ARE WE THERE YET?

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An 80-year-old male with Parkinson’s disease landed in the hospital with an infection last month. Soon, he exhibited signs of dementia and experienced hallucinations. It didn’t look good.

When Christopher P. Cannon, MD, spoke with the patient’s daughter, he learned what sparked this turn for the worse: a newly prescribed antibiotic. “When the antibiotic was added, it increased the level of one of the Parkinson’s medicines and caused a bad side effect. When the antibiotic was stopped, the patient ‘woke up’ and got all better,” said Dr. Cannon, associate physician at Brigham and Women’s Hospital and professor of medicine at Harvard Medical School in Boston, Massachusetts.

Dr. Cannon envisions each patient having access to their own personal, medical “cloud.” With each appointment, various healthcare providers will upload information on all prescriptions, diagnoses, allergies, and drug sensitivities, as well as test results. That way, should you pass out on vacation, the emergency room physician won’t have to live out an episode of TV’s House looking for clues. This brand-new medical world will also allow physicians to use genetic data to determine which drugs will work best and which will cause the least harm, as well as more accurately pinpoint risk factors.

But we’re not there yet. So where are we, and where are we headed?

One step at a time

The first step appears to be gathering information and then having the technology to process, store, and share the data. Next, according to experts, we must figure out how to capitalize on this information to create diagnostics, followed by treatments and, ultimately, preventive strategies.

The amount of information—that first step—is swelling. In fact, there were only 100 laboratories conducting genetic testing in 1993; by 2005, this number had reached 600, very close to the 612 we have today, according to the NIH’s National Center for Biotechnology Information. The number of diseases for which genetic testing is available has skyrocketed, going from 100 in 1993 to 2,634 now. Although tests are available, we’re still figuring out what to do with most of them and learning which ones hold the most promise for future treatments.

Right now the United States spends more than $300 billion per year on pharmaceuticals, but only half of those drugs work as well as anticipated, and some prescriptions prove to be downright dangerous for certain patients.

“Our healthcare system is fabulous, but it’s too expensive,” said Dr. Cannon, who envisions that real savings will enter the picture when we can avoid duplication of care, cut re-hospitalization rates, and decentralize care.

“Soon, we’ll have more home-monitoring devices that will check heart rate and heart rhythm,” Dr. Cannon said. Although a lot of predictions about personalized medicine take on a science-fiction feel, he said the biggest boon will be using...
"That’s where the benefit of personalized medicine lies. It will allow us to spend more time in the sweet spot of medicine."

Widening the lens by tightening the focus

Looking beyond the individual patient, there is the “population approach,” said Clyde W. Yancy, MD, cardiology chief and professor of medicine at Northwestern University’s Feinberg School of Medicine and associate director of the Bluhm Cardiovascular Institute at Northwestern Memorial Hospital in Chicago, Illinois. “The personalized approach is how we deal with the individual who already has disease, the population approach is what we do prior to the onset of disease—can we interrupt the onset of risk?” Dr. Yancy explained.

“There is a journey phenomenon underway. We’re on this path. We’ve actually been doing this for some time, but the tools we have today have been relatively crude: gender, race, ethnicity, etcetera,” said Dr. Yancy, past president of the American Heart Association. To make care more tailored, more specific determinants will be used, such as biomarkers that indicate whether a person will be a super-responder to a treatment or have a potentially deadly adverse reaction. “That’s where the benefit of personalized medicine lies. It will allow us to spend more time in the sweet spot of medicine. Ideally, one day we will know exactly who is at risk for disease and exactly which drugs and treatments will work, saving them from exposure to side effects and adverse reactions. We can be smarter and avoid doing things that might cause harm. But are we there yet? We’re certainly not there yet. We’re on a journey that is very deliberate and methodical.”

“Literally, we start with something that is a physical description, such as race, and refine it further by using biomarker profiles,” Dr. Yancy said. “Now we’re at the threshold to ferret out the signature for that individual disease based on phenotype. That’s the path we’re on.”

