Do Ask, Don't Tell?

Researchers ponder whether to tell patients about "incidental findings" from genomic analyses

As today's tsunami of genomic data answers questions about cancer diagnosis and treatments, it raises new ones about ethics.

Should a participant in a clinical trial for a lung cancer drug, for example, be alerted if sequencing shows that she carries a mutation that puts her at high risk for Alzheimer's disease? If so, who should disclose that information and how? Moreover, if another investigator examines the participant's biobanked samples years later and finds something new, is a plan in place to inform her?

Such questions are now practical. "There are growing signs that many research participants and the public want and expect return of individual research results and incidental findings, yet research practice has been not to return them," says Susan Wolf, JD, a professor of law and medicine at the University of Minnesota in Minneapolis and a faculty member in the University's Center for Bioethics.

Participants and the public aren't alone. "Researchers themselves may feel uncomfortable withholding information of urgent clinical significance," adds Wolf.

Today, even if researchers wanted to provide study participants with test results, they often can't. One issue is that clinical trial consent forms typically don't make provisions for sharing the information.

Another relates to where the testing is done. Generally, sequencing completed as part of a research protocol is a laboratory-developed test (LDT) rather than one done in a facility with Clinical Laboratory Improvement Amendments (CLIA) approval. LDT findings that may affect patient care need validation in a CLIA-certified lab before they can be released to a study participant.

"Who's going to pay for that?" asks Reed Pyeritz, MD, PhD, a senior fellow at the Center for Bioethics at the University of Pennsylvania in Philadelphia.

In addition, while researchers increasingly are thought to have some duty to address findings of clinical importance, Pyeritz says that many genomics specialists have no clinical background. "They are not MDs," he notes, and lack training to answer patients' questions about any needed care.

Meanwhile, a few clinicians are grappling with ethical questions related to genome sequencing, too. Health-conscious patients who have had genotyping completed by a private company may ask their family physician to explain the findings and offer advice. However, most physicians, says Pyeritz, "are woefully unprepared to deal with this."

This challenge will only grow. With costs dropping, patients may soon have whole-genome or whole-exome sequencing done, perhaps due to a family history of breast cancer, instead of having only a small panel of genes checked. All of that information may make its way into the patient's medical record, and the patient may expect to be notified of clinically important findings, even if those findings have nothing to do with why the test was originally ordered.

FOLLOWING UP ON FINDINGS

Whole-exome and whole-genome analyses are sparking debates about the ethics of sharing clinically significant findings with research participants and patients.

The expectation stems from the longstanding clinical tradition of reporting to patients an "incidental" medical finding—a condition with potential health consequences discovered while treating or investigating something else.

Suppose, says Robert C. Green, MD, MPH, a medical geneticist and translational genomics researcher at Boston's Brigham and Women's Hospital, you fall off your bike and go to the emergency room for treatment. After examining your X-ray, the radiologist reports that you have a broken rib. But if he fails to report the obvious lesion on your lung, that could constitute malpractice.

"Whether that analogy holds true with sequencing is still to be determined," says Green.

The radiologist relies on training, expertise, and clinical guidelines to determine what to report, such as the treatable lesion on the lung, explains Green. In the nascent world of sequencing, that deep understanding is missing.

"The genome is a big and complicated place," says Green, "and there's lots of variation in disease genes that *could* mean something. The problem is that we're really not sure" if it does.

PONDERING POLICIES

In April, a 26-member NIH-funded working group led by Wolf published a set of 10 recommendations for biobanks (Genet Med 2012;14:361–84). Broadly speaking, they suggest that biobanks, or tissue repositories, develop policies on whether incidental findings and individual research results should be released; determine which findings and results should be offered to research participants; and decide who is responsible for communicating that information and how.

On the clinical front, the American College of Medical Genetics and Genomics recently outlined points to consider before ordering whole-genome or whole-exome sequencing for clinical diagnosis or screening. One recommendation: guide decision-making by considering sequencing data in the context of an individual's medical and family history.

Beyond a few such steps, it's still early days.

In a recent study led by Green, 16 specialists in clinical genetics or molecular medicine were surveyed about which of 99 conditions or gene variants should be reported back to a patient's physician as incidental findings (Genet Med 2012;14:405–10). All 16 of the experts unanimously favored disclosing just 21 genes or conditions, about half of which were cancer related. They disagreed about disclosing conditions for which few effective treatments exist and about disclosing information about children.

The authors conclude that even genetic specialists "may not be yet fully prepared to deal with the implementation of new genetic technologies." —*Suzanne Rose* ■

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