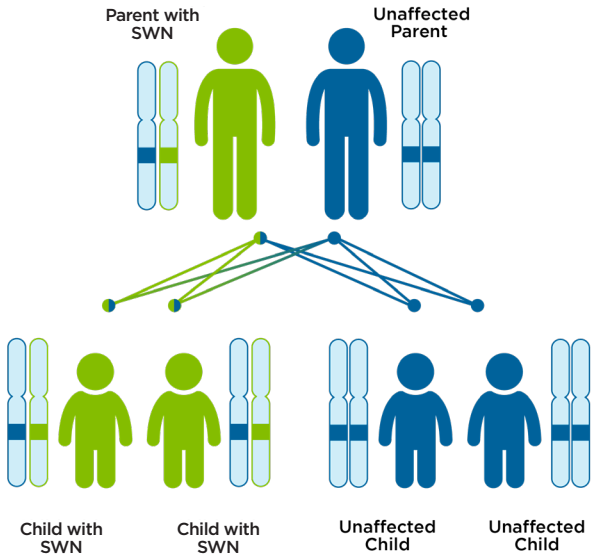
Some cases of schwannomatosis (SWN) are inherited, or familial. This means that there is more than one family member affected by the condition. For most types of SWN, only about 15% of all cases are inherited from a parent.

SWN is inherited based on an autosomal dominant pattern. Autosomal dominant means that inheriting an abnormal gene from only one parent can cause the condition, even though the matching gene from the other parent is normal (we typically have two copies of each gene, one from each parent). A parent with an autosomal dominant condition has a 50% chance of passing along the condition to a child.

However, in familial cases of *LZTR1*-SWN and *SMARCB1*-SWN, symptoms of the condition may skip generations due to a genetic phenomenon called incomplete or reduced penetrance. Penetrance refers to the proportion of people with a particular genetic change who show signs and symptoms of a genetic condition.



Sporadic SWN



Inherited SWN (Autosomal Dominant)

did you know?

A person may carry a SWN gene variant but never develop any symptoms due to incomplete penetrance.

If a genetic condition has complete penetrance, symptoms always occur. However, if a condition has incomplete penetrance, as with SWN, not everyone who inherits the genetic variant will show symptoms. In other words, people may carry a SWN gene variant but never develop any symptoms due to incomplete penetrance.

Sporadic SWN

Most people with SWN did not inherit the condition. They are the first person in their family to be diagnosed with it. We refer to this as sporadic. But people who are the first in their family can then pass it on to their children, who will be designated as having familial cases.

Genetic Testing

Genetic testing for the currently known SWN genes is available and can help confirm the diagnosis, guide clinical management, and inform family members about potential genetic risks (including family planning). Additionally, identifying a specific gene variation can assist in understanding the clinical course of the condition and planning appropriate surveillance and treatment strategies, for both the patient and others with similar variations in the future. Ideally, this testing analyzes the *NF2*, *SMARCB1*, and *LZTR1* genes in a blood or saliva sample, as well as tumor tissue if available.

Consultation with a genetics counselor is recommended to interpret test results and discuss the implications for family planning and future healthcare decisions. It is important to seek the guidance of a professional with genetics expertise to best understand the complexities of how the condition can be passed on from generation to generation.

The Role of Genetic Counseling

It is a good idea for anyone with questions about genetic testing and reproductive options in all types of SWN, including prenatal testing, to meet with a medical geneticist or genetic counselor. A genetic counselor can offer help in the following key areas:

- Provide information about the complex inheritance patterns involved in SWN
- Explain the testing options available and discuss the benefits and limitations of genetic testing
- Interpret and explain the results of genetic testing

CLINICAL FEATURES

Symptoms of Schwannomatosis

The main feature of all types of schwannomatosis (SWN) is the development of schwannomas, distinctive tumors that grow on cranial and peripheral nerves. These tumors develop from Schwann cells, nerve sheath cells that support, protect, and enable the nerves to function properly. These tumors are usually slow-growing and remain on the outside of the nerve. However, they can sometimes push the nerve aside or press it against a bony structure or other tissue, causing pain and other complications.

