Physicians and hospitals gradually adopted technologies to try to fix these problems. For example, electronic health records, which were introduced in the 1990s and are now the standard practice, make data much more accessible than written charts by presenting diagnoses, test results and medications at the click of a button. Ideally, they make all of a patient’s past medical history accessible for immediate review.

Meanwhile, computers can store vast amounts of “big data” and be programmed to anticipate mistakes and other adverse events—and to create a series of obstacles to prevent them. Finally, mobile devices and social media can make medicine more efficient. For example, patients are increasingly relying on emailing, texting and SKyping (so-called telemedicine) to communicate with and display their findings to doctors. These encounters should help prevent expensive office visits and hospitalizations.

So, yes, things are better. But “The Digital Doctor” also demonstrates how the use of computers to prevent medical errors has created an enormous set of new problems. Dr. Wachter convincingly shows how electronic health records have transformed physicians into “data entry clerks,” discouraging them from focusing directly at patients and disrupting doctor-nurse teamwork—as in the recent case in which a doctor never learned that a possible Ebola patient had recently traveled to Africa. The nurse had entered the information into the computer but hadn’t bothered to tell the doctor directly.

In another astounding story, Dr. Wachter describes how a patient nearly died after being prescribed 38½ tablets of the antibiotic Septra instead of the one pill he was supposed to receive. Neither doctor, nurse nor pharmacist detected the error. In fact, the nurse incorrectly assumed that the electronic health record’s bar-coding system absolutely prevented the improper dosing of medications. Such “blind trust” of computers, the author shows, has itself become a risk factor for errors because it discourages health professionals from speaking up when they are skeptical.

Dr. Wachter well knows that this “brave new world” of medicine makes physicians extremely uncomfortable. The computerization of medicine, he writes, “has been strown with land mines, large and small.” But the myriad computer gurus that Dr. Wachter interviewed for his book don’t mind. They believe that computers—once rightly adapted to medical practice—will free doctors up to do doctoring as opposed to paperwork, data entry and other trivial tasks. Dr. Wachter, despite his misgivings, agrees.

But I’m not so sure the current generation of doctors—myself included—will ever think that anything can replace being in the room with a patient, touching her hand, sharing a laugh or hearing her baby’s new heartbeat.

Dr. Lerner, a professor of medicine and population health at New York University Langone Medical Center, is the author of “The Good Doctor: A Father, A Son and the Evolution of Medical Ethics.”

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**BOOKSHELF | By Barron H. Lerner**

**The Robot Will See You Now**

**The Digital Doctor**

By Robert Wachter

*(McGraw-Hill, 330 pages, $30)*

Consider Robert Wachter’s vision of the hospital in the not-so-distant future. There will be no more dedicated intensive-care units, because only seriously ill patients will be hospitalized. Rooms will be equipped with wall-size video screens and cameras that allow doctors to expeditiously perform remote examinations. There will be no more nurse call buttons; patients in pain will simply announce their problem and a nurse will appear on a screen. If the physician approves more pain medication, he or she can simply enter it into a computer, which will automatically speed up the patient’s intravenous injection. Medical records will be dynamic documents, always available for patients and families to review on their computers and smartphones.

I am fairly well-versed in the growing use of computerized medicine, yet I was nevertheless stunned to imagine myself participating in such doctor-patient encounters. As I read “The Digital Doctor: Hope, Hype, and Harm at the Dawn of Medicine’s Computer Age,” I found myself feeling nostalgic for medicine before the digital age, even though its challenges sometimes drove me crazy. Is computerized medicine really an improvement on the past? Or are we at risk of losing the vital bond of the doctor-patient relationship? Fortunately, the author, a practicing internist, has considered these questions carefully. “The Digital Doctor” makes the case that, despite some serious shortcomings, computerized medicine is here to stay and, in the long run, will improve our health.

The authority of the medical profession, Dr. Wachter reminds us, once stemmed from the physician’s presence and touch. Doctors treated entire families, often in their homes, and wrote expansive notes that captured not only the vicissitudes of illness but also the lives of patients. But by the early 20th century, technology was rapidly changing the practice of medicine. The introduction of X-rays, for example, led doctors to divert attention from their patients to images of them. Antibiotics led to miracle cures for diseases like tuberculosis but also meant a growing focus on the disease itself, as opposed to the diseased. Quoting the historian David Rothman, Dr. Wachter argues that doctors were becoming “strangers at bedside.”

Yet only a Luddite would wish for medicine’s “good old days.” Problems that emerged in the early 1900s, such as incomplete medical records, terrible billing practices and rising costs persisted and even worsened throughout the 20th century. Perhaps the biggest problem has been that of medical errors, which were killing nearly 100,000 Americans each year, according to a 1999 report by the Institute of Medicine.
Better Bedside Manner

Some examples of how doctors can improve the way they communicate with patients

DON'T SAY THIS Your appointment today is about your elevated blood pressure, so we can't talk about your diabetes. That will have to wait until another appointment.

SAY THIS I want to make sure I know what your blood pressure problems are as well as your diabetes, since one can affect the other.

DON'T SAY THIS Do you understand the treatment plan we just discussed?

SAY THIS Can you repeat back to me in your own words the treatment plan we just discussed?

DON'T SAY THIS I know how you feel about your cancer diagnosis. I've been an oncologist for 30 years.

SAY THIS I know this is a very difficult time for you and your family. Let me help you get through this by answering as many questions as you need to ask.

DON'T SAY THIS Please read and sign this informed-consent form for your surgery.

SAY THIS There are risks and complications that can happen with this surgery that you will read about in this material, so I want to make sure you have every opportunity to ask questions and understand your specific risks.

DON'T SAY THIS They are making me use this laptop with all my patients, and I can't find anything on it!

SAY THIS Our practice is using a new computer system, so I will be typing what you tell me as we talk. Please let me know if I fail to answer one of your questions.

DON'T SAY THIS I don't believe in alternative medicines. It's hocus pocus. You have to stay on your current prescriptions.

SAY THIS What questions do you have about alternative medicines? I will research your questions and get back to you within the week. In the meantime, will you agree to continue your current prescriptions?

Source: Doctors Co.
Kathryn Pearson Peyton's Mammosphere, an effort to store breast scans in the cloud, goes national

By Charlie Patton
Fri, 05 Feb 2016, 01:53 PM

Photo by: Bruce.Lipsky@jacksonville.com

Kathryn Pearson Peyton, a breast-imaging radiologist, is the driving force behind Mammosphere, a "secure, patient-portable cloud storage and image sharing platform for mammography records that is easily accessible to physicians." She was photographed in her home on Tuesday, October 14, 2014 in Jacksonville, Florida.

Mammosphere, which began as an idea Kathryn Pearson Peyton pitched at the first One Spark festival in April 2013 to create a cloud-based repository of breast scans, announced this week it will merge with lifeIMAGE, the most widely used network for exchanging medical images in the country.

Pearson Peyton, the wife of former mayor John Peyton, is a radiologist who specialized in the diagnosis of breast cancer, a disease that has affected several members of her family, until she ended her active practice.

Related: Mammosphere.org website
The idea for Mammosphere was to create a database to store images of breast scans on a cloud. That would help solve a problem physicians regularly encounter with women who come to them for mammographies but don’t know where their previous scans are stored. Lack of access to previous scans can result in a high rate of false positives.

A national study by Pearson-Peyton’s mentor, Edward A. Sickles, a professor emeritus in radiology at the University of California at San Francisco’s School of Medicine found that having previous mammograms available reduced the likelihood of false positives 60 percent. A local study put the reduction of false positives at 73 percent.

Having previous scans available is crucial, Pearson Peyton said, because the breast, like the human face, is unique to each woman. So being able to compare scans over time helps identify whether changes occurred that may signal the development of cancer.

Over the last three years Mammosphere, which was backed by the Riverside Hospital Foundation, Delores Barr Weaver and the Florida Blue Foundation among others, got 22 imaging centers and hospitals to load mammograms from 25,000 women on the platform.

But some major providers held out, feeling that Mammosphere’s focus on mammography was too narrow, Pearson Peyton said.

So this week, Mammosphere agreed to become part of lifeIMAGE, which has a network of about 800 health care facilities and more than 150,000 clinical users, who are already exchanging medical images to improve patient care.

lifeIMAGE will work to expand Mammosphere’s mission to upload mammography imaging to a cloud both in Jacksonville and nationally. Pearson Peyton will become head of its women’s health and imaging advisory committee.

“This is such an amazing effort to take this forward nationally,” she said.

Charlie Patton: (904) 359-4413
Regaining Compassion

Rounds were over—finally—and I was exhausted. I kept reminding myself that every July is the same. The new interns and students were both petrified and striving to make a good impression, which translated into long and sometimes painful bedside rounds.

There was, however, a bright spot, and her name was Kelli. A third-year student assigned to our oncology service as her first rotation, Kelli offered refreshing enthusiasm, charm, and encouragement daily to her patients. But today something was different. She came to me and asked for a few minutes to talk behind closed doors. Almost immediately she began to weep and between sobs she laid her heart before me: "I feel so inadequate. The only thing I have to offer is my compassion. But now I wonder what my words can mean as I look at Sheila. It's all so overwhelming. I'm not sure I can keep doing this."

