Dear friends,

I am so excited to share with you that our MyCode Community Health Initiative has reached a major milestone: 300,000 of our patients have partnered with us to participate in this groundbreaking program — that’s about 25% of all patients cared for at Geisinger — which is an amazing accomplishment! To date, we’ve sequenced DNA from nearly 185,000 of these participants, analyzed more than 142,000 sequences and returned clinically actionable results to nearly 3,300 people at increased risk for more than 30 health conditions.

MyCode was one of the first DNA screening initiatives to return clinically actionable results to patient-participants through its Genomic Screening and Counseling (GSC) Program, pioneered by Amy Sturm, MS, director of the GSC program, and Adam Buchanan, MS, MPH, director of Geisinger’s Genomic Medicine Institute. We love to share stories from our MyCode patient-participants who learn of their genetic risk. In this newsletter, you’ll hear from Jeff Mylet, who discovered he was at increased risk for thyroid cancer through MyCode, decided to have his thyroid removed in consultation with his doctor, and learned that he actually had an early form of thyroid cancer.

MyCode continues to be the largest healthcare system-based program of its kind in the world, with paired DNA and health data that has contributed to many exciting medical discoveries. We hope you’ll also enjoy reading about some of these discoveries made possible through MyCode.

As we continue to grow our program, I want to thank each of you for being a part of our success to learn from every patient to maximize better health for all. Our participants make MyCode a reality and we couldn’t do this without you!

– Christa Lese Martin, PhD, FACMG
Chief Scientific Officer, Geisinger

“Providing these clinically actionable results to our patients empowers them to take action that may lead to better health outcomes for both themselves and their families,” said Christa Lese Martin, PhD, Geisinger’s chief scientific officer. “The continued growth of the MyCode program not only benefits patients, but also provides crucial information to discover new genetic links to disease.”
As part of the MyCode GSC program, DNA samples are analyzed to look for changes in genes known to increase the risk of developing more than 30 health conditions. These include the BRCA1 and BRCA2 genes known to increase risk for breast, ovarian, and other cancers, and genes for familial hypercholesterolemia (FH), which can cause early heart attacks and strokes. The GSC program also returns genomic risk results for Lynch syndrome, which can cause early colon, uterine and other cancers, and several additional heart conditions, including cardiomyopathies and arrhythmias.

The project has also explored the return of clinically relevant results for other medical conditions, such as neurodevelopmental and psychiatric disorders. While not always clinically actionable, learning these results can provide valuable information to patients about probable genetic causes for their neurodevelopmental and psychiatric conditions like autism, epilepsy, bipolar disorder and schizophrenia.

Analysis of MyCode data has also contributed to a number of groundbreaking discoveries, including a rare genetic variant that protects against obesity. Geisinger researchers have recently received several grants to study the impact of genomics on health, including a study of the genetics of cancer, improvements in the diagnosis of FH, and development of a tool to diagnose genetic disorders in real time.

A northeastern Pennsylvania native, Ms. Evans was excited to join the Geisinger team with a goal of making a positive impact on the health and wellness of her local community. Her favorite part about working at Geisinger is the chance to collaborate with other genetic counselors, providers and researchers from multiple disciplines. In her various roles, Ms. Evans works with people from the start of their MyCode journey at enrollment through receipt of their results and beyond. She’s grateful to have had even a small part in these patient-participants’ experiences and believes the impact that a MyCode genomic screening result can have on the care of a single participant and their family highlights Geisinger’s commitment to quality care and innovative opportunities to improve patient health.

Ms. Evans is an active volunteer with the National Society of Genetic Counselors and participates in educational and mentorship programs for GCAs at Geisinger. When she’s not following her passion for patient care, Ms. Evans enjoys needle arts, spending time with family and friends, live music and traveling.
Thanks to MyCode, a family protects themselves from thyroid cancer.

When Jeff Mylet got the call telling him MyCode had found a change in his RET gene indicating an increased risk of developing thyroid cancer, he was shocked at first — then he gave it some thought. “My mom and grandmother both had thyroid cancer, and I was already on thyroid medication myself,” he explains. “The more I thought about it, the more it made sense.”

Mr. Mylet enrolled and had his blood drawn for the MyCode study in 2017. “It was part of a routine doctor’s appointment,” he says. “I’ve always been interested in genetics, so I thought, why not?” The MyCode team contacted him with his RET gene results in March 2021. Things moved quickly from there.

