MIT Technology Review
BUSINESS REPORT

Data-Driven Health Care

New technologies promise a flood of molecular, environmental, and behavioral information about patients. Will all that data make medicine better?

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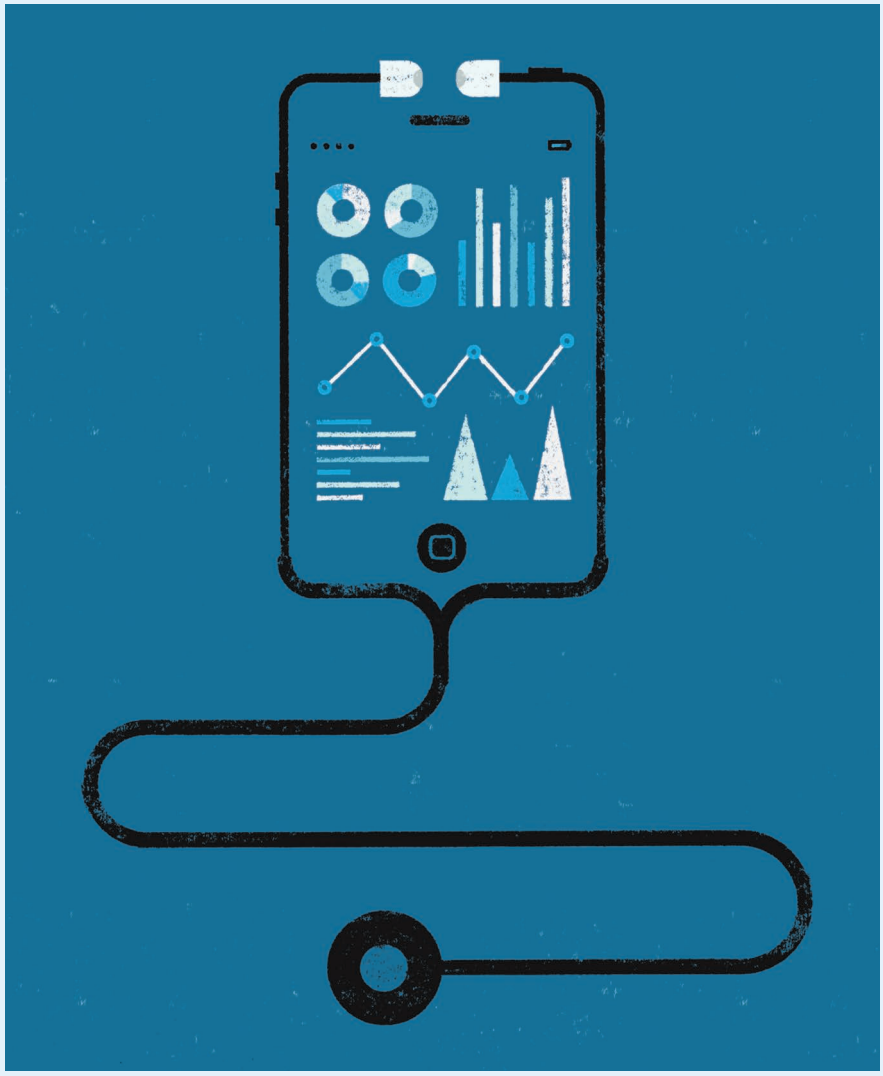


MIKE MCQUADE

The Big Question

Can Technology Fix Medicine?

Medical data is a hot spot for venture investing and product innovation. The goal: better care.

● After decades as a technological laggard, medicine has entered its data age. Mobile technologies, sensors, genome sequencing, and advances in analytic software now make it possible to capture vast amounts of information about our individual makeup and the environment around us. The sum of this information could transform medicine, turning a field aimed at treating the average patient into one that's customized to each person while shifting more control and responsibility from doctors to patients.

The question is: can big data make health care better?

"There is a lot of data being gathered. That's not enough," says Ed Martin, interim director of the Information Services Unit at the University of California San Francisco School of Medicine. "It's really about coming up with applications that make data actionable." →

The business opportunity in making sense of that data—potentially $300 billion to $450 billion a year, according to consultants McKinsey & Company—is driving well-established companies like Apple, Qualcomm, and IBM to invest in technologies from data-capturing smartphone apps to billion-dollar analytical systems. It's feeding the rising enthusiasm for startups as well. Venture capital firms like Greylock Partners and Kleiner Perkins Caufield & Byers, as well as the corporate venture funds of Google, Samsung, Merck, and others, have invested more than $3 billion in health-care information technology since the beginning of 2013—a rapid acceleration from previous years, according to data from Mercom Capital Group.

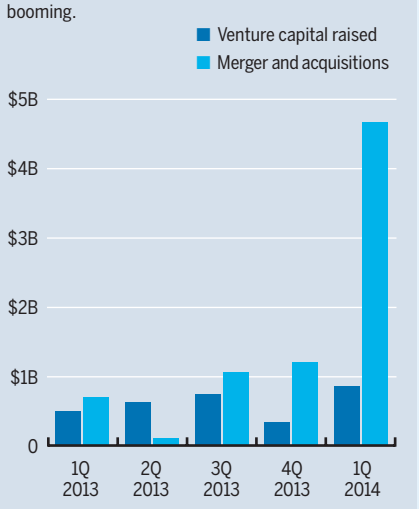
This *MIT Technology Review* Business Report looks at the technologies and companies most likely to survive the boom and the challenges they will face as they push to remake health care.

The groups that control the most medical data today are insurance companies and care providers, and their data analysis is already beginning to change health care. Express Scripts, which manages pharmacy benefits for 90 million members in the U.S. and processes 1.4 billion prescriptions a year, has scoured its data from doctors' offices, pharmacies, and laboratories to detect patterns that might alert doctors to potential adverse drug interactions and other prescription issues. Doctors can now know 12 months in advance, with an accuracy rate of 98 percent, which of their patients may fail to take their medicine. Taking steps to avert that problem could improve patients' health and reduce the $317 billion spent in the United States each year on unnecessary ER visits and other treatment.

Today many companies and health-care providers are adding other layers of information to create an increasingly precise, patient-specific brand of medicine. New mobile technologies, for example, could provide information about a patient's everyday behaviors and health, creating opportunities for care providers to influence patients far more frequently. Data brought in from electronic health records would add doctors' insights, test results, and medical history. Genetic data would offer insight into whether patients are predisposed to certain conditions or how they might react to treatments.

Investor Enthusiasm

Global deal-making involving health-care IT firms is booming.



"We want to believe that most of the things we do in medicine are based on evidence," says Malay Gandhi, managing director of Rock Health, which funds health-care startups. "Some are, but most aren't." The opportunity, he says, is that medicine could become more analytical and evidence-based.

100,000
Number of health apps available for smartphones

Data is also changing the role of patients, offering them a chance to play a more central part in their own care. One way is by using mobile technology to monitor sleep patterns, heart rate, activity levels, and so on. In development are even more advanced devices capable of continuously monitoring such key metrics as blood oxygen, glucose levels, and even stress. And companies like Apple are hoping to become repositories for all this information, giving consumers new ways to track and perhaps improve their health.

This kind of information may be useful and interesting for anyone, but it can become essential for the millions living with chronic conditions like diabetes, heart disease, and depression. WellDoc makes a prescription-only FDA-approved "patient coaching" system, which advises users on how much insulin they should take in light of information recorded on their smartphones: blood sugar levels, recent meals, and exercise. It also offers tailored messages of encouragement and provides the patient's doctor with treatment recommendations based on their data and established medical guidelines. A feature under development would enable the system to predict a hypoglycemic reaction and help users avoid it.

Ginger.io uses data collected (with permission) from a phone and other sensors to assess the behavior of people with mental illnesses such as depression. Are they calling loved ones, or getting enough sleep? When a patient is showing signs of struggling, someone can be alerted.

Over time, both companies will aggregate this information to help doctors study and improve treatment overall. "It's like one of the largest clinical trials in history," says Chris Bergstrom, WellDoc's chief strategy and commercial officer. "And it's not even in an artificial environment—it's in real time."

Families affected by Phelan-McDermid syndrome, a rare condition in which a deletion on chromosome 22 causes problems such as learning and memory deficits, are building a database of information from genomic tests, clinical medical records, extensive family surveys and histories, and more. The goal is to create a central repository where researchers can examine multiple sources of data simultaneously. That's increasingly important as researchers begin to see connections between Phelan-McDermid, autism, and other conditions. Another benefit: data that once would have been locked up in one academic researcher's lab will now be readily available to many different experts.

"So much of that data is already out there," says Megan O'Boyle, whose daughter Shannon was diagnosed in 2001, just two years after chromosome 22 became the first human chromosome to be sequenced. "It's just sitting there waiting to be used." —*Nanette Byrnes*

SOURCE: MERCOM CAPITAL GROUP

Q + A

More Phones, Fewer Doctors

VC legend Vinod Khosla believes that medicine will go mobile and most doctors will be out of a job.

● Famous as the founding CEO of Sun Microsystems, Vinod Khosla has spent the past 28 years as a venture capitalist. As a partner at Kleiner Perkins Caufield & Byers, he was involved in some of the technologies underpinning the Internet. Now 59, he is currently head of Khosla Ventures, where he sees a similar opportunity in medicine and is investing in digital health ventures that he predicts will reinvent the field. In June, he spoke to editor in chief Jason Pontin at the *MIT Technology Review* Digital Summit in San Francisco. Making no apologies for having picked some losers, including some of his high-profile bets on clean tech he declared, "I don't mind failing, but if I am going to be successful, it better be consequential."

Here is an edited version of the full interview.

"Much more precise medicine is possible. And I for one want it. Because our smartphones are on us 24/7, we can start to do much more." —Vinod Khosla

What surprised you the most when you turned your attention to health care?
What surprised me initially was how bad it was. Researchers gave the same data to 40 cardiologists and asked the same question: "Should this person have cardiac surgery or not?" Half said yes and half said no. Whether you get surgery depends on which doctor you happen to pick? That is pretty bad. And that's not the worst part. Two years later they took the same data to the same cardiologists, and 40 percent changed their mind. I could give you 100 examples like that.

You have concluded that about 80 percent of what doctors do can be replaced by machines. So tell me which things we can replace, which things probably should remain human, and why.
Atul Gawande is one of the most famous surgeons. He said machines are much better at the cognitive parts of medicine: diagnosis, writing the right prescriptions. On purely ethical questions, or comforting, humans can do much better. That raises a question that I always ask and that pisses the physicians off. If you want the human element of care, shouldn't we use the most humane humans?

