Rising tides within politics, technology, and science are altering health care in this nation. Pittsburgh is ready to make the most of this moment.
As the 19th century gave way to the 20th, medical schools had taken the place of the traditional physician apprenticeship, so Americans who were ill and injured were at the mercy of the graduates of these schools. And the country had more than its share of shoddy, ill-prepared practitioners.

In 1908, Carnegie Foundation for the Advancement of Teaching President Henry Pritchett summoned the help of the well-regarded educator and Carnegie scholar Abraham Flexner to survey the state of medical education in the United States and Canada and offer his suggestions for improvement. After visiting 155 medical colleges in the course of 18 months, Flexner recommended that all but 31 be closed or undergo serious reform. Of those he suggested be closed, he wrote this in his landmark *Medical Education in the United States and Canada*:

*These enterprises—for the most part they could be called schools or institutions only by courtesy—were frequently set up regardless of opportunity or need … [Students were exposed to lab work and clinical education in only a handful of the better schools.] Little or no investment was therefore involved. A hall could be cheaply rented and rude benches were inexpensive.*
Janitorial service was unknown. Occasional dissections in time provided a skeleton—in whole or in part—and a box of old bones. Other equipment there was practically none. The teaching was, except for a little anatomy, wholly didactic. The schools were essentially private ventures, money making in spirit and object. A school that began in October would graduate a class that next spring; it mattered not that the course of study was [supposed to take] two or three years.

Not surprisingly, admissions standards were lacking at many of these schools: No applicant who could sign his note or pay his fees was turned down, noted the clear-eyed Flexner. And, Many had “graduated” from nonexistent high schools. Favoring the scientific and clinical example he knew from the German model (also used by Johns Hopkins School of Medicine), Flexner suggested the schools would be stronger as departments of universities.

Flexner’s initial impressions of the University of Pittsburgh School of Medicine were tepid. But by 1910, he found a committed dean and physician in Thomas Shaw Arbuthnot. The new dean had high aspirations and within his first year had improved the facilities, hired “increasingly distinguished” and some full-time faculty, and raised admissions standards (a high school diploma was now required)—and he was clearly just getting started. (Soon, two years of college would be required.) Under the management of the University, this School of Medicine proposes to do what is necessary for the development of a Medical School of the First Rank, noted Flexner.

Beyond Pittsburgh, reform was already in the air as Flexner began his study. Yet his famed report was a tipping point that altered the course of medicine, helping bring about the rigorous standards and preparation we associate with modern North American schools and the profession.

Medicine’s next tipping point is now upon us. And Pittsburgh is poised to make the most of this moment.

To use a metaphor Pittsburghers know well, imagine a confluence of rivers. Three, to be exact. A trio of rising forces promises to alter health care in this nation: the push for reform (by that I mean improving quality and lowering cost); informatics (the ability to store and analyze huge troves of data); and an increasingly sophisticated understanding of biology (particularly at the cellular and molecular levels) that is giving us the ability to personalize medicine.

Without delving too deeply into the issue here, especially its politics, I’ll quickly address why medicine costs so much in this country. Physicians, typically highly trained and well intentioned, are using every resource at their disposal to try to help their patients. As Steve Shapiro, an MD who came to Pittsburgh to chair our Department of Medicine and is now UPMC’s chief medical and scientific officer, put in an online interview, “The culture of the United States is just to do more—more medicine, more treatment. Doctors like doing more, and patients like us to do more.”

But too few of those treatments are based on good evidence, and too much is done to avoid litigation. And, to be frank, the financial incentives for testing and treatment are strong and, often, misaligned with proper care. This vice is inherent in the system.

Our clinical partner, UPMC, has another model. It is one of the nation’s two biggest payer-provider systems (the largest that is closely aligned with a research university), meaning it has its own insurance plan. Because it partially finances the cost of the care it provides, it is not marred by a perverse incentive to do unnecessary testing or care. It’s notable that UPMC’s insurance arm came about in the 1990s, not only because its board recognized the opportunity it would provide to affect the future delivery and analysis of care, but also because certain faculty members at Western Psychiatric Institute and Clinic advocated that UPMC enter the insurance business to protect the chronically mentally ill from the possible negative impact of managed care programs. Since then, UPMC’s insurance arm has grown to service more than two million members.