After meeting with his primary care physician and a genetic counselor from the MyCode team, Mr. Mylet was referred to endocrinology and to head and neck surgical oncologist, Nicholas Purdy, DO.

Biopsy of a small nodule that showed up on an ultrasound came back benign, but after consulting with Dr. Purdy, Mr. Mylet elected to have his thyroid removed in July. “And it’s a good thing I did,” he says. “Once it was out, they found cancer. If it hadn’t been for MyCode, I never would’ve known. Finding out early made the whole experience truly worthwhile.”

“The results from MyCode heavily influenced my treatment decision,” says Dr. Purdy. “Once we saw the RET mutation, we knew thyroid cancer was a real possibility, and I felt a prophylactic thyroidectomy was the way to go. Mr. Mylet agreed and now he doesn’t have to worry — MyCode gave him the information he needed to make an informed decision.”

Thanks to MyCode genetic counselor Alyson Evans, MS, CGC, other members of Mr. Mylet’s family are getting the information they need, too. “We’ve tested multiple other relatives based on Mr. Mylet’s genomic result. Some have the RET mutation. Some don’t,” she says. “But the MyCode Genomic Screening and Counseling team is here to make sure they all have the information they need to move forward.”

“Everyone along the way was great, from my primary care provider who first told me about MyCode to my genetic counselor who’s still available to answer my family’s questions,” says Mr. Mylet. “I’m very grateful I agreed to participate.”
A disease-causing genomic variant is discovered. What happens next?

Nicholas Purdy, DO, surgical oncologist

Geisinger’s MyCode program is a valuable resource for patients with a predisposition for certain types of cancer. This is particularly true for people who have a disease-causing variant in a gene known as the RET gene. These patients are at high risk for developing neuroendocrine tumors — particularly medullary thyroid cancer.

Medullary thyroid cancer (MTC) is rare, accounting for about 3 percent of all thyroid cancers. It can occur in sporadic or inherited forms. The prognosis is highly dependent on the stage of disease when diagnosed. The later the cancer is identified, the lower the survival rate. Thus, early diagnosis is important for improving disease outcomes.

Patients found to have a disease-causing variant in this gene are at a much higher risk of developing MTC and other tumors of the parathyroid glands and adrenal glands. By identifying this genetic risk, we can treat disease at an early stage, and sometimes before cancer even develops.

When patients have a genomic risk variant in RET, they’re referred to our treatment team. This tailored clinical treatment includes a team of genetic counselors, endocrinologists, and thyroid surgeons. Patients then undergo an extensive laboratory and imaging workup to assess for various disease states associated with this genetic diagnosis. Initial testing involves a thyroid ultrasound and simple blood draws to check things like parathyroid hormone level, calcium level, urine hormone levels and even tumor markers. Once this testing is complete, patients have a detailed discussion of treatment options with an endocrinologist and a thyroid surgeon. Often family members are also offered genetic testing to determine if they have the same genetic risk.

One of the most important visits for individuals with variants in RET is with the thyroid surgeon. At this visit we focus on the treatment of MTC and possibly overactive parathyroid glands. Based on current guidelines and our experience with treating patients with variants in RET via MyCode, we recommend total thyroidectomy (removal of the thyroid) and lymph node removal from the area around the thyroid gland.

In my practice, patients with variants in RET revealed via MyCode who go on to have thyroid surgery have thrived. In most cases, we've identified thyroid cancer in its earliest stage. Under these circumstances, prognoses are excellent. Notably, many of these patients may not have had their tumors detected by traditional methods. Thus, in my experience, MyCode is often the driving force in their treatment decisions.

Ultimately, traditional methods like routine physical exams and laboratory work may not always indicate there's something wrong. Even traditional imaging methods may not indicate MTC. MyCode is a unique and valuable tool we can use to supplement traditional patient care. It detects medically actionable genetic causes of thyroid cancer and gives many people the opportunity to get more efficient treatment, and a more favorable outcome.

What is genomic research?

Genomic research studies the complex relationship between our DNA and human health and disease. The goal is to identify differences in our DNA that could be used as tools to help the medical community provide more personalized care based on a patient’s DNA. The hope is that this type of genetic information could help to prevent disease, detect it earlier, or treat it better.

How is patient privacy protected?