Doctors don't always qualify.
It's hard to get into good medical schools. You select for IQ and hard work. You don't select medical school students for compassion. I think the role has yet to be defined. I'm not saying humans have no role. If you ask people in the burn unit of the hospital, do we need doctors there? Absolutely. Whether human plus computer is better—whether in certain parts of the world where there is no doctor for 50 miles, the machine will do much better—it's hard to predict.

You have invested in a number of mobile health companies like CellScope, the maker of a smartphone attachment which allows you to peer into the ear, that place the responsibility for health care on the individual. Do people really want that?
Yes. I've often said our goal in medicine should be to make the consumer the CEO of his own health. By that I don't mean the consumer should do his own diagnosis. But every home should have a digital first aid kit that has half a dozen to a dozen devices that let you take your ear image like CellScope, or let you take your EKG like AliveCor [another Khosla investment], or a dermatology image if you have a mole.

With the result being better medicine?
Much more precise medicine is possible. And I for one want it.

Because our smartphones are on us 24/7, we can start to do much more. Take psychiatry. We have a company called Ginger.io that monitors your cell phone with your permission. They collect thousands of data points a day. They figure out over a period of time what day of the week you call your mom. What you do on Thursday evening. Do you call your friends to make plans for the weekend? It figures out that this week you didn't eat. You didn't go from your bedroom to your kitchen. Your cell phone can tell that. They've discovered hundreds of new microbehaviors that can actually be predictive [of mental state]. If you can monitor people 24/7, you can move them from whatever stage of illness to be more healthy. I think that will become possible.

Wellness will become the point of health care. Today it's just sick care.

WIKIMEDIA COMMONS

Data Analysis

IBM Aims to Make Medical Expertise a Commodity

Big Blue thinks its *Jeopardy!* champion Watson can make money by offering health-care providers new expertise without hiring new staff.

● U.S. cancer care is headed for a crisis, warned the American Society of Clinical Oncology in March. Cancer cases are projected to soar 42 percent by 2025 as America's population ages, but the number of oncologists trained to treat →

them will grow by only 28 percent. That mismatch is likely to exacerbate existing inequalities in care between the fraction of patients treated by specialists at major academic centers and the many more who get care at community clinics or hospitals, mainly from general oncologists.

Enter a game show champion to save the day.

An attempt to transform cancer care is a major part of IBM's efforts to make money from its *Jeopardy!*-winning Watson software. The company aims to offer health-care organizations a cheaper way to improve care by turning oncology expertise into a commodity.

This effort to break humans' monopoly on cancer expertise is the advance guard of a model that IBM hopes it can eventually roll out across many areas of medicine. It is also the first real test of the company's claims that Watson can move beyond *Jeopardy!* and earn money.

Whether Watson passes the test could be critical to IBM. The company's revenue has declined for two years as technology's shift to the cloud has left some of its core products behind. CEO Ginny Rometty's promise to spend $1 billion on a new business group dedicated to commercializing Watson is just about the only turnaround prospect in sight.

IBM and collaborators are building two versions of Watson trained in oncology. Memorial Sloan Kettering Cancer Center, in New York, is beta-testing a version for lung, colorectal, and breast cancer. The University of Texas MD Anderson Cancer Center, in Houston, will use one this summer that advises its new fellows on treatments for leukemia. Both help oncologists decide on a treatment plan by ingesting the patient's medical records and pairing that information with knowledge from medical journals, textbooks, and treatment guidelines.

Lynda Chin, a professor of genomic medicine at MD Anderson and a leader of the center's Watson project, anticipates that in the future that kind of product will be highly valued by general oncologists and regional cancer practices. "Physicians are too burdened on paperwork and squeezed on revenue to keep up with the latest literature," she says. That limits the care physicians can deliver, and it has financial consequences: "If you can't make a decision based on your own knowledge, you have to refer the patient out, and that's going to hurt your bottom line."

A version of Watson to be tested this year with brain tumor patients from the New York Genome Center aims to provide oncologists with deep expertise in the new field of genomic medicine that would otherwise be expensive to obtain. This incarnation of Watson suggests treatment options based on details of the mutations detected in a person's tumor by genomic sequencing. Using genome sequencing to direct cancer treatment is just becoming feasible thanks to the plummeting cost of the technology. But in practice, the challenges of interpreting genomic data keep it beyond the reach of most oncologists and clinics.

"Physicians are too burdened on paperwork and squeezed on revenue to keep up with the latest literature."
—Lynda Chin
Professor of Genomic Medicine, MD Anderson Cancer Center

"It requires a heroic level of expertise and is entirely manual," says Ajay Royyuru, director of the computational biology center at IBM's Yorktown Heights lab. Doctors must chase down relevant research papers for the mutations they find in a patient's tumor, try to understand how the mutations change the cancer cells' physiology, and then work out which treatments could target the malfunctioning processes. Getting from a genome sequence to a treatment decision can take five to 10 months says Royyuru—time that cancer patients can ill afford.

80%
Proportion of data that is unstructured, coming from e-mail messages, photos, and doctors' notes

Using Watson, it takes minutes. Doctors need only load in the genomic data. A schematic is then generated showing which of the molecular processes inside a cell have been altered. An oncologist can explore those findings and click a button to see a list of possible treatments that would target the problem pathways.

Though technologically impressive, none of the Watson cancer projects are yet contributing materially to IBM shareholders or helping many cancer patients. Although the deals with medical centers are intended to lead to marketable products, they are for now R&D investments, says Michael Karasick, who leads R&D for the Watson group and was previously director of the company's research lab in Almaden, California. "Revenue comes when the product hits the market," he says.

Some already have. For example, a Watson-based system for the medical insurer Wellpoint helps preauthorize requests for medical procedures. But Watson-based medical products haven't been hitting the market at the rate IBM seems to have expected. A document leaked to the *Wall Street Journal* in January said that the Watson unit was falling behind on a projection that it would bring in $1 billion in revenue by 2018.

One problem is that Watson has struggled to accurately understand technical information. It's been flummoxed by medical jargon, the different ways researchers refer to the same thing in journal articles, and sloppy grammar in doctors' jottings on patient files. Clinicians have had to spend more time than anticipated teaming up with IBM software developers to chase down the misunderstood acronyms or wrongly parsed sentences that caused Watson to misinterpret medical records or suggest incorrect treatments.

Michael Witbrock, vice president of research at the artificial-intelligence company Cycorp, says that IBM's *Jeopardy!* winner was always going to need significant engineering to become an expert in

COURTESY OF MD ANDERSON CANCER CENTER

any specific area. The game show calls for a mastery of general knowledge at a shallow level, not the kind of deep, layered expertise needed to treat cancer. "They went after industrial scope, not industrial depth," says Witbrock.

Eric Brown, director of Watson technologies at IBM's Yorktown Heights lab, says major changes to Watson, informed in part by feedback from the cancer projects, have helped it adjust to its new work. Although there is still a human training process, improved machine learning means Watson now requires less training to get good results, he says.

A company getting started with Watson today can make use of interfaces including one that involves clicking thumbs up or down next to its answers to test questions. In addition, a new team within IBM's technical assistance group is dedicated to helping customers prepare data and use it to train Watson. Late last year the company launched a cloud-based platform where products can be built without having to bring IBM technology on site.

One thing those technical improvements haven't done is shed any more light on whether renting out software that acts like a medical specialist can be a big business. Some people in the health-care industry are unsure.

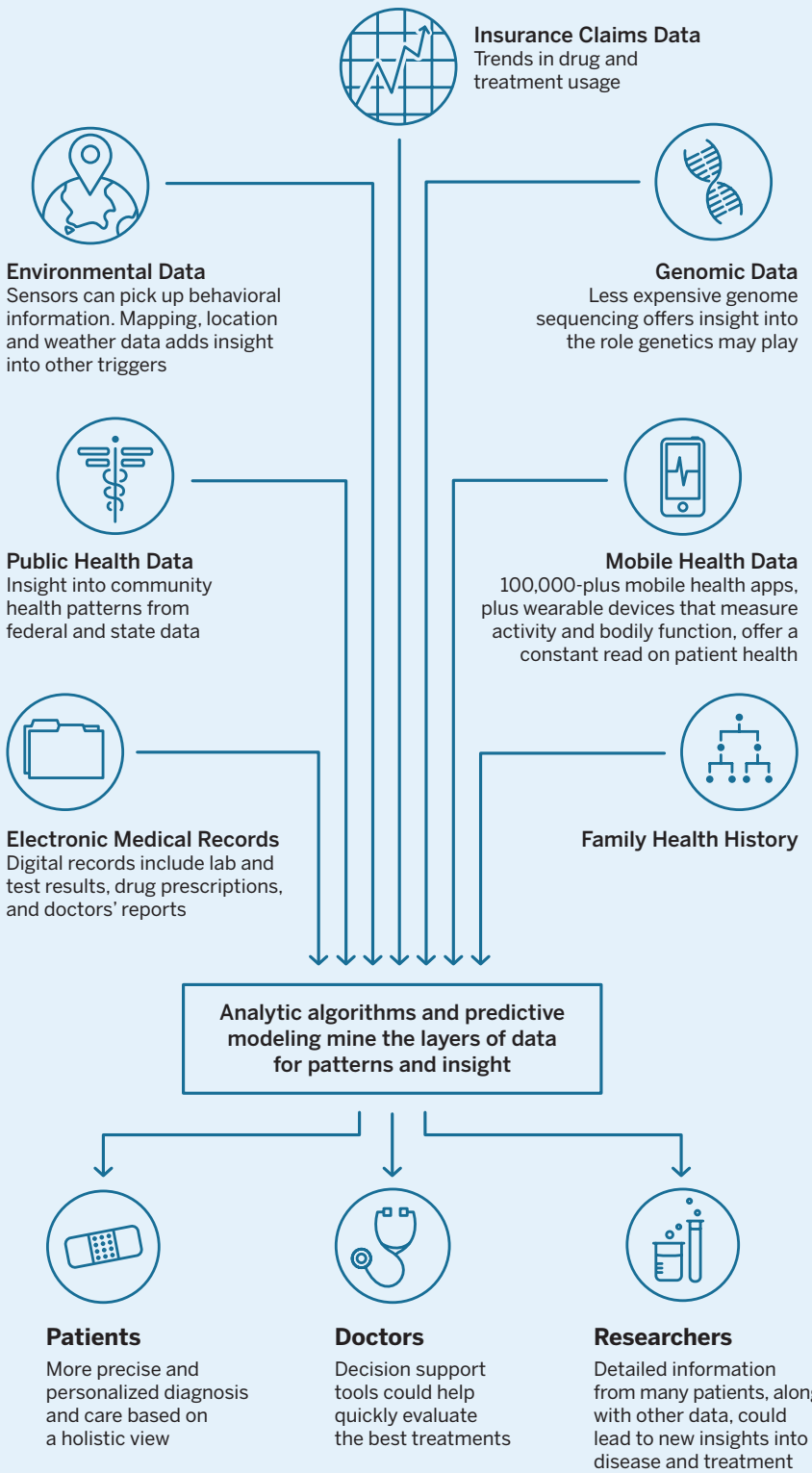
The most successful products built on advanced data processing historically have been focused on managing costs and efficiency in populations of many patients, not improving what doctors do with individuals, says Russell Richmond, a board member for the health-care data company Explorys and previously CEO of McKinsey's health-care division, Objective Health.