At the same time, UPMC has readjusted its physician-compensation system to reward quality and safety. (See pp. 29–31.)

To get back to how medicine can miss the mark, consider how we treat metastatic cancer in adults. With the exception of testicular cancer and chorionicarcinoma (a rare tumor of placental origin), chemotherapy isn’t likely to cure cancer at that runaway stage. (I’m speaking of adults, not children here; both childhood cancers and children tend to respond better to chemotherapies.) What happens instead is heartbreaking: Adults with metastatic cancer are offered highly toxic, intensive chemotherapy cocktails. A small number of patients will have a remission, usually not a very durable one. Most will simply get sick from the drugs and end up spending their last days in the ICU.

This is just one example of how modern medicine is off kilter. I could cite examples for many diseases. So how do we become more effective? What physicians and other scientists intend to do at Pitt—and there are similar efforts at other academic medical centers—is to personalize care. That is, we want to give precisely the right treatment, at the right time, to the right patient. For a handful of drugs, this is already common practice. For instance, in 2008 the American Medical Association reported that 21 percent of patients who receive the anticoagulant Warfarin (a common treatment for pulmonary embolism and thrombosis) experience bleeding events. It is now recommended that physicians test to see whether a patient has certain genomic variations to determine optimal dosing—although the impact of these tests is still under investigation.

In the case of metastatic cancers, if we could identify the genes or other molecular mechanisms that make people responsive to chemotherapy agents as opposed to resistant to them, we would save a great deal of money. And, more profoundly, we would avoid compromising the remaining quality of life that people have.

As of this January, Jeremy Berg—former director of the National Institute of General Medical Sciences and a thought leader in biomedicine—heads our new Institute for Personalized Medicine. The PhD, who has been a member of our faculty since 2011, also serves as Pitt’s associate senior vice chancellor for science strategy and planning and as a professor of computational and systems biology. Jeremy takes the reins as the cost of sequencing a genome (the entirety of an organism’s genetic material) has trended down to almost $1,000. We expect that sequencing genomes of patients (and potentially other molecular “We are able to ask questions we’ve never been able to ask before. Never.”
convincing that Adrian’s new role couldn’t be found at another academic medical center—at least not on the scale he’s operating within.

In addition to pursuing his work as director of UPCI’s Women’s Cancer Research Center, Adrian is leading the research arm of a massive project that will figure out how to use patient data to foster personalized medicine. UPMC announced in the fall that it is investing $100 million throughout the next five years in a data warehousing, integration, and analysis project that will bring together clinical, financial, administrative, genomic, and other information. This is a tall order.

“UPMC’s analytics initiative is one of the most ambitious and comprehensive efforts of its kind in health care,” Neil de Crescenzo, senior vice president and general manager for Oracle Health Sciences, notes in a November 2012 news release. (UPMC is partnering with Oracle, as well as IBM, Informatica, and dbMotion in this effort.) “Given the size, scope, and influence of this leading academic medical center, the discoveries made here are likely to transform the practice of medicine far beyond the walls of UPMC.”

“When a patient walks in the door, we want to be ready to say, ‘You have mutation X, here is therapy Y,’” says Adrian.

To accomplish this goal, we need to link some crucial patient information—genotype and phenotype. Genotype is what we call the specific molecular signature that reveals peculiarities of a patient’s genome, or inheritable characteristics. A phenotype is the broader description of a person that ends up in clinical records (like diseases endured, medications taken, weight, and family history). This information, of course, may already exist for some patients and research participants. The difficulty lies in getting medical center and research data systems to talk to one another. Adrian and his partners at Pitt and UPMC are charged with making that happen.

It’s messy work.

And without an institutional foundation in place to facilitate the process, physicians and researchers who hope to merge clinical and research data for their studies have the odds stacked against them. Think silos of data. Data sets that don’t match up. Absent fields. Data that never made it into the digital realm.

“Data graveyards.”

“Most researchers would just give up,” says Adrian. Some Pitt researchers—in head and neck cancer and melanoma, for instance—have moved such projects forward successfully. But there’s nothing in place systemwide to make the task less arduous. That has meant going back to patient charts and pathology reports to manually extract data, again and again.

