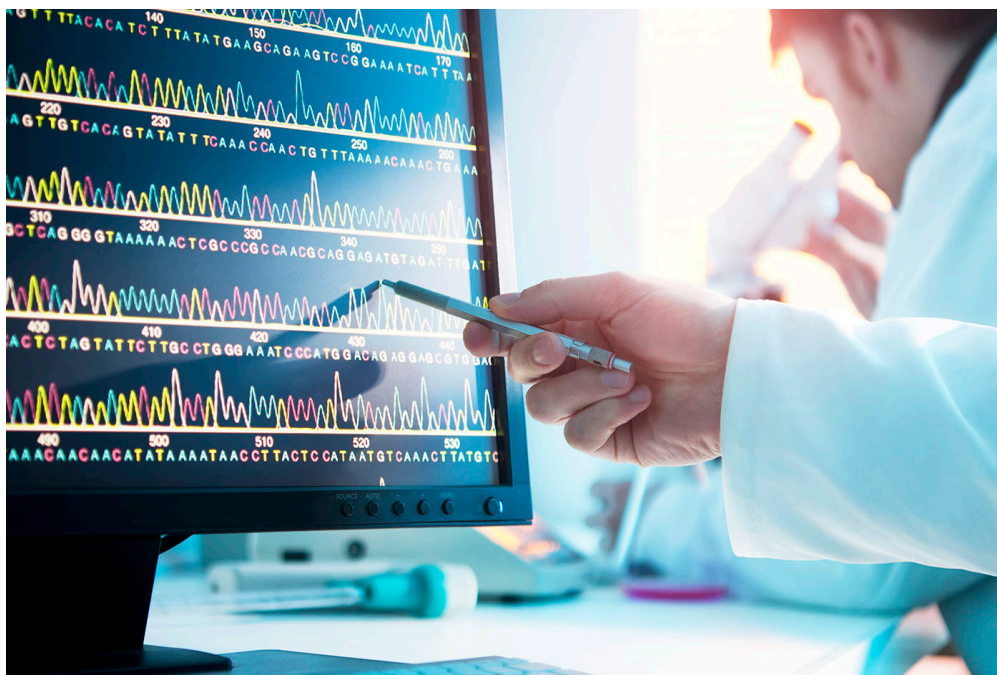


The Double-Edged Code: The Promise and Peril of Personal Genomics

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Kathy Vuksanaj

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At the dawn of the genomic age, the narrative was one of possibility—a race to read the code of life. Thirty years later, the story has changed. The technology has matured, the costs have plummeted, and the question is no longer “Can we sequence everyone?” With uncertainties about who will pay the bill for accessible genomics testing and the effects the results may have on individuals, the question has become “Should we sequence everyone?”

This is the current state of personal genomics: ramping up to becoming a household topic yet still grappling with its own purpose. Across medicine, researchers and clinicians are evaluating how far the human genome can—and should—go in reshaping preventive care. The future of personal genomics no longer hinges on speed or scale, but on implementation and judgment. How will we choose to use the most intimate information we have about ourselves? How will these choices redefine what it means to know, predict, and get (and provide) care?

To conclude this three-part series—which began with a consideration of how far we’ve come in our technological ability to sequence the genome and then shared details of having my genome sequenced and the consequences—we look at a future in which the most profound frontier of precision medicine may be not what our DNA reveals, but how we choose to listen.

From t=0

Robert C. Green, MD, MPH, a medical geneticist at Mass General Brigham and Harvard Medical School, has spent two decades pushing the boundaries of what genomics can do in everyday medicine. His team's pioneering BabySeq Project was the first to comprehensively sequence the genomes of ostensibly healthy newborns, expanding on earlier work in adults done through the MedSeq Project.



Robert C. Green, MD, MPH
Professor, Mass General
Brigham and Harvard Medical
School

“All along the way, the goal has been to integrate genomic results into day-to-day clinical care,” Green told Inside Precision Medicine. His conviction is that genome sequencing should not remain the domain of consumer curiosity or research but become a routine component of preventive healthcare.

In both MedSeq and BabySeq, Green's group analyzed medical findings and outcomes, healthcare spending, and notably, psychological outcomes after returning genomic results. “There was, at the time we began these projects, an expectation of catastrophic psychological distress with predictive genetic risk information. So we [published many] papers on this, including using randomized trial methodology to measure distress and anxiety when people self-selected to learn this information,” explained Green.

