

THE RISE OF GENOMICS

Consumerism, Commercialization and Health Care

JULY 2018

How rising consumerism in health care and technological advances in genomics are driving change in the world of health IT

WITH EXPERT INSIGHTS FROM:

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A report from the Center for Connected Medicine

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GENOMICS EXPERTS



Jill Hagenkord, MD

Chief Medical Officer, Color

A pathologist by training with subspecialty boards in molecular genetic pathology, Dr. Hagenkord is involved in health product strategy, partnerships, and development of provider and patient tools at Color. She is the former Chief Medical Officer of 23andMe.

color



Mylynda B. Massart, MD, PhD

Co-Investigator, All of Us Pennsylvania

A family medicine physician and Medical Director of the Matilda Theiss Health Center at UPMC, Dr. Massart is the Integrating Special Populations Core Co-director of All of Us Pennsylvania, a state-based arm of the NIH-backed 'All of Us' initiative.

All of Us
Pennsylvania



Houman Modarres

Senior Director of IP Networks, Nokia

Mr. Modarres has a long history on the leading edge of networking technology, with expertise on the infrastructure, security and network demands of growing data-heavy fields such as genomics.

NOKIA



Martin Reese, PhD

Founder and CEO, Fabric Genomics*

An expert in machine-learning and bioinformatics who co-created key algorithms for Fabric Genomics' software platform, Dr. Reese previously worked on the Human Genome Project, the groundbreaking initiative that first decoded the human genome.

FABRIC
GENOMICS™



Rasu Shrestha, MD, MBA

Chief Innovation Officer, UPMC and Executive Vice President, UPMC Enterprises

Named a leading innovator in health IT by Health Data Management, Dr. Shrestha also has been recognized by Becker's Hospital Review as one of the 26 "Smartest People in Health IT" and named one of the "Top 20 Health IT Leaders Driving Change" by InformationWeek.

UPMC
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*UPMC Enterprises portfolio company

OVERVIEW OF ADVANCES IN GENOMICS

In the past two decades, understanding of human DNA has had a major effect on health care and is poised to revolutionize the practice of medicine. So far, truly personalized medicine is being delivered in a small number of situations to treat a limited range of diseases. But with advances in technology, a flood of investments and research funding, and surging interest from health systems and industry, the pace of adoption is expected to accelerate.

Genomics, or the study of genes, in health care is about understanding how gene variations affect health and wellness. Scientists and clinicians are still learning about the correlation between genetic variations and disease, but it is known that certain variations, or mutations, can be related to the development of specific diseases. With some mutations, the link is clear. It is known, for example, that the presence of certain mutations will cause sickle cell disease or cystic fibrosis. But with other diseases, such as some cancers, we only know the presence of a specific mutation is related to an increased risk of disease.

Since the Human Genome Project completed the first sequence of the human genome in 2001, there have been incredible advances in the science and technology of genomics, which has made genomics more affordable and accessible than ever before.