That kind of product speaks directly to profit margins and is in fact explicitly encouraged by the Affordable Care Act, which is reshaping the U.S. health-care industry. How products like the Watson-powered cancer advisors will provide that is less clear. As Richmond puts it: "Helping a cancer patient get the best treatment is really good for humankind, but it may not generate a lot of profit."

—Tom Simonite

The New Medical Data Ecosystem

Medical data is being captured today from many sources. Pulling it together and studying what it means is the next challenge.



Genomics

23andMe Tries to Woo the FDA

The DNA testing firm hopes a more coöperative approach with regulators will get its business back on track.

● Anne Wojcicki bounds into a conference room in Mountain View, California, straight from a five-mile ride from home on an elliptical bike. The 40-year-old cofounder and CEO of the consumer genetic testing firm 23andMe is breathless, and not just because of the workout. On this warm day in mid-June, Wojcicki is "super-excited" about an announcement scheduled for two days hence: the Food and Drug Administration has agreed to review a health-related genetic report the company wants to make available to customers.

It's the first step out of the FDA's doghouse for 23andMe. For $99, the company analyzes key components of a person's DNA from a vial of saliva, but last November the federal agency issued a testy warning letter barring it from marketing its service. The FDA said that by selling consumers a test and health reports that outlined their chances of getting dozens of diseases, plus their likely response to various drugs, 23andMe was effectively selling a medical device. That requires explicit approval—and the FDA said 23andMe hadn't come close to providing enough evidence that its test provides accurate, reliable health assessments.

The FDA allowed the company to keep selling the test as long as it provided only raw genetic data and ancestry information, nothing on disease. Sales slowed. Evidently, people care much more about their chances of getting Alzheimer's than about how much Neanderthal DNA they have. "A lot of companies would shut down in this situation, but we looked at how do we double down," Wojcicki says between sips from a water bottle. That meant talking frequently with the FDA, marshalling more data to support health claims, and hiring a number of executives experienced in medical devices.

230
Average number of studies in which a consenting 23andMe customer's genomic data is used

The company's plight reflects just how challenging it is to translate genetic data into useful medical information. Though the company encourages customers to seek a doctor's advice, making medical decisions based on tests like those from 23andMe carries risk. Current understanding of genetics' role in disease is far from complete, often not conclusive, and potentially misunderstood, says George J. Annas, chair of the department of health law, bioethics, and human rights at Boston University's Schools of Public Health, Medicine, and Law.

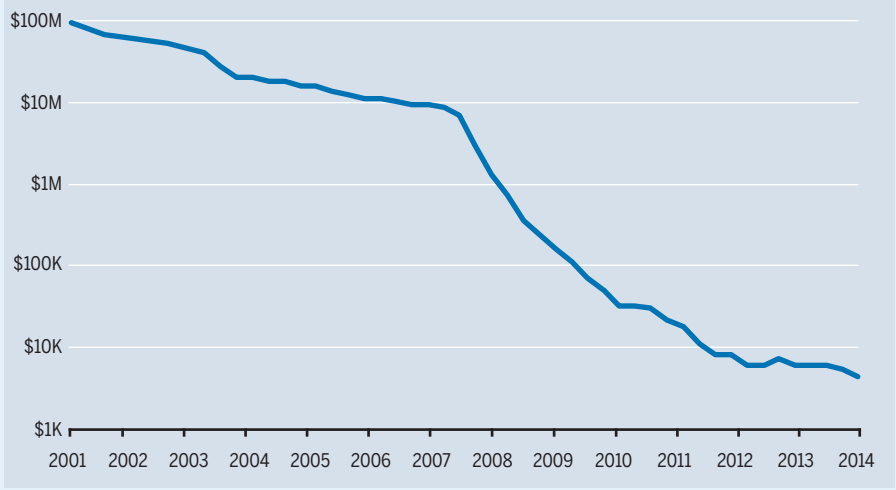
Nevertheless, some experts say it's up to consumers to decide how to use the data, and that access to genetic data and information on what it might mean is a basic right. "It's no different from a family history," says Lawrence Lesko, a 20-year FDA veteran who is now director of the University of Florida's Center for Pharmacometrics and Systems Pharmacology.

At times 23andMe has hurt its own cause. A year after submitting applications for seven health reports in 2012, it stopped communicating with the FDA for six months, according to the agency, at the very time it prepared to launch a television ad campaign. That's what prompted the FDA to clamp down.

The company, which has raised $126 million in funding, needs to fix its FDA issue if it is to meet its goal of creating a database of as many as tens of millions of genetic profiles, up from 700,000-plus today. Coupling those profiles with data from customer health surveys could entice pharmaceutical and medical-device companies to pay 23andMe for the chance to look for connections among gene variations, diseases, and drug response at a small fraction of the cost and time needed to do traditional clinical trials. Genentech has already paid the company to help it recruit breast cancer patients who had taken its drug Avastin in order to assess their response. The strategy of crowdsourcing big data echoes that of one of 23andMe's big investors: Google, which was cofounded by Wojcicki's husband, Sergey Brin. (They separated last year.)

Even before last November's letter, the challenges of meeting regulatory requirements had already prompted 23andMe's U.S. rivals to exit the market for direct-to-consumer genetic tests. Other testing firms bypass the FDA by selling through doctors. If 23andMe can't get FDA approval on at least some health reports, that could spell the end of selling genetic informa-

DNA Data for All?
The cost of sequencing a human genome has dropped.



SOURCE: NATIONAL HUMAN GENOME RESEARCH INSTITUTE

tion directly to consumers within the U.S., says former FDA counsel Patricia Zettler, a research fellow at Stanford Law School.

To win over the FDA, Wojcicki is first shepherding one specific health report—for Bloom syndrome, an inherited disorder that often results in deadly cancer by the mid-20s—through the approval process for medical devices. If it works, it would provide a template. But since 23andMe originally offered more than 200 health reports, it's not yet clear that this process will be enough to attract large numbers of new customers.

Zettler is one of many observers who think 23andMe will eventually get through the FDA process, at least on individual health reports. But the FDA is contemplating new hurdles, like requiring that claims be reviewed by an expert panel.

Wojcicki wonders if too many limitations will simply spur people to take their genetic data to Canada or China for interpretation. "How do you regulate information?" she asks. "I'm not sure you can hold it back." *—Robert D. Hof*

Mobile

Mobile Health's Growing Pains

Full of promise, mobile health still needs to wow patients and nail down its payoff.

● Among technologists, mobile health is thriving. Since the start of 2013, more than $750 million in venture capital has been invested in companies that do everything from turn your smartphone into a blood pressure gauge to snapping medical-quality images of the inner ear. Apple, Qualcomm, Microsoft, and other corporate giants are creating mobile health products and investing in startups.

The idea is straightforward: the increasing number of smartphones means that small, inexpensive sensors, low-energy Bluetooth, and analytic software make it possible for patients and doctors to capture all kinds of data to improve care. Patients can play a more active role in their own health. Doctors and nurses can make house calls without ever leaving the office.

One crucial group, however, remains unsold: the patients. Though one in 10 Americans owns the type of tracking device made by Nike, Fitbit, and Jawbone to monitor steps taken, quality of sleep, or calorie intake, more than half of those devices are no longer in use, according to Endeavour Partners, a consulting firm. Of the 100,000-plus mobile health applications available for smartphones, very few have been downloaded even 500 times. More than two-thirds of people who downloaded one have stopped using it, according to a 2012 study done for the global accounting firm PWC.

"There are unrealistic expectations for when and how mobile health is going to come together," says Patty Mechael, former executive director of the mHealth Alliance, which helped develop early standards for mobile health technologies. In the ⟶

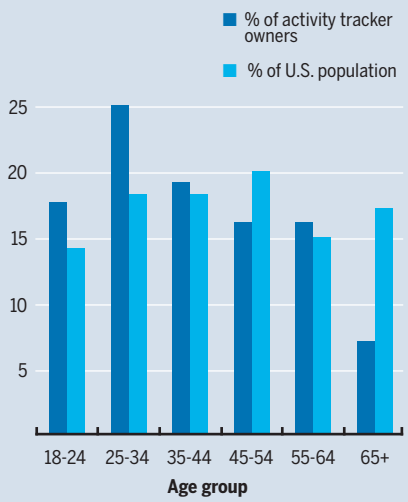
Mobile Health-Monitoring Devices

There's been an explosion in smart devices that measure and monitor various bodily functions. **BY RACHEL METZ**

COMPANY	Propeller Health	CellScope	Google	Withings	Kolibree
FEATURES	Propeller sensor attaches to an inhaler used for asthma or chronic obstructive pulmonary disease and tracks when and where the inhaler is used.	Diagnostic device that attaches to smartphones; the first is a digital otoscope that works with an app to let you view and record images of the inside of the ear.	A contact lens with a circle-shaped layer of electronics for testing the level of glucose in tears—potentially useful for people with diabetes.	The Pulse O_2 includes an optoelectronics sensor and green and red LEDs to measure heart rate and blood oxygen level. An accelerometer tracks activity and sleep.	An electric toothbrush equipped with an accelerometer, gyrometer, and magnetometer to track brushing habits, plus smartphone games controlled by brushing.
PRICE/ AVAILABILITY	Received FDA approval in May.	Price is yet to be determined. Expected to be available sometime this year.	Google is talking with the FDA and intends to find partners to make it.	$120	$129–$199; three replacement brush heads $20 to $25. Expected in late 2014.
DATA SHARING	Users decide what's shared with doctor and whether to share anonymously to help identify asthma hot spots and triggers.	Users can upload ear videos to a CellScope site, where a doctor can see them.	N/A	No data communicated, though data could be shared with your doctor.	You can choose to share data with your dentist.
FINANCIAL BACKERS	Kapor Capital, the Social+Capital Partnership, Calif. HealthCare Foundation	Khosla Ventures, Rock Health	N/A	360 Capital Partners, Ventech Capital, Idinvest Partners, Bpifrance	Angel investors

Stepping Up

Younger age groups are more likely to own an activity tracker.