“I think that’s a major reason we haven’t moved [a lot of promising research] into the clinic,” says Adrian. But with Oracle, Pitt’s team (of mathematicians, biostatisticians, programmers, informatics and IT experts, genomics whizzes, researchers, oncologists and other physicians) is doing the groundwork to make the linking of genotype and phenotype routine for scientists at the University.

“To share data and put it in a ‘warehouse’ is a fundamental change in practice,” both logistically and philosophically for scientists, says Adrian. “We’re laying the foundation for a house—for a mansion. Hopefully we won’t go into foreclosure,” he says with a chuckle.

“We are in a time of massive data,” Adrian says, adding that UPMC now has 3 petabytes of patient data. Not familiar with a petabyte? A petabyte is equal to 1 quadrillion bytes.

“When you go to your doctor, the physician considers a couple of variables on you,” says Adrian. “The human brain can only handle four or five variables at once. But we need to take into account hundreds of variables on you.”

The time is ripe for a big data convergence at UPMC and Pitt. Adrian and his colleagues at the cancer center were working toward this independently when they learned that Steve Shapiro and other UPMC leaders had the same goals. “It’s snowballed since,” Adrian says. In designing the new model, the institutions have pulled together professionals from various disciplines to get their feedback. And Adrian’s IT team now meets with UPMC IT representatives every week.

Adrian’s counterpart at UPMC, Lisa Khorey (vice president for enterprise systems
and data management at the medical center), reports that UPMC has been “methodically studying best practices” in health analytics and data management for years with the braintrust down the street at Carnegie Mellon Software Engineering Institute.

“We’re now ready to turn what we’ve learned into action,” she says.

On a recent chilly Friday in February here, Adrian and his team got a peek at what the future of medical research in Pittsburgh will look like. Their partners from Oracle had been camped out at Pitt for days preparing the team for a trial run on a prototype that would merge clinical and genomic data.

Their first “use-case”? Breast cancer, which is Adrian’s area of expertise.

The system was able to integrate UPMC clinical data from 140 breast cancer patients with molecular findings from The Cancer Genome Atlas. (An impressive portion of the samples for this NIH project has been gleaned from Pitt’s excellent tissue bank.)

“We have the first product from Oracle that allows us to do exactly what we said we’d do—integrate clinical and molecular data,” says Adrian. “We are able to ask questions we’ve never been able to ask before. Never.”

He notes that this “very small, discrete” use-case, and others that will follow, is designed to work out the glitches involved in integrating key data systems. Yet it’s already paying off in terms of what appear to be useful findings (though the work is very preliminary at this point).

“Now we can say—for these 140 patients—’Show me genomic differences in women who are postmenopausal versus those who are premenopausal,’ for example,” says Adrian. “We saw striking differences. We hope these will lead to new treatment strategies.”

In February the system focused on changes in DNA copy number and gene expression. Next fall, it will look at point mutations (like missing or additional nucleotides) and structural variants (e.g., chromosomal segments that have moved to new positions) within the 140 tissue samples. “We will never be finished” using the tool, says Adrian. That said, his team will soon move on to similar use-cases for 10 other cancers, as well as other conditions, including diabetes and acute renal failure.

In the rounds that follow, the product is likely to become more robust. “It’s like Netflix,” Adrian offers. “The system doesn’t know much about you when you first sign up, but after ordering tens or hundreds of movies, then it’s able to more precisely suggest DVDs you would like.” This is how machines learn. They get smarter as we add more data and ask more questions.

The big data world we’re entering is not without complications. Earlier this year, Yaniv Erlich from MIT’s Whitehead Institute for Biomedical Research reported that his team was able to identify about 50 “anonymous” research subjects by comparing their genomic data to data available on genealogy sites and in other public records. This experiment was conducted to illuminate potential gaps in privacy so they could be addressed. UPMC and Pitt are taking such issues very seriously.

Fortunately, we have a very strong group of ethicists at Pitt who will be working with us as we move forward. For instance, Lisa Parker, associate professor of human genetics in the Graduate School of Public Health and a Center for Bioethics and Health Law faculty member, is an expert on informed consent and confidentiality issues in medical research.