Schwannomas are typically located deep inside the body, although sometimes a physician may be able to feel them during a physical exam. Some people with SWN develop tumors throughout their body, while others may have only one or two tumors. About one-third of individuals with SWN have mosaic or segmental SWN (see page 9).

Pain

Pain in SWN is one of the most significant and challenging symptoms associated with the condition. Pain in SWN is caused by the growth of benign schwannomas on nerves throughout the body. The pain can be chronic, severe, and difficult to manage. The nature and intensity of pain can vary widely between individuals, with some experiencing mild, intermittent pain and others enduring severe, debilitating pain that impacts their daily activities and quality of life. Pain can range from sharp stabbing or shock-like sensations to a more persistent deep ache.

People with SWN may experience localized pain in the area in which a schwannoma is directly impacting a nerve. Patients with SWN may also experience referred pain, which is pain in a part of the body where there is not a tumor. Some individuals with SWN may experience generalized pain that seems to affect the whole body. Some people with SWN do not experience any pain associated with their tumors. The exact mechanism by which schwannomas cause pain is not completely understood, which may be frustrating for patients and healthcare providers.

Pain Intensity and Frequency

The intensity (how much) and frequency (how often) of pain experienced by each person with SWN is unique to that person. Some people with SWN have a low level of pain and they don't experience pain very often. Others experience frequent and severe pain that interferes with their daily lives and needs medical intervention.

More from the Children's Tumor Foundation about coping with pain can be found at **ctf.org/pain.**

Other Symptoms

Many people with SWN experience pain as the only symptom. However, some people may also experience other symptoms depending on the location and size of the tumors. Symptoms may be unique and consulting an SWN expert is important. Other symptoms may include:

- Numbness
- Tingling
- Weakness, including facial weakness
- Vision changes
- Headaches
- Problems with their bowels or difficulty urinating
- Lumps or swollen areas under the skin

Dale, who lives with SWN, speaking at CTF's NF Summit

MEDICAL MANAGEMENT

Treatment of Schwannomatosis

The treatment of SWN focuses primarily on symptom management, as there is currently no cure for the condition.

Management of the condition is based on the specific symptoms a person develops. Because SWN can cause pain and other potentially serious complications, it's important to seek treatment from a neurologist (a specialist that treats conditions affecting the brain and nerves), a neurosurgeon (a doctor who performs brain and nerve surgery), and/or a geneticist who is experienced with SWN. It is preferable to go to an NF clinic that provides multidisciplinary care, which means care from a number of different specialists who are familiar with SWN and are working together as a team.

Medical Management of Pain

Pain management is usually an integral part of care. Patients are best served in a clinic where multidisciplinary specialists experienced in SWN can administer pain management protocols that have been shown to be effective for people with this condition. Treatment may include the use of pain medications, physical therapy, cognitive behavioral therapy, and/or procedures such as nerve blocks. If there are not any specialty clinics near you, pain management might require reaching out to several different types of specialists to come up with a good pain management plan.

Surgical Intervention

When a schwannoma causes significant pain or neurological deficits, surgical removal may be an option. This approach may provide relief if the tumor is accessible and the potential benefits outweigh the risks. However, schwannomas may regrow, or new schwannomas may develop, causing symptoms to recur. Additionally, for some people

with SWN, surgery may not reduce pain and may lead to an increase in painful symptoms. Surgery may also be considered for people who have tumors that are causing neurological (related to the nerves in the brain and spine) or organ-related complications.

Anytime surgery is considered, it's important that a surgeon experienced in SWN care be involved to ensure the best possible outcome. Deciding to have surgery is a complex decision and talking with doctors, psychologists and other counselors, along with family and friends can help patients decide if surgery is right for them.

Emotional Support and Self Care

Psychological counseling and emotional support can be extremely important for patients managing pain. It can also be helpful if a person has feelings of anxiety or fear associated with having a genetic condition. Psychologists and counselors trained to assist with pain management strategies can teach you skills, self-care and resiliency strategies to help you live a full and active life. Pain management clinics often include psychologists specializing in this type of support, but you can also ask your doctor to refer you to this type of psychologist or counselor. Additional support for pain resiliency can be found at **ctf.org/pain**.