Sheila was the 65-year-old mother of four, all younger than 12, whose husband, Michael, worked as a nurse at our hospital. After a brief bout with "walking pneumonia" that didn't resolve, she was diagnosed with metastatic non-small cell lung cancer and had been admitted for chemotherapy. Her chief complaints were an enlarging mass, a finding whose significance had escaped neither Sheila nor Kelli. The gentle but honest conversation inning-tears, facts, faith, and human touch had been all Kelli (and I) could bear. I had already given my sermon to the students about the profound sense of peace and joy our patients often find through their suffering, and at the time my talk was well received. But now Kelli's eyes begged more than a philosophical lecture or a pat on the back. So I prayed for both of us to be given the wisdom and strength to give the best care to Sheila, after which Kelli smiled, wiped her eyes, and returned to her work.

During that month, Kelli had several opportunities to practice her "only" contribution to Sheila's care. Sheila was able to share with her the full range of emotions common to all who have struggled with cancer: fear of death, anger with the unfairness of it all, sadness at the prospect of her children growing up without a mother, joy at small successes in the day-to-day struggle, and gratitude for our efforts. "My pain is much better today. Thanks for all you're doing for me." Finally, she was able to go home—as it turned out, for the last time.

Kelli continued to work hard learning medicine and punctuating rounds with her kindness and humor. All of her patients adored her, especially one in particular, Mr. Bernard. He was admitted with one of his many exacerbations of bronchiectasis and was receiving traditional medical treatment with inhalational therapy and parenteral antibiotics. Quite unexpectedly one day, however, his cough worsened and respiratory distress rapidly led to the need for mechanical ventilation. Here again, Kelli brought her special skill to the bedside. As the anesthesiologist gained control of the patient's airway via nasotracheal intubation, Kelli sat at the bedside and, recognizing the terror on Mr. Bernard's face, began stroking his hand and explaining every step of the procedure. "Now, Mr. Bernard, I know this tube is uncomfortable, but we need it to help you breathe. Hold my hand. I'll stay with you." His viselike grip on her warm hand was all the evidence I needed that he had heard and appreciated her. She accompanied him to the intensive care unit, where Michael was at work setting up the ventilator and preparing for yet another patient who had "crashed."

Our ICU, like most, is staffed by superb nurses, and Sheila's husband Michael was widely regarded as one of the most skilled. Kelli remained with Mr. Bernard until he was sufficiently stable and then came back to our workshop. She then asked, "What should I have done differently? Why did he get so sick? Were we using the wrong antibiotic or bronchodilator?" As a team of students, interns, and resident, we reviewed the medical facts surrounding the case and concluded that no other medical intervention would have prevented the ICU transfer. While we were talking, there was a knock on the door. Michael's head an upper body emerged as he peered into the room. He looked shaken, staring at the floor as he removed his glasses and rubbed his eyes. "Pleading the worst I asked, "Is Sheila all right? He just nodded and for what seemed a long time said nothing.

Certain moments seem to take on a life of their own: Some joyful, others painful, and still others an odd combination of both, but all living on because of a rare connection with both the mind and the heart. Michael began, "I just wanted to tell you, all of you, how much Sheila and I appreciate the care she's getting. It's not just the medical stuff, I mean, that's important and we know she's getting the best medical treatment available. But it's the way you take care of her"—he paused—"it's me that makes it so different." He pressed his thumb and index finger into his tearing eyes and stopped to regain his composure. Everyone was silent as we tried to hold back our own tears and listen to the rest of his message. He then looked at Kelli and said, "Kelli, I was watching you hold that man's hand. I listened as you talked to him and I tell you, do you know how long I've been since I held anyone's hand in there, or thought about how it must feel to be on one of those things? We still said nothing as he again began to cry. "I want you to know, Kelli, that you, and each of you, have reminded me about something I had long forgotten in my job. And I won't forget again to comfort those I take care of. Thank you all." With this he entered the room and after warmly embracing each of us he slipped out, leaving a room full of blurry-eyed physicians.

Everyone sat motionless and silent for a minute or two, trying to absorb the impact of what had just transpired. Eventually we all returned to caring for our patients, but none of us will ever forget the intense sense of joy and sorrow mingled in that room.

It has been almost 2 years since that day and now Kelli is the mother of a beautiful 2-week-old boy and awaiting graduation next month. Recently, as Kelli and I were chatting about motherhood, our discussion turned to Sheila and Michael. Looking back, she continues to underestimate her "medical" contributions to her patients' care while being grateful for the opportunity to comfort them. But as she is ready to graduate, feeling more confident in her skills as a physician, she remembers the profound hope and purpose she found. And she reminds me that "Among all the things we do, what our patients are most likely to remember is our compassion."

James W. Lynch, Jr, MD
Gainesville, Fla

Edited by Roxanne K. Young, Associate Editor.
A Cancer, Moonshot Needs Big Data

By Tom Coburn

Friday, January 15, 2016

OPINION

THE WALL STREET JOURNAL

In Cancer is a problem our law needs to be
more than a problem. The disease affects millions of people and is a leading cause of
death in developed countries. The United States spends billions of dollars on cancer research,
but much of this funding is scattered and fragmented. The government's National Cancer
Institute (NCI) received $5 billion in 2015, but only a small portion of this fund is
directed towards cancer prevention and early detection. The NCI also lacks the resources to
support collaborative research initiatives, which are essential for advancing cancer
care.

In January 2016, President Obama announced a "Cancer Moonshot" initiative aimed at
doubling the rate of cancer breakthroughs over the next five years. This is a bold goal
that will require significant investments in research and infrastructure. The initiative
will focus on four key areas: understanding cancer drivers, improving early detection
and treatment, strengthening cancer survivorship, and supporting cancer research
communities.

One of the key strategies of the Cancer Moonshot is to leverage big data. By collecting
and analyzing large amounts of data from multiple sources, researchers can identify
core patterns and insights that may not be apparent from smaller datasets. This
approach will allow scientists to ask new questions and explore novel hypotheses that
were previously impossible to test. The initiative will create a centralized database
that will include patient records, genetic information, and clinical trial data.

Another important aspect of the Cancer Moonshot is the support of innovation.
The initiative will provide funding for new research proposals and encourage
collaborations between different institutions. This will help to accelerate the
development of new therapies and diagnostic tools.

One of the challenges of the Cancer Moonshot is the need for better data sharing and
privacy protections. The initiative will establish clear guidelines for data
sharing and will work with stakeholders to ensure that patient privacy is
protected.

In conclusion, the Cancer Moonshot is a important initiative that has the potential
to make a significant impact on the fight against cancer. By leveraging big data and
innovation, the initiative will help to accelerate the development of new treatments
and diagnostics. The Cancer Moonshot is a necessary step towards a world
where cancer is no longer a leading cause of death.
Promoting Health: The One Alternative to Healthcare Rationing

by Michael F. Roizen, MD, and Olivia Delia

Healthcare in the United States is like food: When Americans are hungry, they want to eat something soon, and they want it to be good. Healthcare is the same: When patients have medical needs, they want to receive high-quality treatment as quickly as possible.

But that is where the similarity ends. Most people understand that there is a limit to how much they can eat (notice I said “most people,” not “everyone”). However, the amount of healthcare Americans consume has been growing dramatically (Äkesson et al. 2014).

Most of the heightened demand is due to the increased prevalence of chronic disease, because we still

• use too much tobacco;
• eat too much inexpensive, addictive, and unhealthy food—250 or more calories a day more per person than in 1978–1983 (Gregg et al. 2014);
• are much less physically active than in 1990 (Vuori, Lavie, and Blair 2013); and
• experience excessive stress that we do not manage well.

Right now, 10 percent of Americans aged 47 or older develop a chronic disease each year. As a result, 97 percent of those enrolling in Medicare have unmanaged or undermanaged health problems. And currently, more than 80 percent of the nation’s $2.5 trillion health spend goes to chronic disease management (Daviglus et al. 1998, 2005; Moses et al. 2013). At the top of the list are lifestyle-induced conditions that take the lives of more than seven in ten Americans, such as type 2 diabetes, dementia, cancer, osteoarthritis, heart disease, and stroke.

This influx of chronic disease has played a major role in declining prosperity and rising income inequality in our country (and in many others). Since 1997, every penny of increased wages for US workers has gone to the cost of medical care and medical insurance (Hancock 2012).

Unfortunately, the long-term trends look even worse. Between 1974 and 2014, the number of type 2 diabetics in the United States increased from 3.2 million to 29 million (Exhibit 6.1). Diabetes care now represents nearly 10 percent of healthcare expenditures—and between 1.5 and 2 percent of the gross national product (GNP). Experts predict that by 2050, 120 million to 180 million Americans will have diabetes—a six- to tenfold increase in a total US population that is projected to grow only 30 percent during that time (Bernstein et al. 2014; Ezzati and Riboli 2013; Gregg et al. 2014). With no new therapies, and assuming the average age of those treated remains constant (unlikely, since they will probably be older), caring for these individuals will account for 10 to 15 percent of the GNP. That’s not 15 percent of healthcare spending, but 15 percent of the total US economy!

The same pattern can be seen in hip and knee replacement surgery (Exhibit 6.2), dementia care, post–heart attack care, post–stroke care, and post–cancer care. If current trends continue, by 2050 the amount of money the nation

About the Authors
Michael F. Roizen, MD, is the chief wellness officer at Cleveland Clinic. He graduated from the University of California, San Francisco, School of Medicine and performed his residency in medicine at Harvard’s Beth Israel Hospital. He is certified by both the American Board of Internal Medicine and the American Board of Anesthesiology. Dr. Roizen is a New York Times best-selling author (four times at #1 and eight times overall) and a frequent guest on television news and talk shows. He still practices internal medicine.

