U.S. Issues Rules for Use of Genetic Information

BY MARY ELLEN SCHNEIDER

The federal government has issued new rules spelling out how it intends to police the use of genetic information by health plans.

The regulations bar health insurers from increasing premiums or denying enrollment based on genetic information. The regulations implement certain provisions in the Genetic Information Nondiscrimination Act (GINA), which was signed into law by President Bush in May 2008.

Beefing up consumer protections for genetic information should help accelerate progress in genetic testing and research, said Health and Human Services secretary Kathleen Sebelius.

"Consumer confidence in genetic testing can now grow and help researchers get a better handle on the genetic basis of diseases," Ms. Sebelius said in a statement. "Genetic testing will encourage the early diagnosis and treatment of certain diseases while allowing scientists to develop new medicines, treatments, and therapies."

In an interim final rule, federal officials provide details on how health plans can obtain and use genetic information. The regulation generally bars health plans from increasing premiums based on genetic information. They also cannot require, or even request, that individuals or family members undergo genetic testing. And health plans cannot request, require, or purchase genetic information at any time for underwriting purposes, or prior to or in connection with enrollment.

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Although the rule bars insurers from charging its members more based on genetic information, it doesn't limit them from doing so because of the manifestation of a disease. However, a health plan can't use the manifestation of a disease in one of its members as genetic information for a family member and raise their premiums, according to the interim final rule.

The rule does allow plans to request limited genetic information if it's necessary to determine the "medical appropriateness" of a certain treatment. Plans also can request that individuals participate in research where genetic testing will be conducted. However, none of the genetic information collected during that research can be used for underwriting purposes.

The interim final rule goes into effect 60 days after publication in the Federal Register.

HHS officials also issued a proposed rule that would modify the Health Insurance Portability and Accountability Act (HIPAA) to comply with the provisions of GINA. Like the GINA rule, the HIPAA rule bars health plans from using and disclosing genetic information for underwriting purposes. However, since HIPAA applies more broadly, the prohibition in the proposed rule also affects employee welfare benefit plans and long-term care policies. It would exclude nursing home fixed indemnity policies.

If the proposed rule is finalized, then plans would have 180 days to comply with the provisions. ■

GENOMIC MEDICINE

Alzheimer's and 'Personal Utility'

Alzheimer's dementia strikes fear in the hearts of elderly patients. The diagnosis can lead families into social and financial chaos, and truly effective treatments have remained elusive. Recently, the mainstream media has drawn attention to genetic testing for Alzheimer's, resulting in patients occasionally requesting "the blood test" to predict their risk. Survey data suggest that a little more than 1 in 10 primary care providers have been asked to provide such testing. Anecdotally, I have been asked twice in the last month—a definite upswing from a few years ago. The request for predictive genetic testing is not unreasonable from the patient's perspective: It's estimated that 60% of the risk for developing Alzheimer's after age 60 years is heritable and that about 25% of Alzheimer's patients have an affected parent. However, commercially available testing for the apolipoprotein E (APOE) gene epsilon 4 has poor predictive value in asymptomatic individuals.

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Not surprisingly, no major medical society endorses the use of APOE testing for screening purposes, and use of the test in a diagnostic setting remains controversial. Testing for mutations causal of the uncommon forms of autosomal dominant early-onset familial Alzheimer's disorder is more predictive and less controversial, but only relevant to about 5% of all Alzheimer's cases. A flurry of high-profile research publications regarding late-onset Alzheimer's in the last few months will probably drive a surge in patients interested in testing, and may cause some to rethink professional guidelines that have discouraged testing to date.

As background, about 40% of Alzheimer's patients have at least one copy of the epsilon 4 version of the APOE gene, and the same risk version of the APOE gene is present in about 30% of the general population. Many individuals with the risk version of APOE gene never develop the disease despite living to an advanced age, and some individuals with comorbidities die before the onset of clinically significant symptoms.

Conversely, substantial numbers of individuals without the epsilon 4 version of APOE develop Alzheimer's. Many health professionals and behavioral scientists have been concerned that APOE testing could result in psychological harm, both because of the relatively poor predictive value of the test and because evidence-based options for risk reduction and therapy are limited. Others argue that such test results are empowering to certain individuals, and that patients are quite capable of dealing with ambiguity.

Two articles appearing in the July 16, 2009, New England Journal of Medicine have added information to this debate. The first demonstrated that some Alzheimer's patients harboring the APOE epsilon 4 variant become detectably (but not necessarily functionally) impaired prior to age 60 (N. Engl. J. Med. 2009;361:255-63). This observation suggests that an earlier and expanded window of opportunity exists to spare neuronal damage and thereby delay the emergence of clinically important symptoms. Though there are no widely accepted risk-reducing or preventive strategies for Alzheimer's, some health professionals argue that lifestyle modifications such as improved diet, exercise, smoking cessation, and moderation of alcohol consumption might affect disease progression over time.

The second article describes a longitudinal study of families affected by Alzheimer's. In the REVEAL (Risk Evaluation and Education for Alzheimer's Disease) study, offspring of affected individuals were randomized to receive or not receive personal APOE testing results under carefully controlled circumstances and then were followed longitudinally. The study authors found little evidence for anxiety, depression, or test-related distress up to 1 year out from disclosure (N. Engl. J. Med. 2009;361:245-54).

Most experts in the genetics community have speculated that revealing a somewhat ambiguous risk for a devastating disease with little opportunity for risk reduction would cause substantial and potentially long-lasting emotional distress. This concern has formed part of the basis for guidelines that recommend against predictive testing for conditions like Alzheimer's; this latest study suggests that such guidelines might be overly paternalistic.

In recent months, genome-wide association studies have begun to yield new, highly validated genomic risk markers. Variants in three genes were described by teams from the United Kingdom and France each conferring a small, yet statistically robust risk for developing disease. The variants occur in or near the genes CLU, which encodes the brain apolipoprotein clusterin; PICALM, encoding a protein associated with synapse function; and CR1, encoding the complement component (3b/4b) receptor 1 protein. These proteins have previously been shown to be associated with biologic processes potentially important to Alzheimer's dementia. These studies are the first to confirm a direct link with the pathologic process in an unbiased way. Each discovery may provide a new approach to prevention and/or treatment, and perhaps improved risk prediction.

Taken together, recent research bolsters arguments made by proponents of the "personal utility" of APOE testing for Alzheimer's. Supporters of "personal utility" argue that genomic testing can empower individuals to make healthy lifestyle choices. The invocation of "personal utility" as justification for genetic testing has arisen in the context of the direct-to-consumer genetic testing movement, often in the absence of controlled trials demonstrating clinical utility of such testing. The concept of "personal utility" has appeal in an extremely fast-moving research and practice environment where trials demonstrating clinical benefits derived from testing may lag availability of the test by years, if not a decade. Despite the appeal, caution seems in order when weighing "personal utility" as a factor for testing in individual cases, particularly when the results might have a profound and poorly defined cascade of effects on patients and their families.

Our understanding of Alzheimer's disease is rapidly expanding, fueled by advances derived from genomics and other disciplines of biomedical inquiry. It is highly likely that Alzheimer's risk prediction and management will improve considerably over the next decade, more closely aligning "personal" and clinical utility. Health professionals and guideline developers will need to monitor advances carefully and adapt as new insights for improved patient care emerge. ■

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