Research News

Geisinger mycode | 250,000+ PARTICIPANTS

A message from David H. Ledbetter, PhD

Dear friends,

Since the launch of MyCode, we've enrolled more than a quarter million participants. Each MyCode participant is motivated to contribute to learning how to achieve better health for everyone.

The data we've gathered supports research that has the potential to improve the health of current and future generations. For a small percentage of MyCode participants, there may be genomic information revealed that allows them to take better control of their health and provide crucial information to their family members, too.

I hope you'll take a few minutes to read about the exciting things happening at MyCode, including new automation, new research — and a great success story, too. And, as always, thank you for being part of MyCode.

David H. Ledbetter, PhD
Executive Vice President and
Chief Scientific Officer
Geisinger

Meet GIA, MyCode's genetic information assistant

MyCode would like you to meet our newest team member — GIA.

GIA (genetic information assistant) is a confidential, secure chatbot. Available to smartphone, tablet and computer users, GIA can talk to people about genetics anytime, anywhere.

Geisinger worked with Clear Genetics, a healthcare technology company in San Francisco, to build GIA for MyCode participants.

Not sure what a chatbot is?

Chatbots are simulated conversation tools. Chances are, you've already encountered them online. They're often used in banking, insurance, customer service, travel and healthcare to answer simple questions using artificial intelligence (AI). They can promote products and services, and many are used to give customers easy access to service providers. Chatbots also often answer frequently asked questions from customers, like, "Is my flight on time?" or, "Can I still return this item?"

In healthcare, chatbots can collect symptoms and triage participants to urgent care.

They can help participants with obesity and diabetes stay healthy or offer therapy to participants with mental health issues. Chatbots can also help teach teens about health risks of sex, drugs and alcohol. And they can help participants with autism talk to others.

In genetics, chatbots answer questions like "Should my children also be tested for this gene change?" and "Will insurance cover the cost of genetic testing?" AI gives chatbots the ability to reply in real-time to user questions. The chatbot pulls the answers from a library of prewritten responses to popular questions. When GIA gets a question that doesn't match an answer, it's sent to the MyCode team. The team can write a new response and add it to the response library, which grows and gets better over time.

Why use a chatbot?

Over 250,000 Geisinger participants are now enrolled in MyCode. At least 2 percent will get a clinically actionable genetic test result. We need to automate some routine study communications to meet this demand. We reviewed the

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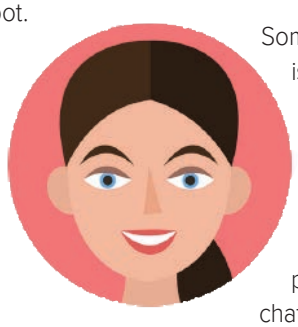
communication tasks in the MyCode study and looked for tasks where we could use a chatbot to help. We chose study consent, follow-up phone calls and family result sharing, which are valuable, but also repetitive and scriptable conversations.

We made a consent chatbot that walks participants through the MyCode consent form to help recruit more Geisinger participants into MyCode. The chatbot allows them to opt to receive more or less detail on key topics (study goals, benefits, risks and so on). It can also record the decision to join or not join the study in the participant's chart. Several Geisinger participants tested the consent chatbot in focus groups last summer. These participants felt the chatbot was easy to use and informative. They also liked the customizable length of the chatbot consent experience. Before using the consent chatbot more, we're planning another study later this year to help us learn more about how well participants understand and recall information shared by the chatbot.



Most people in MyCode will not get a genetic risk result. Participants with a risk result get a phone call from a genetic counselor who can help them make decisions about their genetic health. Participants with results also get a mailed packet that includes the result report, educational material and a result-sharing family letter.

Participants are called by a research assistant one month after getting results to confirm the packet was received. During this call, participants can also schedule a free phone or in-person visit with a genetic counselor. The counselor will explain what the results mean for the participant and their family and connect participants to other healthcare providers. This can help participants start screening and risk-lowering actions.

Six months after getting results, participants get a second call from the genetic counselor, who can answer questions and review progress on recommended actions — like meeting with a doctor, starting screenings, gathering family histories and sharing MyCode results with family members.