U.S. "we are somewhere between the peak of the hype cycle and the trough of disillusionment," she says.

Enthusiasm has been slow to build in part because the technology is often still not perfect, with seemingly simple functions like step counters lacking precision. Another problem is motivation. Many people simply don't seem to like using these apps and devices. It is clear, though, that a well-designed mobile health system can help if patients use it.

At the Center for Connected Health at Partners HealthCare, a health-care network that includes Boston's two leading hospitals, Brigham and Women's and Massachusetts General, a number of mobile programs have been shown to offer strong payoffs both in quality and cost.

One recent study tested whether mobile phones could help increase activity among patients with diabetes. It's an important way to combat the disease's progression, but it's something traditional programs have had little success achieving. Of a group of 130 patients with diabetes, half were given Fitbit activity monitors. By combining feedback from the Fitbit with existing patient records, an algorithm determined which text messages would be sent to the patients. Those falling behind on their goals got messages of encouragement; some messages included information about nearby Zumba classes or jogging paths, based on location data picked up from the patients' mobile devices. On rainy days, the program might send a note about ways to exercise indoors.

Doctors received progress updates via a stoplight system displayed on the patient's electronic medical record. Green meant the patient was doing well. Yellow was caution. Red signaled the patient was not responding to the text messages.

After six months, the average patient was walking about a mile farther each day. In addition, the patients' blood sugar control improved significantly—better results than might be expected with some FDA-approved drugs, says Kamal Jethwani, a doctor who ran the study as the center's leader of research and program evaluation.

For Partners, the program is successful on two counts: patients are healthier, and the cost of caring for them is lower. The payoff of better managing a chronic disease like diabetes comes over many years, but in Jethwani's study, a number of patients have already had drops in blood sugar that equate to savings of $1,000 to $1,200 in doctor visits and other treatments. That's a strong return on a program that costs $300 per patient to run, notes Jethwani.

These are the kinds of results that have enthusiasts convinced that mobile technology can not only fundamentally overhaul how health care is delivered, but also offer sufficient financial benefit to convince insurers and patients to pay for it.

John M. Halamka, a professor at Harvard Medical School and chief information officer of Beth Israel Deaconess Medical Center, expects this kind of technology-enabled monitoring to become standard practice within the next few years. One sign that a heart patient may be about to have a problem is rapid weight gain, he notes. A smart scale that picks up on that could trigger a quick intervention from the doctor and avoid a visit to the ER.

At the University of California San Francisco, which recently announced an initiative to begin testing the effectiveness of mobile devices in health care, one of the biggest technological achievements to date was simply starting to get doctors to move beyond pagers. Now doctors access patient messages via a mobile or Web application, and the message automatically becomes part of a conversation. Under the new system, the whole care team is aware of what is happening, and the doctor has the patient's history available when fielding questions. A program is being tested that would take this to the next level, allowing care providers to send messages to patients.

Getting mobile health technology right can be tricky, however. Fitbit makes some of the most popular activity trackers, but in February the company voluntarily recalled its top-of-the-line $129 Fitbit Force after users complained of skin irritation from the wristband. More serious technological problems have sidelined devices aimed at difficult tasks like measuring blood glucose levels without drawing blood, a desirable feature for people with diabetes.

Though one in 10 Americans owns the type of tracking device made by Nike, Fitbit, and Jawbone to monitor steps taken, quality of sleep, or calorie intake, more than half of those devices are no longer in use.

For all the challenges in mobile health, one issue that dominates many discussions about the technology may fade rather quickly. Privacy concerns have yet to come up in the Partners trial, says Jethwani. "I've never heard any patient say, 'How do you know so much about me?' or 'Why do you know so much?'" he says. "Instead, they say 'Now that you know all this about me, can you give me more useful information?'"

—Nanette Byrnes

SOURCE: ENDEAVOUR PARTNERS; COURTESY OF JAWBONE

Case Study: Mobile Health

Blood Sugar Crash

Many have tried to develop a painless, continuous glucose tracking system, but all have failed. C8 Medisensors may have come the closest.

● In October 2011, Paul Zygielbaum was trapped in a business meeting when he started feeling unwell. Zygielbaum was then CEO of a startup called C8 Medisensors, which was developing a smartphone connected blood sugar monitor, and he has type 2 diabetes. He suspected that his blood sugar was dropping. Stuck in the meeting and surrounded by pastries and Jolly Ranchers, he popped one of the hard candies into his mouth and pulled out his phone. It displayed readings sent wirelessly from a C8 monitor strapped to his abdomen. The phone confirmed that his blood glucose was below normal. As the sugar in the candy took effect, "I was watching my glucose go back up on the phone," Zygielbaum remembers.

The other people at the meeting took notice. "They weren't worried about me," he says. "They were stunned by the technology." One of them, Wade Randlett, an investor, watched as Zygielbaum showed the results to another attendee and was "impressed enough to end up writing him a check," Randlett recalls.

C8 Medisensors was tackling a longstanding and tricky problem: creating a convenient and discreet way for people with diabetes to monitor their blood sugar continuously, without having to draw blood.

It was a technological challenge that some 70-odd companies had already tried and failed to overcome, Zygielbaum says, but by the time of his impromptu conference room demonstration, C8 seemed to have hit on the solution. The company had more than $60 million in funding from investors including GE Capital, GE Healthcare, and private individuals, and a manufacturing facility in San Jose was on board. A year later, in October 2012, European regulators approved the sale of its system. Seemingly on the verge of commercialization, the company began taking reservations through its website.

But before the end of that winter, C8's amazing run would end. The technology was good but needed to be a bit better, and manufacturing was inconsistent. The company needed more money, perhaps $15 million, to fix those issues, says Zygielbaum. C8 couldn't raise it.

Without that cash, C8 quickly failed, closing its doors in February 2013. It was an illustration of how many things—technological, financial, and human—must come together perfectly for a startup to make it in mobile health.

This was not the coda C8's founders had imagined 10 years earlier, when they formed the company after testing ideas in a laser lab built in cofounder Robert McNamara's backyard. McNamara and Jan Lipson, two of Zygielbaum's old Caltech roommates, contacted him to see if he would help. Zygielbaum, a mechanical engineer and MBA, was undergoing cancer treatment at the time, but their idea for a noninvasive way to monitor glucose was so compelling he signed on as a cofounder.

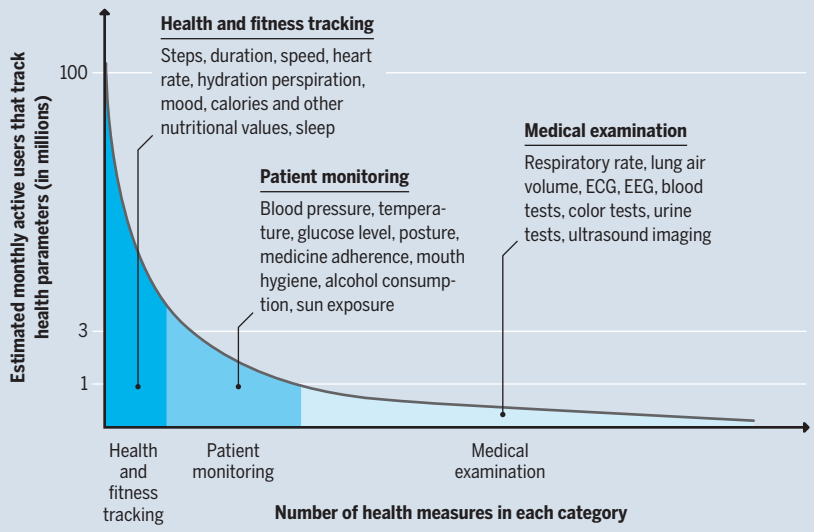
An ideal glucose monitor would avoid breaking the skin, to prevent pain and risk of infections. It would also provide nearly continuous, automatic measurements, to make tracking blood sugar less intrusive and to better meet the needs of insulin-dependent diabetics, who need to keep tight tabs on their blood glucose.

Current options for checking blood sugar are inconvenient and uncomfortable. The most common involves pricking a finger to apply a small drop of blood to a testing strip, which is then read by a glucose meter. While highly accurate, these measurements provide only intermittent peeks into blood glucose levels that change throughout the day. Patients can also wear a continuous glucose monitor that has a needle-like sensor inserted under the skin and usually attached to a larger device taped to the body. Such monitors provide readings every few minutes, and they help people avoid the devastating effects of blood sugar lows or highs, but they're less accurate than a blood test. Both require blood-drop readings multiple times a day for calibration.

C8's team thought it could use a measurement technique called Raman spectroscopy. Its device would be strapped around the abdomen and would shine a beam of light into the skin to measure

What We Measure

Fitness apps are the most popular type of mobile health app



SOURCE: RESEARCH2GUIDANCE

glucose levels in the fluid that bathes skin cells. It could send readings wirelessly to a smartphone for a near-continuous record of glucose changes throughout the day.

The potential market was huge. Today, 382 million people around the world suffer from diabetes, according to the International Diabetes Federation. Market research firm GlobalData estimates that the worldwide market for blood glucose monitoring was $8.9 billion in 2010 and could grow to $12.2 billion by 2017.

To compete in that market, C8 first had to overcome a number of technical challenges. "Glucose is a small molecule in and of itself," explains Ishan Barman, a bioengineer at Johns Hopkins University who is also trying to develop a noninvasive glucose tracker based on Raman spectroscopy. "There are lots of other [compounds] in the bloodstream which are found at a much higher concentration," he says. Because noninvasive systems don't directly test blood glucose, the changes in their readings can lag behind direct readings of the blood, he says. Noninvasive measurements do have advantages, however. Because they can be taken nearly continuously, they can be used to predict whether future glucose levels will move higher or lower. Continuous measurements also provide immediate feedback about the body's response to treatments.

