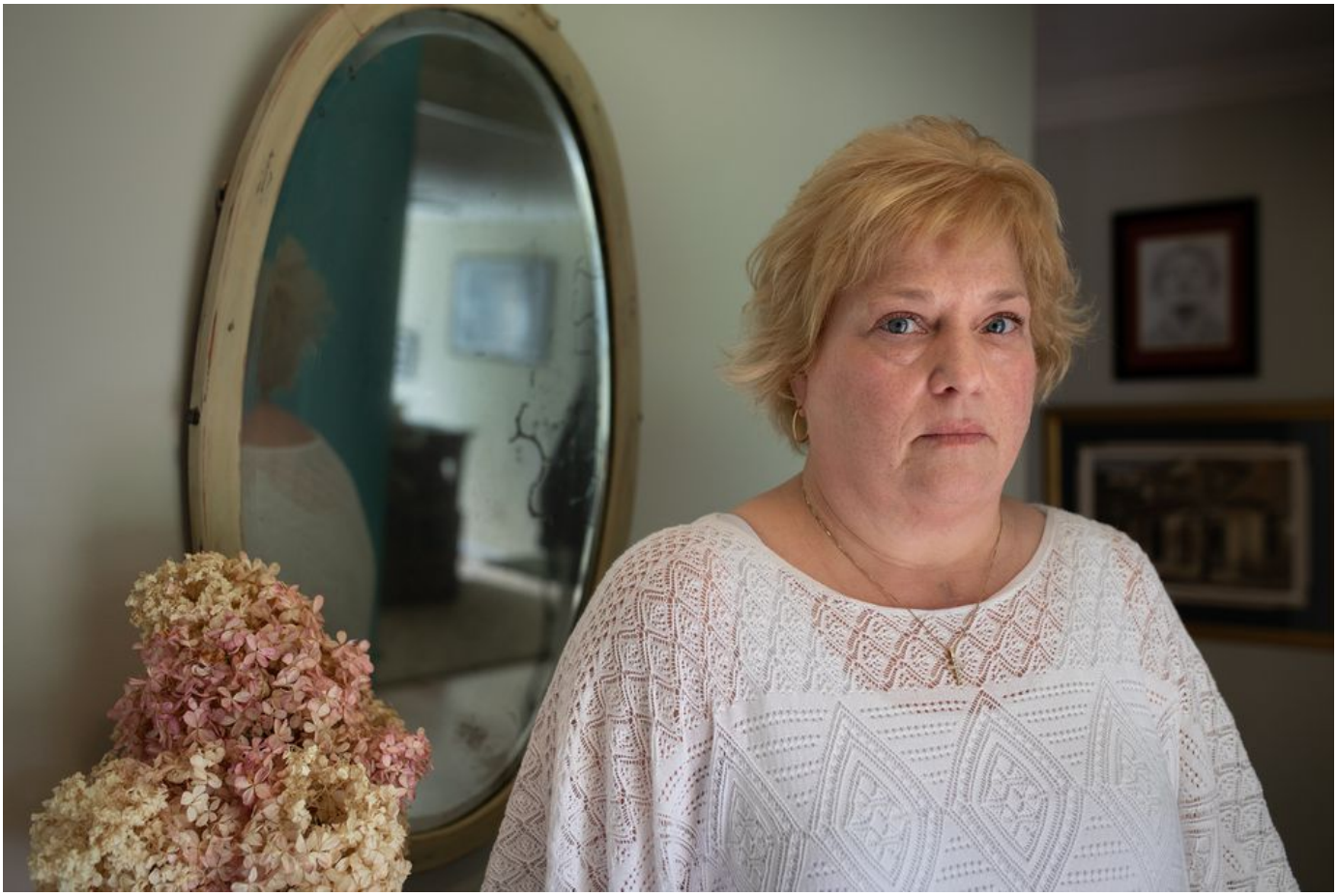
Blood samples reveal valuable data — and life-changing surprises for donors

By **Priyanka Dayal McCluskey** Globe Staff, July 5, 2019, 6:55 p.m.



Kristine Trudeau in her home in West Springfield, Mass. (STEVEN G. SMITH FOR THE BOSTON GLOBE)

During an appointment at Brigham and Women's Hospital last year, Kristine Trudeau agreed to give a little tube of blood for research.

Her sample joined thousands of others in the Partners HealthCare Biobank, a resource for researchers across the Partners hospital network — including the Brigham and Massachusetts General. By analyzing large numbers of blood samples, scientists can learn how genes contribute to disease. Their discoveries eventually could aid in the development of new medications and treatments.

Trudeau said she donated her blood because she wanted to be helpful. Then she forgot about it.

But a few weeks later, she received some startling news. Researchers scanned her sample for genetic trouble signs — as they do with many biobank samples — and they found one. Trudeau's blood showed a variant of the BRCA2 gene, indicating that she had a much higher risk of developing breast and ovarian cancer.

"It was very scary," said Trudeau, a nurse and mother of two who lives in West Springfield.

More than 103,000 patients have agreed to provide blood to the Partners HealthCare Biobank, and their samples are providing valuable data for some 200 studies about Alzheimer's, depression, diabetes, epilepsy, heart disease, and other conditions. But the research initiative is also having another impact, one that is more personal and immediate: It's revealing genetic red flags that patients otherwise might never have seen.

So far, Partners has found genetic variants in more than 300 patients that increase

their risk of cancer, heart disease, or other medical problems.

