A New Heart Disease Test Flings Color Genomics Into A Battle About Genetics In Medicine

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Color Genomics, a Burlingame, Calif.-based startup that has made a name for itself by selling tests for genes that dramatically raise the risk of cancer, is moving into a new area: heart disease. In doing so, it is stepping even more deeply into a raging debate over the medical and economic value of plumbing our DNA.

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Today Color is releasing a genetic test for a condition called familial hypercholesterolemia, or FH, which causes sky-high cholesterol levels and a corresponding increase in the risk of heart attacks and strokes. The test will cost $250, or $150 for people who have already bought Color's cancer tests, although many people are expected to get them from employers or insurers who have paid for access to Color's products. Patients with FH can have cholesterol levels of more than 290 milligrams per deciliter, or levels of low-density lipoprotein (LDL, the "bad cholesterol") of more than 190 mg/dL, both way above normal levels.

"As medical costs soar, the healthcare world is undergoing a transformation from reactive treatment to preventive care," writes Othman Laraki, Color's chief executive, in a blog post on the company's web site. "At Color we're building a preventive health service which helps people learn their genetic risk in important

health areas like heart health and cancer -- and use that knowledge to be more proactive about staying healthy, which could save their families (and our entire healthcare system) lots of money."

But some outside cardiologists say that they're not sure there is value in routinely testing for FH, despite the fact that the disease is a unquestionably deadly, because simple tests for cholesterol and low-density liprotein (LDL, the "bad cholesterol") are so cheap and readily available. Why pull the blueprints, they argue, when you can much more cheaply just listen to the engine? And even one doctor who has worked closely with Color cautions that screening tests like this are likely to add to overall costs – although they can be worth the money.

"This is in-frame with a whole societal moment that's moving toward the option of pre-dispositional genomic sequencing even when experts are still very divided about the long-term downstream consequences of it," says Robert Green, a researcher at the Brigham & Women's Hospital. He cautions that screening will always increase costs, because it always means testing people who won't get sick. "The only question is: For that increased cost, do you get good value?" Green says.

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Some cardiologists who treat people with FH think the value of such a genetic test is suspect.

"Most physicians, including me, do not routinely test for FH," says Steven Nissen, chairman of cardiology at the Cleveland Clinic. "When the LDL-C is super-high, the genetics don't really matter. We give enough LDL-lowering therapy to reduce values to more appropriate levels. Regardless of the genetics, we always ask about offspring and routinely test them."

James Stein of the University of Wisconsin School of Medicine and Public Health, echoed those concerns, worrying about turning 'people' into 'patients' unnecessarily. "There is a perfect storm right now of interest in genetic testing and unlocking its scientific power with availability of new expensive drugs for high cholesterol, patient advocacy (industry-sponsored), and physician champions," Stein writes via email. "Practice has outpaced the science rapidly."

But there is also a building chorus of experts on Color's side, who think genetic testing for FH can help identify and motivate patients in ways that testing for LDL levels cannot. First, some facts everyone agrees on: FH is serious, even if there is only one copy of the gene; in patients who have two FH genes, heart attacks can occur in people's twenties. As with the cancer genes Color tests for, which include the breast-and-ovarian-cancer gene BRCA and genes for a condition called Lynch Syndrome, people who have gene mutations for FH are very likely to have the disease.

In a recent issue of the Journal of the American Medical Association, Joshua Knowles of Stanford University and two cardiologists reviewed using a strategy called "Cascade testing." The idea is that when a person with super-high cholesterol turns up, they are tested, and then their family members are tested. For each new person found, the process is repeated. The argument is that this process finds patients more efficiently than just waiting for them to turn up with high cholesterol levels. Patients with FH usually start having high cholesterol in childhood, but doctors often don't spot the problem until they are at middle age, when years of plaque buildup has already done its damage.

Knowles and his colleagues point to research in the Netherlands that said this approach was highly cost-effective, costing $8,700 for every year of life gained. Generally, anything under $50,000 is a no-brainer. And that's with genetic tests that cost between $500 and $1,000 per person, at least quadruple Color's list price. With Color's tests, the results should be better.

There may also be some value in treating these patients differently from other people who have high cholesterol. A study last year from the lab of Sek Kathiresan, the Director of the Center for Genomic Medicine at Massachusetts General Hospital, used DNA sequencing to diagnose FH in patients who donated samples for other studies. It found that patients with an LDL of more than 190 mg/dL with no FH genes had a 9-fold increase in the risk of coronary artery disease. For those with FH genes, there was a 22-fold increase in risk. This may be like smoking: patients who just have high cholesterol are like those who smoke intermittently, whereas those who have the unlucky genes are analogous to those who smoke almost constantly. But the study also emphasized how rare the condition is: even in people with an LDL of more than 190 mg/dL, only 2% of people had FH.

Jill Hagenkord, Color's chief medical officer, points out another benefit of testing. When people are just told they have high cholesterol, they stop taking their cholesterol medicines 60% of the time. That drops to 20% when they are told they have FH. In this case, turning people into patients may have a long-term benefit. The company says it is dedicated to only working on genetic tests where the value of testing is incontrovertible.

"A lot of that thinking is around the assumption that genetics is a very explosive undertaking," says Othman Laraki, Color's chief executive. "It's just turning out to be wrong in the world where genetics is unlike, for example, a lipid panel or mammogram. Those are things you get single snapshot of a current state. One of the biggest values of the genetic side is that is part of the program you're running. That can then be used to change a lot of the thinking."

That's an emotionally appealing argument. But many doctors are skeptical because they've been conditioned to believe the opposite: that a test is likely to add to costs, lead people to get treatments they don't need, and cause harm. A discussion about testing for FH can start to feel more like a discussion over whether it's better to try to fix the current healthcare system, which should be identifying all the kids in the

country with super-high cholesterol but isn't, or to add some new product to our crazy Rube-Goldberg system on top of the system as another fix. Sorting this out is going to require a lot of energy, and plenty of that one thing none of us have enough of: Time.