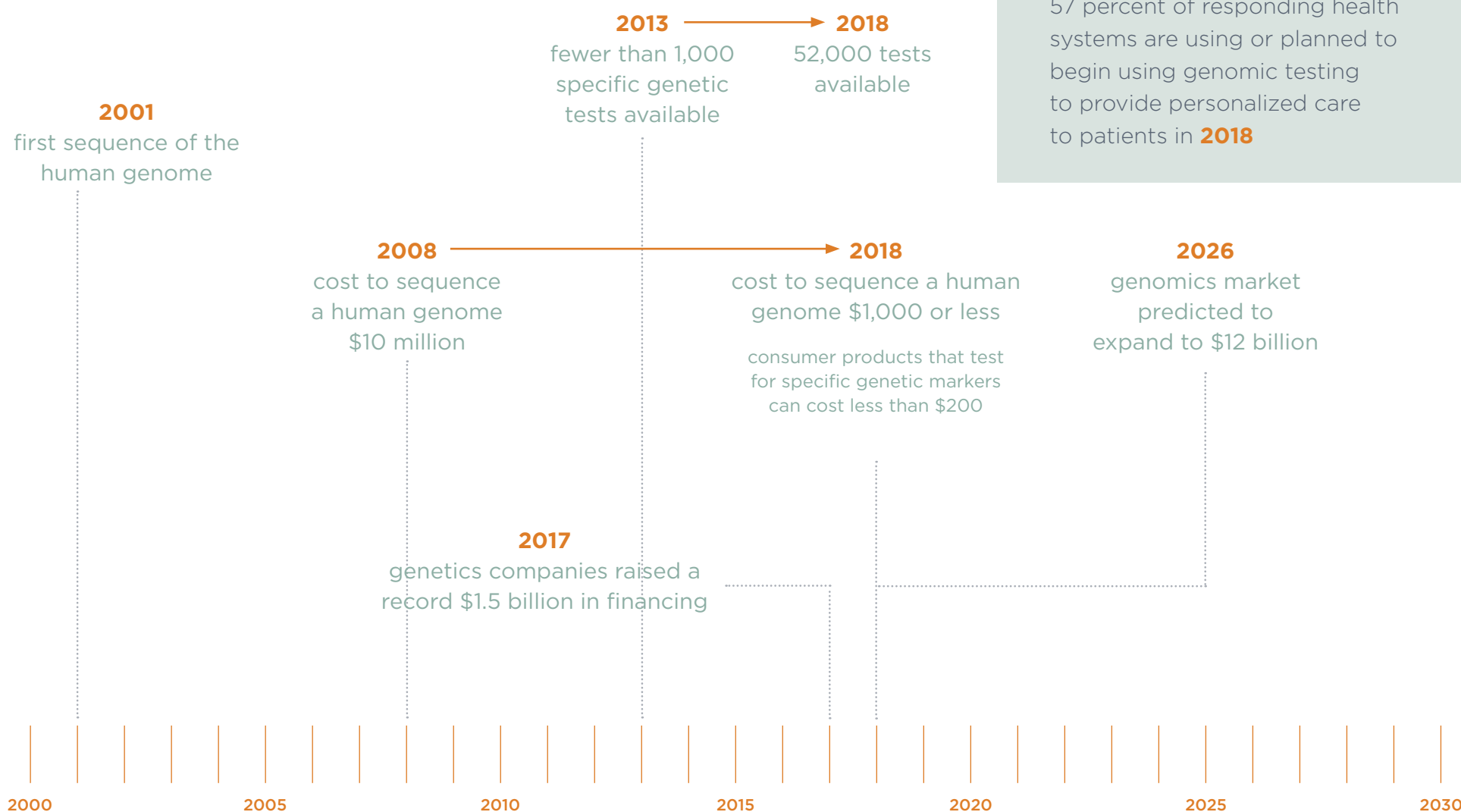
- Five years ago, there were fewer than 1,000 specific genetic tests available. Today, there are more than 52,000.

- Over that same period, the cost to sequence a person's DNA dropped from \$10,000 to less than \$1,000. And some direct-to-consumer products that test for specific genetic markers can cost less than \$200.
- To sequence a full human genome can still take up to two and a half days – however, tests that sequence the exome, or only specific genes, can take hours and yield valuable data.

Meanwhile, industry and investors have taken notice. Investment in genomic startups is growing, driven in part by consumer demand for genetic tests. Genetics companies raised a record \$1.5 billion in financing in the first 10 months of 2017, according to Pitchbook, led by \$250 million for 23andMe – the largest-ever investment round for a VC-backed genetics company. The value of the genomics market is predicted to expand to nearly \$12 billion by 2026, more than double the value of \$5.1 billion in 2017, according to Inkwood Research.

At the same time, medical center researchers are hoping to unlock more effective care for populations by collecting large sets of genomic and other health data. An example of this is the National Institutes of Health-backed All of Us project, which is attempting to sequence the genomes of 1 million Americans. And many of the largest health systems in the United States are moving into personalized medicine by employing genomics. In the Center for Connected Medicine's Top of Mind 2018 digital health trends survey, 57 percent of responding health systems said they were using or planned to begin using genomic testing to provide personalized care to patients in 2018.

Advancement of Genomics



OVERVIEW OF ADVANCES IN GENOMICS

While this report is focused on genomics in health care, genetic testing is also being used in ancestry and wellness contexts. These products are regulated differently from those used in a medical setting, but there can be overlap. Direct-to-consumer ancestry companies also offer products with potential clinical implications. For example, 23andMe sells tests that screen for the BRCA1 and BRCA2 gene mutations, which indicate an inherited risk for breast and ovarian cancers.

