MyCode®

Fall 2023

Research News

Geisinger

300,000+ participants have made the success of MyCode possible

Christa Lese Martin, PhD, FACMG

Dear MyCode participants:

This year, we're celebrating a new milestone. Close to 20% of Geisinger patients have had their DNA sequenced through our MyCode Community Health Initiative. That means we have one of the largest healthcare-based groups in the world! In this newsletter, we're excited to share updates and discoveries that have been made thanks to partnerships with our MyCode participants.

One main MyCode project is our Genomic Screening and Counseling (GSC) program. This program lets us alert participants who are at higher for certain conditions, like cancer or heart disease, due to their genetic makeup. The information can also be shared with their care team, so they can better shape patient care plans. Our GSC program recently reached a major milestone, too, returning results to 4,000 participants.

We're also always looking to use genetic testing and data to alert people to risks for more conditions. In this newsletter, you can read about recent additions to our MyCode gene list.

We also work to provide researchers with more and more data resources, so they can find new relationships between genes and disease and find new ways to prevent disease, detect it earlier or treat it better. We're excited to share some of these stories with you, too.

Last but not least, we want to thank you for participating in MyCode. None of our discoveries or the related impacts on patient care would be possible without participants like you. You're helping make better health easier for everyone. I look forward to sharing more exciting updates with you in the coming year.

Genomic Screening and Counseling Program returns results to 4,000 people, names new co-directors

Juliann Savatt, MS, CGC

Melissa Kelly, MS, CGC

The MyCode Genomic Screening and Counseling (GSC) program uses genetic testing to let MyCode participants and their families know if they're at a higher risk for potentially life-threatening conditions. These include heart disease, some breast and colon cancers and familial hypercholesterolemia, which raises levels of LDL cholesterol — the "bad" cholesterol that can lead to heart disease.

The GSC team helps participants understand their genetic results, empowering them to work with their care providers to prevent or detect disease in its early stages. The team also encourages them to share their results with family members who may have the same genetic risk. This year, the GSC program returned genetically actionable results to more than 4,000 MyCode participants — a major milestone.

Juliann Savatt, MS, CGC, and Melissa Kelly, MS, CGC, were recently appointed co-directors of the GSC program. They hope to return genetic results to about 500 more MyCode participants in the coming year. Everyone who receives a result is offered genetic counseling and resources to help decide what they should do next.

Ms. Kelly joined Geisinger in 2017 after working as a research coordinator and genetic counselor.

Ms. Savatt joined Geisinger in 2015 and has experience in cancer genetics and working in Geisinger's Autism & Developmental Medicine Institute.

"Our goal is to empower patients and their families to act on their genetic results to help prevent disease or diagnose disease earlier," Ms. Savatt said.

"It is important that we share lessons learned from MyCode to inform other genomic screening efforts, to shape how genomic screening is used in clinics and look for gaps in research that we can fill," added Ms. Kelly.

DNA 101: What is a variant?

Gretchen Thone, genetic counselor

All of our cells contain chromosomes, which are made up of our genetic information, or our DNA. DNA is our body's instruction manual, telling our bodies how to develop and function. Each person usually has two copies of each chromosome, except for the X and Y chromosomes. People assigned as male at birth usually have an X and a Y. People assigned female at birth usually have two X chromosomes.

We all have changes in our DNA, and these changes are known as variants. Some DNA variants don't affect our health while others can increase risk for certain diseases. If a variant puts a person at risk for a health condition or increases the chance of having a child with a certain condition, we call that variant pathogenic. Variants that aren't known to cause health issues are called benign.

DNA variants can be passed from parent to child or can be new and unique to a person. If a variant is passed from parent to child, it is said to be inherited. If a variant is new and wasn't passed down from a parent, it's called *de novo*.

Some variants aren't inherited from parents and happen during a person's lifetime. These are called somatic variants. These variants aren't passed to children and can be caused factors such as our environment.

MyCode is working to better understand the relationship between genetics and health. We're excited to continue this work to better support and serve our patients.

that we're helping to lead this type of research to lead to more targeted treatments and precision medicine.