382 million
Number of people who suffer from diabetes worldwide

Developing software to translate the spectrographic readings into glucose levels is tricky, says Barman. Because the light used in Raman spectroscopy doesn't penetrate very deeply, the system calculates blood glucose levels on the basis of glucose levels in the skin, and that calculation can vary from person to person, he says.

That variability from user to user, and even from spot to spot on the same user, proved to be C8's greatest challenge. Some problems were driven by manufacturing variability, says Zygielbaum. The way the device was mounted on the skin could change the readings as well.

Compounding those technical challenges were a series of incredible personal misfortunes. One of the founders, Jan Lipson, died in a biking accident in July 2010, just as the first prototypes of the final, miniaturized version of the device were being tested by volunteers. The progression of Zygielbaum's cancer slowed but later picked up again, which was probably what caused him to develop diabetes. Zygielbaum had to step down in the middle of the last round of fund-raising for the $15 million, and his replacement died in an ice-hockey accident just five weeks after.

"That took the heart out of the investors," says Zygielbaum.

Even under the best of circumstances, funding the development of a new medical device is difficult, says Fred Toney, chief financial officer at C8 during its final two and a half years. "One reason the venture capital community has increasingly been stepping back from funding private medical-device companies is they are hard and take a lot of capital," he says.

After C8 shut down, the technology was sold to a small private equity group that continues to work on it, says Toney. "Whether used for glucose or other things, it's a technology that will certainly come to market," he says.

Some diabetics had been closely watching C8's progress. "If it had worked with sufficient accuracy, I believe many would have jumped at the chance of buying C8's product," says Mike Kendall, who was diagnosed with type 1 diabetes in 1991 and writes a well-read blog about living with the disease. "I know I would have."

Others continue to chase the dream of a needleless, continuous glucose monitor for commercial use. An Israeli company called Integrity Applications expects to begin selling its GlucoTrack system, which detects glucose using ultrasonic, electromagnetic, and thermal measurements through an ear clip, in Europe this year. Barman's team is starting to test its system as well. Despite C8's demise, he thinks the field has advanced impressively. "I see this as a much more hopeful time than 10 years back," he says.

—Susan Young Rojahn

Case Study: Mayo Clinic

Data in Action

Data is helping one of the country's leading hospitals solve tough medical questions.

● At Mayo, big data is already improving health care. Consider the case of Javrie Burdell.

The six-year-old from Clovis, New Mexico—a cheerful lover of cartoon movies like *The Nut Job*—had his first seizures at two years old. Josiah and Renata Burdell, both 29, took him to a local hospital. That first night, Javrie's respiration slowed to four breaths a minute. "Watching your child lie unconscious on a table for an hour is pretty real," Renata says.

Puzzled doctors sent the family to Lubbock, 100 miles away, then 220 miles in the other direction to Albuquerque. Seizures continued, diagnoses multiplied, and his parents say Javrie's development regressed. The Burdells went to four hospitals before, fed up, they Googled the top pediatric neurology departments in 2010, then wrote to Mayo.

The tests continued at Mayo. A spinal tap, an MRI, and tests for genes linked to known disorders were all negative.

In September 2012 the hospital opened its Center for Individualized Medicine, an interdisciplinary effort to use genomics to identify diseases that have stumped the world's top hospitals, and Javrie became one of the first patients in its Disease Odyssey program. The idea of Disease Odyssey: to sequence patients' exomes—a subset of the human genome that includes all the body's important instructions for building proteins—and use resulting data to comb for clues.

After years without a diagnosis, some 37 percent of patients get one within about three months, says Gianrico Farrugia, a gastroenterologist who directs the center.

Javrie's journey took longer. Even after he came to Mayo, it took years for members of the hospital's team of 369 data

scientists to invent the technology that would diagnose him as one of 10 children on earth with a mutation so rare the syndrome it causes has no name. To a six-year-old, it was a simple blood draw, taken last July. Javrie's parents also supplied DNA samples. Behind the scenes, much more was happening, Farrugia says. In cases like these, samples are sent out for sequencing and analysis. Data is compared with medical records, published literature, and normal genomic patterns to try to forge a diagnosis. A team of as many as 20 people, from geneticists and pathologists to ethicists, review each pending case every Wednesday.

On January 3, the Burdells were told that their results were ready. After an 18-hour drive, they learned that Javrie has a mutation on the *PACS-1* gene. That accounts for his balance problems and subtle facial abnormalities—a slightly bulbous nose and widely spaced teeth that many people don't initially notice.

Big data gave the Burdells the comfort of understanding the cause of their son's challenges, but it did not provide a cure. "It's really kind of a bittersweet deal, but our life's better," Renata Burdell says. Still juggling symptoms and medications, she and her husband hope the next wave of data unlocks therapies for a little boy who still knows only 160 words.

Most times, of course, big data in health care focuses on simpler problems that affect more people—crunching data from many sources to spot similarities between cases, identifying treatments that work best and cost least. At Mayo, that means efforts like the three-year-old Center for the Science of Health Care Delivery, which studies innovations in organizing care. The center's projects include a series of departmental clinical engineering labs, each managed by a clinician in that specialty and a data scientist. The first lab was built for emergency medicine.

The ER at Mayo's Saint Marys campus is now taking advantage of an ongoing renovation to embed RFID equipment in the walls, the better to study patient flow. In a year, Mayo hopes to have better data on how it keeps track of patients, how long it takes to get them seen by a doctor, and how long they stay in the ER, says Tom Hellmich, a pediatric ER doctor and one of the managers of the lab studying the emergency room. Of special note: a project to understand and solve the problem of psychiatric ER patients who need to quickly find spots in programs that can help them. Data from that effort should be useful to both hospital administrators and legislators interested in mental-health reform, says Kalyan Pasupathy, co-director of the Emergency Department Lab.

Of all Mayo's data initiatives, the effort that may have the most long-term impact is the partnership last year with United Health Group's data-analysis unit, called Optum Labs.

The idea is to study claims records from 109 million patients, contributed by Optum, and 30 million medical records, including five million from Mayo. Research under way is investigating such topics as how compounds' performance in clinical drug trials compares with their effectiveness in large patient populations once approved; how medical practice varies in different locations; and how to attack problems like excessive hospital admissions.

As changes in policies and insurance shift more cost to patients and providers, there are financial as well as medical reasons to pursue this kind of research.

One study of joint-replacement patients under 65 found that weight and diabetes played previously unknown roles in knee and hip problems, says Nilay Shah, associate professor of health-care policy and research at Mayo. Early intervention could mean fewer operations.

"Is this big data, or just lots of data?" Mayo CEO John Noseworthy said at a conference last year. "This really is big data. This looks for associations we didn't predict or anticipate and lets us really change the story." *—Tim Mullaney*

Personal health data flows in hundreds of directions. The Data Privacy Lab at Harvard University found that only half of those transmissions are covered by HIPAA, the federal law that governs patient privacy and data sharing.

The lab's interactive maps show where patient data is sent and by whom, noting the potential privacy breaches.

Q+A

Big Data Mining

Isaac Kohane is inventing new tools for medical analytics.

● Over the past decade, health-care providers have spent tens of billions of dollars to digitize their patients' medical records. In theory this should be providing researchers with a treasure trove of data to dig through for evidence of the effectiveness and efficiency of care. In practice, it's more complicated.

Data from these records can be hard to access and difficult to make sense of once it is in hand. Patient privacy issues and data security are of increasing concern and have yet to be fully addressed.

Isaac Kohane, co-director of the Center for Biomedical Informatics at Harvard Medical School, has spent the last 20 years working to pull meaning out of large sets of health data. A pediatrician with a PhD in computer science, Kohane mined medical data to discover the risk of heart attack for patients on one widely prescribed diabetes medicine, Avandia. After his study the drug was pulled off the market. His other research has identified early warning signs of domestic abuse and revealed the variations and patterns among patients with disorders such as autism. He spoke with senior editor Nanette Byrnes.

Has this multibillion-dollar investment in electronic health records led to better health care, or at least a better understanding of the quality of care?
You can't have accountable care if you can't count. But you'd be dismayed. If you ask any large health-care system, "How many patients do you have with this characteristic? How many patients of this kind did your doctors see? What was their average length of stay?" they will not know.

I do not believe it's overly cynical to note that many electronic-health-record vendors have touted the ability to bill more effectively for care using electronic records than paper records. [Records that doctors submit to insurance companies] for reimbursement are obviously biased to maximize the income of the health-care system. It may not necessarily reflect the on-the-ground biological or clinical truth.

One oft-cited goal of medical analytics is to combine a patient's health records with information from his or her genome to create a very precise kind of personalized medical care. But that also seems far off.
In addition to all the challenges of genomic data by virtue of its volume and complexity, no major electronic-health-record vendor supports it. A lot of electronic health records, if you look under the hood, are fairly antiquated. Even though they have a modern skin, they are really state-of-the-art 1980s technology, so integrating them with all the existing genomic tools is a very high bar. Even perhaps more important sometimes than the genome is knowing family history and knowing it in a structured way. But that is not done in most electronic health records, either. The bulk of our health-care data comes from [insurance] claims data and electronic health records, period. And maybe a little bit of public health data.

You and your colleagues have created two platforms with the idea that developers would write apps that could unlock what is in electronic health records.
I do not believe the answer is to tear down all these [electronic-health-record] dinosaurs. Work has gone into them, a lot of thought has gone into them, and you don't want to rebuild all the back-end stuff. The apps give you modern functionality.

What's an example?
A detailed family history is on average the most informative [information] for understanding inherited disease risk. Yet very few electronic health records provide the capability to easily enter a family history and link it to the broader genealogy of the family. There are several highly successful Web apps that are low-cost and yet allow entry of highly detailed family history—and by virtue of their market success allow linking of a small family's history to a much larger genealogy. With a platform like ours you can adapt these modern Web apps to provide a legacy electronic health record with a state-of-the-art family history record.

Even with the technology to mine these records, you say doing that accurately can be tricky.
I am concerned that it's all too easy to see the data and say, "I've been doing big-data analysis for Target and now I can do it for medicine." That turns out not to be true. You really have to know something about medicine. If statistics lie, then big data can lie in a very, very big way.

