riscover™
HEREDITARY CANCER

Result Navigator

⊕ Positive Test Result: *VHL*

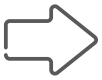
Positive test results identify a change, or "misspelling," of DNA that is known or predicted to cause an increased risk for cancer. DNA is the blueprint of life—it carries all of the genetic information needed for our bodies to function. A section of DNA with a specific job is called a gene. A pathogenic variant is a change in a gene that is known to cause increased risk for cancer. A likely pathogenic variant is a change in a gene that is very likely to cause increased risk for cancer. Another name for these types of variants is mutation.

After a positive test result, there can be many questions about what to do next.

This guide is a supplement to Riscover™ Hereditary Cancer test results, helping patients and healthcare providers understand the results and together determine the best path forward.

Navigate Your Results

Learn | *page 2*
Review the test results along with this guide, and discuss the meaning of these results with your healthcare provider.



Plan | *page 3*
Develop a healthcare plan for early detection and prevention of specific cancers.

Share | *page 4*
Understand the risks for other family members, and consider how to inform relatives of their risks.

Connect | *page 5*
Reach out to medical experts and find local and national groups that can provide more information and support.

Glossary of Terms

Audiologic evaluation: Hearing test and treatment if hearing loss is identified.

CT (CAT Scan): Computerized tomography; combines a series of X-ray pictures taken from different angles.

Gene: A section of DNA with a specific job.

Hemangioblastoma: Benign (noncancerous) tumor in the central nervous system (brain, spine, eyes) that arises from cells in small blood vessels.

MRI: An abbreviation for magnetic resonance imaging, a test that provides detailed pictures of a specific part of the body.

Mutation: A change in a gene that causes or is capable of causing disease. Another word for pathogenic/likely pathogenic variants.

Paraganglioma: Type of tumor that is most often benign and forms in structures called paraganglia. Paraganglia are groups of cells that are found near nerve cell bunches called ganglia. Paragangliomas usually occur in the head, neck, or torso.

Pathogenic: Causing or capable of causing disease.

Pheochromocytoma (pheo): Type of paraganglioma that forms in the adrenal glands.

Risk: The chance, or possibility, of developing a disease.

Variant: A change, or "misspelling," in the DNA sequence. Variants can be benign (not associated with disease), pathogenic (associated with disease), or of uncertain significance.

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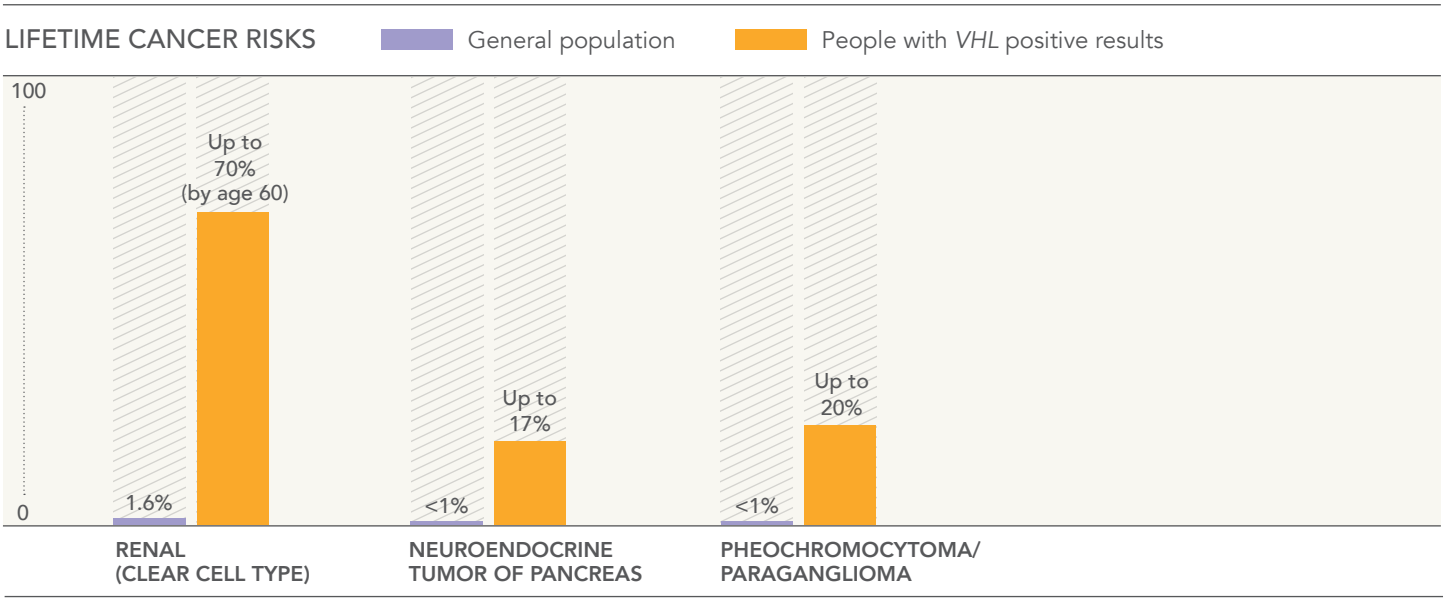
Your Diagnosis: Von Hippel-Lindau Syndrome