MyCode Genomic Screening and Counseling Program expands genetic conditions

Zoe Lindsey-Mills, genetic counseling assistant

We're excited to share that the MyCode Genomic Screening and Counseling program recently started screening and returning results for variants in more genes. We did this after reviewing recommendations from genetics experts (see table).

What does this mean for your sample?

We re-analyze all MyCode samples as more genes and conditions are added to our list. This means, when you share a sample, you may receive a result after a long time has passed. This also means some participants who previously received a MyCode result may be contacted about an additional result. If an important genetic change is found in your DNA, the MyCode genetic counseling team will reach out to tell you about it.

Remember, participation in MyCode doesn't replace clinical care. If you have questions or concerns about your personal or family history, talk to your doctor. Clinical genetic counseling is available and genetic testing may be recommended for some patients. You can also contact the MyCode team at 844-250-8031 with questions about clinical genetic counseling or genetic testing.

New Conditions* Returned by MyCode

Condition Name	Increased Risk For
PALB2-related cancer syndrome	Cancers including breast, ovarian, and pancreatic cancers
Maturity onset diabetes of the young (MODY)	Diabetes in the teens or early adulthood
Biotinidase Deficiency	A buildup of too much of a B vitamin that could cause neurological problems
Pompe Disease	A buildup of glycogen that could cause muscle problems throughout the body
Hereditary hemorrhagic telangiectasia (AVMs)	Abnormal blood vessels that can cause a risk of bleeding or poor blood flow to certain body parts
Retinopathy	Gradual vision loss that can lead to blindness
Amyloidosis	A buildup of amyloid in the body that can lead to heart and nervous system disease

**MyCode has also added new genes in three previously returned conditions*
See all results retuned to date

Genetic counselor spotlight: Kristy DiLoreto

Kristy DiLoreto, MS, CGC

Kristy DiLoreto, MS, CGC, is a licensed, board-certified genetic counselor at Geisinger. She began as a student intern for Geisinger in 2018 and stayed on as a genetic counseling assistant before enrolling in Case Western Reserve University's genetic counseling program. She received her Master's in Genetic Counseling in 2022.

After graduating, Ms. DiLoreto's passion for expanding genetic counseling services to rural communities drew her back to Geisinger. She is now a genetic counselor in the Cardiovascular Genetics and Genomics Clinic, providing genetic counseling for cardiovascular patients through in-person and telemedicine visits. She also works closely with Geisinger's Heart and Vascular Institute. In this role, Ms. DiLoreto helps providers order genetic testing for patients who could benefit from the results. She also offers in-person counseling for MyCode participants with a risk for cardiovascular diseases and other conditions in Geisinger's Western region.

In both clinics, she's seen how learning genetic information can impact patients and their healthcare. MyCode allows her to play a role in many patients' health journeys as she works with providers across many specialties.

Ms. DiLoreto is an active member of the National Society of Genetic Counseling and the Pennsylvania Association of Genetic Counselors. Outside of work, she enjoys hiking and being outdoors, live music, and spending quality time with family, friends and dogs.

Watch:

What is a genetic counselor?

Bloomsburg Fair recap

The MyCode team was excited to be at the 2022 Bloomsburg Fair to share research opportunities with our community. Geisinger patients could enroll in MyCode — and give a blood sample right on site. Fair attendees could also learn more about MyCode, other research at Geisinger and how participating in research benefits the health of our entire community.

Pictured are Paul Francis and Karinna Troutman.

Need to submit your MyCode sample?

Request a free saliva kit.

By consenting to participate in MyCode, you've already taken the first step toward helping us improve healthcare by identifying medical conditions earlier — before symptoms show up — and finding new treatments.