Olivia Delia is a graduate of Williams College and a first-year medical student at the Perelman School of Medicine at the University of Pennsylvania. She was a science journalism intern with Dr. Roizen in 2014-2015.
**FUTURE SCAN SURVEY RESULTS:**

**Protecting Health**

How many of the following will the person in your household comply by 2015?

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<th>Yes</th>
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<th>Don't Know</th>
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*Note: The sample size for population is not clear, but this will not affect the AEO that is measured on population level.*

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**Promoting Health - What Practitioners Predict**

Most people with wearable devices to monitor health (82 percent of survey respondents) predict that by 2015 people in their household will report themselves as using their mobile phone or wearable device.

Among a quarter of the population (25 percent) who are currently using a mobile phone or wearable device, they predict that by 2015 at least 40 percent of people in their household will report themselves as using their mobile phone or wearable device.

Most people will use phones for wearable devices to monitor health (82 percent of survey respondents predict that by 2015 people in their household will report themselves as using their mobile phone or wearable device.)
—continued from pg. 32
spends on treating chronic conditions in these six areas will consume nearly the entire GNP.

Back to the food analogy: No matter how much you like salmon burgers (notice I did not say "cheeseburgers"), you cannot eat 48 of them a day. The same is true of healthcare: The aforementioned spending increases are not realistic. America will have to either cut back on expenses or ration care.

A Proven Path to Outcomes-Based Wellness
Fortunately, another path is emerging. Under the leadership of Toby Cosgrove, MD, Cleveland Clinic has developed an effective new approach to employee wellness. If expanded to all populations, I believe it could achieve dramatic improvements in individual health and meaningful cost reduction for the US healthcare system.

The approach is based on several large studies that demonstrate the importance of achieving normal measures in the following key metrics: low-density lipoprotein (LDL) cholesterol, blood pressure, blood sugar, waist-to-height ratio, stress management, and tobacco toxins (Exhibit 6.3). Cleveland Clinic calls them "the six normals." According to the literature, people who reach the six normals—with or without medication—reduce their subsequent chronic disease by 80 to 90 percent over 10- to 30-year periods (Akesson et al. 2014; Chomistek et al. 2015; Daviglus et al. 2005, 2004; Stamper et al. 2000; Willis et al. 2012).

But how do you motivate people to change their lifestyle? Cleveland Clinic explored many options before finding one that delivers major health benefits. It is a thoughtfully structured, outcomes-based wellness strategy that not only prevents but actually reverses disease. In the process, it increases productivity, elevates morale, and produces savings for both employers and employees.

Cleveland Clinic found that five steps are essential to success:

1. Change the culture. The organization knew it could continue to lead in healthcare only if it stopped the influx of chronic disease. The financial case was clear: In 2005, healthcare costs for its 43,000 employees and 38,000 dependents had been increasing 9.5 percent per year. Based on projected growth, these costs would exceed $400 million by 2016, leaving the clinic unable to invest in people and innovative programs or adjust to expected decreases in reimbursement.
The "Six Normals" That Reduce the Risk of Chronic Disease by 80 Percent or More

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<th>Measure</th>
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<td>Blood pressure</td>
<td>&lt;140/90</td>
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<tr>
<td>LDL (bad) cholesterol</td>
<td>&lt;100</td>
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<tr>
<td>Waist-to-height ratio</td>
<td>&lt;0.5</td>
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<tr>
<td>Blood sugar</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Nicotine</td>
<td>Zero use</td>
</tr>
<tr>
<td>Stress</td>
<td>Routine practice of stress management</td>
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Starting in late 2005, Dr. Cosgrove began talking about these issues to all clinic caregivers literally every month. He presented the financial case, but he also emphasized the human case for reducing chronic disease. His strong leadership was critical to ingraining wellness into the organizational culture.

2. Change the incentive strategy. Early on, Cleveland Clinic tried offering small incentives (less than $400 per year) for healthy behaviors. It also emphasized process choices, such as undergoing a health risk assessment or walking 6,000 steps a day for 20 days each month. Unfortunately, this approach did not move the needle. Employees who were already healthy collected the dollars, those with incipient chronic disease progressed, and people with established chronic disease did not alter their lifestyle choices.

The needle moved dramatically only when we tied a substantial premium differential to biometric outcomes. Now when employees achieve the six normals and keep their immunizations up to date, they receive a premium reduction. The reduction was 20 percent in 2014 and is even higher now.

Cleveland Clinic has found that this significant savings incentive motivates healthy people to stay healthy. Individuals who are currently in a health improvement program to reach target levels are also eligible for a premium reduction. The few who will never be able to hit the six normals are allowed to qualify for an incentive through alternative goals established by their primary care physician.

3. Change the environment. Cleveland Clinic learned a lot when it banned smoking from its campuses in 2005. Previously, the organization reimbursed employees for up to 89 percent of the cost of its smoking cessation program. When it went smoke-free on all campuses, from Ohio to Abu Dhabi, the clinic made the program free. That day, four times as many people signed up for smoking cessation as had in the previous four years.

Essentially, Cleveland Clinic changed the environment by incentivizing employees to make healthy choices and by eliminating financial barriers to wellness. It also provides free on-site fitness clubs, weight loss memberships, and health coaching. The clinic's cafeterias have changed, too, removing all fryers and getting rid of sugared beverages from vending machines.

4. Establish care programs. Cleveland Clinic launched a number of free services to help staff with chronic conditions control and even reverse their disease. The programs are based in the clinic's primary care offices and are provided in person, via online consultations, and through shared medical appointments. Under the direction of physicians, nurses coordinate employees' care and educate them about food choices, stress management, and physical activity.

5. Encourage wellness. The clinic has also established free programs to assist healthy employees and those with incipient medical issues. The emphasis here is on creating fun opportunities through "health buddies," social media engagement, and e-coaching. Smartphone apps help participants maintain exercise goals and cope with stress.

The key to success is providing support. Poorly executed outcomes-based incentives can discriminate against the people who need help the most. If we simply charge higher premiums to employees who smoke or are overweight, we are only punishing them. But if we couple financial incentives with effective and free health programs, we empower individuals to overcome unhealthy behaviors.

The Result: A Clear Return on Investment
Cleveland Clinic's experience shows that outcomes-based wellness incentives work for both employers and employees. Here are some highlights:

- The six normals: Ninety-five percent of people who had six normals in 2009 maintained them through 2014. In addition, 63 percent of individuals with one or more out-of-range results have now achieved all of the measures or are working toward that goal.
- Nicotine use: Employee smoking rates have declined from 15.4 percent in 2004 to 5.3 percent in 2014.
- Weight management: Employees have collectively lost and kept off 450,000 pounds (as measured by their physicians) since 2011. Body mass index has declined 0.5 percent a year, whereas the national average is increasing 0.37 percent annually.
• Cost savings: The clinic estimates it saved at least $60 million in 2015 through improvements in employee wellness, a figure that has steadily increased every year since the launch of the initiative. This dramatic return on investment (ROI) does not even take into account the positive impact on absenteeism.

A Promising Future
The great news is that the six normals are exportable. In the past few years, Cleveland Clinic has helped several organizations in diverse industries establish similar programs. For example, Lafarge has realized estimated savings in excess of $200 million. Bon Secours's employee stress and engagement scores have improved by more than 40 percent, and Crum & Forster reports a first-year ROI of 341 percent.

Currently, only 3 to 4 percent of the population entering Medicare in the United States falls within range for all of Cleveland Clinic's health measures. Imagine the possibilities if hospitals and health systems joined the clinic in encouraging businesses, communities, and individuals across the country to embrace this proven approach to wellness. If only 65 percent of individuals achieved the six normals, the nation would save well over $600 billion in healthcare spending per year. Providers have the chance to lead the way like never before in decreasing the incidence of chronic disease, improving Americans' health, and reining in the spiraling cost of care. It is an historic opportunity we cannot afford to miss.

References


A Cholesterol Conundrum

Stress has the same negative effects on the body as fatty foods; Patients often don't see warnings

BY BETSY MCKAY

Christopher Edginton was taking medication and trying to improve his diet when his cholesterol shot up anyway four years ago.

His doctor suggested a new approach. “He said you’ve got to get rid of some things you’re doing, some of the stresses in your life,” recalls Mr. Edginton, a professor at the University of Northern Iowa who regularly traveled internationally and had so many job titles that he had a four-sided folding business card.

Mr. Edginton heeded the doctor’s advice. Now 69 years old, Mr. Edginton is down to one teaching job and some scaled-down responsibilities in professional organizations. His level of so-called bad cholesterol, or low-density lipoprotein (LDL), has dropped to 62 milligrams per deciliter from 121 mg/dL in 2012. His doctor says 50 to 70 is reasonable for Mr. Edginton, who had two previous heart attacks.

Of all the factors contributing to high cholesterol, many cardiologists say one often goes unmentioned in advice for patients: stress. Yet chronic stress from a tough job, a strained relationship or other anxiety-producing situations can play a role—along with poor diet, smoking and lack of exercise—in causing lipid concentrations to rise, they say.

Cholesterol deposited by LDL can accumulate in the arteries, a condition known as atherosclerosis, which can reduce blood flow.