Michele, who lives with SWN

HOW YOUR DOCTOR MAKES A DIAGNOSIS OF SWN

Healthcare providers use a list of criteria (like a checklist of signs and symptoms) to determine whether or not a patient may be given a diagnosis of a condition or disease. Healthcare providers will obtain a detailed medical history from you and discuss symptoms, such as chronic pain, the presence of masses or lumps, and any neurological issues like muscle weakness or sensory changes. Family history is also reviewed, as it can provide clues to the genetic basis of the condition, although SWN is often sporadic rather than inherited. Imaging studies such as magnetic resonance imaging (MRI) may be used to identify schwannomas. It provides detailed images that help locate and evaluate the number, size, and distribution of tumors along the nerves. Genetic testing may confirm a diagnosis by identifying variations in genes associated with SWN, such as *SMARCB1* or *LZTR1*. Testing can be done on blood samples or tissue obtained from biopsies of schwannomas in uncertain cases.

While the diagnostic criteria below were developed for healthcare providers, it may help enhance your understanding of the diagnostic procedures for SWN and in your discussions with clinicians about your diagnosis.

2022 Diagnostic Criteria Update

The diagnostic criteria for all types of SWN was carefully reviewed, and an update was published in 2022. The revisions aimed to improve diagnostic accuracy so that clinicians can make the best decisions to help improve the health and well-being of patients.

For Healthcare Providers and General Practitioners

Complete information about the diagnostic criteria for all types of NF, including links to the *Genetics in Medicine* publication, summary documents, and an NF Diagnosis mobile app, may be found at **ctf.org/criteria**.

Schwannomatosis Diagnostic Criteria

A brief glossary of the scientific terms and phrases used below is included on page 20.

Diagnostic Criteria for *SMARCB1*-related schwannomatosis (*SMARCB1*-SWN)

A *SMARB1*-SWN diagnosis can be made when a patient meets **one** of these criteria:

- At least one pathologically confirmed schwannoma or hybrid nerve sheath tumor AND a *SMARCB1* pathogenic variant in unaffected tissue such as blood or saliva
- A common *SMARCB1* pathogenic variant in two anatomically distinct schwannomas or hybrid nerve sheath tumors

Note: diagnosis requires surgical specimen to confirm

SUMMARY: A patient is diagnosed with *SMARCB1*-SWN when genetic testing of one schwannoma tumor and a genetic test using blood or saliva shows a gene change in the *SMARCB1* gene OR, two different schwannoma tumors are tested and show the same *SMARCB1* gene change (without a blood or saliva test).

Diagnostic Criteria for *LZTR1*-related schwannomatosis (*LZTR1*-SWN)

A *LZTR1*-SWN diagnosis can be made when a patient meets **one** of these criteria:

- At least one pathologically confirmed schwannoma or hybrid nerve sheath tumor AND an *LZTR1* pathogenic variant in an unaffected tissue such as blood or saliva
- A common *LZTR1* pathogenic variant in two anatomically distinct schwannomas or hybrid nerve sheath tumors

Note: diagnosis requires surgical specimen to confirm

SUMMARY: A patient is diagnosed with *LZTR1*-SWN when genetic testing of one schwannoma tumor and a genetic test using blood or saliva shows a gene change in the *LZTR1* gene OR, two different schwannoma tumors are tested and show the same *LZTR1* gene change (without a blood or saliva test).

Diagnostic Criteria for 22q-related schwannomatosis (22q-SWN)

A diagnosis of 22q-SWN can be made when an individual **does not meet** criteria for *NF2*-SWN, *SMARCB1*-SWN, or *LTZR1*-SWN, and has **both** of the following molecular features:

- Loss of heterozygosity (LOH) of the same chromosome 22q markers in two anatomically distinct schwannomas or hybrid nerve sheath tumors, AND
- A different *NF2* pathogenic variant in each tumor which cannot be detected in unaffected tissue

Note: diagnosis requires at least two surgical specimens

SUMMARY: A patient is diagnosed with 22q-SWN when a genetic test using blood or saliva shows no variants in the *NF2, LZTR1* or *SMARB1* genes. However, the testing of two of their tumors (removed by surgery) show the absence of one copy of a part of chromosome 22q, and a different *NF2* pathogenic variant in each tumor.