Follow-up and family sharing bots

We also made a "follow-up" chatbot that repeats the questions asked during the one-month follow-up phone call. This lets participants tell us if they:

- Got a result packet
- Gathered their family history
- Shared results with family members
- Met with a healthcare provider to talk about their results
- Want to schedule a visit with a genetic counselor

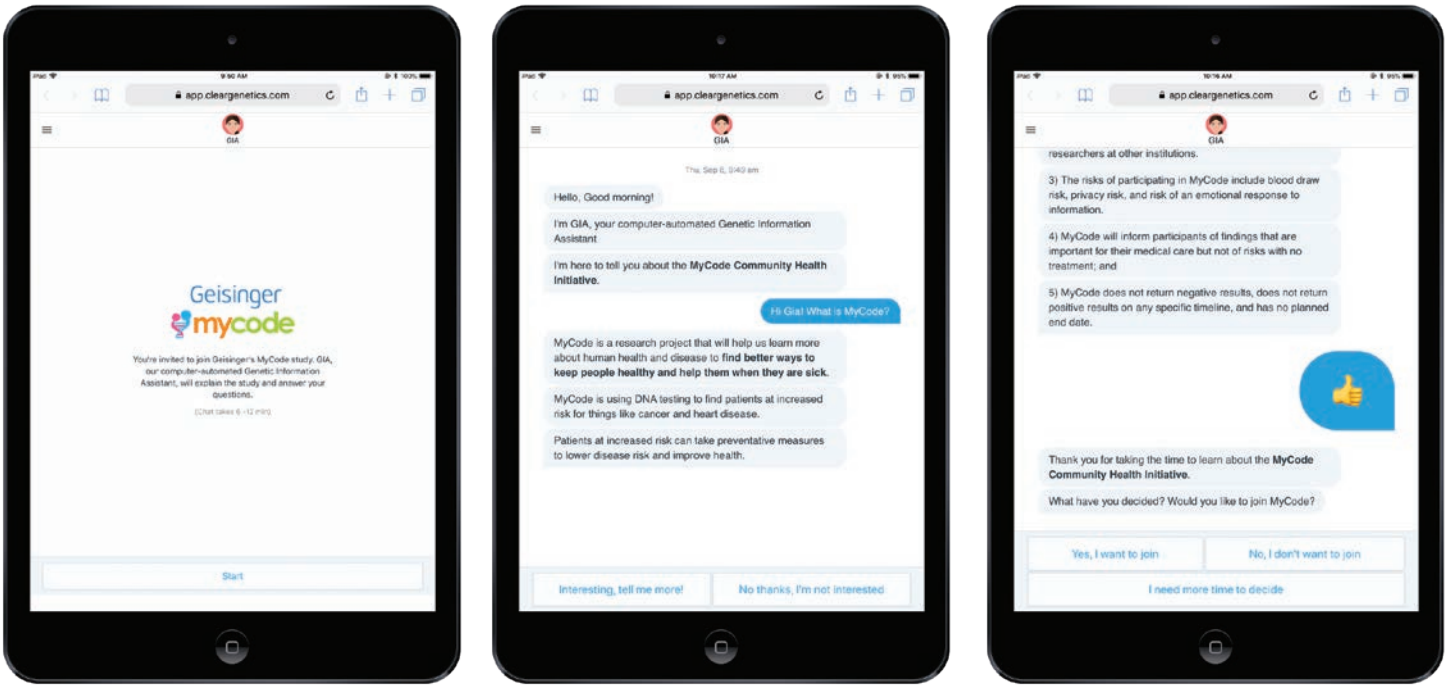
Users can even type in their own questions at the end of the "conversation."

In addition, we created a family sharing tool to help participants share their MyCode results with relatives. This tool allows the participant to send their family members a link to a family sharing chatbot, using a text, email or Facebook message. The chatbot explains the participant's result and why the family member may also have the same risk. It also explains the disease risks and recommended screening and risk-lowering actions. And this chatbot tells a participant's family members about the importance of genetic counseling and testing.