Contrary to fears that genomic findings would overwhelm patients, the studies showed that people generally welcomed the data—and used it. The numbers were striking: sequencing roughly 6,000 genes revealed that 10–20% of healthy children and adults carry a monogenic disease risk, and nearly all had variants relevant to reproductive health or pharmacogenomic sensitivities.

While newborn screening has long relied on biochemical tests from the heel-prick blood spot, Green argues that the system could be expanded through genomic data. Yet the challenge, according to Green, is structural: “There are 53 state labs and territories who are struggling every day to save children despite under-budgeted systems.” To address this, Green and collaborators are launching Building Evidence and Collaboration for GenOmics in Nationwide Newborn Screening (BEACONS), the first multi-state genomic newborn screening initiative in the U.S.

Funded by a \$27 million award—\$14.4 million from the National Institutes of Health (NIH) Common Fund Venture Program and \$12.6 million from GeneDx and Illumina—BEACONS will pilot the integration of whole genome sequencing (WGS) into existing state newborn screening systems. BEACONS will recruit, consent, and enroll up to 30,000 newborns in as many as 10 states over the next three years. This multi-state effort will send samples to a central sequencing lab and focus on 400–500 treatable conditions that manifest in the first year of life.

“It aligns with the urgency inherent in the newborn screening ecosystem,” Green said, drawing parallels to the rapid interventions for newborns with phenylketonuria (PKU) or galactosemia that prevent irreversible harm.

For Green, these stories illustrate a “life cycle” of genomic interpretation that evolves as technology improves. “We’ve reached a real inflection point around newborn genomic screening,” he said. Despite reimbursement and policy hurdles, he is encouraged by the momentum. “It’s astounding that the needle has moved this far in the 10 years since we began this work with the BabySeq Project.”

The policy and payment puzzle

While genomic sequencing promises to revolutionize newborn screening, Kathryn A. Phillips, PhD, a leading health policy researcher in precision medicine, warns that implementation is far from simple.



Kathryn A. Phillips, PhD
Professor, UCSF Institute for
Health Policy Studies and
UCSF Comprehensive Cancer
Center

“Although there can be great value from one-time sequencing, let me correct what I think is a mistaken idea that you could get sequenced once and you’re done,” said Phillips, professor of health economics and health services research in the department of clinical pharmacy at the University of California, San Francisco (UCSF) “Technology changes and you may need to redo testing to get an updated result. And someone’s got to store the data.”

Phillips argues that sequencing newborns to identify conditions that can be treated immediately is a fundamentally different proposition from a one-time lifetime test. It raises logistical questions about how data are maintained and how results evolve as technology and

interpretation improve.

The challenges, she notes, also extend to state-by-state inequities in current newborn testing. All U.S. states mandate newborn blood spot testing for a wide range of serious but treatable genetic, metabolic, and endocrine disorders. “Currently, different states do different things,” Phillips said. “It has always really bothered me that every state’s not the same. And if you’re in a less resourceful state, your newborn receives less testing. Why is that? That doesn’t make any sense at all.” She finds it troubling that while new national efforts are pouring resources into genomic sequencing, the longstanding blood-spot programs “still require further attention.”

Even when sequencing demonstrates clinical value, the question remains: who pays? “We must remember that the cost of the test itself is only the beginning of what someone has to pay,” Phillips said. “You have all these follow-up cascades of additional testing and data storage and reinterpretation.”

Phillips draws parallels to the financial dilemmas posed by multi-cancer early detection (MCED) and Alzheimer’s blood biomarker tests—technologies that may generate costly downstream imaging and specialist visits. “Payers generally avoid paying for screening the general population because, on a population basis, the cost often outweighs the value.”

As precision tests flood the market, she emphasizes the need for evidence-based policy, “We must base policy on evidence, not ideology,” Phillips said. “While people’s perspectives and preferences are valuable inputs, they should not dictate the decisions made at the population level.”

Phillips is the founding director of the UCSF Center for Translational and Policy Research on Precision Medicine, where she studies how stakeholders—payers, government agencies, labs, benefit managers, and patients—make decisions and what evidence they demand.

“Understanding how payers think is really important to develop the appropriate policies that take that into account,” she explained. The goal, she said, is not advocacy but objectivity: assembling empirical data so that policymakers can move forward “in a reasonable way.”

Less is more

The thought of a full genetic blueprint for everyone, decoded at birth, guiding health decisions across a lifetime sounds quite appealing. But Sean Tunis, MD, a veteran health policy thinker, doesn’t think the WGS approach will be a healthcare panacea. Rather, it may create more problems than it solves.