At Geisinger, we are both a clinical care provider and a healthcare system that offers our patients the opportunity to join research studies. Therefore, we take the utmost responsibility in protecting our patients’ privacy for both their clinical care and participation in research. We have developed a multi-layered approach to securing and protecting participants’ personal, medical, and DNA information for both clinical care and research purposes. When MyCode data is compiled for use in other research studies, it is “de-identified,” meaning that any information that would allow personal identification is removed to minimize the possibility that a connection with a patient-participant can be known or re-established. Our agreement with our industry partners includes a pledge that they will use data security measures as rigorous as ours, and they won’t try to re-identify participants. We’re confident that the chance that any study volunteer’s personal information will be lost or divulged is as low as it can possibly be.
Researchers at Geisinger recently discovered that DNA screening can help identify patients who are at risk for heart disease associated with amyloidosis, the build-up of abnormal proteins in the organs and tissues.

Transthyretin amyloidosis (ATTR) can be hereditary and lead to a spectrum of other diseases and conditions, including cardiomyopathy, a heart muscle disease that is a common precursor to heart failure. One known cause of ATTR is the presence of a disease-causing variant in the transthyretin (TTR) gene. A team of researchers at Geisinger hypothesized that identification of disease-causing variants in MyCode participants could lead to the discovery of undiagnosed disease.

New treatments for ATTR have improved survival rates, but diagnosis based on symptoms is challenging. Using data from MyCode, combined with electronic health records, our researchers are studying patients with and without specific TTR variants to determine how often they showed signs of cardiomyopathy and compared those results to findings from cardiac imaging.

Out of 134,753 patient-participants studied, the research team identified 157 patients who carried a known disease-causing TTR variant. Related heart-disease diagnoses, including cardiomyopathy and heart failure, were significantly more likely in those 60 and older, but only two of the 157 patients identified already had a clinical diagnosis of amyloidosis.

“We not only found that patients with variants identified by DNA screening had increased risk of heart disease after age 60 but also that the amyloidosis causing that heart disease is likely going to be undiagnosed without knowledge of the genetic variant,” said Brendan Carry, MD, Geisinger cardiologist and one of the study’s lead authors. Dr. Carry, who co-leads the Geisinger multidisciplinary amyloidosis clinic with neurologist colleague David Avila, MD, plans to evaluate, test, and treat high-risk patients who carry a TTR variant.

The research has positive implications for the future of population health as well as treatment of amyloid cardiomyopathy, heart failure, and other amyloid-related conditions.

“Historically, hereditary amyloidosis has been underdiagnosed, which can be a burden on families for generations,” said Christopher Haggerty, PhD, associate professor in translational data science and informatics at Geisinger and the senior author of the study. “A DNA-screening approach to identifying TTR gene variants has the potential to diagnose previously unrecognized cases of ATTR and identify patients at risk for developing cardiomyopathy and other diseases. If we can identify this risk earlier in a patient’s life, we’ll have opportunities to improve treatment.”

The full study can be read in the Journal of the American College of Cardiology: CardioOncology.
Scientists from the Regeneron Genetics Center (RGC) and Geisinger have discovered rare genetic variants in the GPR75 gene that are associated with protection against obesity.

As part of the research that led to the finding, published in the journal Science, scientists analyzed deidentified genetic and associated health data from 645,000 volunteers from the United Kingdom, United States and Mexico, including participants in Geisinger’s MyCode Community Health Initiative.

It’s estimated that more than one billion people will be severely obese (BMI of 35 or higher) by 2030. Working with collaborators, RGC scientists found that people who have at least one inactive copy of the GPR75 gene have lower BMI and, on average, tend to weigh about 12 pounds less and face a 54 percent lower risk of obesity than those without the inactive copy. Protective genetic variants were found in about one of every 3,000 people sequenced.

“Discovering protective genetic superpowers, such as in GPR75, provides hope in combatting global health challenges as complex and prevalent as obesity,” said George D. Yancopoulos, MD, PhD, co-founder, president and chief scientific officer at Regeneron. “Discovery of protective genetic variants – many of which have been made by the Regeneron Genetics Center in its eight-year history – will allow us to unlock the full potential of genomic medicine by instructing on where to deploy cutting-edge approaches like gene-editing, gene-silencing and viral vector technologies.”