There are also several models for where and how tests are available to patients and consumers. Direct-to-consumer companies sell genomic sequencing products directly to consumers, who pay for testing out of pocket, without oversight from a genetic counselor or other health care professional. This is an important model because it is helping to drive awareness of genomics testing capabilities and spur the industry forward. Easy access companies sell directly to consumers, who typically pay out of pocket, but the companies support consumers in obtaining physician prescriptions for products that require them; they also facilitate licensed genetic counseling, which is currently required to accompany certain tests. In a clinical model, a health care provider or physician is responsible for recommending and facilitating genomic testing and counseling through a traditional health care setting. Health insurance companies may or may not reimburse for testing, depending on the circumstances.

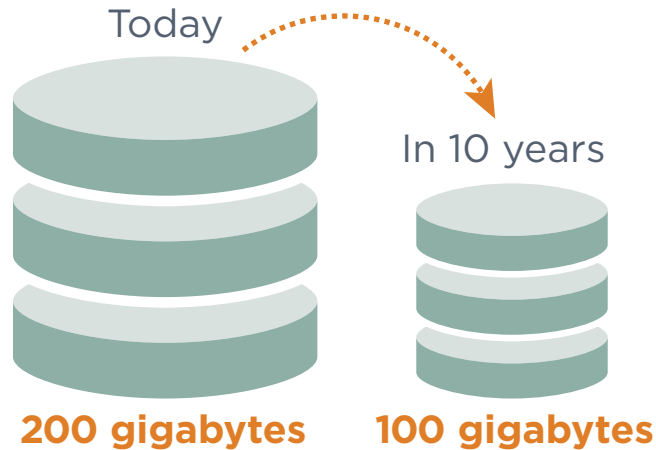
While there are reasons to be excited and hopeful for the future of genomics in health care, there are many challenges for the industry, including around reimbursement, privacy, and data storage and management.

- So far, limited reimbursement from payers for genetic testing has limited access primarily to those consumers willing to pay out of pocket.
- While some consumers have no problem handing over their genetic information to a private company, a Rock Health survey reported that nearly 90 percent of consumers believed they should be in control of who has access to their genetic data, and nearly 89 percent want to be informed when findings result from accessing their data.
- For health systems, genomic sequencing generates huge amounts of data – sequencing one tumor can create 2 terabytes of data – leading some to question how they will store, manage, secure, and analyze the information.
- Patients and providers are wondering how best to interpret and act upon the knowledge of a genomic abnormality.

To address these issues and the potential of genomics for the health care field, the CCM tapped a range of experts for insights on the opportunities, challenges, excitement, and concern surrounding genomics.

Storage + Infrastructure

RAW DATA
STORAGE FROM
ONE GENOME
TAKES



Some experts
estimate between
**100 million
& 2 billion**
human genomes will
be stored by 2025.

Sequencing
1 tumor
creates
2 terabytes
of data

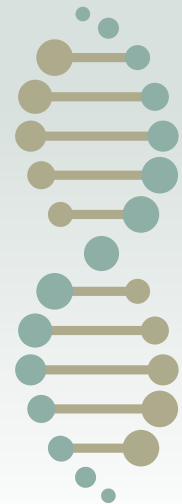
2 terabytes of storage holds:

 **34,000** hours of music

 **620,000** photos

 **1,000** hours of video

Growth to
exceed the data
requirements for
YouTube or the
entire field of
astronomy.



CONSUMERS AS A DRIVING FORCE

The significant decrease in the price of genetic testing means more consumers than ever have access to a new frontier in personal health information. And greater numbers of curious, health-conscious consumers are taking advantage of testing to learn about what their genetics say about their health and predisposition to disease. Health systems should know that their patients are seeking out this information and have a plan to cater to their needs.

The rise of genomics offers potential benefits to the overall health system because engaged patients, armed with their genetic information, are often open to making healthy lifestyle changes and talking to family members about their health. The potential for genetic testing to lead to early detection of some diseases could reduce health costs for treating those diseases. And patients who receive genetic testing often are willing to



If you want to get genetic testing covered by insurance, you have to meet criteria, which means you have to have a significant personal or family history of one of these hereditary conditions. But the data actually shows that those criteria are too stringent, and we are leaving behind anywhere from 20 percent to 50 percent of mutation carriers of these three conditions.”