“What ‘genetic privacy’ can mean is complicated,” she says. “We leave behind our DNA on every restaurant water glass. [Still, most people don’t] have the scientific resources to analyze DNA and connect genetic information to a name on a credit card slip. What is most important is not possession of genetic material or even genetic information, but how genetic information is used. We need regulations and penalties regarding misuse of information. A federal act (GINA) prohibits health insurers from discriminating on the basis of genetic information; other protections are patchwork at this point.

Lisa also notes that Pitt and UPMC won’t presume patient consent: “We want to ask people to participate after we explain the importance of their contribution and the measures we have in place to protect their privacy.”

Big data is going to be key to moving personalized medicine forward. Think about how many genomes or partial genomes would be needed to find patterns that will lead to personalized outcomes for patients: “Any given two people have literally millions of differences in their genomes,” says Jeremy. “We are very, very similar to each other, but if there are three billion DNA base pairs [in the human genome], and if we are 1 percent different—that’s probably a little high—but, 1 percent of three billion is 30 million. So that’s lots of differences from one person to another. To try to get enough information to get patterns out of that, you need lots of samples, perhaps a thousand.”

In addition to casting a wide net for patient samples, Pitt researchers will be diving deeply into molecular goings-on.

The University is exploring partnerships with other organizations to bring deep sequencing (“deep” because it allows us to detect rare mutations and other molecular anomalies after sequencing an individual genome perhaps hundreds of times) and other new technologies into our portfolio. And our own researchers are helping to uncover the many mysterious compensatory and regulatory machinations at work that were previously tossed aside as “junk DNA.”

“What Pitt and UPMC bring to the table is really first-rate basic and clinical science, as well as the patient population,” Jeremy notes. UPMC’s network now includes 20 hospitals and 400 outpatient sites.

He reminds that correlation is not causation: “There’s an idea that you take all the data, put it in a bag, and shake it up, and you’ll find out what you need. That didn’t work in finance or other fields. Mechanisms really matter. Weather prediction, for example, has gotten better because it’s based on solid principles of physics.”

That’s where strong science enters in. We need to understand the organ and build on that, he says: “One of the most important things in scientific discovery is knowing when you should be surprised. If you are just looking at correlations, that’s not a basis for being surprised. It’s unlikely to lead you anywhere productive.”

What I keep hearing from my colleagues here is we have an extraordinary opportunity in Pittsburgh. Consider the research strength of this University (which shot up to number five in terms of National Institutes of Health research funding a few years ago), UPMC as the largest payer/provider linked to a research university, the technology powerhouse Carnegie Mellon University in the same neighborhood, corporate technology partners like Oracle and IBM. And the secret ingredient: Pittsburghers.

Pittsburghers love their town and are more likely to stick around
than are folks who live in other biomedical meccas—like Boston.

“In the early days of genetic research, places with stable populations, like Salt Lake City, were the powerhouses,” reminds Jeremy. That stability, he notes, will be “good for a research tool and good for Western Pennsylvania.” And because this stable patient population is so large, we are in an excellent position to make advances in understanding and treating both common and rare diseases that arise within it.

The Salk vaccine could have been called the Pittsburgh, or Pitt, vaccine, Jonas Salk’s son, Peter Salk, has said. And according to some, Dr. Salk would have wanted it that way. In the ’50s, Pittsburgh scientists, practitioners, and community members (including thousands of children) literally rolled up their sleeves to make history.

This is another Pittsburgh moment.

Arthur S. Levine is dean of the School of Medicine and senior vice chancellor for the health sciences. Erica Lloyd is editor-in-chief of this magazine. Michael Fitzgerald and Elaine Vitone contributed to this report.

In a Maelstrom

At Health Care’s Stormy Front, an Opportunity to Rethink How Medicine Is Delivered

By Michael Fitzgerald

Diane Holder might forgive you if you accidentally called her Diane Hold-on.

Much of her job involves handling the accelerating pace of change coming with health care reform. As president of UPMC Health Plan and its Insurance Services Division and executive vice president of UPMC, Holder is effectively dealing with a maelstrom.

