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SEQUENCE
Decoding news and trends for the medical genetics community

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RESEARCH UPDATE

LEGAL, ETHICAL ISSUES LOOM OVER TOPIC OF RECONTACTING PATIENTS

Advances in research, next-generation sequencing lead geneticists to consider approaching former patients with results about genetic variants

The genetics community should address whether certain new genetic findings and circumstances warrant contacting former patients, a recent paper suggests.

Genetic tests often deliver results that labs cannot interpret, known as variants of uncertain significance (VUS), which are becoming more common with the expanded use of next-generation sequencing techniques. New research increasingly shows that such mutations may have both positive and negative implications for patient health, or that variants believed to be pathogenic are actually benign.

A paper by researchers from the Netherlands and the United Kingdom recently published in *Genetics in Medicine* says the explosion in new genetic information warrants closer examination of the ethical, legal, and social issues involved in telling former patients about VUS results (Otten et al., 2014).

"Our research shows that recontacting is considered desirable by both professionals and patients, but experience with it is limited," says Ellen Otten, MD, a PhD candidate in the Genetics Department at the University Medical Center Groningen in the Netherlands.

Dr. Otten's paper concluded that informing former patients about relevant new findings is considered unfeasible in most cases, but she urges the genetics community to reach a consensus about which situations merit recontacting.

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As genetics research expands, geneticists debate the ramifications of informing former patients about new genetic findings.

The Study

The researchers reviewed 61 articles that discussed the duty to contact former patients in clinical settings, with an eye toward conclusions about when to do so, and the ethical, legal, social, and practical issues involved.

While the authors of most papers regard recontacting as ethically desirable, they also note that geneticists have no legal requirement to do so, Dr. Otten and her colleagues write. Although contacting former patients "seems more obvious for definite and actionable information than for less certain information," they do not support creating a general duty to recontact patients with such information, Dr. Otten's report notes.

However, given continuing advances in genetics findings and information technology capability, contacting former patients in some circumstances may be regarded as "a reasonable degree of care" in the future. To that end, Dr. Otten and her colleagues are preparing a pilot study of an online application that would allow patients to view new genetic and testing information that applies to their own health, to change their preferences about whether to receive new information, and to contact physicians online.

Current Policy

The American College of Medical Genetics and Genomics (ACMG) is one of the few organizations worldwide with a policy statement that addresses telling former patients about genetics advances that could impact their health. Its statement directs primary care physicians, who, unlike most geneticists, maintain ongoing, long-term contact with their patients, to encourage patients who have consulted geneticists to "recontact geneticists or genetic counselors as relevant changes in their lives occur."

The policy was published without full endorsement by the ACMG board

TESTING UPDATE CONTINUED

and is now being reconsidered, says Reed E. Pyeritz, MD, PhD, a member of the committee that wrote the policy. He is Professor of Genetics and Vice-Chair for Academic Affairs in the Department of Medicine at the Perelman School of Medicine at the University of Pennsylvania in Philadelphia.

In a commentary published in the *New England Journal of Medicine,* Dr. Pyeritz points to another problem, that is, implications for relatives of a patient who receives a different interpretation of a result (Pyeritz, 2011). "Determining who, if anyone, is responsible for telling them involves clinical, ethical, and legal questions," he writes.

How to Proceed

Geneticists should not promise to contact former patients with new genetic information unless they can reliably do so for all patients, Dr. Pyeritz says, warning that having such a policy would create a legal obligation. Instead, he suggests telling families that want updates to call the clinic in a year to request a review of new pertinent literature.

Regularly contacting former patients about new genetic findings would require a tremendous amount of work, which is not feasible for most genetics clinics with small staffs and budgets, notes former ACMG President Wayne Grody, MD, PhD, Professor in the Division of Medical Genetics and Molecular Diagnostics and Director of Molecular Diagnostics Laboratories and the Clinical Genomics Center at the UCLA School of Medicine.

"It's impossible to keep up with the entire genome," says Dr. Grody. "Most of us keep up mainly with the genes in our areas of expertise. If patients are reasonably educated, probably they are constantly looking for information on the Internet."

Benjamin S. Wilfond, MD, Director of the Treuman Katz Center for Pediatric Bioethics at Seattle Children's Hospital and Chief of the Division of Bioethics in the Department of Pediatrics at the University of Washington School of Medicine, recommends that geneticists educate families about rapid increases in genetics knowledge and the understanding of variants' significance.

"I tell patients, 'Right now, this is the best information I can give you, but it may change,'" Dr. Wilfond says. "It's reasonable to suggest that they check back with someone in five years."

References

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TREATMENT UPDATE

SETTLEMENT REACHED OVER MEDICAID COVERAGE OF CYSTIC FIBROSIS DRUG

Arkansas federal court case highlights medical necessity, high cost of targeted therapies

A recently settled federal court case around access to the targeted cystic fibrosis (CF) drug ivacaftor (Kalydeco) involved questions about medical necessity, access, and cost. Though settled, the case raises concerns about state Medicaid programs' future ability to pay for other expensive new therapies.

In the case settled last February, three patients with CF sued Arkansas-based Medicaid officials, alleging that they violated the patients' civil rights by denying them access to the drug Kalydeco, marketed by the Boston-based company Vertex Pharmaceuticals.

The U.S. Food and Drug Administration (FDA) has approved Kalydeco—which costs more than $300,000 per year—for patients with CF who are age six and older and who have at least 1 of 10 rare CF mutations.

The FDA is currently reviewing applications to expand the drug's use in children age two to five who have some of these mutations, and for its use in combination with the drug lumacaftor in patients with two copies of the most common CF mutation, F508del, according to the Bethesda, Maryland–based Cystic Fibrosis Foundation, which helped pay for Kalydeco's development.

The Case

The case pitted sick children with CF—who may need Kalydeco for the rest of their lives at a potential cost of millions of dollars—from low-income families against a Medicaid program interested in controlling spending as healthcare costs skyrocket.

In their lawsuit filed June 2014 in an Arkansas federal court, the plaintiffs alleged that Medicaid officials blocked their access to Kalydeco because of the drug's cost and argued that a Medicaid-imposed waiting period and medical criteria violated their rights under the federal law governing Medicaid. That law obligates state Medicaid agencies to pay for treatment—including FDA-approved drugs—deemed medically necessary.