Jill Hagenkord, MD

Chief Medical Officer, Color

participate in research studies, which can further advance the knowledge of how human genetics influences health.

However, there are hurdles that need to be overcome to make genetic testing a more common practice in routine medical care. Clear links between genetic mutations and disease are still being discovered by researchers, but more evidence needs to be gathered on the economic benefits that go hand in hand with understanding these links. There are three cases in which strong evidence points to genetic mutations increasing the risk of developing breast and ovarian cancer, Lynch syndrome, and familial hypercholesterolemia, said Jill Hagenkord, MD, Chief Medical Officer of Color, a genetic testing company. Yet it can be a challenge to convince payers to reimburse for genetic testing for those diseases without showing a significant family history, Dr. Hagenkord said.



As we accrue more information and the health economic benefit for testing becomes evident, I believe we'll see a monumental leap forward in testing.”

Rasu Shrestha, MD, MBA

Chief Innovation Officer, UPMC

PRIMARY CARE PHYSICIANS ON THE FRONT LINES

Patients who receive genetic testing frequently turn to their primary care physicians (PCPs) for advice on interpreting their results and understanding steps they should take to reduce risk of disease and improve their health. However, physicians have been wary of engaging patients on questions of genomics and health. As the trend of consumer genomics continues to grow, PCPs will need to be prepared to respond to patients seeking information.

PCPs have a clear role to play as the frontline responders in an era of molecular medicine. Relying on genetic counselors and other specialists to provide information will not meet the needs of a growing patient base. Genomic specialists will be needed

for more complex cases, meaning genetic screening and preventive use of genomics will fall to the primary care work force, said Mylynda Massart, MD, PhD, Co-investigator, All of Us Pennsylvania.

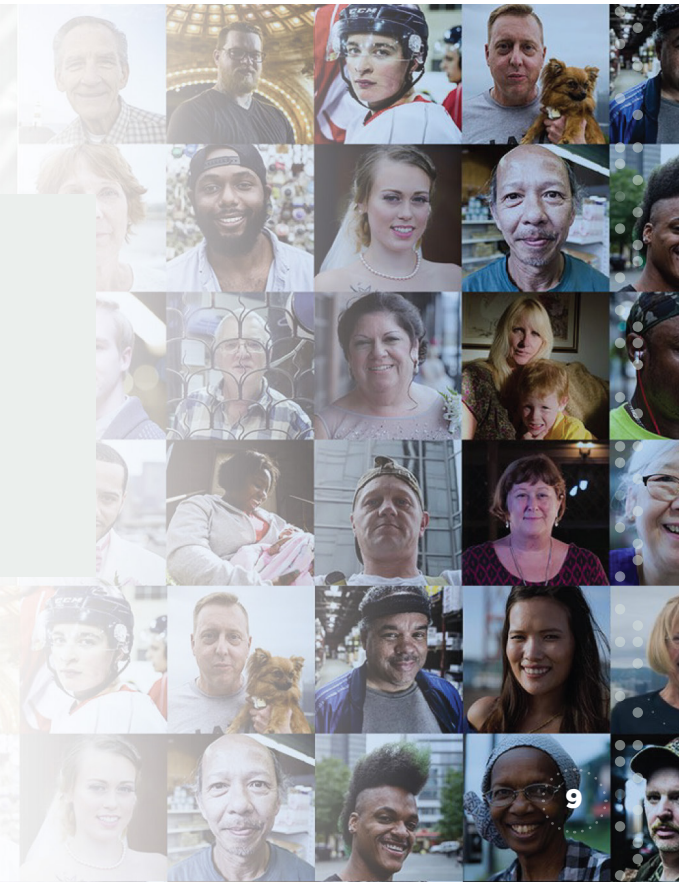
Primary care doctors have broad medical training and knowledge, and genomics is one more subspecialty in which they need to enhance their knowledge base and clinical skills. Continuing education courses are becoming available, such as the Test2Learn program at University of Pittsburgh, which are giving primary care physicians the skills needed to address their patients' needs, Massart said.



“Now that we are seeing this clinical level of genetic data, providers are starting to recognize that they need to get on board and seek that education and prepare themselves to be able to respond to results that will be returned by their patients.”