When you are looking for adverse events in drugs given for diabetes, for example, it's pretty tricky if one of the adverse events you are looking for is heart attacks, because heart attacks are also a result of poor diabetes care—the same reason for which the drug is being given. So consequently, if you just willy-nilly said "Just give me all the drugs with a high rate of heart attack," of course all the diabetes drugs would light up. Instead what we did was say, "Let's compare the different drugs that are used in the same way and belong to the same class of drug and see if we can see different rates of heart attack if we control for all the other aspects." And sure enough, we found one such drug. It was called Avandia, and compared to another similar drug, it had a much higher heart attack rate.

"I am concerned that it's all too easy to see the data and say, 'I've been doing big-data analysis for Target and now I can do it for medicine.' That turns out not to be true. You really need to know something about medicine. If statistics lie, then big data can lie in a very, very big way."

There is a lot of concern that compiling databases of health records could result in personal information becoming public. Does that worry you?
The more I know about someone, the more I can do useful things for them, and the more I know about them the more I can discover. And the more you blind me to things, the less useful I'll be. The only real protection is that the people who have the authorized use of the data have to understand what is the right code of conduct.

Transparency

Big Pharma Opens Up Its Big Data

Normally super-secretive, pharmaceutical companies open up in the hope that sharing data will get sluggish drug pipelines flowing.

● When British pharmaceutical giant GlaxoSmithKline announced in October 2012 that it planned to make detailed data from its clinical trials widely available to researchers outside its own walls, the scientific community was stunned. For a company that spends $6.5 billion a year on research and development, it was a sharp turn away from the system of data secrecy that had made it one of the world's

largest drug companies, with 2013 sales of $43.6 billion.

The announcement came a few months after the company pled guilty to misdemeanor charges in the U.S. that it had marketed drugs for unapproved uses, based on improperly reported clinical trial data, and failed to report safety data on another drug later shown to raise the risk of heart attacks. Given the timing, many wondered if GSK's move was more about rehabilitating its image than embracing data transparency.

GlaxoSmithKline's efforts since could turn those skeptics into believers. In May 2013, the company began posting its own data online. Then it invited others to join ClinicalStudyDataRequest.com, where GSK and six other drugmakers have already uploaded data from nearly 900 clinical trials, and more than a dozen research projects are under way.

Trial transparency is appealing thanks to a growing sense that it could make drug development more efficient, saving the industry billions while also getting breakthrough therapies to patients more quickly.

In the United States, health reform has increased the pressure on insurers and government payers such as Medicare to control costs, in part by paying for treatments that are targeted to the patients most likely to benefit from them. If researchers could see the mistakes made by rivals in the past—compounds that were too toxic or not potent enough—they could design better trials. Those could, in turn, get new drugs to market faster—tempting to an industry that spends $150 billion a year on R&D globally but still fails to find enough new hits to replace its aging blockbusters.

Balancing secrecy and privacy concerns with the potential benefits of data sharing required new technological tools and an unprecedented level of coöperation among companies that typically consider themselves fierce rivals.

For GSK, the project started several years before the 2012 announcement as an internal platform that allowed researchers to scrutinize data from past clinical trials. Moving that data outside the company required scouring away any details that might compromise patient privacy.

To preserve the integrity of the data—to prevent users from e-mailing it to people who weren't authorized to see it, or surreptitiously altering it in any way—GSK hired the software analytics firm SAS to build a sort of data castle and moat, says Matt Gross, SAS's director of the health and life sciences global practice. SAS built a secure environment in which approved researchers could access a suite of tools to allow them to crunch the numbers.

The site allows researchers, for the first time, to obtain data on the same topic from many companies simultaneously. "We can combine all of the evidence from many studies to get one overall result," says Sarah Nolan, a research assistant in medical statistics at the University of Liverpool. Nolan is working on a three-year research project designed to determine the clinical utility and cost-effectiveness of various epilepsy treatments. She uses ClinicalStudyDataRequest.com to look at factors such as whether the age of the patients affects their responses to drugs and what prompts some patients to drop out of trials—details that speak to the tolerability of drugs but are rarely reported in standard published trials.

Transparency is spreading. France's Sanofi, in addition to putting its trial results on ClinicalStudyDataRequest.com, has posted three prostate cancer trials on Project Data Sphere, a pharma-supported site aimed at using data sharing to speed up the development of new cancer cures. Companies such as Johnson & Johnson and Pfizer are erecting their own data-sharing sites.

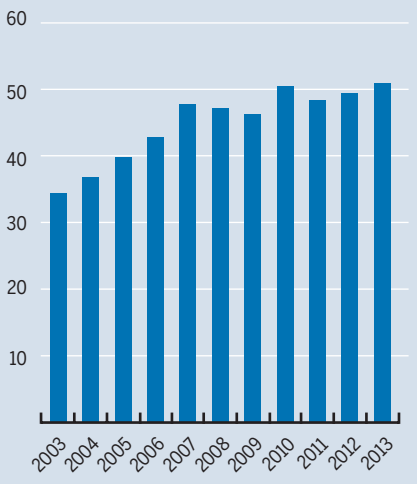
As for GSK, widely credited with starting the transparency trend, it continues to build upon the platform it invented. The company has posted 450 studies online, says Perry Nisen, GSK's vice president for science and innovation. And after having initially promised to release clinical trials from 2007 forward, it is now disclosing research dating back to 2000.

This new age of openness could lead to further and wider-reaching changes. Philip Huang, vice president of strategic planning and operations for Sanofi, says the next step will be to unify the procedures followed in clinical trials. In September 2012, Sanofi, GSK, and Roche helped found TransCelerate BioPharma, a nonprofit that creates standards for collecting and reporting clinical-trial data. "It will essentially give investigators a single playbook, if you will, for how to do clinical research," Huang says.

—Arlene Weintraub

Big Spender

Research and development expenditure of the U.S. pharmaceutical industry (in billions of U.S. dollars)



SOURCE: THE PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA

"If you asked my mother her attitude toward privacy, she would say, 'Oh, I never want anyone in the community to know my medicines or my diseases.' What you see in the 20-year-olds is, 'What's the big deal?' Over time the medical privacy preferences of individuals will change."

—John D. Halamka

Chief Information Officer, Beth Israel Deaconess Medical Center

Digital Data

Modernizing the Medical Record

As medical data goes digital, patients gain power.

● In April, a San Francisco–area startup called BaseHealth announced health-management software that integrates diet, exercise, genetic tests, and medical records, then calculates a patient's risk for more than 40 diseases—including type 2 diabetes, lung cancer, and Alzheimer's disease—and suggests ways to lower the risk of developing them.

Along with Apple's recent announcement of its Health app, which compiles data from other apps that track activity and medical data into a single dashboard, and a similar initiative from Samsung, BaseHealth's software is part of a push for a new kind of electronic health records that integrate both personal and medical information.

BaseHealth founder and CEO Hossein Fakhrai-Rad calls the current approach to medicine fragmented. "You don't have a 360-degree complete view of health," he says. Looking at just one piece of the puzzle hampers preventative health care, he adds. Type 2 diabetes, for example, which runs in Fakhrai-Rad's family and was the subject of his doctoral research, remains, for all its complexity, a preventable disease. Doctors often look at diet but ignore other risk factors like genetics, he says.

"[Genetic data] is one more piece of patient care data that helps motivate and excite patients," says Katherine Sutherland, a physician in Silicon Valley who recently began offering BaseHealth's application to some patients. "No matter what any results show, you are going to recommended improving diet, exercise, and lifestyle, but you've got a lot more force to show them why it's going to work," she says.

BaseHealth's program integrates lifestyle information, genetic data, and medical records data, all under the guidance of a doctor. Other offerings from companies like Apple promise to integrate medical information with lifestyle data, but those products don't require the involvement of a doctor, whereas patients using BaseHealth can't even get their full results until a doctor grants them access after an in-person consultation. "We are including physicians because we believe they are a key factor in the health ecosystem," says Fakhrai-Rad. That involvement distinguishes BaseHealth from other personal genetics companies like 23andMe, which was censured by the FDA in November 2013 for marketing health reports directly to consumers.

$24.4 billion
Federal incentives paid to doctors and hospitals for adopting EHRs

Before a patient can use BaseHealth, a doctor must upload information, such as prescription history and physiological measures like blood pressure, that would commonly be found in an electronic medical record. The patient can then upload lifestyle and family history data. The doctor can add a patient's genetic analyses by ordering genotyping or whole-genome sequencing from one of BaseHealth's lab partners. All that information is then crunched together to provide an overall risk assessment for various diseases and recommendations for changes to the patient's diet or exercise routine, based on peer-reviewed journal articles. Doctors can tweak the recommendations according to their own familiarity with the patient. "Physicians can override to say don't do this, do that," says Fakhrai-Rad.

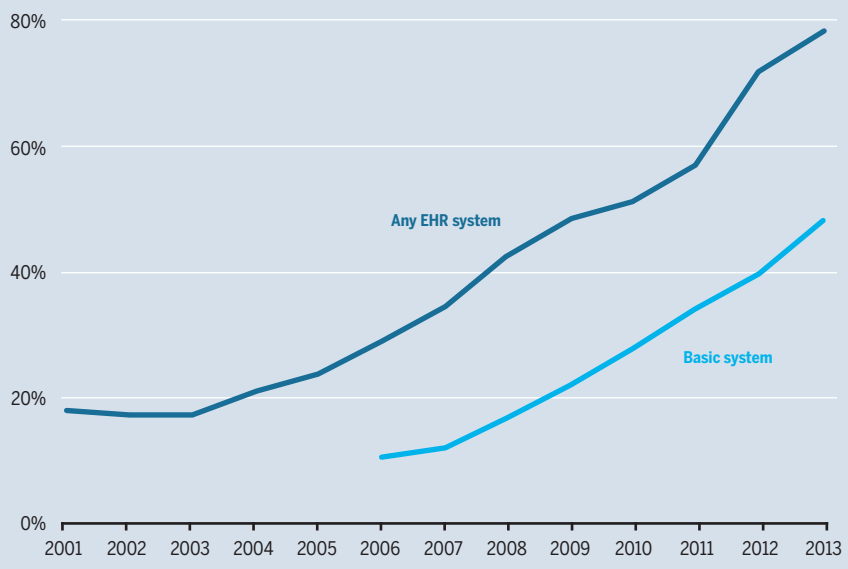
Increasing patients' access to their medical records could help them and their doctors make health decisions together, says Helen Burstin, chief scientific officer at the health-care-focused National Quality Forum.