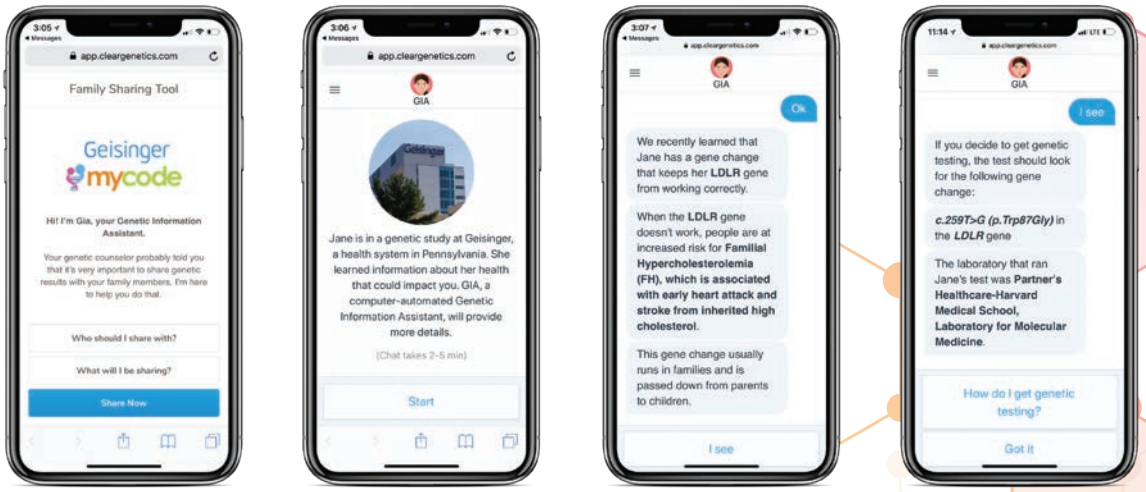
A MyCode participant's at-risk family member can ask for a genetic counseling visit via the chatbot. They can also type in questions. Participants who tested the family sharing chatbot said they liked being able to see what their family member would see. They also liked that GIA gave "answers that wouldn't be on the tip of your tongue" when talking to family members about genetic test results.

Some may be worried that "the bots are taking over." The goal is not to replace our MyCode staff with chatbots. Instead we'll give some of the communication tasks that are repetitive, time-consuming and scriptable to GIA. This frees up more time for our MyCode team to do things better done by humans, like explaining what MyCode results mean for your healthcare. If you are one of the 2 percent to get a MyCode result, we hope you'll choose to chat with GIA and let us know what you think.

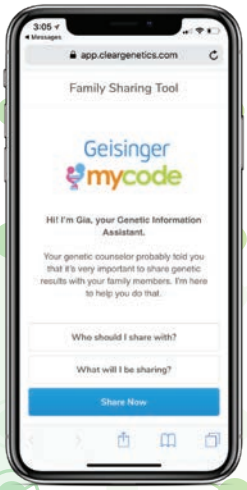
Consent



Family sharing



Follow up



Cascade testing — Helping to share crucial information

"Cascade testing" is a way to identify people who are at risk for hereditary conditions.

The process starts with the identification of one person with a gene variant associated with a condition. From there, testing is expanded to that person's blood relatives, with the goal of sharing important health information with as many potentially at-risk people as possible.

Most of the genetic disease risks looked at in the MyCode study are "dominant." Parents, brothers, sisters and children of a person with a dominant genetic risk factor have a 50 percent chance of having the same risk factor. Cascade testing is repeated ("cascaded") in a family until all people with the genetic risk factor are found.

This process can find people with genetic risk factors much younger than they would usually be found. It also saves money by alerting people to genetic risk factors before they get sick. This gives them a better chance to prevent the disease that runs in their family. People with genetic risk can lower their disease risk by getting extra screening tests, taking medications or having surgery. These steps can also help people find disease sooner, which often leads to a better outcome if they do get sick.

Family members must first be told they're at risk to start the cascade testing process. When a MyCode participant gets a result, a genetic counselor explains why sharing the result with family is important.

How are results shared?

The MyCode study has several ways to help participants share results with their family members.

We give MyCode participants letters that can be mailed to family members to explain the genetic risk result, the health risks and how to get genetic counseling and testing.

We also have a web-based family sharing tool, which lets participants send a chatbot to their family to explain the genetic risk. (See the article on GIA, our genetic information assistant.)

We're also working on a direct contact program that will give MyCode participants the option to have a healthcare provider contact their family. We surveyed participants with a result, and 42 percent said it would be helpful if Geisinger contacted their family members. Only 16 percent said that wouldn't be helpful at all. More than 40 percent said they would use a direct contact program. (For more information, see the article on the IMPACT-FH study.)

Sharing genetic risk information with family members can be lifesaving. If you have ideas about how we can help people share their genetic risk with family, contact us. We'd love to hear from you.

Unexpected MyCode result impacts multiple generations

When State College resident Matt Farley's MyCode screening showed he has the *BRCA2* gene — a predictor of breast, ovarian and prostate cancers — his life didn't change right away. But the results were life altering, and possibly lifesaving, for his mother.

Mr. Farley, 29, joined the MyCode study two years ago, after he was approached by a team member at his doctor's office. He quickly put the initiative out of mind — until he received a letter with his results in June 2018. "Honestly, when I got the results, it was a bit of a surprise," he says. "It said I have the *BRCA2* gene and described what that means for men."

