# **Genetic Insights:** quick reference guide for healthcare providers

This guide is intended to facilitate discussion between a provider and their patient.

## Genetic Insights test results: **Loeys-Dietz syndrome**

### Key results

A pathogenic or likely pathogenic variant associated with Loeys-Dietz syndrome (LDS) was found in the *TGFB2* gene.

People with LDS have a significantly increased risk of developing an aortic aneurysm and/or dissection and may have other health concerns.

### Next steps

| Clinical recommendations | Resources |
|---|---|
| *Genetic Insights is a screening test and not intended for diagnosis. A follow-up genetic test should be performed in a clinical setting before any other action is taken.* | **Ready to order?**<br>Check with your institution and/or patient's insurance about the preferred testing laboratory.<br>Blueprint Genetics® offers LDS testing. To confirm this test result, **targeted variant testing** for the variant identified is available. You can order a confirmation test here: Blueprint Genetics/TVT<br>**Have questions?**<br>Call **1.866.GENE.INFO** (1.866.436.3463) to speak to a specialized Quest genetic counselor or geneticist available to healthcare providers to discuss test selection and results. |
| *Refer your patient to a genetic counselor.*<br>*Genetic counselors can provide counseling on the implications of this test result and next steps for your patient.* | Your patient can schedule a 1-on-1 remote genetic counseling session through their online Genetic Insights Connective Tissue Disorder Report at no additional cost.<br>To find a genetic counselor with expertise in connective tissue disorder genetics practicing in your patient's area for an in-person session, please visit FindAGeneticCounselor.NSGC.org |

**Patient conversation starters:**

Patient conversation starters summarize the preceding information in plain language to support meaningful conversations between you and your patient.

FindAGeneticCounselor.NSGC.org

Your Genetic Insights test is a screening test. The next step is to have your result confirmed with a second genetic test.

It's also important that you talk with a genetic counselor. Genetic counselors are experts in genetics and can help you understand this result and potential next steps.

You can access a genetic counselor through your online Genetic Insights dashboard at no additional cost to you, and we can discuss a referral to a local genetic counselor.

**Visit QuestDiagnostics.com/Genetic-Health-Screening for more information about this test.**

## What is LDS?

LDS is a hereditary connective tissue disorder characterized by vascular, skeletal, craniofacial, and cutaneous findings.[1,2]

People with LDS are at a significantly increased risk of developing an aneurysm, dissection, and/or rupture of the aorta or along the arterial tree.[1,2]

Arterial aneurysms are often asymptomatic, and individuals may first present with an acute aortic dissection with high morbidity and mortality.[2,3]

There is clinical variability between individuals with LDS.[1] Features outside of vascular involvement may include scoliosis, joint laxity, cleft palate, easy bruising of the skin, and allergic diseases.[1,2]

Diagnosis is typically made by a specialist, such as a medical geneticist, and management is best coordinated by a multidisciplinary care team.[1]

*See the Management options section for more detail.*

**Patient conversation starters:**

Loeys-Dietz syndrome (or LDS) is caused by having a DNA variant in a certain gene.

LDS is a connective tissue disorder; that means the tissues that help connect our bodies together—like the blood vessels—can be affected.

People with LDS have a higher than typical chance of having a tear in a major blood vessel like the aorta. But not everyone with LDS will have a tear in a blood vessel.

People with LDS should see a specialist, including a geneticist, to help monitor for and prevent health issues.

## What this result means for family members

There are 2 primary ways someone can have a DNA variant associated with LDS:

The DNA variant can be inherited from a biological parent. In this case, at least 1 parent has the same DNA variant. Each full sibling and each child of someone with the variant has a 50% chance of having the same variant.

The DNA variant can arise in someone for the first time (also called a de novo variant). In this case, their children have a 50% chance of having the variant. Neither biological parent nor any siblings are likely to have the variant.

In people with a confirmed DNA variant associated with LDS, genetic testing for family members may help inform their risks and screening protocols.[3] Therefore, it is strongly recommended that individuals share these results with their biological relatives.

**Patient conversation starters:**

There are 2 ways someone can end up having a DNA variant linked to LDS.

- First, it can be passed down from a parent. In this case, 1 parent would have that same DNA variant. Siblings would have a 50% chance (1 in 2 chance) of having the DNA variant
- Second, it is possible that the DNA variant happens in someone in a family for the first time. In this case, parents and siblings are not likely to have the DNA variant

However, in either case, each child of someone with a DNA variant linked to LDS has a 50% chance of having the same DNA variant.

Sharing this result with your family members is important so they can talk to a healthcare provider about genetic testing for LDS.

## Management options

There are management and treatment options for people with LDS. Select clinical guidelines from the American College of Cardiology Foundation/American Heart Association[3] include:

| Scenario | Option(s) |
|---|---|
| *Screening* | People with a confirmed genetic variant associated with LDS should undergo complete aortic imaging at initial diagnosis and 6 months thereafter to establish if enlargement is occurring, and yearly magnetic resonance imaging of the cerebrovascular circulation to the pelvis |
| *Surgical aneurysm repair* | Surgical repair of the aorta in all adult patients with LDS should be considered at an aortic diameter based on clinical guidelines |
| *Control of hypertension* | Stringent control of hypertension, some exercise restrictions, and other risk-reducing measures may be recommended |
| *Pregnancy* | Individuals considering pregnancy should be counseled about the risks. Optimal care includes involvement with a high-risk maternal-fetal team along with an aortic specialty team[3] |

**Patient conversation starters:**

It's recommended that people with LDS make a plan to monitor their health. This way, any health problems can be found as early as possible, and a treatment plan can be made.

If your genetic test result is confirmed, it's important to work with the right specialists, including a geneticist, to make a plan that's right for you.

See the American College of Cardiology Foundation/American Heart Association[3] and expert reviewed clinical guidelines[1] for complete recommendations. Guidelines and recommendations may change over time.

If this result is confirmed, a medical geneticist should be consulted for further clinical management. To locate a genetics center, please visit the American College of Medical Genetics and Genomics.

## Additional resources

The following advocacy groups have additional information and resources about LDS:

**Loeys-Dietz Syndrome Foundation:** LoeysDietz.org
**John Ritter Foundation:** JohnRitterFoundation.org

### References


1. MacCarrick G, Black JH 3rd, et al. Loeys-Dietz syndrome: a primer for diagnosis and management. *Genet Med.* 2014;16(8):576-87. doi:10.1038/gim.2014.11
2. Loeys B and Dietz H. Loeys-Dietz Syndrome. February 28, 2008. Updated March 1, 2018. In: Adam MP, Ardinger HH, Pagon RA, et al, editors. GeneReviews® [Internet]. University of Washington, Seattle; 1993-2022. https://www.ncbi.nlm.nih.gov/books/NBK1133/
3. Hiratzka LF, Bakris GL, et al. ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the diagnosis and management of patients with thoracic aortic disease. *Circulation.* 2010;121(13):e266-369. doi:10.1161/CIR.0b013e3181d4739e