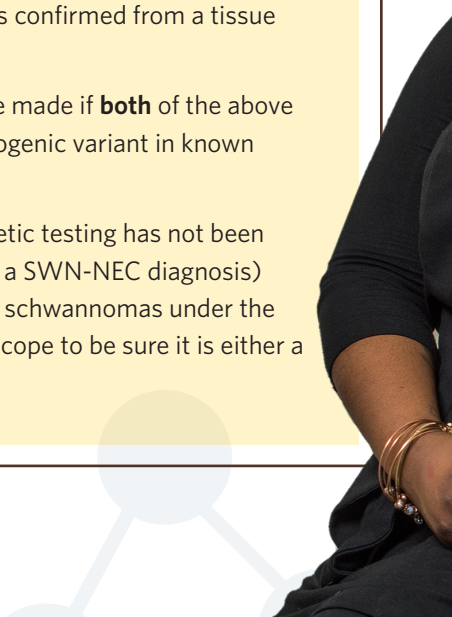
Diagnostic Criteria for schwannomatosis-NOS (SWN-NOS) or schwannomatosis-NEC (SWN-NEC)

A diagnosis of SWN-NOS (not otherwise specified) can be made if **both** of the following criteria are met, and genetic testing was not performed or is not available:

- Presence of two or more lesions on appropriate imaging consistent with non-intradermal schwannomas, AND
- At least one schwannoma or hybrid nerve sheath tumor is confirmed from a tissue sample

A diagnosis of SWN-NEC (not elsewhere classified) can be made if **both** of the above criteria are met, and genetic testing does not reveal a pathogenic variant in known schwannomatosis-related genes.

SUMMARY: A diagnosis of SWN-NOS can be made if genetic testing has not been completed, OR did not reveal a gene change (which will be a SWN-NEC diagnosis) - **however**, an MRI shows at least two tumors that look like schwannomas under the skin, and at least one tumor must be tested under a microscope to be sure it is either a schwannoma or a hybrid nerve sheath tumor.



Diagnostic Criteria for Mosaicism

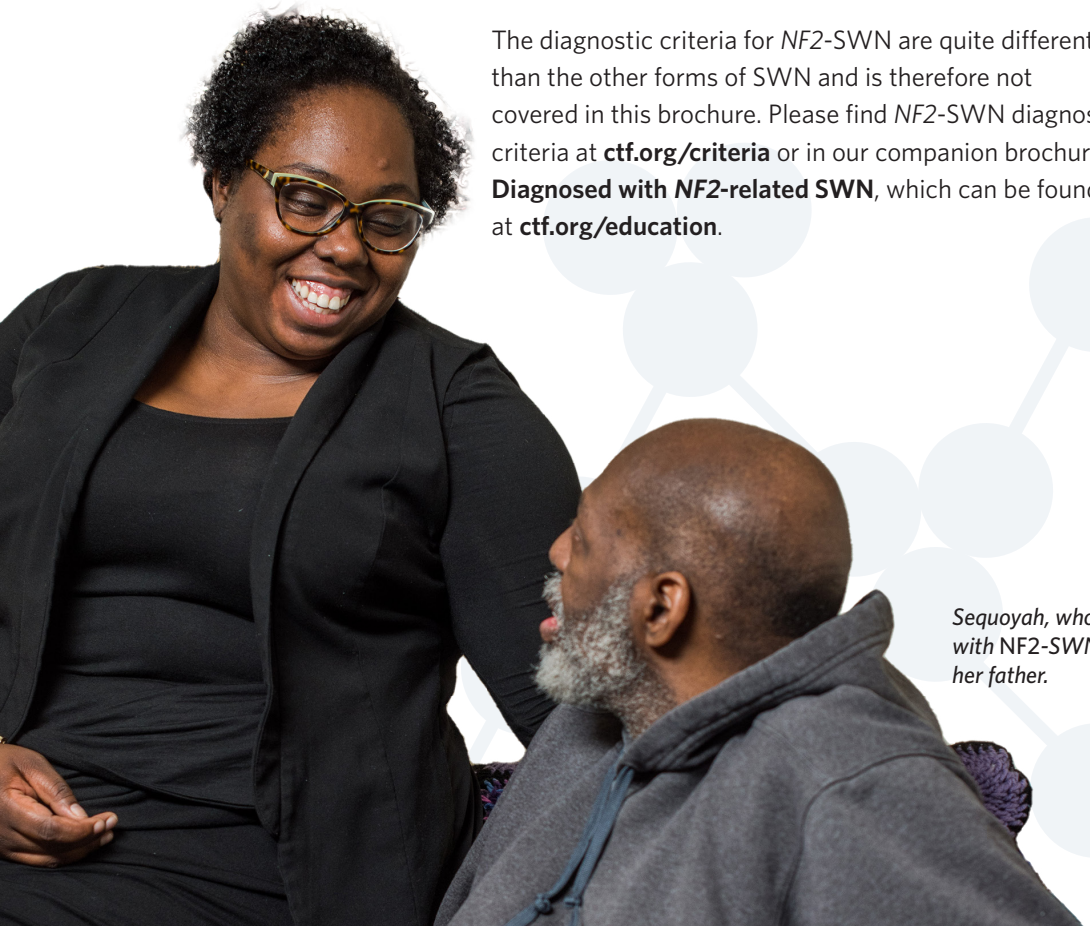
Mosaicism is confirmed for *LZTR1*-SWN, *SMARCB1*-SWN, or *NF2*-SWN by **either** of the following:

- Clearly less than 50% pathogenic variant allele fraction (VAF) in blood or saliva OR
- Pathogenic variant is not detected in blood or saliva but a shared pathogenic variant is found in two or more anatomically unrelated tumors

SUMMARY: Mosaicism for schwannomatosis is confirmed when blood tests show that less than 50% of the cells being tested show the same gene variant or when blood or saliva shows no pathogenic variant. A variant must be found in two separate tumors.

Diagnostic Criteria for *NF2*-related SWN (*NF2*-SWN)

The diagnostic criteria for *NF2*-SWN are quite different than the other forms of SWN and is therefore not covered in this brochure. Please find *NF2*-SWN diagnostic criteria at **ctf.org/criteria** or in our companion brochure, **Diagnosed with *NF2*-related SWN**, which can be found at **ctf.org/education**.



Sequoyah, who lives with NF2-*SWN, with her father.*

Diagnostic Criteria Glossary

In the order in which these terms appear on pages 17 - 19.

- **pathologically confirmed schwannoma** – a tumor that has been tested under a microscope to confirm that it is a schwannoma and not some other type of tumor
- **schwannoma** – a type of tumor that grows on nerves of the central nervous system (brain and spine) or the peripheral nervous system (other parts of the body) that develop from Schwann cells, which are nerve sheath cells that support and protect the nerves
- **hybrid nerve sheath tumor** – a noncancerous tumor which has the combined features of more than one type of tumor when looked at under a microscope
- **pathogenic variant** – a change in a gene that keeps the gene from working normally (formerly called a gene mutation)
- **unaffected tissue** – part of the body that does not have tumors
- **anatomically distinct** – in more than one area of the body; tumors that are not touching
- **surgical specimen** – a part of a tumor, or an entire tumor, that has been removed by surgery in order to test under a microscope
- **molecular features** – aspects of blood or human tissue that can only be seen and tested under a microscope
- **loss of heterozygosity (LOH)** – a change in DNA that results in the loss of one copy of a patient's gene or group of genes. Human cells normally have two copies of each chromosome — one from each parent — so in the case of LOH, only one copy is present
- **chromosome 22q markers** – a small fragment of chromosome 22
- **lesions** – damaged tissue; tumors are lesions but not all lesions are tumors
- **non-intradermal schwannomas** – schwannoma tumors that are not located in the layers of the skin
- **pathogenic variant allele fraction (VAF)** – a percentage used to measure whether or not the cells being tested can be classified as a pathogenic variant

DISCUSSING YOUR DIAGNOSIS

Telling Others

Navigating how and when to share a new diagnosis of SWN with close family and friends can feel challenging. Here are some suggestions that may help make the process a bit smoother and more comfortable.