Seeking more answers, Mr. Farley made an appointment with genetic counselor Miranda Hallquist, LGC, who assured him that he would likely be fine. "She told me that for a guy my age, there's not much to do to manage risks associated with the *BRCA2* gene," he notes.

However, Mr. Farley did have concerns about his family — especially his mother, Diane Farley, and his unborn child.

"When Matt came in to discuss the *BRCA2* genetic variant, he had so many great questions," Ms. Hallquist says. "He's expecting his first child and wanted to know what it means for that little guy's future. And he had questions about his mom, too."

Soon after that initial meeting, Mr. Farley's mother scheduled her own consultation with Ms. Hallquist. "I wanted to know if I was the parent who was carrying the *BRCA2* gene," Ms. Farley explains. "When we met, Miranda gave me information on the gene and let me know what to expect if I had the positive result."

By September, Diane learned she was *BRCA2*-positive. "I had made up my mind: If I had the gene, I was going to be aggressive with my options," she says. "Miranda referred me to a gynecologic oncologist, because there is a great risk of developing ovarian cancer with *BRCA2*."

Ms. Farley had her ovaries and fallopian tubes removed on Oct. 15. "I am so lucky," she says. "I learned I had an increased

risk of ovarian cancer and did something about it. I'll never get ovarian cancer now."

Mr. Farley and his mother are both grateful. "We got so lucky," Mr. Farley says. "I could have walked right by the MyCode recruiter two years ago, and we wouldn't know any of this information. Genetics and technology are amazing. Miranda is amazing. We need people like her. We need genetic counselors who can explain to people exactly what the risks are of developing diseases based on their DNA. My wife and I are having a baby, due on Christmas day. Knowing about this *BRCA2* gene will prevent diseases in his future. And seriously, that's just incredible. We are living the future of medicine."

"I gave Matt life," Ms. Farley adds. "And he saved mine. I could have developed ovarian cancer and not known about it until it was too late to treat. Now, that's not going to happen. Miranda has helped so much, and she still guides me. I call her and message her through myGeisinger whenever I need help."

Today Ms. Farley is talking with a breast surgeon about her options, including the possibility of having both breasts removed. "I'd rather prevent the cancer than confront the cancer cells," she says. "I have the luxury of options, now that I know I have an increased genetic risk of developing these cancers."

Identification Methods, Patient Activation and Cascade Testing for Familial Hypercholesterolemia: The IMPACT-FH Study

Geisinger scientists were recently awarded a grant from the National Heart, Lung and Blood Institute to fund a new study called IMPACT-FH. The research will focus on the genetic disease familial hypercholesterolemia (FH). People with FH have very high levels of "bad cholesterol" (LDL) in their blood, putting them at higher risk for a heart attack over time.

More than 90 percent of U.S. residents with FH aren't aware they have this common condition, which affects about 1 in every 220 people. If FH isn't found and treated early, men have a 50 percent chance of having a heart attack by age 50. For women with FH, there's a 30 percent chance of having a heart attack by age 60. If people with FH are found young enough and treated, they can greatly lower their risk for heart disease.

The IMPACT-FH study will focus on the best ways to find people with FH. It will also develop new ways for people with FH to share this risk information with their family members. The study team will design novel tools and programs to improve the uptake of cascade testing. (For more about cascade testing, see the article on page 4). The study will interview patients with FH, their family members, healthcare providers and others on how best to find other patients with FH and get their family members tested.

IMPACT-FH is led by Amy Sturm, a professor and genetic counselor at Geisinger who also co-leads the MyCode Genomic Screening and Counseling program. The IMPACT-FH team includes Geisinger experts in genetics, clinical informatics, implementation science and FH. Geisinger is also working with the FH Foundation (thefhfoundation.org) on this study. Data from this novel study will help other healthcare systems design and start programs for FH.

If you have questions, contact project manager Andrew Brangan at ambrangan@geisinger.edu or 570-714-6631.