Von Hippel-Lindau syndrome (VHL) is an inherited disorder caused by a pathogenic variant in the *VHL* gene. VHL is associated with an increased lifetime risk of kidney cancer, neuroendocrine tumor of the pancreas, and pheochromocytoma/paraganglioma. Additional risks include hemangioblastomas of the brain, spinal cord, and retina; renal and pancreatic cysts; endolymphatic sac tumors; and cystadenomas of the epididymus (males) and broad ligaments (females).

About 1 in 36,000 people have VHL. Many people with pathogenic variants in the *VHL* gene have a family history consistent with the disorder, while about 1 in 5 are the first in the family to be affected.

Your Risk

Not all people with positive test results will develop cancer, but the chance for cancer is higher than the general population risk. The graphs below show how much the risk for cancer increases when a pathogenic variant is found. The cancer risks are presented in ranges based on multiple studies of families who have a pathogenic variant. There is not enough evidence available to give a specific risk to a person or family.



Hemangioblastomas are non-cancerous tumors that occur frequently in VHL. Risks vary by site:

- Retina: 25 – 60%
- Cerebellum: 44 – 72%
- Brain stem: 10 – 25%
- Spinal cord: 13 – 50%

Your Screening and Management Options

Listed below are the intervention options that are recommended by medical experts for individuals who carry this cancer gene variant. Your healthcare provider can explain these options in more detail, and together you can make a plan for cancer prevention and/or early detection.

RENAL FINDINGS, PHEOCHROMOCYTOMAS/PARAGANGLIOMAS, PANCREATIC FINDINGS

Abdominal ultrasound	An abdominal ultrasound is recommended every 2 years beginning at age 8.
CT or MRI of the abdomen	CT or MRI of the abdomen is recommended every 2 years, beginning at age 16. It may be considered earlier based on ultrasound or laboratory results.
Monitor blood pressure	Blood pressure should be monitored on an annual basis beginning at age 1.
Lab tests	Annual lab tests (blood and urinary fractionated metanephrines) are recommended beginning at age 8, or earlier if indicated.
Avoid contact sports	If adrenal or pancreatic lesions are present, it is recommended that contact sports be avoided.

CNS HEMANGIOBLASTOMAS

Physical and neurologic exam	An annual physical and neurologic exam performed by your healthcare provider is recommended beginning at age 1.
MRI of brain and spine	Consider an MRI of the brain and spine every 2 years beginning at age 16.

RETINAL HEMANGIOBLASTOMAS

Ophthalmologic evaluation	An annual ophthalmologic evaluation is recommended beginning at age 1.

ENDOLYMPHATIC SAC TUMORS

Audiologic evaluation	An audiologic evaluation is recommended every 2 – 3 years beginning at age 5.
MRI of the inner ear	An MRI with contrast of the internal auditory canal using thin slices is recommended as directed by your healthcare provider beginning at age 5.

ALL CANCERS

Avoid tobacco	Tobacco use increases cancer risks and should be avoided.
Avoid chemical/industrial toxins	Certain chemicals may affect the organs associated with VHL and should be avoided. Review your workplace and home exposures with your provider.