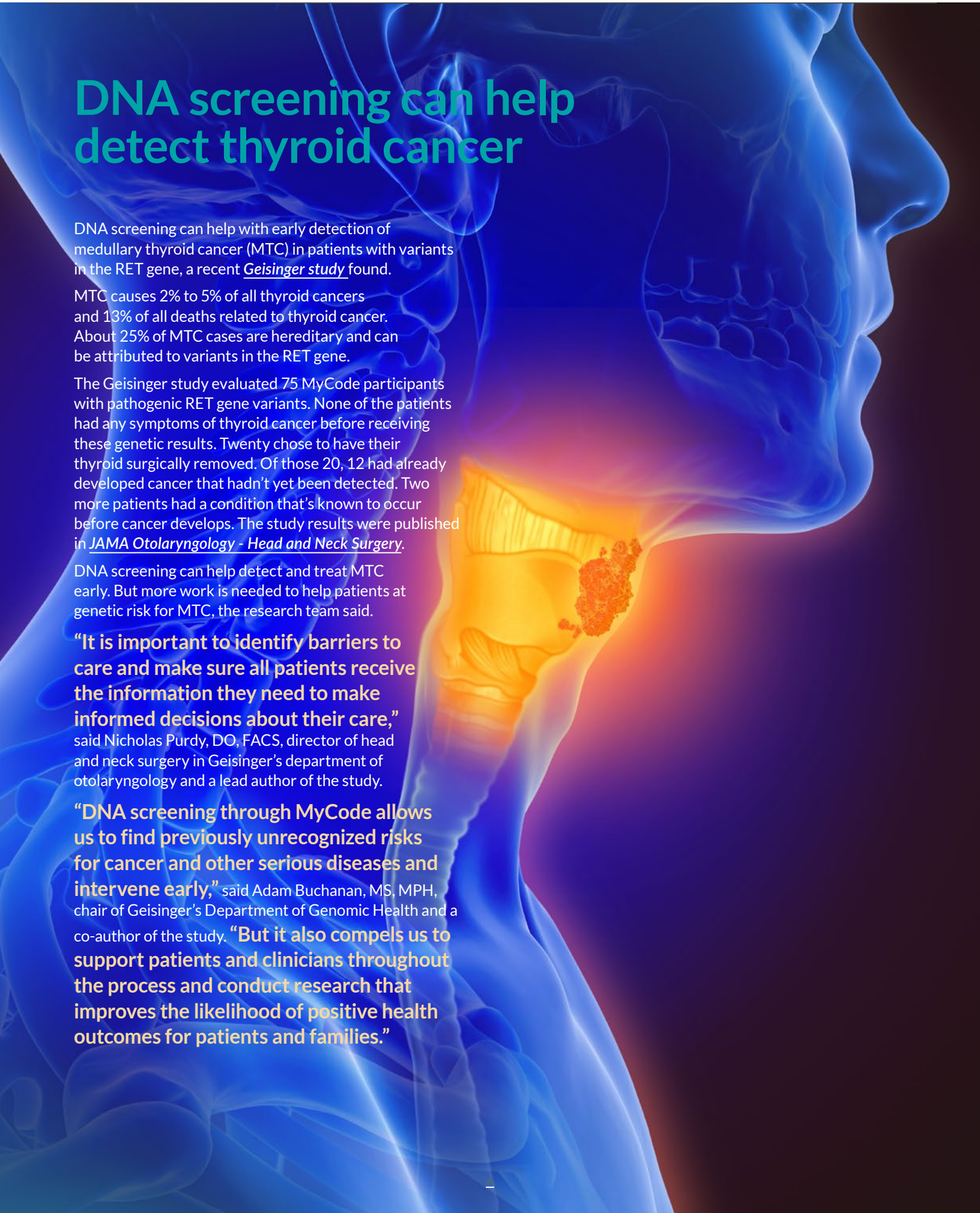
If you haven't done so, the next step is to provide a sample so we can add your genetic (DNA) information to the study.

Your DNA may also hold important information about your health. If you haven't given your MyCode blood or saliva sample yet, it's quick and easy. Choose one of these two ways:

- **Go to any Geisinger outpatient lab** to give a blood sample. Find one near you: *go.geisinger.org/lab-locations*.
- **Request an at-home saliva collection kit** that you'll mail back to us. **Call 855-636-0019 or visit** *go.geisinger.org/mycode-samplekit*.

Questions? Call the MyCode team at the number above. Thank you for being part of MyCode!

DNA screening can help detect thyroid cancer



DNA screening can help with early detection of medullary thyroid cancer (MTC) in patients with variants in the RET gene, a recent *Geisinger study* found.