Regeneron scientists, collaborating with scientists at New York Medical College, replicated their finding in mice that were genetically engineered using Regeneron’s VelociGene® technology to lack copies of the GPR75 gene. Such mice gained 44 percent less weight than mice without the variant when both groups were fed a high-fat diet. Regeneron scientists are pursuing multiple therapeutic pathways — such as antibody, small molecule and gene silencing approaches — based on this newly discovered genetic target.

“This is a potentially game-changing discovery that could improve the lives and health of millions of people dealing with obesity, for whom lasting interventions have often been elusive,” said Christopher D. Still, DO, director for the Geisinger Obesity Research Institute at Geisinger Medical Center. “While the behavioral and environmental ties to obesity are well understood, the discovery of GPR75 helps us put the puzzle pieces together to better understand the influence of genetics. Further studies and evaluation are needed to determine if reducing weight in this manner can also lower the risk of conditions commonly associated with high BMI, such as heart disease, diabetes, high blood pressure and fatty liver disease.”
Engaging patients at Geisinger 65 Forward clinics for MyCode

Geisinger 65 Forward is a unique approach to healthcare for everyone 65 and older. Members spend more time with their doctors and get personalized attention from a team that includes nurses, a nutritionist, a pharmacist and wellness specialists.

65 Forward also puts everything under one roof. Imaging and lab work are done right on site. Members have access to state-of-the-art fitness equipment and there are plenty of opportunities to socialize and make new friends. So, why wouldn’t we provide an opportunity for these patients to participate in, and be engaged with, our MyCode project?

“Our presentations are designed to inform members about the MyCode Community Health Initiative and explain the benefits to our community at large, as well as to individual patients and their families,” explains Precision Health Associate Paul Francis, who led the initiative. “We coordinate with the 65 Forward Community Program Specialists — who have all been amazing — to find different ways to best serve their members.”

In some cases, the MyCode presentations are available to members who sign up to hear about MyCode in a small group setting that’s open for questions and answers. Other presentations are set up to tell members about MyCode before exercise classes or arts and crafts activities. The MyCode team was even invited to take part in the 2021 Holiday Party at the Shamokin Dam location.

“Thus far, the results have been very positive,” says Mr. Francis. “We’ve only had five events so far and they’ve been to small groups, so the overall totals aren’t high, but as these continue on a bi-monthly or monthly basis we expect similar positive results moving forward.”

“Many people say they’re doing it for their grandkids — or great grandkids,” says Mr. Francis. “And even if nothing is found, they’re helping the community at large.”
DNA 101: The DNA-cancer connection

In the last newsletter, we talked about the basics of DNA. But how exactly do differences in our DNA cause disease? Here we use the example of a difference in the BRCA1 gene and share how it leads to higher chances of developing certain cancers.

A DNA difference in BRCA1 is linked to hereditary breast and ovarian cancer syndrome, a condition in which someone is born with an increased risk for breast cancer, ovarian cancer in women, prostate cancer in men, pancreatic cancer and melanoma.

BRCA1 is a “tumor suppressor” gene. It plays a protective role in the body. Our cells naturally divide and multiply to grow and replace damaged cells. BRCA1 works with other genes and proteins to prevent cells from multiplying out of control. We all have two copies of the BRCA1 gene. When someone is born with a difference (or misspelling) in BRCA1, one copy of BRCA1 works properly and the other copy does not. Over time, with certain environmental exposures, lifestyle habits and aging, the second copy of BRCA1 loses its normal protective function. When both copies of BRCA1 can’t do their job as a tumor suppressor, the cell loses control of dividing and multiplying. That is when we see cancers develop.

We often use a car analogy to describe this process. Think of BRCA1 as the brakes on a car. One copy of BRCA1 is your regular brake and the second copy is your emergency brake. When your regular brakes fail, you can rely on your emergency brake. But over time, wear and tear can cause the emergency brake to fail, too. Without functioning brakes, the car can lose control.

But there’s hope. Knowing that someone has a BRCA1 variant can guide them to take steps to help prevent cancer or find it early, like preventive surgery or more frequent screening. This knowledge can also help doctors select the best cancer treatment. By studying DNA differences, we can discover the root cause of a cancer. The DNA difference can be the “Achilles’ heel” of a cancer and drugs can be designed to stop a cancer’s growth by targeting the area of weakness caused by that difference. For BRCA1, targeted cancer treatments have been developed from this concept. We’re excited that we’re helping to lead this type of research to lead to more targeted treatments and precision medicine.