Such efforts by Partners and some other hospital systems around the country represent a milestone in the movement to incorporate genetic information into patients' medical care. Yet they also raise thorny questions about when to share sensitive information and how patients should act on it.

Such knowledge could be life-changing: Patients can sometimes take medications or seek treatments to prevent disease. But knowing they are at higher risk of serious illness could also cause stress and anxiety for otherwise healthy adults.

Partners, which launched its biobank in 2014, has analyzed the DNA of more than 30,000 patients and is planning to expand genetic testing to the entire biobank.

Dr. Scott T. Weiss, Partners' director of personalized medicine, said most patients have been enthusiastic about getting this information, although some have opted out.

"We think this is going to increase participation [in the biobank]," Weiss said. "Instead of just doing this for medical research, you have the opportunity to get something back."

Partners researchers have been scanning blood samples for variants of more than 100 genes with known links to specific diseases. It's a far more detailed analysis than is typically done by consumer services like 23andMe. With a federal grant, Partners and other health systems are studying the implications of this kind of testing.

It's a complex endeavor: A single gene can have hundreds of variants, and scientists may understand only some of them.

How do they know what to look for? Weiss said Partners is working from a list of genes nationally recognized by genetics experts.

"It's got to be done very carefully," Weiss said. "We're erring on the side of being very conservative about what information we give back. We want to give people stuff that's important, and we want to leverage this to improve cost-effective care."

This approach — broad-based screening of healthy people — is a shift from years past, when genetic testing was usually limited to those who had a specific reason to scan their DNA, such as a family history of disease.

"This is very different, because what we don't want to do is wait until that heart attack happens, or that colon cancer happens, or that breast cancer happens," said Amy Sturm, president of the National Society of Genetic Counselors. "We would like to identify people who have risk before that."

Trudeau, the Brigham patient, gave her blood to the Partners Biobank during a routine appointment last year.

She soon learned that it contained something suspicious, and she was asked to provide some saliva to confirm the results. She spit into a test tube and put it in the mail.

Trudeau was asked to meet with a genetic counselor. At that appointment, she learned about her increased risk for breast cancer.

"I knew right away I had to act on it," said Trudeau, 55. "I went through that anger, denial, acceptance rather quickly."

She had a breast MRI, then a biopsy, and discovered she had early-stage breast cancer. Armed with the information from her genetic test, she opted for the most intense treatment available: surgeries to remove her breasts, ovaries, and fallopian tubes.

"I knew I wanted to protect myself," said Trudeau — who had endured a lung

transplant for her pulmonary fibrosis a few years before her brush with cancer.

But not every result from a genetic test is so clear-cut. And not every patient reacts the way their doctors may expect.

At Vanderbilt University Medical Center in Nashville, Dr. Dan Roden recalled a woman who was so worried that her daughter's genetic test results raised the risk of cardiac arrest that she wanted a defibrillator implanted in her daughter's chest. Vanderbilt doctors told her that wasn't necessary: The genetic test results were not cause for alarm, and other tests came back normal. The woman went looking for another doctor to implant the defibrillator.

"Returning results is extraordinarily complicated," said Roden, Vanderbilt's senior vice president for personalized medicine.

Vanderbilt has a large biobank with blood samples from about 250,000 patients. The medical center has returned results to about 150 patients so far — information that could help them take the most effective medications and get the proper cancer screenings to ward off disease. But Roden said he sometimes wonders: "Why are we looking for trouble in a bunch of healthy middle-aged people?"

"There are a group of people who say, 'It's my genetics; I should know everything about it,' " Roden said. "On the other hand, you're going to create a huge amount of anxiety and create a lot of testing that is useless."

Those additional tests would come at additional cost to patients, and to the health care system.

Dr. Wylie Burke, a bioethics expert at the University of Washington, said researchers should tell patients about any reliable information that could help them reduce their

risk for a serious disease. But the evidence on genetic testing of broad populations — as opposed to testing of people with a known family history of disease — is lacking, she noted.

“Participants in these testing programs could experience overdiagnosis and unnecessary medical follow-up,” Burke said in an e-mail. “The cost to patients and the health care system could be substantial.”

At Geisinger Health in rural Pennsylvania, researchers have analyzed the DNA of more than 64,000 patients since 2013 — and they’ve found concerning genetic variants in more than 1,000.

“We’re not going to feel very comfortable finding clinically important information about your health and not telling you,” said David Ledbetter, chief scientific officer at Geisinger.

Ledbetter’s team held focus groups with patients and asked how they would feel about receiving this kind of information. The patients said they wanted to know.

“When we made this decision,” Ledbetter said, “a fair number of the people in the genetics and scientific community thought it was premature. We felt confident.”

Nearly 300 Geisinger patients have learned about their higher risk for breast and ovarian cancer. More than 100 were at higher risk of familial hypercholesterolemia (early heart attacks and strokes), and more than 70 learned about their increased

chance of cardiomyopathy, a heart muscle disease. Others have learned about their risks of developing rare conditions.

Because genetic risks run in families, one person’s troubling test results can trigger additional testing among blood relatives.

After Trudeau learned about her higher risk for cancer, she talked to her sister, Karen Larkin, who also was tested — and learned she, too, had a variant of BRCA2. Larkin had her ovaries and Fallopian tubes removed to avoid cancer, and she plans to have more frequent breast-imaging tests.

Now it's up to Trudeau's twin daughters, who are 20, to decide if they want to learn about their genetic risks for cancer.

"In my case, it was a good thing," Trudeau said. "But I don't think it's for everyone. Some people just don't want to know."

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