Who should I tell?

Who you tell is up to you. It is all right not to tell anyone about your diagnosis if you do not want to. However, it can be helpful in some relationships to explain what you have been experiencing and also to receive support from other people.

What should I tell them?

When you decide to share your or your family member's diagnosis with others, you must also decide how much information to share. You might only feel like sharing in a limited way, such as discussing the fact that pain is usually the main issue you are dealing with. Other times it is helpful to have someone with whom you can share more details, including all of the potential ups and downs that go along with the diagnosis.

Sample Message to Family & Friends

Dear _____,

I want to share with you that _____has been diagnosed with a rare genetic condition called schwannomatosis, or SWN.

Schwannomatosis can cause painful tumors, called schwannomas, to grow on spinal and peripheral nerves anywhere in the body. These tumors are usually benign (not cancerous) but sometimes need to be surgically removed due to their location or to lessen pain. People with schwannomatosis need special medical care and lifelong monitoring.

Although people are born with the condition, it may not be diagnosed until adulthood. It is caused by a genetic change and occurs in about 1 in 70,000 births. It is not contagious. There is no cure yet, but scientists and doctors are working toward understanding and treating schwannomatosis.

There is a lot of hope for people living with schwannomatosis, and new research is underway. The support of family and friends makes a difference on this journey.

If you would like to learn more, please visit the Children's Tumor Foundation website at ***ctf.org****.*

We appreciate all of your love and support.

Sincerely, Your Name

ADDITIONAL SUPPORT AND RESOURCES

Connecting With Other Patients and Families

After your diagnosis, you might experience a range of feelings that could include shock, sadness, anger, and uncertainty. While all of these feelings are completely normal, it can be difficult to deal with these emotions by yourself. In addition to getting love and support from friends and family, it can also be helpful to connect with other patients and families who are facing similar challenges. These individuals might have a special understanding of your thoughts and feelings and offer a uniquely personal perspective about their own experiences and challenges with the condition.

It may be comforting and useful for you to read stories about others living with SWN and their families. The CTF newsfeed at **ctf.org/news** frequently posts stories of NF. You may also benefit from sharing your personal story with us at **ctf.org/storiesofnf**.

Numerous videos featuring SWN patients of all ages can be viewed on the Children's Tumor Foundation and Make NF Visible YouTube channels.
YouTube.com/ChildrensTumor
YouTube.com/MakeNFVisible

> *"When I was diagnosed with schwannomatosis, I learned that I have a genetic condition that I could pass down to a child. Despite this, I am hopeful about starting family some day because increased awareness around NF and advancements in genetics allow people like me to have more knowledge and options than ever before."*
>
> —Renee, who lives with SWN

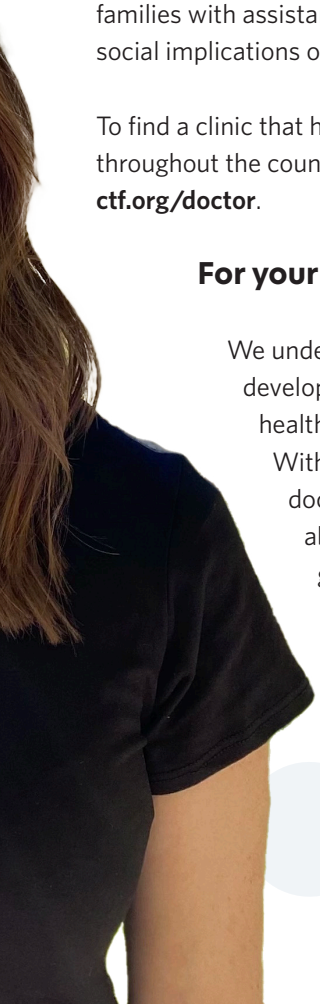
Finding Specialized Care

Because SWN is a rare genetic condition, it can be challenging to find a specialist with experience in diagnosing and managing the condition. If you have a confirmed or suspected diagnosis of SWN, it's important to look for a trusted, experienced clinician.

