Whole-genome sequencing: a new liability tsunami for doctors?

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Will whole-genome sequencing create a new liability tsunami for physicians?

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Just over 10 years ago, the sequencing of the first human genome was announced at a White House press conference. In the decade since, the practical application of genomic information has been disappointingly slow. That is about to change. We are rapidly—much faster than many anticipated—approaching the widespread clinical use of whole-genome sequencing. WGS involves the complete sequencing of all 6 billion-plus base pairs of DNA in our individual genomes. Just 10 years ago, it cost $100 million to sequence an entire genome. Today, WGS is commercially available for less than $10,000, and several companies are racing to get the cost below $1,000 within the next few years. The $1,000 price tag is the magical flip point at which the National Institutes of Health and many experts in the field believe WGS will be economically feasible for routine use in medical care.

Though we haven't reached that $1,000 milestone yet, WGS is already being rapidly adopted across the country. In 2009, fewer than 100 people had ever undergone WGS, but that number jumped to more than 2,000 in 2010 and is expected to reach 30,000 this year. The accelerating adoption of WGS brings with it much promise, but as with any rapid technology change, it will also have disruptive consequences, at least in this transition period. Unfortunately for doctors, they will likely bear much of the brunt of this disruption.

On the positive side, a number of patients have already reaped dramatic benefits from WGS. A 6-year-old Wisconsin boy received a life-saving umbilical-cord-blood transplant after WGS showed that a unique DNA mutation was responsible for his mysterious bowel disease. A pair of 14-year-old San Diego twins suffering from a debilitating movement disorder were successfully treated after WGS revealed they had a rare mutation that could be corrected by a simple amino acid supplement. A family of four in Silicon Valley recently underwent WGS, revealing that a teenage daughter had several mutations putting her at high risk of blood clots. That information will help let her doctors treat her before the blood clots become a problem, instead of only when the damage has been done. More generally, a growing number of cancer patients have benefited from tailored therapies based on new mutations in their tumor discovered by comparing the complete genomes of their healthy cells with those of their tumor cells.

Given these dramatic successes, it seems clear that WGS is going to be good for patients, enabling them to receive treatment tailored to their personal genetic makeup. However, should genomic sequencing become nearly as routine as, say, a colonoscopy or cholesterol check, doctors—most of whom have no formal genetics training—may find themselves in a precarious position. These doctors may be extraordinarily vulnerable to lawsuits regardless of whether they embrace or resist the use of WGS with their own patients. While other players such as the testing labs may also be subject to lawsuits if they negligently conduct or interpret genetic tests, it is doctors who will be required to communicate and explain test results to patients, which is the step that involves the greatest duty to the patient and carries the biggest risk of liability.

As with any new technology, many doctors will resist adopting WGS, at least initially. As the cost of sequencing continues its precipitous decline, and ever-more doctors and patients use the technology, the performance gap between those who adopt it and those who resist will inevitably grow larger. At the same time, many courts are moving toward a national rather than local standard of care. Essentially, this means that doctors, whether they work in underfunded hospitals or prestigious academic medical centers, are expected to offer the same quality of care. Let's say that two patients, living across the country from each other, are suffering from the same medical problem. The one in a rich, technology-friendly hospital is offered WGS by her doctor. Her life is saved as a result. But the other patient, either because his hospital doesn't have the resources or because his doctor is not comfortable with WGS, doesn't have the test and dies as a result. That doctor may be now be liable for that patient's death.

Even doctors who eagerly adopt WGS will be vulnerable to lawsuits. It is estimated that each of us have more than 100 variants that could significantly increase our risk of genetic diseases. WGS can detect every one of those variants. That's an overwhelming number of potential problems for doctors to evaluate. There are nowhere near enough genetic counselors or medical geneticists to meet this demand, leaving the burden of understanding and communicating this information to doctors who have little or no training in genetics. Under these circumstances, it is likely that many doctors will fail to recognize some of these variants' potential significance—and if that happens, a doctor can expect a major malpractice claim when his patient suffers illness or death that could have been prevented. A number of court cases dealing with existing genetic testing demonstrate that juries fully expect doctors to recognize and understand a broad range of genetic conditions, no matter how rare. For example, a Florida doctor recently was hit with a $23.5 million verdict for failing to recognize a rare genetic condition called Smith-Lemli-Opitz syndrome. When these expectations are applied to the hundreds of variants that will inevitably be revealed in every use of WGS, doctors will be easy prey for savvy trial lawyers.

Yet another potential source of liability will relate to a doctor's duty to disclose medically significant genetic findings to a patient's relatives. Unlike most medical tests, genetic information is relevant not only to the individual patients being tested but also to their family members, since they may harbor the same genetic variants. While physicians' professional codes of ethics and federal laws discourage disclosure of genetic test results to family members, courts have decided this issue inconsistently to date, in some cases holding doctors liable for failing to warn family members about potential genetic risks. Settled legal and ethical principles on confidentiality and disclosure issues will be upended by widespread use of WGS.

Other dynamics of WGS will exacerbate these physician liability risks. There will be constant and rapid changes in our knowledge about the significance of various genetic variants, requiring doctors to constantly re-evaluate the diagnosis, prognosis, and treatment of their patients. Moreover, as patients become increasingly familiar with genetics, they'll start asking more informed and nuanced questions of their doctors about genetic factors, creating new liability risks if the physician fails to respond accurately or completely. For example, consider a patient who expresses concern about his or her risk for a particular type of cancer, which may be affected by dozens of genes. If the doctor fails to note a significant mutation in one of those genes, she may be at an increased risk for liability given her affirmative assurance to the patient. In this environment, doctors will be forced to learn genetics on the job (and quickly) or will be spending much of their time and income in litigation. Perhaps the greatest hope is that a new generation of doctors being trained today will respond to these potential issues before they are overwhelmed by them, though most medical schools are not training today's students to deal with the challenges and implications of WGS.

There is one thing we do know. As instructors of a Genetics & Law course at a law school, a new generation of law students will be ready and hungry to jump on the coming tidal wave of genetics-based medical malpractice lawsuits. It remains to be seen whether the medical profession will step up to the plate and meet

this challenge, but they better start soon. If not, it will be a good time to be a patient, and a lawyer, but perhaps not a physician.