Mylynda Massart, MD, PhD

Co-investigator, All of Us Pennsylvania



THE FOUNDATIONS OF BIG DATA SECURITY AND STORAGE

Genetic testing creates challenges for traditional health system networks and data storage. On the infrastructure side, there is the challenge of handling the additional volume of data, and doing so securely and efficiently. “There’s big data coming at us and it’s our job to get it to the right systems,” said Houman Modarres, Senior Director of IP Networks, Nokia.

Health systems are generating an estimated 150 exabytes of data a year, and the amount is doubling every two years. While genomics is not the biggest driver of this growth, it is a significant and expanding source of health information for health systems. Large health systems that have invested in their data networks should be prepared for the onslaught of data from genomics, radiology, and other sources. Those networks will be built with redundancy to handle the traffic and include multiple layers of security.

The security and privacy measures include strict vetting of how data are stored and encrypted, attention to separating samples from patient identifiers, and clinical redundancy. “Leading providers are deploying networks for real-time health systems, and building in real-time multi-dimensional threat analysis to ensure they scale with reliability, availability, security, and threat mitigation,” Mr. Modarres said.



Health care was nine times more susceptible to data breaches than banking. Five million patient records – on average more than an incident a day – and the problem with a lot of the breaches, as a lot of your IT teams know, the thing that keeps your CIO and medical records officers awake all night, is that these breaches are silent killers.”

Houman Modarres

Senior Director of IP Networks, Nokia

ANALYTICS SPEEDING GENETIC RESULTS

Sequencer technology has advanced significantly in recent years to the point where genome and exome sequences can be turned out relatively quickly. Instead, there is often a bottleneck created in the big data interpretation of a patient's genetic information. "It's no longer a problem with the sequencing technology," said Martin, Reese, PhD, Founder and CEO of Fabric Genomics.

In the past five to 10 years, the industry has experienced tremendous progress in applying genomics to health care. For example, more than a half million people received a genetic test for breast and ovarian cancer in 2017, nearly triple the number who received the test in 2013. There have been even

larger increases on a percentage basis for other cancer tests, and for whole exome testing in the pediatric market.

So, while it is encouraging to see many consumers and patients being tested, much of their genetic data is separated from their other health data, which is typically locked away in proprietary electronic health record systems. In order for science and medicine to advance, researchers need access to all patient data. Dr. Reese called for "closing the circle" of personalized medicine by encouraging more genetic testing, using that data in the clinical environment, and opening all data to research to develop more personalized drugs and novel diagnostics.



Honestly, I hope and believe that every patient gets a full genome sequence in the health care system in a couple of years. But what we really need to do is link to the EMR data. If we can do that, that will generate a tremendous source of knowledge that pharma would love to tap into."

Martin Reese, PhD

Founder and CEO, Fabric Genomics

BALANCING PATIENT ACCESS AND PHYSICIAN GUIDANCE

The Food and Drug Administration in 2017 granted approval for 23andMe to provide results directly to its customers for genetic predisposition to 10 diseases or conditions. Since that first-of-its-kind approval, there has been discussion within the industry about whether consumers should have direct access to their genetic test results or if they should be required to receive results from a genetic counselor or other health professional. Anne Wojcicki, CEO of 23andMe, has argued that receiving genetic test results at home should be as easy and common as at-home pregnancy tests. Yet some in the medical community have concerns about the complexity of genomics causing confusion among the average consumer.

Dr. Hagenkord said as long as reports are written well and user comprehension is demonstrated, there should be no requirement to have physician oversight. However, it's important to also remove as many barriers as possible on the clinical side to make it easy for patients to access genetic testing via their health care provider. "There are ways to provide those touch points using telemedicine or other techniques that

still help ensure that the consumers understand the results and what the next steps should be," Dr. Hagenkord said.

Patients should be in control of their health information, Dr. Reese said, but there are nuances and complexities when it comes to interpreting and acting on genetic test results that require the guidance of a physician. Because of this, health systems should do more to provide easy access to the appropriate counseling and clinical interpretation. "Patients should have access to the right medical professionals to help interpret these genomic data," Dr. Reese said.