Money drives the maelstrom. Health care sucks up money at a far higher rate here than in other developed nations. Yet compared to the citizens of those nations, the health of Americans is mediocre.

To try to slow down the storm, the U.S. government, which this year will pay for more than half of the medical care doled out to Americans, is beginning to integrate “value-based payments” to hospitals. Instead of paying by volume—number of patients, tests, and procedures—quality of care will dictate payments. In another effort to economize, we will see more care delivered by highly trained nurses and physician assistants working with doctors.

Meanwhile, technology is giving patients access to and control over their entire medical histories. It also allows medical professionals to make virtual house calls. Such trends increase the potential for competition, which should reduce costs.

“We’re seeing a lot of changes,” Holder says. UPMC is not just waiting to get buffeted by this storm. It has begun shifting away from the pay-for-service model, adopting “shared savings,” in which UPMC’s Health Plan splits cost savings if quality-of-care targets (such as whether patients get better or stay healthy) are met. In 2012, it also boosted its roster of advanced-practice providers like physician assistants by 16 percent.

With UPMC’s partner the University of Pittsburgh, a storied medical research institution, “we have the opportunity to do things differently,” says Holder (who is also an assistant professor of psychiatry). UPMC is becoming well positioned to, for example, combine research findings with a database of care information to help suggest more individualized treatments for patients, depending on their unique genetic characteristics. (See Arthur Levine’s article, p. 24, for more on how this is unfolding.) Such combinations should reduce inefficiencies and improve outcomes at the same time.

The Health Plan even does its own research: The nonprofit UPMC Center for High-Value Health Care, established in 2011, examines ways to improve service and payment policies for different types of patients and providers.

UPMC has been investigating ways to reduce the incidence of chronic conditions, the source of some 70 to 75 percent of all health care spending in the United States.

For instance, UPMC changed its threshold for paying for nutritional and support services for overweight children. Where once those services were not paid for until the child was officially obese, now UPMC’s Health Plan kicks in at a threshold below obesity, which should help reduce the long-term costs associated with the condition.

In another experiment aimed at a chronic condition, UPMC focused on reducing the percentage of smokers on its own staff, which stood at 19 percent, about the same as the national average. UPMC found that patients who combined smoking-cessation coaching with medication to combat cravings were more likely to quit smoking than patients who’d just picked one method. So the health plan waived co-pays for the medication for patients who also worked with a coach. The number of smokers on staff fell by 9 percent.

Solid science may show us the way out of this maelstrom.

Chronic Challenges

70–75% of every health care dollar is spent on someone with a chronic condition.

35.7%: adult Americans who are obese.

16.9%: Americans ≥19 who are obese.

33%: Americans with high blood pressure.

54% of these do not have their condition under control.

20%: adult Americans who smoke.

8.3%: Americans with diabetes.

0.26%: Americans under 20 with diabetes.
THE PittsBuRGh MODEL
FOr TRANSFoRMING HEALTH CaRE

Health care reform. Three words that promise systemic, wholesale change in the way Americans receive health care.

“People question whether health care reform is going to happen or not,” says Steven Shapiro, the MD executive vice president and chief medical and scientific officer at UPMC, as well as president of its Physician Services Division and a professor of medicine in the School of Medicine. “It has to. Our country simply can’t afford to spend 17 or 18 percent of GDP on health care.”

And the UPMC/Pitt medical community is not waiting around to see what politicians might imagine; it has a vision for the future of medicine. That vision is built upon what could be called the Pittsburgh Model, which integrates the medical center’s care providers and payment system with the University’s impressive research power in a way that perhaps no other academic medical center in this country is attempting. “Transform” is a more apt word for what is happening here than “reform.”

The big idea? Smarter care that will lead to fewer unnecessary tests, more precise treatments, and healthier Pittsburghers.

Here’s how the future is unfolding.

—Compiled by Michael Fitzgerald and Erica Lloyd

200 DIFFERENT DATA SOURCES in different systems across UPMC operations—previously “silos” of information—are being accessed and integrated with data sources from Pitt researchers.