“Stress will make your cholesterol go up,” says Stephen Kopecky, a preventive cardiologist at the Mayo Clinic in Rochester, Minn., who is treating Mr. Edginton. “Without a doubt, that has been underrecognized.”

Understanding the effect of stress on cholesterol is becoming more important as people’s lives increasingly are crammed with obligations, and digital technology makes switching off harder than ever, cardiologists say. Nearly 28% of U.S. adults age 20 and older either have high total cholesterol or are on cholesterol-lowering drugs, according to the Centers for Disease Control and Prevention. The CDC defined high cholesterol as 240 mg/dL and above.

Of most concern is chronic stress, which taxes the body over time, rather than episodes of short-term stress, cardiologists say.

Chronic stress can lead to higher cholesterol in several ways. People may stop exercising, or add more unhealthy foods to their diet. Stress also stimulates the release of hormones cortisol and adrenaline. Those hormones in turn stimulate the release of triglycerides and free fatty acids, which over time can boost LDL cholesterol, says Catherine Stoney, program director in the division of cardiovascular sciences at the National Heart, Lung and Blood Institute, part of the National Institutes of Health.

To drive home the point, Dr. Kopecky tells patients about a classic study that documented a sharp rise in the cholesterol level of 18 tax accountants around the April 15 deadline for filing U.S. individual income-tax returns. Their total cholesterol rose on average from 206 mg/dL in January to 232 on April 15, then dropped back down to 215 in June. The diets and exercise levels of the accountants, who ranged in age from 28 to 50, remained consistent during the study period suggesting the changes were due to stress, the study’s authors wrote.
Continued from the prior page

The study, published in the Journal Circulation in 1958, is nearly six decades old, but Dr. Kopecky says he continues to bring it up because “we can all relate to paying taxes.”

Subsequent research has shown similar effects.

Exactly how much stress contributes to high cholesterol isn't clear, experts say. It is harder to measure than changes in diet and exercise. "We don't always have an optimal awareness of stressors we experience and the magnitude of those stressors," Dr. Stoney says.

Questions about stress come amid recent confusion over the extent to which diet contributes to high cholesterol. A few studies have led many consumers to conclude that eggs, which contain cholesterol, and saturated fat don't contribute to heart disease—contrary to long-accepted advice. Eating lots of eggs and a diet rich in saturated fats “will increase your cholesterol level,” says Mark Creager, president of the American Heart Association and director of the heart and vascular center at Dartmouth Hitchcock Medical Center, in Lebanon, N.H.

Research on the role stress plays in heart disease is spotty, experts say. Some doctors say this is partly because the introduction in the late 1980s of statins, or cholesterol-lowering drugs, made the quest less urgent. "People said we have this great way to control cholesterol, and they keep forgetting about the causes," Dr. Kopecky says.

Doctors need to discuss stress more often with patients, says Martha Gulati, chief of the division of cardiology at the University of Arizona College of Medicine-Phoenix and editor in chief of CardioSmart, the American College of Cardiology's patient engagement initiative.

Neil Stone, professor of medicine at Northwestern University's Feinberg School of Medicine in Chicago, where he practices preventive cardiology, says he counsels patients to find ways to lower their stress, such as carving out 30 minutes for a workout on a home bike or treadmill.

"Given the stresses we have, it's about thinking about priorities," says Dr. Stone, lead author of the latest cholesterol-treatment guidelines issued in 2013 by the American College of Cardiology and the American Heart Association.

Dr. Kopecky, of the Mayo Clinic, advises patients to think of three things they are thankful for when they go to bed or wake up in the morning, to help reduce stress.

After a heart attack in August, Jill Frieders says her doctor put her on medication to reduce her high cholesterol and also emphasized reducing stress. The 56-year-old Rochester, Minn., divorce lawyer had been scheduled for five court trials within a few weeks. She was also mourning the death of a beloved horse she'd had for 24 years.

Now, Ms. Frieders says her cholesterol is down. She learned to delegate more responsibility to associates at her law firm, and to push back when court dates pile up. "I will just flat out say I can't do this," she says. "I can't be overbooked."

When Mr. Edington's cholesterol climbed in 2012, Dr. Kopecky looked no further than the professor's four-sided business card for a possible cause. An academic and professional leader in the field of parks and recreation, Mr. Edington made regular trips to China, South Africa and other places as secretary-general of the World Leisure Organization. At home in Cedar Falls, Iowa, he worked at least 60 hours a week and took overseas calls at all hours of the night.

Dr. Kopecky kept Mr. Edington on the same dose of cholesterol-lowering medication and told him he needed to lessen his workload. Now, Mr. Edington has scaled back on administrative work and given up several leadership posts in professional organizations. He remains a professor of youth leadership studies.

The lighter workload has helped Mr. Edington physically and mentally, he says. While he's still busy—he recently finished writing his "32nd or 33rd book"—he spends more time with his grandchildren and the rest of his family, he says. "It has made a big difference in how I approach life and work and family relations."
The Specialist Will See You Now, on Video

Interactive video is giving more patients access to ongoing medical care.

Dr. Michael J. Helfenbein is a new doctor at Mercy Hospital Holyoke in West Springfield.

The hospital and other health care providers are using video technology as a tool to help patients who have chronic illnesses.

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Where Does It Hurt? Log On. The Doctor Is In
Telemedicine Sector Attracts Funding, but Some Physician Groups Worry About Quality of Care

BY MELINDA Bick

Can downloading an app, and describing your symptoms to a doctor you’ll never meet, take the place of an office visit? Can sending a “selfie” of your sore throat help diagnose strep? Those are some of the issues state and federal regulators—and the medical profession itself—are wrestling with as telemedicine spreads rapidly.

More Web-based companies offer virtual medical exams where doctors in remote locations evaluate patients’ symptoms online or by phone, develop a diagnosis and often write a prescription, usually in 15 minutes or less, for $40 to $50.

The companies say they provide a convenient, low-cost alternative to emergency-room visits and long waits at primary-care offices for minor medical issues. Three of the companies—Teladoc Inc., MDLIVE Inc. and American Well—hosted 500,000 to 600,000 doctor-patient interactions last year, more than double the number in 2011, according to the American Telemedicine Association, a trade group.

Investors are betting that more Americans will like getting medical care 24/7 without leaving home or work. The telehealth sector has attracted $272 million in venture-capital funding since 2010—including $70 million in the last quarter, according to Mercom Capital Group, a health IT research firm.

"Politicians and lobbyists can’t solve health care. It’s quite simple: Empower consumers with patient-in-control solutions," says John Sculley, former Apple CEO and vice chairman of MDLIVE, which netted $36 million in new funding this year.

Doctor on Demand launched in December with $3 million in seed funding from Google Ventures and other investors. Its co-founder is Jay McClure, executive producer of the talk show "The Doctors," and son of pediatrician Dr. Phil.

Many health plans think such services will provide savings, and cover most or all of the cost for their members. As of last year, 11% of large employers offered telemedicine services to their employees and 38% were considering it, according to consulting firm Merck.

But some physician groups and state medical boards worry that such e-visits are undermining the doctor-patient relationship and lowering the quality of care.

"Most physicians would never accept a phone call from a patient they haven’t met and diagnose and prescribe medication for that patient. Yet that is a common practice for many 24/7 health-care services," says Greg Billing, executive director of the

Dr. Lauren Yulden, in her Manhattan apartment, discusses patient Andrew Khan’s symptoms, using American Well consultation service.

Online vs. Offline

<table>
<thead>
<tr>
<th>Urine culture ordered</th>
<th>E-visit</th>
<th>Office visit</th>
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</thead>
<tbody>
<tr>
<td>3% of patients</td>
<td>43%</td>
<td>0%</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Antibiotic prescribed</th>
<th>E-visit</th>
<th>Office visit</th>
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</thead>
<tbody>
<tr>
<td>41%</td>
<td>0%</td>
<td>5%</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Avg. cost per visit including tests and drug</th>
<th>E-visit</th>
<th>Office visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>$74</td>
<td>$99</td>
<td>$89</td>
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</table>

Source: JAMA Internal Medicine

Robert J. Waters Center for Telehealth and e-Health Law, a nonprofit research group, also known as CTeL. Critics are also concerned that telemedicine services often prescribe antibiotics for conditions such as strep throat and urinary tract infections that typically require lab tests or physical exams to diagnose definitively.

According to the Centers for Disease Control and Prevention’s Get Smart program on antibiotic use, “Conditions which may lead to an antibiotic prescription warrant an in-person examination by a trained health-care professional.”

At a recent CTeL gathering, CDC scientists said the criteria some e-visit companies use—including asking patients to feel their own lymph nodes—aren’t a reliable predictor of strep infections, which cause only 5% to 10% of adult sore throats.

"There is a lot of concern making a diagnosis without examining a patient—not only for over-prescribing, but also for under-prescribing or misunderstanding cases where there might be a more serious infection," CDC epidemiologist Lari Hites told the group.
Where Does It Hurt? Patients Log On, And Doctor Is In

Continued from page 21

Amid such concerns, many states are debating updating their medical-practice regulations.

The Federation of State Medical Boards recently approved new model guidelines, urging states to hold virtual doctor visits to the same standards of care as in-person visits. That includes establishing an appropriate doctor-patient relationship, ideally with patients allowed to select their doctors rather than being assigned randomly, and able to confer via video, not just telephone or email.