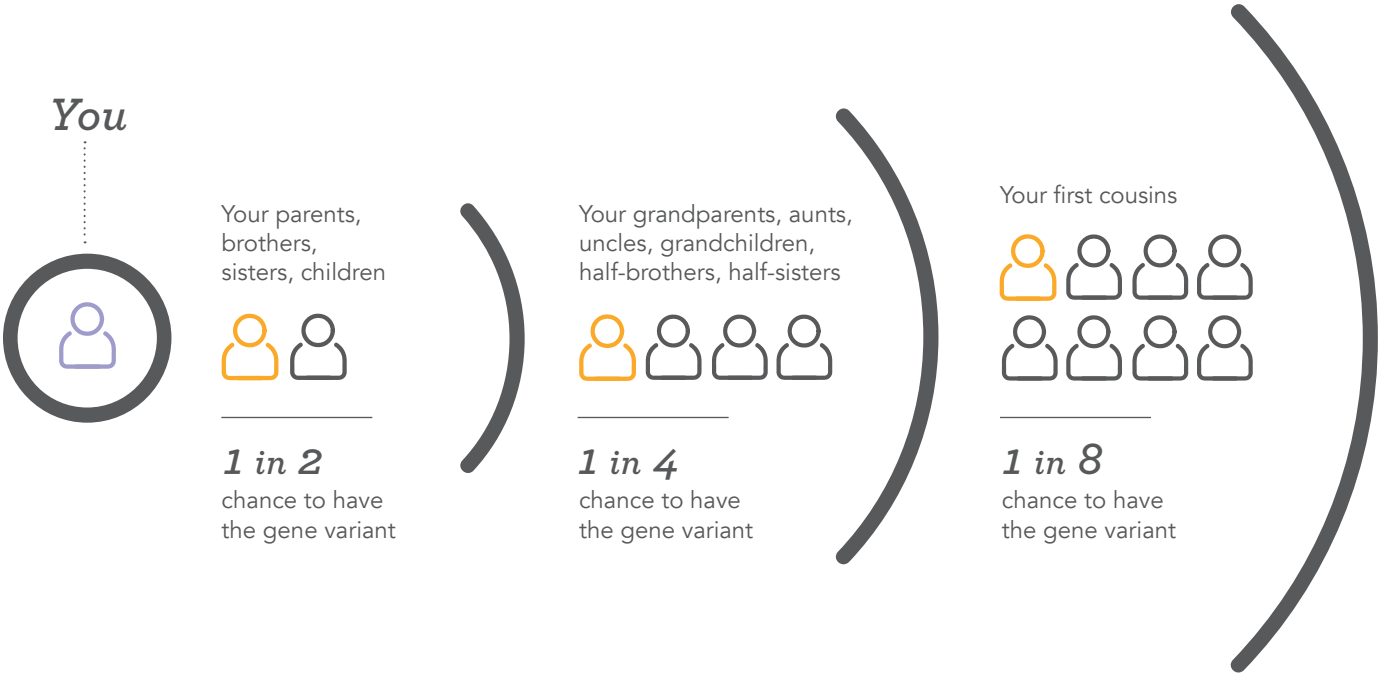
Your Family Matters

Cancer gene variants are inherited in an autosomal dominant manner. This means that when a parent tests positive, each child has a 1 in 2 chance to inherit the variant. Some people who inherit the variant will develop cancer, and some will not, but the risks are significantly increased compared to the average person. People in the same family may develop different types of cancers at varying ages, and the pattern of cancer and age of onset can differ from family to family.

Gene variants can be passed through families for many generations. When a gene variant is identified in one person in the family, relatives can be tested for just that variant. Sharing information about test results with family members is important, because it allows them to make informed choices about their healthcare and to decide whether they want genetic testing.

Some people who have pathogenic and likely pathogenic variants are interested in learning how to avoid passing these variants on to their children. If you are planning to have a child, you may wish to consult with a reproductive medicine specialist to discuss all of your reproductive options, including use of an egg or sperm donor, preimplantation genetic diagnosis, and prenatal genetic testing.

The likelihood for family members to carry the same gene variant depends on how closely related they are to the person with a known gene variant.



Your Expert Team

As you take your next steps, it can help to have a team of experts on your side. This team may include your primary care provider and a number of specialists who will help along the way.

If you haven't already done so, you may wish to speak with a genetic counselor. Genetic counselors are healthcare professionals with specialized training in medical genetics and counseling. They can help you understand your test results, discuss your healthcare plan, and connect to other resources in your area. Your healthcare provider may be able to provide a referral to a local genetic counselor. You can also find a genetic counselor through the National Society of Genetic Counselors at www.nsgc.org.

For questions about your test results, Progenity's genetic counseling team is available to help.
To reach a genetic counselor, call +1 855-293-2639 and select option 3.

Helpful Resources

GeneReviews
ncbi.nlm.nih.gov/books/NBK1463
A detailed clinical summary of von Hippel-Lindau syndrome written for healthcare providers.

VHL Allliance
vhl.org
An organization dedicated to research, education, and support to improve awareness, diagnosis, treatment, and quality of life for those affected by VHL.

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