Health care is firmly in the era of patient-driven medicine and patients have a right to access their health data, Dr. Massart said. However, the community should be doing more to ensure patients and providers are educated about genomics and about the limitations of test results. In the All of Us research initiative, researchers will be working to make sure that educational and other resources are in place to support the research participants and their physicians.

EXPANDING GENOMIC EDUCATION FOR PHYSICIANS

As precision medicine develops and becomes a reality in clinical settings, experts say patients, researchers, and clinicians are being forced to respond. “The direct-to-consumer market has led the role in leading genomic awareness. Patients are bringing in questions to their doctors, using the internet, and creating an era of patient-driven medicine,” Dr. Massart said.

PCP genomic education is vital for the execution of precision medicine to prevent and treat disease because it provides clinicians the ability to use the data in a targeted and useful manner. Dr. Massart is a faculty expert for the Test2Learn education program, which could serve as a model for PCP genomic education. Test2Learn is an online education model created by the University of Pittsburgh in the field of pharmacogenomics, the study of how genes affect a person’s response to drugs. Dr. Massart expects a similar program designed specifically for primary care physician education to be available online within the next year.

“The premise of this program is for participants to test their own genetics and practice using their own results. This gives the doctor the opportunity to be the patient, which increases engagement in the program,” Dr. Massart said.

Dr. Massart said a PCP education model to implement genomics should be carried out in three phases. The first phase would occur during medical school and provide an in-depth understanding of genomics role in each organ system.

Secondly, during residency, training would transition from book learning to clinical and bedside training. Thirdly, mandatory continued education through the PCP’s career would round out the education model.

“This year specifically, the tide is turning. For a long time when people heard about genomics, they thought about the future,” Dr. Massart said. “People are starting to grasp that the future is now.”



OUR EXPERTS ANSWER QUESTIONS ABOUT GENOMICS

The CCM gathered questions from its audience on Twitter and from a [webinar](#) on genomics for our experts to answer.

When Dr. Hagenkord mentions that the clinical criteria are too stringent, what criteria is she referring to? Also, what is the data that she is referencing that shows that many are missed by the current criteria?

Payers will only pay for inherited disease testing if there is a significant personal or family history of a specific genetic condition. For the Centers for Disease Control and Prevention Tier 1 genetic conditions, studies have been done where they tested everyone in the population (rather than just those that met criteria). These studies have shown the current coverage criteria would disqualify 20-50 percent of mutation carriers from getting tested. [See here for an example.](#)

Where do you see pharmacogenetic/PGx testing playing a role in the overall genomic ecosystem?

Pharmacogenomics involves the investigation of the effects of genetic variation on drug response with the aim of offering clinical decision support to improve the benefit-risk profile of prescribed medications ([you can find an overview of pharmacogenomics here](#)). PGx has been around for over 30 years, but is rarely ordered or utilized. However, consumer genomics enables PGx to arrive in doctors' offices for "free" in real time, and doctors may be more likely to consider the information if it is there at the right time.

Can data from a testing kit can be integrated with the electronic medical record?

Typically, when a diagnostic test is performed, test performance statistics and design details for the genomic test are included in the test description field. These statistics and details can include items such as: number of genes, names of genes tested for, sequencing platform, analysis pipeline version, as well as testing kit information. The amount of detailed test description pushed into the EMR typically depends on the provider's customization of the EMR.

What is the industry's dependency on different brand sequencers, and what is the role of file formats extracted and databases for genomics data processing?

The majority of clinical next generation sequencing (NGS) has been done on the suite of Illumina sequencers from the MiSeq, HiSeq to the NovaSeq, followed by IonTorrent sequencing on the Proton platform (predominantly in oncology sequencing). Some of these machines are FDA approved. Sequencing machines are installed with a CLIA laboratory, and each machine is individually validated by the CLIA laboratory for their laboratory developed test (LDT). New sequencers such as BGISEq and Oxford Nanopore sequencers are slowly coming online as well.

With respect to file formats, various standard file formats have been developed from the FASTQ-format (raw sequence reads), to BAM-format (aligned read sequences) and to the variant call format (VCF-format). With respect to databases for genomics, there are over 90 databases and algorithmic sources used for interpreting genetic variants. These databases and sources grow daily. Standardization and quality are an unsolved problem in the industry. Some software provider companies tackle these challenges by providing best-practices suggestions to CLIA laboratory customers.