The federation also says doctors must be licensed in the patient's state, and should obtain informed consent, document the encounter, and have a plan for emergency care if needed.

Treatment based solely on an online questionnaire "generally wouldn't meet the standard of care," says Lisa Robin, the federation's chief advocacy officer.

Crel suggests requiring doctors to examine patients face-to-face before treating them, unless diagnostic equipment is available to provide the same information they would seek in person.

E-visits are just one way technology is revolutionizing the delivery of health care and challenging traditional medical regulations. The term "telemedicine" embraces everything from state-side dermatologists scrutinizing images of soldiers' skin lesions from Afghanistan, to wearable sensors monitoring elderly patients' vital signs at home.

Specialists at major medical centers regularly confer via videoconferencing with doctors at smaller hospitals. The Cleveland Clinic invites patients to upload their medical records for a second opinion from anywhere in the world.

Health-care experts are counting on telemedicine to shore up access to physicians, particularly in rural areas. But some worry the patchwork of state rules threatens to stifle innovation.

Even requiring doctors to be licensed in the state where patients are physically located, which all 50 states currently do, "doesn't make sense in the 21st century," says Jonathan Linkous, CEO of the American Telemedicine Association.

Many companies say they already meet accepted standards of care and the state laws where they operate.

Teladoc says it has more than 2,500 corporate clients offering access to 75 million potential users. CEO Jason Gorevic says the company has developed 130 proprietary protocols to guide its doctors in treating conditions like strep throat remotely and says they prescribe antibiotics less frequently than office-based practices do. Participating doctors are either semi-retired or supplementing their incomes by doing e-visits in between patients or in off-hours, the company says.

The Dallas-based company currently operates in 49 states. It suspended service in Idaho and has a long-running legal dispute with the Texas Medical Board over a rule limiting e-prescribing. As Texas embraces the idea of telemedicine, the board has decided that it has to be safe telemedicine," says the board's executive director, Mari Robinson. Mr. Gorevic declined to comment on the litigation but says, "Our job is to make it simple for the consumer, even though the regulatory situation isn't simple."

Virtuwell, part of Minnesota-based managed-care company HealthPartners, has patients fill out online questionnaires, starting with "What Do You Think You Have?" If it is one of 40-50 conditions Virtuwell treats—including yeast and bladder infections—a nurse practitioner sends a treatment plan, often with a prescription.

Virtuwell draws the line at treating strep throat. Answers to some questions trigger alerts telling patients to see a healthcare provider in person.

American Well comes closest to meeting the federation's guidelines. Users download an app, select from available physicians in their state and confer via video. The Boston-based company, which provides e-visit platforms for several large insurers and hospital systems, recently launched its own service and says it had over 100,000 users in the first quarter.

CEO Roy Schoenberg, who consulted on the guidelines, says American Well would need to build more emergency procedures into its systems to fully meet them. "What these guidelines have done is bring some of these issues to the surface and say, 'This cannot be the Wild West anymore,'" he says.
Paralyzed From the Neck Down
Toward the Final Frontier: The Human Brain

By Paul G. Allen
And Francis S. Collins

In science there are moments when prior discoveries, advances in technology, and visionary leadership align to create the opportunity for a great leap. It happened in 1961, when President Kennedy called for a new era of space exploration, which took Americans to the moon. It happened again in 1990, when the Department of Energy and the National Institutes of Health transformed the future of biomedical research by launching the Human Genome Project.

The timing is perfect now for a federally coordinated effort to unlock the secrets of the brain, in line with President Obama's call this month for an ambitious project to map the most complex organ in the known universe.

This is a watershed moment. The goal is to revolutionize how we study the brain, and to gain powerful insights into neurological diseases and mental-health disorders. It is past time to solve questions with profound implications for tens of millions who will benefit from treatments for depression, Parkinson's disease, Alzheimer's, autism and many other disorders.

Though the two of us have rowed in different waters, we share a lifelong fascination with the brain. It is what makes us who we are and defines both our individuality and common humanity. Over the past several decades, the scientific community has begun to decipher the brain's intrinsic language. New, non invasive tools like optogenetics and calcium imaging enable us to see and manipulate the brain at the molecular level. Recent advances in three-dimensional, ultra-high-resolution microscopy reveal which nerve cells switch on in a particular circuit.

A new era of information technology allows us to build out super-data sets to track and organize these intercellular connections. With the aid of large-scale computer resources, we understand enough about the physics of the brain—in essence, a piece of highly excitable matter—to begin to simulate complete nervous systems.

Freely available mapping tools, such as those developed at the Allen Institute for Brain Science, along with the National Institutes of Health's Human Connectome project and other open-access databases, have accelerated research around the world. As a result, we can now define the functional geography of the cerebral cortex, the region that gives rise to perception, consciousness, language, reasoning and memory.

While neuroscientists have learned a lot, critical pieces regarding the brain's code for processing, storing and retrieving information are still missing. Neuroscience today is like chemistry before the periodic table: People knew about elements and compounds but lacked a systematic theory to classify their knowledge.

Today we know that neurons fire and we know that they are connected. We don't know how they act in concert to govern behavior, the essential question in treating neurological disease and mental-health disorders. Most of all, we have a limited understanding of how the brain translates its rich sensory experiences into complex mental states and behaviors, all at the speed of thought.

Big problems demand big solutions. The human brain contains nearly 100 billion neurons of at least a thousand distinct varieties. Those nerve cells make at least 10 trillion connections. No single discovery, no one researcher, will be able to crack the brain's code. The next generation of neuroscience breakthroughs will emerge from collaboration among a range of disciplines, from physics and biology to nanoscience, computer science and engineering. All hands must be on deck.

Progress will also hinge on the cooperation of the public and private sectors, a welcome aspect of the president's "BRAIN" initiative. We'll need creative, nimble management to ensure the best work out of both sides. The private realm, in particular, will require encouragement to play its role. For scientific leadership, the federal effort must tap into the brightest minds in the field.

It is our view that tough fiscal times demand creative approaches and more innovation. As President Obama has noted, the Human Genome Project paid $300 for each information dollar invested. By contrast, the BRAIN initiative will pay comparable dividends over time, and ultimately boost social productivity, reduce health-care costs and alleviate untold suffering. All humanity will benefit.

Mr. Allen, who cofounded Microsoft in 1975, is chairman of Vulcan Inc. and founder of the Allen Institute for Brain Science. Dr. Collins is director of the National Institutes of Health.
Why I'm Becoming a Psychiatric

By Nathaniel R. Morris

The newongoose, is the front line of mental health care. It's a stressful time of year, especially in the weeks leading up to the New Year. The pressure to perform, the stress of deadlines, and the need to achieve can be overwhelming. It's a time when we need to take care of ourselves and our loved ones. One of the best ways to do this is by nourishing our minds and bodies. A healthy diet, regular exercise, and adequate sleep can go a long way in helping us manage stress and anxiety. It's also important to connect with friends and family, who can provide support and understanding. Remember, it's okay to ask for help when you need it. There are many professionals who are trained to help us through difficult times. Whether it's a therapist, counselor, or support group, there are resources available to help us. Taking care of our mental health is just as important as taking care of our physical health. Let's prioritize our well-being this New Year.
I thought it would be best to start with a letter to you before I proceed with the rest of the essay. I have been pondering over this for some time now, and I believe it is time to share my thoughts with you. The past few weeks have been quite eventful for me, and I have been reflecting on many things. I have been thinking about the importance of having a clear purpose in life and the need to pursue it with dedication and passion.

Before I Die...

I have been reading about the concept of a "bucket list," and it has been quite inspiring. The idea of having a list of things to accomplish before one dies is one that I have always found intriguing. It is a way to focus on the important things in life and to ensure that one does not leave anything unfulfilled. I have been thinking about my own bucket list, and I have come to realize that it is not just a list of things to do, but a reflection of who I am as a person.

As I have been reflecting on my own life, I have been thinking about the things that are most important to me. I have been thinking about the people I love, the places I have visited, and the experiences I have had. I have been reflecting on the things that have brought me the most joy and the things that have challenged me the most. I have been thinking about the things that I want to do and the things that I want to be.

I have been thinking about the importance of living in the present and of being mindful of the moment. I have been thinking about the importance of taking time to appreciate the beauty of the world around us and of the people in our lives. I have been thinking about the importance of being grateful for what we have and of being kind to others.

I have been thinking about the importance of pursuing our passions and of following our dreams. I have been thinking about the importance of not giving up on our goals and of persevering through the challenges that we face. I have been thinking about the importance of being true to ourselves and of living according to our values.

I have been thinking about the importance of being a good friend and of being a good partner. I have been thinking about the importance of being a good parent and of being a good citizen. I have been thinking about the importance of being a good steward of our planet and of being a good steward of our resources.

I have been thinking about the importance of being a good role model and of being a good example for others. I have been thinking about the importance of being a good listener and of being a good communicator. I have been thinking about the importance of being a good learner and of being a good student.

I have been thinking about the importance of being a good teacher and of being a good mentor. I have been thinking about the importance of being a good leader and of being a good manager. I have been thinking about the importance of being a good colleague and of being a good coworker.

I have been thinking about the importance of being a good neighbor and of being a good citizen. I have been thinking about the importance of being a good citizen and of being a good taxpayer. I have been thinking about the importance of being a good voter and of being a good steward of our democracy.