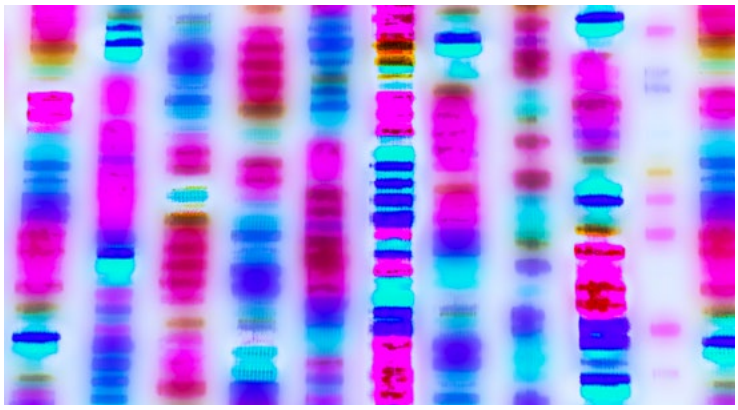
MTC causes 2% to 5% of all thyroid cancers and 13% of all deaths related to thyroid cancer. About 25% of MTC cases are hereditary and can be attributed to variants in the RET gene.

The Geisinger study evaluated 75 MyCode participants with pathogenic RET gene variants. None of the patients had any symptoms of thyroid cancer before receiving these genetic results. Twenty chose to have their thyroid surgically removed. Of those 20, 12 had already developed cancer that hadn't yet been detected. Two more patients had a condition that's known to occur before cancer develops. The study results were published in *JAMA Otolaryngology - Head and Neck Surgery*.

DNA screening can help detect and treat MTC early. But more work is needed to help patients at genetic risk for MTC, the research team said.

"It is important to identify barriers to care and make sure all patients receive the information they need to make informed decisions about their care," said Nicholas Purdy, DO, FACS, director of head and neck surgery in Geisinger's department of otolaryngology and a lead author of the study.

"DNA screening through MyCode allows us to find previously unrecognized risks for cancer and other serious diseases and intervene early," said Adam Buchanan, MS, MPH, chair of Geisinger's Department of Genomic Health and a co-author of the study. **"But it also compels us to support patients and clinicians throughout the process and conduct research that improves the likelihood of positive health outcomes for patients and families."**



Geisinger study confirms link between genetics, neuropsychiatric disorders

A *Geisinger study* of more than 90,000 patients found that about one in 100 carried at least one rare gene variant known to increase risk for neuropsychiatric disorders (NPD), such as schizophrenia and autism spectrum disorder. A third of those with a variant had a diagnosed mental health condition.

The results, published online by the *American Journal of Psychiatry*, confirm a strong link between genetics and NPD.

The Geisinger team, led by Christa L. Martin, Ph.D., analyzed genetic and electronic health record (EHR) data from 90,595 MyCode participants. Researchers evaluated the DNA sequences of 94 genes that increase the risk for NxPD. They also reviewed electronic health records for NPD, including autism, schizophrenia and bipolar disorder. More than 1% of patients in the study group had genetic variants, and a third of those had been diagnosed with a corresponding NPD.

"We know that hundreds of genes contribute to neuropsychiatric disorders. But, for this study, we focused on those that are now best understood," said Hermela Shimelis, PhD, a lead author of the study.

"This study confirms the important role of rare genetic variants in neuropsychiatric disorders. It also highlights the potential for using DNA-based approaches in studying and diagnosing these conditions," Dr. Martin said. "Our findings indicate that using genetic screening in routine healthcare could improve the prevention and treatment of neuropsychiatric disorders."

More MyCode discoveries

- A *Geisinger study* could help providers identify patients with autosomal dominant polycystic kidney disease (ADPKD) who are at the highest risk of complications, so they begin treatment earlier.
- People with an additional X or Y chromosome have *an increased risk of developing blood clots* known as venous thromboembolism (VTE).
- *VEXAS syndrome*, a genetic disease that causes a variety of inflammatory and blood conditions, is more common than originally expected.
- Using data from MyCode, researchers have *discovered genetic changes* that can provide protection against developing liver disease, including nonalcoholic steatohepatitis (NASH) and cirrhosis.

For the latest MyCode and research news, visit *geisinger.org/research*.