The Children's Tumor Foundation (CTF) knows how important it is to find healthcare professionals with experience diagnosing and caring for patients with SWN. CTF has established a nationwide network of NF clinics called the **NF Clinic Network (NFCN)** that recognizes clinics that provide comprehensive medical care for NF.

Clinics specializing in SWN provide a comprehensive, multidisciplinary approach to care led by experienced specialists who collaborate in the treatment and management of all forms of SWN and its related complications. These specialized clinics also offer access to genetic counselors, nurses, and other caring specialists who can provide patients and families with assistance and support in managing the lifelong medical, psychological, and social implications of a SWN diagnosis.

To find a clinic that has been accepted into the NFCN, as well as other specialists throughout the country who are familiar with NF, go to our Find a Doctor page at **ctf.org/doctor**.



For your General Practitioner

We understand that not everyone has access to an NF specialist, so CTF has developed the NF Diagnosis mobile app for general practitioners and other healthcare providers, which is available for iPhone and Android phones. Within the app is up-to-date SWN diagnostic information specifically for doctors and clinicians. There are also links to important publications about all types of SWN for the general practitioner. Ask your doctor to go to **ctf.org/nfapp** for more information.

The NF Registry

The NF Registry is a patient-centered resource for sharing information about your symptoms to help guide SWN research. This safe and effective tool will empower patients and their caregivers by inviting them to take an active role in advancing NF research.

When you join the NF Registry, you have access to the latest discoveries about the many ways living with NF can affect individuals and families. This will help you and your family find the best possible care. As an NF Registry participant, you complete a yearly health survey. This data helps researchers study how NF affects everyone differently, potential correlations between various symptoms or outcomes, and how NF changes over time. You can then choose whether to receive personalized emails about any or all of the following topics:

- Clinical trials and research studies relevant to you or your child
- Updates to NF care recommendations
- Research announcements and news
- Surveys designed to get patient input on key NF challenges
- Educational materials specific to you
- Resources to help you on your path with NF

did you know?

Joining the NF Registry will give you access to the latest SWN research, and can alert you to clinical trials and research studies relevant to you.

The NF Registry's first principle is that patients are always in control of their own information. You only share what you want to share, and you control the permissions on when or if you are to be contacted. All information is carefully protected, and the strictest privacy protocols are in place. Even if you choose not to be contacted, your participation helps researchers learn from the real experts – NF patients and families.

To learn more or join the NF Registry, go to **nfregistry.org**

Schwannomatosis Research

The Children's Tumor Foundation is committed to finding treatments for all forms of NF, including all types of SWN.

Finding Potential Drug Treatments for Schwannomatosis

Since the breakthrough discoveries of the genes associated with SWN, *SMARCB1* and *LZTR1* genes (discovered in 2007 and 2015 respectively), scientists have been working to design studies that test potential drug treatments that target the function of these genes. Other research continues to focus on the discovery of new genes associated with SWN as well as exploring how the *SMARCB1* and *LZTR1* genes contribute to the condition.

The Children's Tumor Foundation is proud to support ongoing vital research into treatment options for SWN. In 2017, CTF launched Synodos for Schwannomatosis, a two-year consortium focused on pain. The data from this research was released into the NF Data Portal (a database for NF researchers to share and integrate data from various studies) in early 2021.

The Children's Tumor Foundation also hosts and supports SWN workshops to identify priorities for advancing research and funding SWN research initiatives. You can follow this progress by signing up for the Children's Tumor Foundation newsletter and watching for updates at **ctf.org/news**.

International Schwannomatosis Database

The establishment of an International Schwannomatosis Database has helped cultivate collaborative efforts for developing new experimental models for SWN and new approaches to treatment. The database aims to accelerate SWN research by connecting researchers and patients who have expressed a desire to participate in future studies. For more information or to join this registry, visit **schwannomatosis.org**.

Searching for information is a positive step that can empower you as a patient. Keep in mind that your doctor is the best resource for information or to answer questions. If you come across any information that you find confusing or strange, it's important that you talk to your doctor.