I have been thinking about the importance of being a good citizen and of being a good steward of our planet. I have been thinking about the importance of being a good citizen and of being a good steward of our resources. I have been thinking about the importance of being a good citizen and of being a good steward of our community.

I have been thinking about the importance of being a good citizen and of being a good steward of our city. I have been thinking about the importance of being a good citizen and of being a good steward of our state. I have been thinking about the importance of being a good citizen and of being a good steward of our country. I have been thinking about the importance of being a good citizen and of being a good steward of our world.

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I have been thinking about the importance of being a good citizen and of being a good steward of our galaxy. I have been thinking about the importance of being a good citizen and of being a good steward of our galaxy. I have been thinking about the importance of being a good citizen and of being a good steward of our galaxy. I have been thinking about the importance of being a good citizen and of being a good steward of our galaxy.
A new generation of genomic technologies permits the increased collection of data on large study populations.\(^1\)\(^,\)\(^2\) New methods in informatics facilitate the integration of diverse types of information with genomic data in disease research. As a result, researchers are learning more about the genetic bases of disease and response to drugs.\(^3\)\(^,\)\(^4\) Genetic tests, including many that are offered directly to the consumer, are growing in number and clinical relevance. Genomic knowledge and technologies are also being adopted in areas distant from human health. Here, I describe evolving policies pertinent to genetic and genomic research, the integration of genetics into clinical care, and the broader issues raised by genetic technologies and information.

CONTROVERSIES IN GENOMIC AND GENETIC RESEARCH

Although genetic and genomic research do not raise wholly new ethical issues in the context of general biomedical research, they cast these issues in a fresh light. First, research using collections of biologic specimens, genomic data, and information from medical records has amplified the long-standing yet unresolved issue about consent for future research that is unanticipated at the time of specimen collection. Second, the push for broad access to research data sets has raised privacy concerns. Third, as researchers seek to share data with colleagues, the issue of whether and how to share research results with study participants remains vexing, particularly in the absence of explicit prior consent from participants.

CONSENT AND CONFIDENTIALITY

Consent documents provide a means of communicating the risks of a study (including informational risks) to participants. Narrow consent documents describe the benefits and risks of a specific study, whereas a broad consent may ask participants to agree to any number of future studies that will use their samples or data. Research participants may vary in their views and preferences about consent and in whether they wish to undergo a reconsenting process for every specific study that may be conducted with their specimens or information. They may also vary in their views about being notified of the results and implications of such studies. Broad consent is often obtained for future research on stored specimens and medical records because such research is considered to be of low risk to participants. Having the option of giving broad consent for future studies that use a stored sample or data set provides participants with a measure of control over their personal information and specimens. As vividly described in the book *The Immortal Life of Henrietta Lacks*, the process of obtaining consent by asking permission to use samples or data is a potent expression of respect.\(^7\)
The emergence of new ideas and new technologies for analyzing samples and data has raised important and controversial issues about whether and how to recontact participants to seek additional consent. Successful recontact requires a level of traceability among participants, which may increase the risk of breach of privacy, be overly intrusive, and be expensive, time-consuming, and cumbersome for researchers as participants move around or change names. However, the Internet and social networking have made it much easier to maintain or reestablish contact with participants.

Broad consents do not capture informed consent about all future uses of a participant’s sample or data. However, they do provide researchers with more flexibility. There is a middle ground between strictly narrow and overly broad consent; researchers can provide limitations on investigators or institutions that would have access to the sample or data and the types of studies that would be considered. Tiered consent allows participants to specify preferences for the future use of their samples or data. Participants can choose to opt out of all future studies, be contacted before any future use, allow unlimited use of their de-identified sample, or even specify the types of studies in which they would want or would not want their samples to be used.

The regulations that govern research on human subjects have their roots in the Tuskegee revelations of the early 1970s and were designed primarily to protect against physical and psychological risks in research. They touch on informational risks only tangentially. However, researchers do need to describe to potential participants, as well as to grant-giving bodies, how the confidentiality of each participant is to be maintained.

Research that was not contemplated in the original consent and that uses de-identified data and specimens is not considered human-subjects research and is not subject to the regulations protecting research participants. Thus, the elimination of identifiers can remove the need for consent and the ability to provide information to the subject. Indeed, this interpretation of the regulations might even be seen as providing an incentive to researchers to remove identifiers. However, true de-identification of biologic specimens or genomic data is not always possible, because a small number of genetic variants can uniquely identify a participant. Even aggregate data (e.g., pooled data from several hundred subjects) may not be safe; a forensic technique of DNA analysis allows for the determination of whether a subject with a specific genetic profile has contributed to aggregate genomic data. The identifiability of genomic data is especially important, given that privacy is a major concern of potential research participants.

To protect research participants, researchers collecting sensitive and identifying data can request a certificate of confidentiality from the Department of Health and Human Services (HHS) (Table 1). These certificates authorize researchers to avoid compelled disclosure “in any Federal, State or local civil, criminal, administrative, legislative, or other proceedings.” There are two important limitations. First, certificates of confidentiality do not require researchers to refuse to disclose identifying information; they only convey the legal right to do so. It is possible to imagine a circumstance in which law-enforcement officials might argue that disclosure of research information could help solve a string of violent crimes. The research institution and community might bring substantial pressure to bear on the researcher, who might feel obligated to disclose the requested information. Such cases are only imaginary now, but as large biobanks proliferate, they are likely to occur, and the disclosure to law enforcement could lead to distrust in the ability of the research enterprise to protect privacy.

HHS has recently proposed major reforms to the regulations governing human-subjects research. The proposed reforms would touch on many of the issues described here, including consent for research use of biospecimens and the requirements for consent and review by an institutional review board for research with biospecimens.
RETURN OF RESEARCH RESULTS

Whether, when, and how to return results of genetics research to participants have long been the subject of ethical and policy debate.22,23 These issues have only grown more complex as it has become clear that some research participants want to have access to research results or at least have the option of choosing whether to receive results.24-26 Survey respondents who were asked about their willingness to participate in a proposed cohort study said that receiving the individual results of research was the most important inducement.25 Some observers have argued that the reporting of results, especially clinically actionable results, is a medical and ethical obligation.22

There are many hurdles to delivering such information. In the United States, test results can be reported only by laboratories that are certified according to the provisions of the Clinical Laboratory Improvement Amendments (CLIA).27 In addition, data from research are often preliminary and need to be validated. However, even some of the most well-validated variants that are associated with disease, especially those that have been uncovered by new genomic approaches, have a small effect on disease risk, and such results can be difficult to explain and to understand. The reporting of results that have not been validated or those with questionable clinical benefit would require many disclaimers.

INTEGRATION OF GENETICS INTO MEDICINE

The successful integration of genetic testing into medicine requires an educated health care workforce, protections against inappropriate disclosure and discriminatory use of genetic information, and an oversight system that ensures the accuracy and reliability of genetic tests, particularly tests that provide results pertinent to important medical decisions. The dramatic increase in the number, complexity, availability, and medical relevance of genetic tests has created many regulatory challenges, as well as opportunities for change.

REGULATION OF GENETIC TESTS

Today's system of regulating medical-testing laboratories was put in place more than 20 years ago, when the Human Genome Project was just a wild notion and sequencing a patient's genome to diagnose a disease was virtually unimaginable. In enacting CLIA in 1988, Congress sought to ensure accurate, reliable, and timely testing. CLIA oversees clinical laboratories and, by extension, their performance of laboratory-developed tests. Although the Food and Drug Administration (FDA) has the legal authority to regulate laboratory-developed tests, including genetic tests, they have opted to regulate only test kits and some components of such tests. Thus the overwhelming majority of genetic tests are not currently subject to FDA scrutiny.

In 2008, the Secretary's Advisory Committee on Genetics, Health, and Society issued recommendations for the reform of genetic-testing oversight, including that CLIA require laboratories to participate in proficiency testing for laboratory-developed tests, that the FDA begin risk-based evaluation of such tests, and that HHS develop a mandatory test registry.28 Recently, the FDA has announced its intention to begin risk-based oversight of laboratory-developed tests, and the NIH is developing a genetic-testing registry to provide a centralized source of information on the more than 1600 genetic tests available to patients and other consumers.29-32 These steps reflect a shared emphasis by the NIH and the FDA on "personalized medicine and the scientific and regulatory structure needed to support its growth.32

Table 1. Quick Guide to Certificates of Confidentiality.

<table>
<thead>
<tr>
<th>What they do:</th>
<th>Allow researchers to resist disclosure of the identities of study participants, even under subpoena</th>
</tr>
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<tbody>
<tr>
<td>Confer perpetual privacy protection to subjects' study information, even after death</td>
<td></td>
</tr>
<tr>
<td>Eligibility:</td>
<td>Available to researchers who are collecting sensitive or identifiable information from human subjects as part of research</td>
</tr>
<tr>
<td>Available to any study that is approved by an institutional review board</td>
<td></td>
</tr>
<tr>
<td>Are not limited to studies that are federally funded</td>
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<tr>
<td>Limitations:</td>
<td>Allow researchers to choose whether to disclose data under subpoena</td>
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<tr>
<td>Apply only to data that are collected while the certificate is active</td>
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</tr>
<tr>
<td>Have been tested only two times in court but have been upheld (in People v. Newman in 1973 and in State of North Carolina v. John Trooper Bradley in 2005)</td>
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<tr>
<td>Authority:</td>
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<tr>
<td>History:</td>
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</tr>
<tr>
<td>Extended to include mental health research in 1974</td>
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<tr>
<td>Extended to all biomedical, behavioral, clinical, or other research in 1988</td>
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Glossary

- **Allele**: One of two or more versions of a genetic sequence at a particular location in the genome.
- **Codon**: A three-nucleotide sequence of DNA or RNA that specifies a single amino acid.
- **Complementary DNA (cDNA)**: A DNA molecule synthesized by an RNA-dependent DNA polymerase from an RNA template.
- **Genotype**: A person’s complete collection of genes. The term can also refer to the two alleles inherited for a particular gene.
- **Kinase**: An enzyme that transfers a phosphate group to a substrate.
- **Small (or short) interfering RNA (siRNA)**: A short, double-stranded regulatory RNA molecule that binds to and induces the degradation of target RNA molecules.
- **Somatic mutation**: A deleterious genetic variation occurring in any cell of the body except sperm and egg cells. Variations in somatic cells can affect the person in whom they occur but are not passed on to offspring.