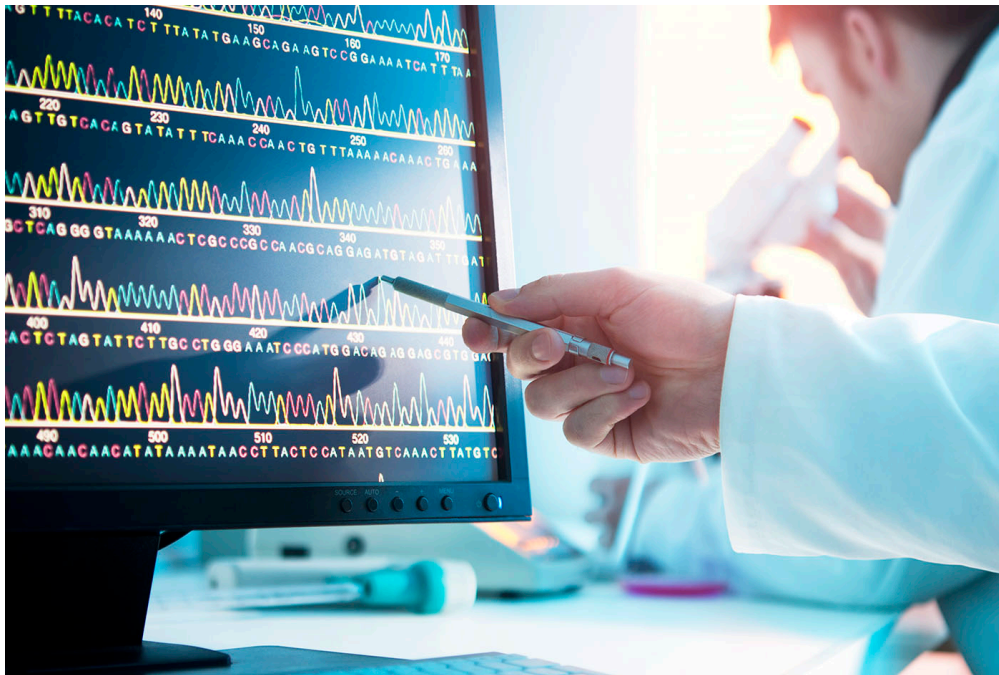
Sean Tunis, MD
Principal, Rubix Health
Senior Fellow, Tufts Center for
the Evaluation of Value and
Risk in Health

Tunis, principal at Rubix Health, advises public and private sector organizations on health technology issues at the intersection of regulatory and reimbursement policy, market access, comparative effectiveness, outcomes measurement, and assessment. “The overarching challenge,” Tunis said “is how much data and evidence you need to know that these things have clinical utility.” Translation: when does knowing more actually make us healthier?

It’s a deceptively simple question with massive implications. Tunis, who was the founder and executive director of the Center for Medical Technology Policy, has spent the past few years looking into the clinical utility of MCED tests, which can spot molecular traces of up to 50 cancers at once, many of them currently undetectable by standard screening. The results look dazzling on paper. These tests may flag pancreatic or ovarian cancers long before symptoms appear. But there’s a catch: no one knows for certain whether catching them early actually saves lives or improves patients’ quality of life.

“To show that these tests reduce cancer mortality, you’d have to follow hundreds of thousands of people for a decade or more,” said Tunis. “By the time you had the answer, the technology would already be obsolete.” Clinical studies suggest that these tests reduce the number of late-stage cancers detected, while finding more early cancers. We don’t yet know for sure whether that reduces mortality.

The problem, in essence, is that diagnostic accuracy means little without effective intervention. Tunis learned that lesson firsthand as the chief medical officer for the Medicare Program in the early 2000s, when the agency debated whether to cover positron emission tomography (PET) scans for early Alzheimer’s detection. “The scans seemed to work,” he said, “but available drugs didn’t.” It’s only now, with monoclonal antibodies that may slow disease progression, that early diagnosis has a shot at real utility.



Credit: nicolas_ / Getty Images

That logic extends to the latest genetic risk tools: polygenic risk scores, WGS, and predictive AI. A test that predicts a 60% drop in Alzheimer's risk sounds miraculous, but it's only useful if there's something you can do about it. "Otherwise," Tunis said, "it's just information for its own sake."

And even if sequencing became virtually free, the real costs would remain: the cascade of false positives, unnecessary biopsies, and anxious follow-ups triggered by data of uncertain meaning. In health systems like Medicare or the NHS, those downstream effects become questions of opportunity cost: what proven, underfunded care do we sacrifice to chase uncertain promise?