It could also help patients to make medical decisions based on their own judgment, rather than relying completely on a physician's advice. "When patients are armed with better information about the potential risks and benefits, they may make a decision that may be different than what a clinician would have decided for them," says Burstin.

—Susan Young Rojahn

Health Records Go Digital

The proportion of U.S. physicians keeping patient health records electronically has increased dramatically over the past decade



SOURCE: CDC/NCHS

Hospitals

Big Money, Uncertain Return

Hospitals are spending billions collecting and analyzing medical data. The one data point no one is tracking: the payoff.

● Ten years ago, Kaiser Permanente began building a $4 billion electronic-health-record system that includes a comprehensive collection of health-care data ranging from patients' treatment records to research-based clinical advice. Now Kaiser has added advanced analytics tools and data from more sources, including a pilot program that integrates information from patients' medical devices.

Faced with new government regulations and insurer pressure to control costs, other health-care organizations are following Kaiser's example and increasing their use of analytics. The belief: that mining their vast quantities of patient data will yield insights into the best treatments at the lowest cost.

But just how big will the financial payoff be? Terhilda Garrido, vice president of health IT transformation and analytics at Kaiser, admits she doesn't know. Nor do other health-care leaders. The return on investment for health-care analytics programs remains elusive and nearly impossible for most to calculate.

"We can all accept the fact that analytics contribute to the outcomes, so that justifies more investments into analytics. But I don't think anybody can definitely put together a proven case," says Stephen M. Stewart, CIO of the Iowa-based Henry County Health Center, which is spending $100,000 to $150,000 annually on analytics.

Although the health-care industry has long used data to determine medical protocols, the use of computerized records and analytics software is still in its infancy. Most organizations only started to install electronic health records in recent years, encouraged by nearly $24 billion in federal grants. Those digital records are crucial for analytics programs because they pull in and computerize reams of data on each individual patient, allowing health-care organizations to access exponentially greater amounts of information than what was contained in old paper records or disparate computerized files. They also allow clinicians to look across populations of patients for evidence of which treatments work best.

Opportunities to identify the most effective treatments could slip away if CIOs and their teams aren't able to quantify the return on their analytics investments. Health-care providers are under increasing pressure to cut costs in an era of capped billing, and executives at medical organizations won't okay spending their increasingly limited dollars on data warehouses, analytics software, and data scientists if they can't be sure they'll see real benefit.

A new initiative at Cleveland Clinic shows the opportunities and challenges. By analyzing patients' records on their overall health and medical conditions, the medical center determines which patients coming in for hip and knee replacements can get postoperative services in their own homes (the most cost-effective option), which ones will need a short stay in a skilled nursing facility, and which ones will have longer stints in a skilled nursing facility (the most costly option). The classifications control costs while still ensuring the best possible medical outcomes, says CIO C. Martin Harris.

That does translate into real—and significant—financial benefits, but Harris wonders how to calculate the payoff from his data investment. Should the costs of every system from which patient data is pulled be part of the equation in addition to the costs of the data warehouse and analytics tools? Calculating how much money is saved by implementing better protocols is not straightforward either. Harris hesitates to attribute better, more cost-effective patient outcomes solely to analytics when many other factors are also likely contributors. *—Mary K. Pratt*

INDUSTRY GUIDE

Data-Driven Health Care

Industry resources, upcoming events, and companies to watch.

Companies to Watch

Apple

COMPUTING HARDWARE AND SOFTWARE

A new health app will be built into Apple's next-generation operating system

Vital statistic: 150.3 million iPhones were sold in 2013, for $91 billion in revenue

There are already tens of thousands of third-party fitness and health applications for the iPhone, but in June, Apple executives revealed that the company would be launching one of its own. As part of the new iOS8 operating system, a new app called Health will give users a comprehensive view of vital signs—including blood pressure—plus weight, activity, and diet. Some data will be gathered from monitors that users wear and some recorded by them manually. Apple also plans to release a developer tool called HealthKit that will enable Health users to share these statistics with existing applications, like Nike's fitness tracker and the Mayo Clinic app. The hope is that this will improve the apps' performance and offer potential benefits ranging from an improved workout to automatic doctor calls at signs of danger.

Epic Systems

ELECTRONIC RECORDS

Makes the software health-care organizations and hospitals use to manage electronic records

Vital statistic: 100 million patients' records are accessible to companies using Epic's health information exchange, Care Everywhere

Privately held Epic Systems provides electronic medical records and software to 315 hospitals and health-care providers, including the Cleveland Clinic, the Dartmouth-Hitchcock Medical Center, and several Kaiser Permanente health plans, and has been a major beneficiary of a federal program reimbursing health-care providers for adopting digital record-keeping. Next, Epic has its eye on the Department of Defense, and it's teaming up with IBM to compete for a contract covering more than 9.7 million people. Apple's new Health app will be able to add data to MyChart, Epic's mobile tool for patients, with which they can view test results, schedule appointments, pay bills, and send messages to health-care providers.

Google

WEB SEARCH GIANT

A new Android app platform is Google's second attempt at building a health business

Vital statistic: There are more than 40,000 health apps available for Android phones, but only a handful have been downloaded by more than 500 users

In June, Google joined Apple in launching Google Fit, a new developer platform for fitness-tracking apps. Sensors on mobile and wearable devices—including Google's new smart watch and Android phones, but also items from other manufacturers, like the Withings smart scale—would help users track their data. The company's first foray into health care, Google Health, a digital health record analogous to Microsoft's HealthVault, was discontinued in January 2012. The company said that it "didn't catch on the way we would have hoped."

Illumina

GENOME SEQUENCING

Sells genome-sequencing machines and tools for analyzing the data

Vital statistic: $1.42 billion in fiscal 2013 revenue

Illumina was at the top of the list of *MIT Technology Review*'s smartest companies earlier this year after its CEO, Jay Flatley, announced that the firm had hit a long-held goal—sequencing a human genome for $1,000, a price seen as low enough for widespread use in a clinical context. The MyGenome iPad app enables doctors and patients alike to visualize genome data, highlighting genetic variants and predicting how they may affect health. "One of the biggest challenges now is increasing the clinical knowledge of what the genome means," Flatley told *MIT Technology Review* late last year. Illumina, he said, intends to be "at the apex of that effort."

Merck Global Health Innovation Fund

VENTURE CAPITAL ARM OF PHARMACEUTICAL MAKER

Invests in new digital health technologies

Vital statistic: $500 million has been invested in more than 20 companies

One way drug giant Merck stays abreast of new technology is by investing in digital health-care startups through its venture capital fund. Investments focus on remote monitoring, data analysis, and personalized medicine. They include ElectroCore, a company developing technology to treat headaches with electrical signals; Preventice, the creator of an FDA-approved patient monitoring system that tracks biometrics like heart rate through a wearable sensor; and GenomeDX, which develops genomic tests for prostate and urological cancers.

Microsoft

COMPUTING HARDWARE AND SOFTWARE

Markets tablets and cloud-based software tools to health-care providers

Vital statistic: $77.8 billion in fiscal 2013 revenue

Microsoft has been dabbling in health records since at least 2007, when it launched software called HealthVault to manage medical records. Now adapted to smartphones, it connects to third-party apps from Aetna, the American Diabetes Association, and others that allow users to manage prescription information and track fitness statistics. The software giant has not shared how many people are using the service, which is free, but it does not seem to be a major part of Microsoft's business; HealthVault has nearly 9,700 followers on Twitter and 5,300 on Facebook. Health-care companies are also using Microsoft's products to collect digital health data such as electronic clinical questionnaires.

Philips

DIVERSIFIED TECHNOLOGY COMPANY

In-home monitors and other devices connect patient to physician

Vital statistic: In 2013 health-care sales were 9.6 billion euros, 41 percent of the company's total. Its home health care and informatics businesses grew modestly.

Philips already makes monitors that enable doctors to monitor heart patients at home and informatics programs to help care providers evaluate data. That's just part of its sizable health-care business. Facing the possibility that some of these functions could move to mobile phones, the firm is expanding the focus of its "Hospital to Home" program and creating health sensors for wearable devices. In June it announced a collaboration with cloud computing company Salesforce.com to launch a secure platform that would connect data from personal and wearable devices with clinical data like labs and medical records.

Qualcomm Life

QUALCOMM SUBSIDIARY FOCUSED ON WIRELESS HEALTH TECHNOLOGIES

Sells wireless health monitoring systems and services to health-care providers

Vital statistic: more than 400 health-care companies use a Qualcomm-supported wireless tracking "ecosystem" to connect health data with doctors, patients, and payers

Qualcomm Life technology sends data wirelessly from medical devices to the cloud through a connectivity gateway called the 2Net Hub. This new technology, unveiled last September, allows patients to use their Android smartphones to transmit information gathered from devices like blood glucose meters, weight scales, blood pressure cuffs, and pulse oximeters. The phones connect to the medical devices via software built in with the help of a developers' kit.

Samsung Electronics

ELECTRONICS MANUFACTURER

Makes electronics products aimed at tracking activity and fitness

Vital statistic: Top smartphone manufacturer, with 31 percent of the market in 2013

Days before rival Apple unveiled its health monitoring application, Samsung shared its latest vision for health tracking: a wearable device called the Simband that tracks real-time information like temperature and heart rate and can share that information with cloud-based applications. Meanwhile, Samsung has partnered with the University of California San Francisco to open a new lab dedicated to testing and validating these gadgets.

SAS

DATA ANALYSIS

Makes software tools to help health-care providers lower costs and interpret data

Vital statistic: Privately held, $3.02 billion in revenue

As more hospitals adopt electronic health records, spending on tools to analyze that data is expected to increase. Last year, 59 percent of U.S. hospitals were using a basic electronic-health-record system, up from just 9.4 percent in 2008. SAS makes analytic tools that allow hospitals to visualize information about issues like how health-care costs are distributed across regions and how chronic illnesses affect health-care costs. Beyond assessing costs, SAS is now looking for ways to help improve health-care quality, such as a program recently implemented with a large pharmaceutical company that provides a secure way for researchers to access data from clinical trials.