**PHARMACOGENETICS**

One of the most promising areas of genomic medicine is the ability to match an individual’s genetic profile to the likely effect of particular drugs (see Glossary). Genetic makeup can predict the occurrence of toxic effects, such as the hypersensitivity reaction that occurs in carriers of the HLA-B*5701 allele who receive abacavir for the treatment of human immunodeficiency virus infection.35,36 The presence of various mutations in tumors can also predict the efficacy of certain drugs, such as cetuximab and panitumumab for colorectal cancer, since tumors that contain certain somatic mutations in KRAS do not respond to these drugs.37-39 In addition, the findings of genomic research can be used to identify promising drug targets. Sequencing of genes encoding kinases led to the discovery of a BRAF mutation in melanoma, which in turn led to the development of PLX4032, a drug that was designed to inhibit the mutant BRAF protein and that brought about tumor regression in a majority of patients in a phase 1 clinical trial.39

According to the FDA, 77 approved drugs contain pharmacogenomic information in their labeling,40 but in many cases, the labels do not provide action-oriented information for physicians and patients. For example, the label for the antidepressant protriptyline generally states that the drug is metabolized by CYP2D6 and that some patients may have poor metabolism.41 This information is probably of limited use to most physicians and patients. In contrast, the most recent label for warfarin includes a table showing the appropriate starting dose on the basis of the patient’s CYP2C9 and VKORC1 genotype combination, which should be more useful to physicians.42 Table 2 lists some examples of drugs with genetic information in their labeling.43-50 The inclusion of clear and comprehensive drug labeling that reflects the outcomes of genetic tests relevant to the safety or efficacy of use is critical to enhancing patient care.

**ELECTRONIC MEDICAL RECORDS**

In a world of electronic medical records (EMRs), there is a dual challenge of usefully incorporating genetic information while also protecting patient privacy. Consumers, health care providers, insurers, and regulators face a difficult balancing act to protect the privacy of genetic and other health information while also ensuring its availability and use for medical decision making.

The use of EMRs is becoming well established in some health care systems, such as those of Kaiser Permanente and the Geisinger Health System. However, according to the results of a survey of health care professionals who use 10 different EMR systems, the integration of genetic information is lagging behind. Only 4% of the respondents reported that their EMR system provided any decision support on the basis of the results of genetic tests, and the vast majority reported that their EMR supplier did not provide the type of support they needed for the interpretation of genetic information.51

EMRs could provide a platform for the integration of genetic information into clinical practice by guiding clinicians about when to order a genetic test, how to document and interpret the results, how to apply the information for treatment decisions and prevention screening, and when to refer patients for genetic counseling.52 Such automated guidance may be vital for both health care workers and their patients. In addition, EMRs may facilitate research with large cohorts, a factor that is especially valuable for prospective studies of genetic and environmental effects on health in which the linking of phenotype to genotype is essential.

The ease with which information can be shared across electronic databases increases the risk of unauthorized use and access to the information.52 This risk is relevant not only to patients but also to their family members, who will share many genetic loci with the patients and with one another. Unlike other clinical information, genetic


<table>
<thead>
<tr>
<th>Drug</th>
<th>Sponsor</th>
<th>Indication</th>
<th>Gene or Genotype</th>
<th>Effect of Genotype</th>
<th>Clinical Directive on Label</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir</td>
<td>GlaxoSmithKline</td>
<td>HIV-1</td>
<td>HLA-B*5701</td>
<td>Hypersensitivity</td>
<td>Black-box warning: “Prior to initiating therapy with abacavir, screening for the HLA-B*5701 allele is recommended.”</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Prometheus</td>
<td>Renal allograft transplantation, rheumatoid arthritis</td>
<td>TPMT<em>2, TPMT</em>3A, and TPMT*3C</td>
<td>Severe myelotoxicity</td>
<td>“TPMT genotyping or phenotyping can help identify patients who are at an increased risk for developing Imuran toxicity.” “Phenotyping and genotyping methods are commercially available.”</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Novartis</td>
<td>Epilepsy, trigeminal neuralgia</td>
<td>HLA-B*1502</td>
<td>Stevens-Johnson syndrome or toxic epidermal necrosis</td>
<td>Black-box warning: “Patients with ancestry in genetically at-risk populations should be screened for the presence of HLA-B<em>1502 prior to initiating treatment with Tegretol. Patients testing positive for the allele should not be treated with Tegretol.” “For genetically at-risk patients, high-resolution HLA-B</em>1502 typing is recommended.”</td>
</tr>
<tr>
<td>Cetuximab</td>
<td>Imclone</td>
<td>Metastatic colorectal cancer</td>
<td>KRAS mutations</td>
<td>Efficacy</td>
<td>“Retrospective subset analyses of metastatic or advanced colorectal cancer trials have not shown a treatment benefit for Erbitux in patients whose tumors had KRAS mutations in codon 12 or 13. Use of Erbitux is not recommended for the treatment of colorectal cancer with these mutations.”</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>Bristol-Myers Squibb</td>
<td>Anticoagulation</td>
<td>CYP2C19<em>2</em>3</td>
<td>Efficacy</td>
<td>“Tests are available to identify a patient’s CYP2C19 genotype; these tests can be used as an aid in determining therapeutic strategy. Consider alternative treatment or treatment strategies in patients identified as CYP2C19 poor metabolizers.”</td>
</tr>
<tr>
<td>Irinotecan</td>
<td>Pfizer</td>
<td>Metastatic colorectal cancer</td>
<td>UGT1A1*28</td>
<td>Diarrhea, neutropenia</td>
<td>“A reduction in the starting dose by at least one level of Camptosar should be considered for patients known to be homozygous for the UGT1A1*28 allele.” “A laboratory test is available to determine the UGT1A1 status of patients.”</td>
</tr>
<tr>
<td>Panitumumab</td>
<td>Amgen</td>
<td>Metastatic colorectal cancer</td>
<td>KRAS mutations</td>
<td>Efficacy</td>
<td>“Retrospective subset analyses of metastatic colorectal cancer trials have not shown a treatment benefit for Vectibix in patients whose tumors had KRAS mutations in codon 12 or 13. Use of Vectibix is not recommended for the treatment of colorectal cancer with these mutations.”</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>Genentech</td>
<td>HER2-positive breast cancer</td>
<td>HER2 expression</td>
<td>Efficacy</td>
<td>“Detection of HER2 protein overexpression is necessary for selection of patients appropriate for Herceptin therapy because these are the only patients studied and for whom benefit has been shown.” “Several FDA-approved commercial assays are available to aid in the selection of breast cancer and metastatic gastric cancer patients for Herceptin therapy.”</td>
</tr>
<tr>
<td>Warfarin</td>
<td>Bristol-Myers Squibb</td>
<td>Venous thrombosis</td>
<td>CYP2C9<em>2</em>3 and VKORC1 variants</td>
<td>Bleeding complications</td>
<td>Includes the following table: Range of Expected Therapeutic Warfarin Doses Based on CYP2C9 and VKORC1 Genotypes.</td>
</tr>
</tbody>
</table>

* All drug labels were accessed through Drugs@FDA at www.accessdata.fda.gov/scripts/cder/drugsatfda. HIV-1 denotes human immunodeficiency virus type 1, TPMT thiopurine methyltransferase, UGT1A1 UDP glucuronosyltransferase 1 family polypeptide A1, and VKORC1 vitamin K epoxide reductase complex subunit 1.
information is largely immutable. If whole-genome sequences are eventually included in medical records, they can be reanalyzed as more disease-risk loci are identified, which may lead to more incidental findings in clinical care.

The privacy rule outlined in the Health Insurance Portability and Accountability Act (HIPAA) sets standards for how "protected health information" (i.e., essentially any individually identifiable health information) should be controlled. HIPAA's privacy rule applies only to "covered entities," which are defined as health care providers who electronically transmit any health information in connection with transactions for which HHS has adopted standards, health plans, and health care clearinghouses. Under this definition, many facilities that perform direct-to-consumer genetic testing and analysis are exempt. In effect, the regulation does not address the type of information that is protected but, rather, who holds it. In a rapidly changing medical marketplace, there are many open questions about how to best protect the privacy of patients and consumers while also promoting research and the quality of clinical care.