For Tunis, who is also a senior fellow in the Tufts Center for the Evaluation of Value and Risk in Health, the path forward isn't maximalist, it's measured. He points to the American College of Medical Genetics' approach of identifying the highest-value applications first. "The real risk," he warned, "is becoming overly enthusiastic about the value of information for its own sake." In a data-driven future, restraint may be the most radical form of wisdom.

The knowing effect

As WGS approaches the clinic and nursery, bioethicist Amy L. McGuire, JD, PhD, urges that the real ethical frontier of genomics is what we do with the information it reveals. "Individual preferences play a role in the question of whether we should do it," she told Inside Precision Medicine. "As long as people understand that much of the information generated by [WGS] may be uncertain, and we may not fully understand the implications of what we're discovering."



Amy L. McGuire, JD, PhD
Professor and Director of
Center for Medical Ethics and
Health Policy
Baylor College of Medicine

For McGuire, who directs the Center for Medical Ethics and Health Policy at Baylor College of Medicine, the question is less about the generation of genetic data and more about its consequences—social, psychological, and practical. While the Genetic Information Nondiscrimination Act prohibits genetic data use in health insurance and employment, it leaves gaps in other areas. Life, disability, and long-term care insurers can still legally request disclosure of genetic testing and use it to determine eligibility or premiums. “You can still be required to disclose if you’ve had a genome sequence or genome test,” McGuire noted. “And there are concerns about how this could be used against you.”

Beyond discrimination, McGuire studies how genomic knowledge affects self-identity and treatment. Psychologists found in the 1960s that telling teachers certain students had high potential for intellectual growth impacted their academic achievement. McGuire sees echoes of this skewing in genomics, especially when communicating results related to non-medical or behavioral traits. “I’m more concerned about the nuanced responses,” she said. “Does newborn sequencing change the way parents subtly treat their children?”

Early research already hints at this phenomenon. At least one study has shown that people who learn they carry the high-risk APOE4 variant, which is a well-known risk factor for Alzheimer’s disease, perform worse on memory tests than those who are not told, a self-fulfilling prophecy effect. The opposite is also true: those told they don’t carry the APOE4 variant perform better. “It’s fascinating,” McGuire said. “It’s not that people become clinically depressed or anxious. It’s that they may unconsciously change how they see themselves, how they behave, or even how others perceive and treat them.”

Large-scale studies like the NIH-funded Clinical Sequencing Evidence-Generating Research consortium have allayed fears of widespread psychological harm from genetic results, but McGuire claims they often overlook the more nuanced effects on identity and social behavior. “There hasn’t been a lot of attention paid to these more subtle ways genetic information might influence how we think about ourselves and others,” she said. “That’s where I find it really interesting.”

McGuire has also wrestled with these questions personally. After sequencing her genome, she initially declined to see the results. “I know the science, I know it’s not deterministic; but I still worried about how my family might look at me differently,” McGuire said. “How would my kids react? My partner? Even if you understand intellectually that genetic risk isn’t destiny, emotionally it’s harder to separate.”

In an age when DNA can influence medical treatment and matchmaking, McGuire believes the challenge is managing meaning, not just data. “Most genetic information is probabilistic, not prescriptive,” she said. “Our task now is to learn how to live with that uncertainty without letting it quietly shape who we become.”

Living by a code

Personal genomics began as a quest to decode the body. What it is revealing, instead, is how deeply our biology and our beliefs intertwine. The genome may be written in individual biomolecular encyclopedias, but its interpretation unfolds in the language of medicine, policy, and psychology—of what we decide to know and what we choose to do with that knowledge.

The next frontier of genomics won’t be defined by another breakthrough in sequencing speed or data storage. It will depend on how responsibly and humanely we interpret and apply the astronomical amount of personal genomics data we will have in hand.

This article is the third and final part of the personal genomics series by Jonathan D. Grinstein, PhD. View part one [My Personal Genomics Journey in 23andMe’s Resurrection Era](#) and part two [I Got My Genome Sequenced At Home—Now What?](#).

Jonathan D. Grinstein, PhD, North American editor for Inside Precision Medicine, investigates the most recent research and developments in a wide range of human healthcare topics and emerging trends, such as next-generation diagnostics, cell and gene therapy, and AI/ML for drug discovery. He is also the host of the Behind the Breakthroughs podcast, featuring people shaping the future of medicine. Jonathan earned his PhD in biomedical science from the University of California, San Diego, and a BA in neural science from New York University.

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