Genetic Insights: quick reference guide for healthcare providers

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

Genetic Insights test results: **Peutz-Jeghers syndrome**

Key results

A pathogenic or likely pathogenic variant associated with Peutz-Jeghers syndrome (PJS) was found in the *STK11* gene.

People with PJS have a significantly increased risk of developing gastrointestinal polyps and certain cancers, especially colon cancer, and in females, breast cancer.

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?** Check with your institution and/or patient's insurance about the preferred testing laboratory. Blueprint Genetics® offers hereditary cancer 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 **Have questions?** 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 specializing in hereditary cancer. *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 Cancer Risk Report at no additional cost. To find a genetic counselor with expertise in hereditary cancer 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 Peutz-Jeghers syndrome?

Peutz-Jeghers syndrome, or PJS, is a hereditary cancer predisposition syndrome characterized by the presence of hamartomatous gastrointestinal polyps, mucocutaneous hyperpigmentation, and a higher lifetime risk of certain cancers, typically with an earlier age of onset.[1,2]

Polyps can appear anywhere in the GI tract and may lead to complications such as obstruction and bleeding.[1] Hyperpigmentation often presents in childhood with characteristic freckling on the mouth, eyes, and nostrils that fades over time.[1] There is clinical variability between people with PJS.[1]

PJS is primarily associated with DNA variants in the *STK11* gene.[1,2] Clinical diagnosis may be made based on standardized clinical criteria.[1,2]

Individuals with PJS are recommended to undergo more frequent cancer screening, starting at a much earlier age than in the general population.[2]

Management is best coordinated by a specialized care team.[1,2]

See the Management options section for more detail.

Patient conversation starters:

Peutz-Jeghers syndrome, or PJS, is caused by DNA variants in a gene called *STK11*.

People with PJS have a higher than typical chance of developing certain cancers, especially colon cancer. Not everyone with PJS will develop colon cancer.

People with PJS should have cancer screenings earlier in life and more often than typical. This increases the chance that if cancer develops, it's detected as early as possible.

What this result means for family members

There are 2 primary ways someone can have a DNA variant linked to PJS:

- 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 variant
- The DNA variant can arise in someone for the first time (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 PJS, 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 PJS.

First, it can be passed down from a parent. In this case, 1 parent would have that same DNA variant. Full siblings would have a 50% chance (1 in 2 chance) of having the DNA variant too.

Second, it's 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.

In either case, each child of someone with a DNA variant linked to PJS 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 PJS.

Cancer risk

Select estimated cancer risks in people with PJS compared to the general population are included below.[2] Individual cancer risks may be higher or lower depending on the specific variant identified, in addition to personal and family health history. Associated cancers and risks may change over time as medical research advances.

Cancer type	Approximate lifetime risk with PJS	Approximate lifetime risk in the general population
Males and females:		
Colon	39%	4.5%
Stomach	29%	<1%
Small intestine	13%	<1%
Pancreas	11%-36%	1.5%
Assigned female at birth:		
Breast	32%-54%	13%

Additional increased risks include lung cancer, ovarian or testicular sex cord/Sertoli cell tumors, and uterine cancer.[2]
See NCCN® for a full description of associated cancers and risks.[2]

Management options

There are options for cancer prevention and early detection for people with PJS. Clinical guidelines from the National Comprehensive Cancer Network® (NCCN®) in adults with PJS and no personal history of an associated cancer include[2]:

Cancer/tumor type	Guidelines for adults with PJS
Colon and stomach	Colonoscopy and upper endoscopy every 2-3 years starting in late teens
Small intestine	Small bowel visualization starting in late teens
Pancreas	Magnetic resonance cholangiopancreatography with contrast or endoscopic ultrasound annually starting around age 30-35 or earlier based on clinical judgment and family history
Breast (female)	Mammogram and breast MRI annually starting at age 30 Clinical breast exam every 6 months starting at age 30
Ovarian/cervical/uterine	Pelvic examination, pap smear, and pelvic ultrasound annually starting around age 18-20
Testicular	Annual testicular exam

Patient conversation starters:

It's recommended that people with PJS have cancer screenings earlier and more often than typical. This way, cancer is more likely to be caught in the early stages when it's most treatable. In fact, colon cancer can even be prevented if pre-cancerous colon polyps are found and removed during a colonoscopy.

If your PJS result is confirmed, it's important to work with the right specialists, like a medical oncologist or gastroenterologist and a geneticist, to find cancer screening and risk-reducing options that are right for you.

See NCCN for complete recommendations. Recommendations may change over time.
If the test result is confirmed, local centers for excellence in hereditary cancer may be considered for further clinical management.

Additional resources

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

FORCE: Facing Our Risk of Cancer Empowered: FacingOurRisk.org

References

1. McGarrity TJ, Amos CI, Baker MJ. Peutz-Jeghers Syndrome. February 23, 2001. Updated September 2, 2021. In: Adam MP, Ardinger HH, Pagon RA, et al, editors. GeneReviews® [Internet]. University of Washington, Seattle; 1993-2022. www.ncbi.nlm.nih.gov/books/NBK1266/
2. National Comprehensive Cancer Network®. Genetic/Familial High-Risk Assessment: Colorectal (Version 2.2022). NCCN Guidelines®. Accessed December 13, 2022. www.nccn.org

This information is not a substitute for medical advice, diagnosis, or treatment. The diagnosis or treatment of any disease or condition may be based on personal history, family history, symptoms, a physical examination, laboratory test results, and other information considered important by a healthcare provider.

Individuals should talk with a healthcare provider about the meaning of genetic test results and before stopping, starting, or changing any medication or treatment.

Genetic Insights is a test developed and performed by Quest Diagnostics. The test results are not diagnostic and do not determine overall chances of developing a disease or health condition. The tests are not cleared or approved by the US Food and Drug Administration.

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