Not Star Trek yet

When people hear personalized medicine, often futuristic images arise. We imagine a drop of our blood will tell everything we’ve ever done, predict every disease we’ll develop, and then correctly choose the medicine that will cure us—sans side effects. “Even though it’s relatively easy and inexpensive to genotype an individual, much of that information is virtually impossible to understand,” Dr. Yancy cautioned. There is surprisingly little information on how a person’s specific genetic profile will impact medication choices and other treatments. “We need to respect the complexity of the genotype.”

Genes, of course play a large role in our current and future health, but so does environment. Add in pharmaceuticals and you’ve reshaped those original building blocks. “It’s really, really important to measure our enthusiasm to understand the true impact of how genes relate to disease and not immediately jump to genetic profiling,” Dr. Yancy added. “I’m very concerned that, in our rush to increase genetic testing and genetic descriptors of disease, we may do more harm than good. If we do that, the information could lead to a less-than-ideal experience.”

An example: if a person learns early in life that they’re genetically predisposed to develop a rare, incurable heart disease and may die young, that information could very likely result in them paying more for health and life insurance—if they’re able to get it at all. Then there is the impact on the person’s quality of life, as they may make very different life choices and suffer from increased stress.

“We still must have the important ethical discussions about what we do when we discover something adverse in a patient’s genotype,” Dr. Yancy said. “How do we manage that? Do we modify our behavior? We don’t want to replicate the difficult experiences of disparate care that was based on race, ethnicity, age, and gender. This isn’t a trivial concern since we’re being equipped with such power and the information is so descriptive of a single individual.”

Ethics should be tackled now, while this movement is young, Dr. Yancy urged. “It’s going to take some time and I don’t believe it’s immediately upon us,” he said. “Medicine has been a beautiful journey. We’re on the precipice of comparative effectiveness research. We’ve gone from eliminating many infectious diseases, changing the mode of death from things like pneumonia to cardiovascular disease.”

At the heart of the matter

As medicine as a whole adapts and eventually adopts new technology and methods, cardiology as a specialty is ahead of the pack in some areas, while still moving slowly in others, said Eric Topol, MD, a cardiologist and chief academic officer of Scripps Health, a nonprofit integrated health system in San Diego, California.

“Cardiologists are very gadget-oriented. We know they’re into their iPads and iPhones,” said Dr. Topol, who is no stranger to new medical technology. “You’ve heard the one about the cardiologist who responds to the call, ‘Is there a doctor aboard?’ during a cross-country flight? Well, that was Dr. Topol last fall, when, at 30,000 feet, he whipped out his iPhone equipped with a portable EKG to correctly diagnose that a passenger was having a heart attack. ‘After we landed and got him safely whisked off in the ambulance, all of the flight attendants and pilots wanted their cardiograms done.’

Soon, Dr. Topol predicts, these handheld tools won’t be so novel. He envisions people with hypertension continuously monitoring and tracking their blood pressure through a noninvasive wristband that sends readings directly to a smartphone. “I’ll get hundreds of readings from patients that will give you a look at their blood pressure when they’re sleeping or when they’re having an argument. We’ll get a lot of data from individuals that we never had access to before.”

Keep the change

“The deep problem is getting the medical community to change,” said Dr. Topol, who describes it as a slow process. He and other experts pointed to clopidogrel as an example of what’s right and what’s wrong. The information is available to determine which patients will respond to clopidogrel after having a stent implanted or which will be the non-responders at significantly higher risk of dying from a heart attack. “This can be screened,” Dr. Topol said. “Some physicians aren’t comfortable using this genomic information and haven’t incorporated it into their cardiology practices. It really needs to be a rapid, inexpensive test.”

Dr. Topol wrote his latest book, The Creative Destruction of Medicine, as a way to take his message to the public, so the average patient can act as change agent. “They should know about this stuff because, ultimately, it will affect their care. Individuals can capture their own data and drive these
changes more rapidly.”

While cardiologists are leaders when it comes to adopting new gadgets, when dealing with genetic information they lag behind, Dr. Topol said. “We’re behind the curve compared to oncologists, because cancer is a genomic disease.” But he expects that to change. “Eventually most medicines we will have genomic information.”