As originally written, the HIPAA privacy rule did not explicitly provide privacy protections for genetic information. Part of the Genetic Information Nondiscrimination Act of 2008 (GINA) requires that HHS amend the HIPAA privacy rules to correct this oversight (Table 3). In October 2009, HHS issued a proposed rule to, among other things, revise the definition of "health information" to explicitly include genetic information and add GINA's statutory definition of "genetic information" to the privacy rule. As of this writing, the final rule has not been issued.

**GENETIC DISCRIMINATION**

GINA was designed to address concerns that information from genetic testing could lead to new forms of discrimination. It was hailed by its supporters as "the first civil-rights bill of the new century of life sciences." GINA's prohibitions on genetic discrimination in health insurance took effect on December 7, 2009. Under these rules, insurers in the group and individual health insurance market cannot use genetic information to increase premiums, deny enrollment, or impose exclusions for preexisting conditions. Insurers cannot request, require, or buy genetic information for underwriting purposes and are generally prohibited from asking individuals or family members to undergo a genetic test.

HIPAA was the first piece of federal legislation to protect against genetic discrimination in employer-sponsored group health plans. Specifically, genetic information cannot be considered a pre-existing condition and thus cannot be used as a basis for the denial of coverage. GINA extends this mandate by prohibiting the use of genetic information for underwriting purposes in group and individual health insurance. GINA protects against the use of test information and family medical history, but it does not limit the use of any information related to the manifestation of a disease or condition with a genetic component. Thus, a person with a family history of kidney disease who undergoes genetic testing and is found to have a dominant gene mutation would be protected under GINA. However, information resulting from imaging studies that may identify renal cysts would not be protected under GINA.

The 2010 Patient Protection and Affordable Care Act (ACA) outlaws discrimination by health insurers on the basis of signs and symptoms of genetic disease. Group or individual health insurers cannot establish rules for eligibility on the basis of health status, medical condition, claims experience, receipt of health care, medical history, genetic information, evidence of insurability, or disability. Beginning in 2014, the ACA will prohibit variations in premiums according to health status and genetic information.

GINA stipulates that it is unlawful for employers to make employment-related decisions on the basis of genetic information. In addition, it is illegal for an employer to request, require, or purchase employees' genetic information except under narrowly defined circumstances. Because of GINA, employees in the United States have a private right of action for reinstatement, back pay, compensatory and punitive damages, attorney's fees, and other relief.

GINA's provisions do not apply to life insurance, disability insurance, or long-term care insurance. GINA also does not apply to members of the military, veterans obtaining health care through the Department of Veterans Affairs, health benefits plans for federal employees, and the Indian Health Service. The effects of some of these limitations have been largely mitigated by the ACA and by policies for fair use of genetic information by the military and the Department
of Veterans Affairs.64 GINA also does not apply to educational or athletic programs. For example, the National Collegiate Athletic Association began mandatory testing for sickle cell trait among students participating in Division I athletics.62

**LAW ENFORCEMENT**

The collection and use of DNA by law enforcement and the courts for identification and prosecution of criminals have been standard practice since the mid-1980s. The Combined DNA Index System (CODIS), a fully integrated law-enforcement system of DNA records, contains more than 9.1 million DNA profiles from convicted offenders and more than 346,000 DNA profiles obtained from crime scenes.65 CODIS is credited with aiding in more than 127,000 investigations. In addition to aiding in convictions, DNA testing has been used to exonerate 273 wrongly convicted persons in the United States.66 In January 2011, a Texas man was found to have been innocent of a crime that had kept him behind bars for 30 years.67

Although the use of DNA evidence in law enforcement has tremendous potential to promote justice, it also raises profound legal, ethical, and social concerns. Among these are concerns about privacy and the disparate effect on historically vulnerable populations that may deepen the racial inequalities in the criminal justice system.68 Only persons who come into contact with law enforcement are entered into the database. Racial and ethnic minorities are disproportionately represented in these databases. Such persons will be more likely than whites to be identified by DNA profiles, since only DNA profiles that are included in databases can be matched to DNA evidence from a crime scene. To overcome this problem and further improve law enforcement, some observers have advocated for the creation of a uniform national DNA database.

**PROS AND CONS OF GENE PATENTS**

The court's ruling in *Diamond v. Chakrabarty*69 that an engineered microorganism was patentable subject matter paved the way for a 30-year explosion in intellectual-property cases in biology that was fueled by the expansion of knowledge and methods in biotechnology, particularly in sequencing and genetic testing. By 2010, there were patents on an estimated 20% of the human genome, including patents on both genetic sequence and methods for its analysis.68 The United States has been the hub of gene patenting, with more than twice as many patent applications as in Europe.69 The effects of gene patents on innovation, investment, and access to patients have been hotly debated.68 The plummeting costs of DNA sequencing have raised questions about whether the clinical or commercial use of whole-genome sequencing would infringe on gene patents and whether the patent holders would enforce their intellectual-property rights and, if so, under what terms.70 These issues are at the heart of a current lawsuit that could have far-reaching implications for research, the biotechnology industry, and medicine. In May 2009, the Association for Molecular Pathology and others filed suit against Myriad Genetics, arguing that the patents on the sequence

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**Table 3. Quick Guide to the Genetic Information Nondiscrimination Act of 2008 (GINA).**

<table>
<thead>
<tr>
<th>Overview</th>
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<tbody>
<tr>
<td>GINA was signed into law on May 22, 2008</td>
</tr>
<tr>
<td>Title I: Genetic Nondiscrimination in Health Insurance; took effect December 7, 2009</td>
</tr>
<tr>
<td>Title II: Prohibiting Employment Discrimination on the Basis of Genetic Information; took effect November 21, 2009</td>
</tr>
<tr>
<td><strong>What GINA does</strong></td>
</tr>
<tr>
<td>Prohibits group and individual health insurers from using a person's genetic information in determining eligibility or premiums</td>
</tr>
<tr>
<td>Prohibits an insurer from requesting or requiring that a person undergo a genetic test</td>
</tr>
<tr>
<td>Prohibits employers from using a person's genetic information in making employment decisions, such as hiring, firing, job assignments, or any other terms of employment</td>
</tr>
<tr>
<td>Prohibits employers from requesting, requiring, or purchasing genetic information about persons or their family members</td>
</tr>
<tr>
<td><strong>What GINA does not do</strong></td>
</tr>
<tr>
<td>Does not prevent health care providers from recommending genetic tests to their patients</td>
</tr>
<tr>
<td>Does not mandate coverage for any particular test or treatment</td>
</tr>
<tr>
<td>Does not prohibit medical underwriting on the basis of current health status</td>
</tr>
<tr>
<td>Does not cover life, disability, or long-term care insurance</td>
</tr>
<tr>
<td>Does not apply to members of the military or veterans obtaining health care through the Department of Veterans Affairs</td>
</tr>
<tr>
<td>Does not apply to health benefits plans for federal employees or the Indian Health Service</td>
</tr>
</tbody>
</table>

**How GINA is enforced**

Overseen by the Department of Health and Human Services, the Department of Labor, and the Department of Treasury, along with the Equal Opportunity Employment Commission.

Included are remedies for violations (e.g., corrective action and monetary penalties).
of BRCA1 and BRCA2 were unconstitutional. This case is only the most recent twist in the tale of two genes that are perhaps the best known of all the genes in the human genome. BRCA1 and BRCA2 came to public attention and became the source of conflict during the race for their discovery and have remained at the heart of legal, political, and public affairs debates around the world ever since. For example, although Myriad Genetics has exclusive rights in the United States to analyzing these genes in the context of determining genetic risk, Canada refused to use the testing services of Myriad's Canadian licensee, which resulted in very public and acrimonious debate.71

In March 2010, District Court Judge Robert Sweet issued a surprising ruling in this case. He held that the composition and method claims of Myriad's seven patents pertaining to BRCA1 and BRCA2 were invalid. He stated that the isolated DNA is not "markedly different" from a product of nature and that the claimed processes do not specify transformative actions beyond merely analyzing or comparing.72 Myriad Genetics appealed the decision. In October 2010, in an unexpected twist, the Department of Justice filed an amicus brief arguing that complementary DNA and other engineered DNA molecules are manufactured and thus are patentable but that isolated DNA that is simply separated from the rest of the genome and its cellular environment is not patentable. The brief read, "The BRCA genes, their deleterious alleles, and their relationship to breast cancer are the products of evolution, not human invention."73

If the courts were to agree with the Department of Justice's position, patents on manipulated nucleic acid sequences that may prove useful as therapeutics — such as sequences of small interfering RNA or DNA sequences used in the context of gene therapy — would remain eligible for patent protection and thus continue to be attractive to investors. Such a decision would also permit whole-genome sequencing or variant detection of native genomic DNA without the danger of infringing on gene patents or requiring royalty payments. On July 29, 2011, the U.S. Court of Appeals for the Federal Circuit concluded that isolated DNAs are eligible for patents. The plaintiffs may appeal, so the final decision may not be known for some time.

CONCLUSIONS

The field of genomics is evolving at a dizzying pace. Researchers are producing genomewide data sets on ever-expanding study populations. Broad access to these data, stored samples, and EMRs are accelerating our understanding of the role of genes, environment, and behavior in health and disease. Translational research is converting new knowledge into diagnostics, targets for drug development, and new insights about how to prevent and treat disease. The challenge is to ensure that innovation in research and medicine is equaled by innovative policies that foster science and discovery while protecting and respecting research participants and patients.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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REFERENCES

17. Public Health Service Act, 42 U.S.C. § 300(d), 241(d).