Controversial guidelines suggest patients should be informed what risks lurk in their DNA

Dr. Robert C. Green, a medical geneticist at Harvard Medical School and Brigham and Women's Hospital who co-led the group that wrote the recommendations *–courtesy of Robert C. Green*

By Carolyn Y. Johnson March 21, 2013

Doctors who sequence a patient's full set of genes for any medical reason should look for two dozen unrelated

genetic conditions and tell the individual if they find any of them lurking in the DNA, according to a long-awaited report led by a medical geneticist from Boston.

Released Thursday morning, the recommendation by an organization of genetics specialists is the first real effort to delineate how broadly testing laboratories should look for additional potential genetic problems, and the specific information that doctors should tell patients.

Should patients whose genome is sequenced to help diagnose a cardiac condition be tested for a gene that predisposes them to later develop breast cancer, or one that will cause them to have a life-threatening reaction to anesthesia?

Yes, the new guidelines suggest, even if that person is a child.

The guidelines were issued as rapid technology advances have made whole-genome sequencing cheaper and faster — enough so that genetics specialists predict that within a few years, it will be a routine part of patient care.

"I'm pretty proud of this, as the first response by an organized medical body to the completely revolutionary aspects of using whole genome sequencing in the practice of medicine,'' said Dr. Robert C. Green, a medical geneticist at Brigham and Women's Hospital and Harvard Medical School. He co-led the

group that winnowed the list from 90 genetic risk factors to a minimum of 24 that should be searched for in routine testing. "You simply can't do business as usual, once this [technology] is scaled up and is affordable, and is part of everyone's medical care.''

All of the genetic conditions on the list, approved in a vote late Tuesday afternoon by the board of the American College of Medical Genetics and Genomics, are rare. They are a diverse set of conditions, causing predisposition to heart conditions or cancer, and the group focused only on conditions where the knowledge of having a particular gene could be used to prevent or treat a condition.

Physicians and bioethicists had mixed reactions to the recommendations, which were hammered out over weekly 90-minute conference calls over the course of a year and reviewed by 15 outside experts. Most commended the bold effort to establish some ground rules and principles for how to deal with the vast amount of information in the genome, even as they raised concerns — especially about whether patients should have a choice in what they want to be told about their genes.

"We're in a transitional time, where a lot of the knowledge of the genome is not yet available, in the sense we have the sequence, but we don't know what its meaning is for large swaths of the genome,'' said Dr. Isaac Kohane, chair of the informatics program at

Boston Children's Hospital. He anticipated the problem of sequencing turning up unexpected findings in the genome, and in 2006 coined the term "Incidentalome'' to describe the problem.

For example, he said, the list includes mutations in two genes — BRCA1 and BRCA2 — that dramatically increase risk of breast and ovarian cancer in women with a family history of the disease. The problem, he said, is that the risks such mutations confer are far less well understood in the general population. Since the preventive action women could choose to take is extreme — surgery to remove their breasts or ovaries — providing the information could be fraught, especially because many physicians do not have enough grounding in genetics and there will not be enough genetic counselors.

"We can actually envisage the following: It's going to be affordable, almost immediately, if not next year, to get a genome sequence for less than the price of an MRI,'' Kohane said. "Does that mean we're going to have all these BRCA1 mtuations now presented to a health care system whose doctors are not well-equipped to assess the meaning of those mutations?''

The recommendations also make two major departures from typical practice in medicine and research.

Instead of allowing patients to opt out, telling

physicians there are some results they don't want to learn, the recommendations suggest patients be told if they have any of the mutations. Green said it was similar to how medicine already handles incidental findings. If a radiologist sees a dark spot on an X-ray, for example, the doctor would inform the patient and investigate it further. Doctors do not as a matter of course counsel patients before every X-ray that they may find something they do not anticipate, such as lung cancer.

The recommendations also specify no age limit on any of the conditions, suggesting that if an genetic risk relevant only in adulthood is found in a child, the parents should be told. Their reasoning was that such information could have benefits for the parents or other family members, who might learn of a life-threatening disease risk from their son or daughter. But ethicists talk of the importance of maintaining an "open future'' for children and not using children for parents' benefit.

The guidelines "go very far in privileging the concerns of the lab and the concerns of the clinician over the rights of individual patients, and the rights of kids to be protected from certain information'' until they are old enough to make the decision for themselves, said Susan Wolf, a professor of law and medicine at the University of Minnesota. "I'm troubled by them going that far in demoting these core concerns of [patient] autonomy, which in the clinical sphere have been such

important bedrocks.''

Even the team that put together the recommendations noted that this was far from the final word, suggesting that the list evolve over time. The recommendations are not binding. They are intended to guide the use of genetic information in health care.

"This is not some list we expect to be maintained for all time or take some sort of pride in getting it right,'' Green said. "We're sure we didn't get it right; we're sure people will find evidence something shouldn't be on the list and some things should be. But it's a starting point.''