These advances are expected to improve health while cutting costs. Patients with chest pain will be able to monitor their hearts at home, and a doctor will tell them remotely if a trip to the emergency room is necessary. “If you don’t have people going to the hospital for heart rhythm, you have more control of blood pressure and you can prevent clotting of stents—preventing heart attacks—you have a great potential for lowering costs,” Dr. Topol said. “We’re talking about cutting costs quite substantially. We do 20 million echocardiograms per year. Probably 10 million are unnecessary and can be prevented by using pocket echocardiograms as screenings. We could gut costs, not just cut costs; but we’re not taking advantage of that yet.”

“In 10 years, the biggest difference will be that the individual will have so much information,” Dr. Topol said. “It will be like the Gutenberg printing press. Not just the high priest will have access to the Bible—everyone will have access to their information to learn about themselves. We’re re-booting how they relate to doctors. It will become, ‘Here’s my information, doctor. What do you think I should do?’ instead of doctors having all of the information in their domain. Now here comes the real empowerment.”

Getting comfortable with ‘new’ genes

Although considered the Holy Grail of, well, life, the Human Genome Project was the opening act, but not the curtain call, said Christopher O’Donnell, MD, senior advisor to the Director of the NHLBI for Genome Research and Associate Director of the Framingham Heart Study.

Mapping the human genome gave us the ingredients, now researchers work to figure out the right recipes.

“We don’t have any drugs right now from this new information,” Dr. O’Donnell said. “We’re in a very exciting position of discovery—particularly in the area of genomics. We’ve taken the information from the Human Genome Project and applied that entire human genome sequence to cardiovascular disease and cardiovascular risk factors. As a result of a set of genome-wide association studies, we have a whole new set of gene variants that we know are very strongly associated with cardiovascular disease and cardiovascular disease risk factors. We literally had virtually none of this information 7 years ago.”

Like a multi-layer cake, new research builds upon those earlier discoveries giving investigators more insight into genetics and disease. With the mapped genome serving as the base layer, now researchers continue to delve into specific topics, such as rare diseases in families as well as the usual suspects, the common causes of MI: high blood pressure and elevated cholesterol.

“We have all of these discoveries and we’re definitely in a phase of taking stock of what we’ve discovered and prioritizing next steps,” Dr. O’Donnell said.

“We’re understanding for the first time the actual genetic underpinnings of various cardiovascular disease. We’re learning there may be many new pathways that may have not been known. This will require work understanding the biology. New treatments will be tested in small clinical trials and then larger trials, it will take time. It’s a 10-plus year process,” Dr. O’Donnell said.

“One of the great things about cardiology is that we have one of the strongest evidence bases for our practices for preventing and treating diseases,” he continued. “To some extent, the new discoveries will have a higher hurdle to overcome to demonstrate that genetic discoveries are comparable to existing treatments. We know that most drug treatments now only reduce burden of disease by, at most, 15% to 20%. That’s considered a good result. Anything that improves on that will be very important. We need to stay with our evidence-based practice and integrate new knowledge into that practice.”

This new knowledge will take new, multifaceted training methods to educate doctors.

“For practitioners, continuing education will be needed to allow decision-making about personalized care at the level of the primary care physician or general cardiologist, not just at the level of the genetic counselor,” Dr. O’Donnell said.

In addition, he agreed with Dr. Yancy that, while we’re laying the foundation for a digitized future of voluminous personalized data, now is the time to hash out ethical considerations. “We need to think carefully about the ethical implications of genetic information that can be used to discriminate in terms of health insurance and life insurance.”

Dr. O’Donnell also raised the concern that we must ensure that all segments of the population are appropriately represented in research. “The initial research was largely conducted in people of European descent.”

In all, finding ways to personalize medicine comes down to improving care for patients, which means increasing effectiveness and decreasing risks while saving money and lives.

Dr. O’Donnell, for one, has high hopes: “The area of personalized medicine and personalized genomics has a great potential to change the way we practice cardiovascular medicine.”