“We’re starting to build these pathways so we can do the appropriate care, not unnecessary care.” —Michael Becich, chair of Pitt’s Department of Biomedical Informatics

3 PETABYTES: estimated volume of current UPMC patient data.

$100 MILLION, 5 YEARS: investment in melding those sources into a new data warehouse, with help from IBM, Oracle, Informatica, and dbMotion (partly owned by UPMC).

1ST QUARTER, 2013: when the first version of the new data warehouse goes into service.

AN EXPANDED CARE TEAM makes sense on a number of fronts, studies show. You probably don’t need an MD to treat poison ivy, for instance. “Intraprofessionalism” is now part of the medical students’ curriculum at Pitt.

“All sorts of market forces are pushing us toward team delivery of care.”

—Benjamin Reynolds, director of the UPMC Office of Advanced Practice Providers

1,400: advanced-practice providers (nurse practitioners, nurse midwives, certified registered nurse anesthetists, and physician assistants) practicing at UPMC in collaboration with or under the supervision of a physician.

16%: increase in UPMC advanced-practice providers from 2012 to 2013.

500: new advanced practice providers UPMC expects to hire within the next four years.

REMOTE CONTROLS
Virtual house calls and telemedicine allow expertise to reach patients from a distance.

3,714: patients served through UPMC telemedicine from 2007 to March of this year at clinics and in-home programs. And Children’s Hospital of Pittsburgh of UPMC faculty will soon bring remote pediatric emergency care to four rural hospitals.

“For the average worker with employer-based health insurance, growth in premiums and cost sharing has largely eroded wage gains over the past decade.”

—The Commonwealth Fund, May 2012

$7,960: what the U.S. spent per person on health care in 2009.

$3,960: what the median spending was for health care in 2009 in 13 other industrialized nations, ranging from $2,828 in Japan to $5,352 in Norway.

5%: reduction in revenues for most U.S. medical centers in 2012 because of unofficial health care reform by insurers.

$1,080: average MRI scan cost in United States in 2011.

$599: cost in Germany in 2011.

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SOURCES: CDC, UPMC, UNIVERSITY OF PITTSBURGH.
**WHERE THE HEART IS** The relatively stable and diverse population in Pittsburgh is “good for a research tool and good for Western Pennsylvania.”

—Jeremy Berg, who directs the new Pitt–UPMC Institute for Personalized Medicine

1,000: approximate number of patients at UPMC whose genomic data has been gathered for various research efforts (631 for NIH’s The Cancer Genome Atlas).

10,000–100,000: guesstimate of number of patients whose genetic data UPMC will have in five years (to be gathered with their consent). That data will feed back into research efforts to improve and personalize care.

**ACROSS THE DIVIDE**
Bridging patient clinical information with a deep understanding of genetics and organ systems will lead to important discoveries and better, more customizable care. It’s also likely to change the way doctors run clinical trials.

55,000: employees at UPMC.
5,500: physicians affiliated with UPMC.
20: hospitals within UPMC.
400: outpatient sites.
234,000: patient admissions in 2012.
4.8 MILLION: outpatient visits in 2012.

**THE CLOUD IS THE LIMIT**
Big data and sophisticated informatics from the new data warehouse will be powerful tools for researchers.

“If you have Siri [Apple’s nifty voice-driven personal assistant], you say, ‘Tell me [which] planes are above me.’ In microseconds, it tells you the planes. It uses data and triangulates. Why can’t we do that? ‘Tell me the last 500 patients with the BRCA mutation. How was the response of this treatment versus that?’ This is what will drive good care.”

—Adrian Lee, who leads Pitt’s end of the data warehouse effort

12 (FIRST) STEPS
A dozen “use-cases” (or pilot projects) will inform the infrastructure for the massive Pitt/UPMC data warehouse in its first five years. Among them: diabetes, utilization of blood products, acute renal failure, breast cancer, prostate cancer, and other cancers.

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**THE COMPENSATION SYSTEM**
UPMC now rewards care providers for quality of care, not just quantity (of exams, tests, etc.).

250: primary care practice sites involved in the savings-sharing program at UPMC Health Plan, which has focused on Medicare patients in the first stages of this program. The program will expand in 2013 into more of the 2,000-plus practices in the network.

32%: improvement in the specific quality measure University Health Services is evaluating.

4%: cost improvement experienced with the new program.

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