THE CHILDREN'S TUMOR FOUNDATION

The Children's Tumor Foundation (CTF) is the drug discovery engine for NF. By bringing together patients, doctors, scientists, and pharma, we drive treatments, advance care, and deliver faster results for millions affected by all types of neurofibromatosis or schwannomatosis. Our patient-first collaborative approach accelerates drug development and brings life-changing therapies to patients faster – driven by our mission to end NF.

The Mission of the Children's Tumor Foundation:
Drive research, expand knowledge, and advance care for the NF community.

Our Vision: End NF.

> *My diagnosis of schwannomatosis did not come until I was 37 years old. My family was a rock, and they helped me research the right doctors and treatment options.*
>
> —Adam, who lives with SWN

CTF Educational Resources

There is a lot to learn about when you or someone you love receives a diagnosis of SWN. The unpredictability of the condition requires keeping up with new and innovative research and clinical information. This can feel overwhelming at times. However, there are resources to help make your journey feel a little more manageable.

Stay Informed

Visit the CTF website at **ctf.org** to stay informed about NF research and join our email list by going to **ctf.org/newsletter.**

Get the Facts

Read the information in this booklet, and visit the Foundation's website at **ctf.org** to learn more about the different types of SWN. Attend a local clinic symposium or a national event like the CTF NF Summit, which is held each year.

Translations

The Children's Tumor Foundation is a global organization and is working to translate our educational resources, including this one, into Spanish and additional languages. To find our translated patient resources, go to **ctf.org/education**.

Download the NF Care Patient App

For patients and caregivers, the Children's Tumor Foundation NF Care app contains quick access to the CTF newsfeed, research updates, patient resources, and more. Learn more at **ctf.org/nfapp**.

Sign Up for Research

Join the NF Registry at **nfregistry.org** to learn about and participate in advanced scientific research for NF. Read more on page 24 of this brochure.

Get Involved

Getting involved is a great way to meet others who are also affected by SWN.

CTF National Programs

Fundraising opportunities with the Children's Tumor Foundation include Shine a Light NF Walk, NF Endurance, Cupid's Undie Run, and Fight NF Your Way. These are great ways to empower yourself in the fight for treatments and a cure for all types of SWN.

The NF Summit

An annual gathering of patients, families, volunteers, and clinicians, the NF Summit allows those living with SWN and their families to connect, support, and learn from one another while attending seminars on relevant topics pertaining to SWN.
Find out more at **ctf.org/nfsummit**

Spread the Word

Families and organizations worldwide participate in NF Awareness Month each May and join the Children's Tumor Foundation's **Make NF Visible** and **Shine A Light** activities and campaigns. You can share our infographics and videos on social media, secure a proclamation in your local town or state, light up a local landmark, and even advocate for NF research funding. Learn more at **ctf.org/nfawareness**.

Get Social

In addition to in-person events nationwide, you can connect with NF patients and families on any of the Children's Tumor Foundation's social media channels.

facebook.com/childrenstumor
twitter.com/childrenstumor
instagram.com/childrenstumor
youtube.com/childrenstumor
linkedin.com/company/children's-tumor-foundation
tiktok.com/childrenstumor

CTF Europe

The Children's Tumor Foundation Europe (CTF Europe) is a partner organization to CTF in the United States. A patient-centric drug discovery engine for NF, CTF Europe drives treatments, advances care, and delivers faster results for over four million patients affected by neurofibromatosis or schwannomatosis. Find out more at **ctfeurope.org**.

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This patient brochure was prepared by the Children's Tumor Foundation and approved by the 2024 CTF Clinical Care Advisory Board.

Remember that you are not your diagnosis.

Yes, it is a major part of your journey. Yes, it is very difficult. However, remember that you are a unique individual with talents, skills, personal strengths, and resources—even if there are many challenges to living with SWN. The world can be a better place because of you in so many ways.

We're here to help.

For more information about all types of schwannomatosis, please contact the Children's Tumor Foundation.

CHILDREN'S TUMOR FOUNDATION
ENDING NF THROUGH RESEARCH

ctf.org

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