What if patients don't want their genome sequenced?

Patients are partners in their own health care, and no patient should be forced to take a test that he or she doesn't want to take. However, as precision medicine and genomics become more valuable, common and integrated into health care best practices, physicians will have greater expertise in outlining its benefits.

What is going to be the value of large whole genome shotgun (WGS) databases? Will having a base of the genomes of 1 million people be an economic asset?

It is not clear that the All of Us research project will use a shotgun sequencing approach. The intent will likely be to sequence a subset of the million participants and to balance the economic gain from this knowledge versus the cost. These are all discussions still currently in progress.

The economic value of WGS remains to be proven. Health economic studies (with respect to sequencing data and the impact on preventative health), reduced harm, and quality-adjusted life years will be some areas of potential research that will be appropriate within the All of Us study.

If a genetic test suggests a genetic predisposition to a disease, and an individual informs their physician of this information, how might this impact his or her insurance?

The Genetic Information Nondiscrimination Act (GINA) bars health insurance companies from denying coverage to those with a gene mutation. However, GINA was passed 10 years ago, and some believe it should be reviewed considering rapid changes and growth in the genomics industry.

How do we accelerate precision medicine into everyday practice?

Development of precision medicine education programs is imperative to improve the confidence of providers and accelerate precision medicine integration. In addition, health systems need to develop robust support and ongoing education for both providers and patients as the integration of precision medicine for clinical decision-making support becomes more prevalent.

Does physician resistance occur because doctors don't believe in the efficacy of the genetic tests, or are they worried about potential liability insofar as tests revealing something they should have caught?

Primary care physicians have historically been cautious of genomics due to lack of education and confidence in the field. Physician training is one way to help physicians embrace the rise of genomics. For example, Test2Learn is a course being developed at the University of Pittsburgh that will provide primary care physicians with the ability to advance their comfort, knowledge and skills in the field of precision medicine and genomics.

What's driving breaches in genomics data? Financial gain? Creating chaos?

In the case of most health care related data breaches, cyberattacks are executed with the intent of soliciting financial gain through ransomware or the sale of stolen data on the dark web. Attacks with the intention to engage chaos or protest are relatively less common.

Is DevOps (or DevSecOps) almost a requirement for the IT environment to be stable and nimble enough to support the needs and demands genomics will place on IT?

The appeal of the DevSecOps mantra and mode of operations is the agility it delivers to the IT environment. It is successful in highly dynamic environments where code and configurations can change over a dozen times weekly. It is unlikely to be a requirement for the support of genomics workloads or in most health care IT environments. Stability and security of the infrastructure in support of the application is a far more critical consideration, as the application environment is not prone to daily churn. That said, a good DevOps environment never hurts!

Is the industry looking at blockchain technology as a solution to genomic data privacy and security challenges?

Yes. Blockchain technology is already being used by [some genomics companies](#) to protect genomic data. The appeal is that blockchain can ensure control and security without centralization.



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The Center for Connected Medicine (CCM) serves as a thought-leadership incubator and content hub where health care leaders from around the globe explore more efficient and effective models for delivering patient-centered care through strategically integrated health information technology.

The Center, jointly operated by GE Healthcare, Nokia, and UPMC, facilitates connections among those who deliver, receive, and support health care, exploring firsthand how emerging models and integrated technologies can help them address the opportunities and challenges of their own organizations and regions. Visitors are exposed to comprehensive, quality driven, cost-conscious health care inspired by new care models and new technologies.

Watch “**The Rise of Genomics**” webinar

Learn more about our experts’ organizations:

The logo for 'color' features the word in a lowercase, sans-serif font. The letter 'o' is stylized with a multi-colored arc passing through its center.The logo for 'All of Us Pennsylvania' features the words 'All of Us' in a bold, dark blue font, with 'Pennsylvania' in a smaller, lighter blue font below it.The logo for 'FABRIC GENOMICS' features a stylized icon of three horizontal lines of varying lengths to the left of the word 'FABRIC' in a bold, black font, with 'GENOMICS' in a smaller font below it.The logo for 'NOKIA' features the word in a bold, blue, sans-serif font.The logo for 'UPMC' features the letters in a large, purple, serif font, with 'LIFE CHANGING MEDICINE' in a smaller, purple, sans-serif font below it.

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