Conferences

July 22–24, 2014
The 2nd International Conference on Big Data and Analytics in Healthcare, Singapore, www.bdah.org

October 6–7, 2014
Predictive Analytics World Healthcare 1st Annual Conference, Boston, www.predictiveanalyticsworld.com/health/2014/

October 10–11, 2014
5th Annual Workshop on Health IT & Economics, Washington, D.C., www.rhsmith.umd.edu/centers-excellence/center-health-information-decision-systems/initiatives-programs/workshops-white

October 22–23, 2014
Data 360 Conference, Santa Clara, California, www.data-360.com

November 4–5, 2014
Big Data & Analytics for Pharma Summit, Philadelphia, theinnovationenterprise.com/summits/big-data-analytics-for-pharma-2014-November-philadelphia

January 26–28, 2015
Personalized Medicine World Congress, Mountain View, California, www.pmwcintl.com

January 26–29, 2015
Arab Health Congress, Dubai, www.arabhealthonline.com/AHCongress/

February 24–25, 2015
World BioPharma Big Data Congress, London, www.healthnetworkcommunications.com/conference/biopharma-big-data/index.stm

May 20–22, 2015
Big Data in Biomedicine Conference, Palo Alto, California, bigdata.stanford.edu

May 31–June 3, 2015
Health Datapalooza, Washington, D.C., healthdatapalooza.org/

August 12–13, 2015
National Forum on Data & Analytics, Washington, D.C., www.ehidc.org

U.S. National Center for Telehealth and Technology

GOVERNMENT ORGANIZATION

Vital statistic: Operating budget of $28.3 million in fiscal 2013; established in 2008

In 2012, 250,000 former members of the U.S. military were diagnosed with post-traumatic stress disorder (PTSD). One app created by the center, the PTSD Coach, has been downloaded more than 100,000 times and is the subject of a randomized controlled research study at Stanford University to evaluate its long-term efficacy. The BioZen app uses brainwaves, respiratory rate, skin temperature, and electrocardiogram data, all captured by sensors the user wears, to calculate a relaxation level that can be displayed on a smartphone. The information is transmitted wirelessly to an Android device.

Verizon

TELECOMMUNICATIONS

Provides IT and telehealth products for health-care companies

Vital statistic: $120.6 billion in revenues

As a carrier, Verizon benefits if more data travels over mobile phones, and it's promoting mobile health through a number of programs. Verizon Virtual Visits allows patients to remotely consult clinicians by smartphone, and clinicians can electronically file prescriptions at a patient's local pharmacy when needed. Verizon also has FDA approval for a platform known as Converged Health Management, which runs on Apple's iOS operating system and allows clinicians to remotely monitor patient information like blood glucose levels and weight through several different devices. Verizon has not announced any customers for the system yet but confirms that it is undergoing one clinical trial.

Outside Reading

David Lazer et al., "The Parable of Google Flu: Traps in Big Data Analysis," *Science*, March 2014

When Google launched Flu Trends in 2008, hopes were high that the company would use its algorithmic magic to save lives by analyzing the search terms of millions of users worldwide to track the progress of flu strains in real time. A widely publicized 2013 study revealed, however, that Google greatly overestimated the prevalence of flu cases during the 2011–2012 season. In an article published earlier this year in *Science*, four social scientists reveal that this was not an isolated failure. They argue that Google's approach provides a cautionary tale of "Big Data hubris."

"Using Big Data to Transform Care," *Health Affairs*, July 2014

Exploring the connections between big data and policy, the journal taps top academic experts for insight into how data is changing health care. Several pieces look at predictive analytic tools that could help doctors give better care; others cover patient-powered research networks and the policy challenges of genomics.

Alberto Gutierrez, "Food and Drug Administration Warning Letter," November 2013

Last fall, the FDA addressed an uncharacteristically scathing letter to Anne Wojcicki, CEO of the genetic testing company 23andMe, ordering the company to stop selling its "personal genome service" because of concerns that the information it was providing to customers was not clinically validated. The letter specifically mentioned 23andMe's screens for cancer-associated mutations and genetic drug sensitivities, citing "the potential health consequences that could result from false positive or false negative assessments for high-risk indications such as these." The Google-funded company's effort to bring personalized genomics into the mainstream is at a standstill while it seeks resolution of the regulatory impasse.

Peter Groves et al., "The 'Big Data' Revolution in Healthcare: Accelerating Value and Innovation," McKinsey & Company, January 2013

In this white paper, McKinsey consultants make the case that after years of effort and billions of dollars spent digitizing, organizing, and networking patient health records, the industry is now at a tipping point: new tools, apps, and devices will help providers and patients make use of this data to improve care and lower costs. The authors estimate that if certain proven technologies were instituted system-wide, the U.S. could see a $300 billion to $450 billion reduction in annual health-care spending, but they caution that significant industry inertia must be overcome.

Francis S. Collins, *The Language of Life: DNA and the Revolution in Personalized Medicine*, Harper Perennial, 2011

The former head of the Human Genome Project and current director of the National Institutes of Health makes the case that the genomics revolution will lead to a new era of medicine optimized for each patient's genetic heritage. Collins opens the book on a personal note, explaining how he helped his family make use of discoveries about the genetic basis for diseases such as breast cancer and Charcot-Marie-Tooth disease to access genetic testing, quantify their risk, and ultimately guide their health-care decisions. Increasingly, he argues, DNA will unlock the secrets of the 6,000 known rare diseases as well as common ailments like heart disease and asthma. His early research found genetic factors in diseases including type 2 diabetes and cystic fibrosis.

From the Archives

"Too Much Information," January/February 2014

With a number of companies marketing noninvasive genetic tests that promise to identify abnormalities early in a pregnancy, Amanda Schaffer looked at how expecting parents and their doctors will make sense of this newly available data and the thorny ethical issues surrounding it.

"A Hospital Takes Its Own Big-Data Medicine," November/December 2013

As part of last year's Business Report on rising health-care costs, Courtney Humphries described how one major research hospital bet on big data: by investing in supercomputing and recruiting Facebook's chief data scientist to help analyze the vast amount of information doctors collect.

"Bases to Bytes," May/June 2012

Research editor Mike Orcutt put the genomic revolution into visual focus with a series of charts illustrating how the plummeting cost of DNA sequencing has led to an exponential increase in the number of full genomes sequenced. If the trend continues, it may test the limits of our ability to store data.

"The Patient of the Future," March/April 2012

In a big-data detective story, Jon Cohen recounted how computer pioneer Larry Smarr used wearable sensors to gather a wealth of data about himself, which he then analyzed to help doctors diagnose his Crohn's disease. The process reflects how tech-savvy individuals are using data analytics to take control of their own health and treatment.

"Kenya's Startup Boom," March/April 2012

When chief correspondent David Talbot paid a visit to Nairobi, a hotbed of the mobile health movement sweeping Africa, he met an inspiring group of young programmers developing phone-based tools that could allow social workers and the patients they serve to access health information, communicate with doctors, and report disease outbreaks to health authorities.

"Prescription: Networking," November/December 2009

The data doctors collect from patients is of little use if it can't be instantly accessed wherever care is provided, so chief correspondent David Talbot took readers on a tour of hospitals and community health centers in one city to show how they were attempting to build a network to exchange this information.

A Primer on Reimbursement

Who decides if a treatment is worth the price? Once that was the domain of insurance companies and Medicare, but today the answer is more complicated. More than one-third of Americans today have high-deductible insurance plans and must cover medical costs up to $1,250 per year themselves ($2,500 if family is covered as well), creating a new category of price-conscious health-care consumers. The Affordable Care Act's promotion of accountable care organizations, which are paid a certain amount per patient no matter how much care they require, means more caregivers will now be the ones making those cost decisions.

Traditional insurance and government programs remain the most common way for Americans to pay for health care, and the pace at which data-driven medicine is adopted will be decided by the extent to which these programs reimburse genetic testing or mobile health devices.

A study performed by UnitedHealthcare in 2012 determined that the company had spent $500 million on genetic and molecular tests in 2010, of a total $5 billion spent nationally, and predicted that by 2021, spending on these tests nationwide could reach $15 billion to $25 billion. Yet insurance companies remain skeptical about the health benefits of many genetic tests.

Here is what is being paid for today, according to interviews with genetic counselors, hospital administrators, pharmacy advisory firms, academic studies, and consulting reports.

GENOMICS AND GENE TESTING:

- Sequencing a human genome has dropped in cost significantly, but the price remains high at $3,500 or so—up to five times that when interpretation of the results is added. Only about half of insurance submissions are approved. Reimbursement is most likely when the cost of the other tests that would have to be done for diagnosis outweigh the cost of sequencing. Illumina, the leading sequencer, does not bill insurance.

- Sequencing the exome, the subset of the human genome that includes all the body's important instructions for building proteins, has reimbursement rates comparable to those for established genetic tests. In one recent study, 98 percent of submissions were approved.

- Targeted genetic testing for rare diseases and hereditary cancers, like colorectal and breast cancers associated with certain mutations of the *BRCA1* or *BRCA2* gene, is generally covered when family history or other factors indicate a risk. The specific amount varies. In January, Medicare reimbursement for the *BRCA1* and *BRCA2* tests dropped from nearly $3,000 to a maximum of $1,440 after competition among testing firms picked up. Screening expectant parents to see if they carry genes for conditions like cystic fibrosis is generally covered, as is testing fetuses for Down syndrome.

- Multigene panel testing has been broadly available for just over a year, following a Supreme Court ruling that opened up testing for some mutations by suggesting that genes can no longer be patented. The test is often covered by insurance, but genetic counselors report that coverage is increasingly being denied on the basis of cost and a preference for less expensive single-gene testing, though early studies have shown that multigene hereditary-cancer panels have benefits over the cheaper tests.

- Pharmacogenetic testing, which provides information about how well a patient is likely to respond to a given medication, is beginning to be covered. Pharmacy benefits manager Express Scripts has established about 20 tests for which the evidence supports reimbursement.

MOBILE HEALTH:

- The FDA is regulating diagnostic apps and accessories that turn a mobile phone into a medical device like an electrocardiogram or blood pressure monitor. More than two dozen apps and devices are FDA approved and eligible for insurance reimbursement. Still, insurance companies deem many of these items "experimental and investigational" and hold that their clinical value is not yet established, so they will not cover their costs.

- A limited number of insurers pay for activity-tracking mobile devices and apps. Nearly one-third pay for the cost of mobile communications to patients about drug adherence and other health-related issues, according to a study performed by the Economist Intelligence Unit for the consulting and accounting firm PWC. According to that same study, 29 percent are paying for medical professionals to receive mobile data as a tool for patient monitoring, and 30 percent cover practitioners' analysis of health and wellness data gathered by mobile devices.