Hereditary hemochromatosis: MyCode gives participants a headstart on management

Marc S. Williams, MD, Director, Genomic Medicine Institute

Iron is an essential element for health — a key component of the hemoglobin that carries oxygen in our blood (and gives it the red color). Low iron can cause decreased energy, low blood counts (anemia) and, if severe, heart problems and death. Having enough iron is a good thing. But you can have too much of a good thing, too. People who have too much iron can develop significant medical problems that affect multiple organs including:

- Heart (heart failure)
- Liver (cirrhosis and liver cancer)
- Pancreas (diabetes)
- Thyroid (low thyroid levels called hypothyroidism)
- Joints (arthritis)
- Pituitary gland (decreased secretion of some hormones, which could lead to low testosterone and sexual dysfunction)

There are many different reasons a person can have high iron levels. MyCode is looking at a genetic cause — a disease called hereditary hemochromatosis (HH). The most common form of HH is caused by changes in a gene called *HFE*. The *HFE* gene provides the recipe for our body to make the HFE protein. This protein helps control how much iron is absorbed from food and released in the body. Certain changes (also called variants) in this gene lead to the body making an abnormal HFE protein. This can cause HH and affect the way iron is absorbed from food.

The abnormal HFE protein in people with hereditary hemochromatosis due to changes in *HFE* (*HFE*-HH for short) causes iron to build up starting in childhood. Not everyone with *HFE*-HH will have health problems. And it may take many years for the extra iron to cause issues. Males usually don't have symptoms until they reach ages 40 to 60. Females usually don't have symptoms until after menopause. This is because the blood loss from menstruation also results in loss of iron. Some of the first symptoms of *HFE*-HH may be extreme tiredness, stomach pain, weakness, reduced sex drive, weight loss, painful and stiff joints, and darkening of the skin.

The good news is, there's an effective treatment for people with elevated iron levels due to *HFE*-HH. Removing blood removes iron from the body. By removing blood over time, the iron can be completely removed from places where it can do damage and help people become healthier. Blood can be removed through regular blood donation. This also has the benefit of helping with the national blood shortage. The amount of blood removed depends on the level of iron and whether there's evidence of organ damage. Unless the organ damage is severe, removal of iron can allow early damage to be reversed in hopes of avoiding long-term health problems. This makes *HFE*-HH one of the most treatable genetic conditions we're reporting as part of MyCode.

HFE-HH is the most common genetic disease in European-Americans. It occurs in people of other ancestries (such as Hispanic, African American and Asian), but less often. About 90 percent of European-Americans with *HFE*-HH have two copies of an *HFE* variant called C282Y (one in each copy of the *HFE* gene).

As of 2019, over 200 MyCode participants who have 2 copies of the C282Y variant in the *HFE* gene have been identified. When a patient is notified of an *HFE* gene variant, a blood test is done to measure the iron level in the blood. If iron levels are high, the iron may be damaging the liver. Liver enzyme tests may be ordered to assess liver health. Other tests may be ordered to assess damage to other organs. If the blood tests are normal, that means there is no evidence of *HFE*-HH at the present time. However, the person will be monitored closely, as high iron levels may develop later.

HFE gene changes and risk for disease can be passed to other family members. People with *HFE*-HH should share their MyCode result with relatives, so they're aware they could be at risk for disease.

If you have questions about caring for people and families with *HFE*-HH, call our team of genetic counselors and geneticists at 844-250-8031. This team is also studying how MyCode participants with the *HFE*-HH gene use this information for their healthcare. This will be the first assessment ever done of the impact of *HFE*-HH in a large population. We'll report our findings in a future newsletter.

Specialties

DNA and health data from MyCode research participants like you has contributed to over 250 research studies initiated since 2009. With the help of our participants, we've been able to study a broad range of health and disease.

50+ Brain Studies:

- Neuroscience
- Parkinson's disease
- Autisim & developmental medicine
- Psychology
- Addiction
- Behavioral health

40+ Heart & Blood Studies:

- Atrial fibrillation
- Peripheral vascular disease
- Cardiomyopathy
- Blood lipids
- Coronary artery disease
- Hemochromatosis

10+ Liver Studies:

- Fatty liver disease

10+ Kidney Studies:

- Chronic kidney disease
- End-stage renal disease
- Kidney stones
- Polycystic kidney disease

30+ Obesity & Nutrition Studies:

- Diabetes drug response
- Gestational diabetes
- Obesity
- Monogenic studies
- Gestational weight gain

10+ Bone & Joint Studies:

- Joint infection
- Osteoarthritis
- Pediatric orthopaedic conditions

20+ Cancer Studies

- Bladder cancer
- Breast cancer
- Colon cancer
- Endometrial cancer
- Esophageal cancer
- Familial cancers
- Lung cancer
- Melanoma
- Prostate cancer

Pulmonary/Sleep Studies:

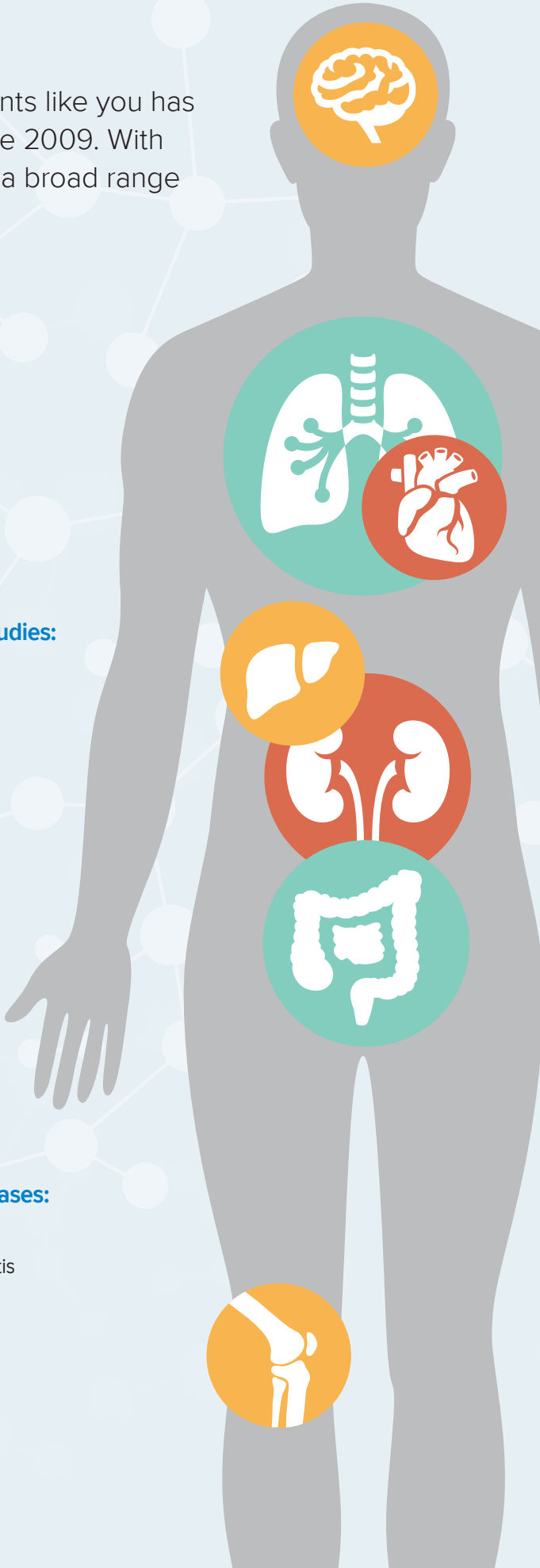
- Asthma
- Smoking
- Sleep disorders
- Pulmonary hypertension
- Chronic obstructive pulmonary disease
- Respiratory distress syndrome
- Cystic fibrosis

Research Studies:

- Population health
- Genomics
- Stem cell
- Pharmacogenetics
- Social media

Digestive Tract Diseases:

- Crohn's disease
- Eosinophilic esophagitis



Geisinger

Geisinger Medical Center
100 N. Academy Ave.
Danville, PA 17822

PROGRESS: Pediatric Reporting of Genomic Results Study

MyCode participants have helped Geisinger researchers secure a grant from the National Institutes of Health for a study called PROGRESS, which addresses a question that has been hotly debated among genetics experts:

Is it harmful or helpful to tell children about genetic risks that will not affect their health or change their care until adulthood?

Disclosing these adult-onset results can spur life-saving preventive measures in these children's parents. But some experts worry that these results might be distressing to children, or that children might be treated differently by their families. There's little research to support either position, and the lack of data prevents genetics clinicians from deciding how to best care for children and families at risk for genetic disease.

PROGRESS is designed to provide this data. The study will report adult- and pediatric-onset genomic results to MyCode pediatric participants through a supportive clinical program. It will then ask several questions:

- How do children and their parents respond to these results?
- Do parents use the results to make medical decisions?
- Are there any legal doctrines that apply to reporting genomic results?

The **PROGRESS** team is led by Adam Buchanan, MS, MPH, LGC who co-leads the MyCode Genomic Screening and Counseling program. The team includes Geisinger and external experts in genetics, pediatrics, psychology, bioethics and health law. Data that's gathered will guide national and international groups that might screen children for genomic risk.

Contact project manager Amanda Lazzeri, **570-714-6639**, with any questions about **PROGRESS**.

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