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Editorial

Genetic Risk of Alzheimer's Disease: Three Wishes Now That the Genie is Out of the Bottle

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Abstract. The availability and increasing popularity of direct-to-consumer genetic testing for the presence of an APOE4 allelle led the Alzheimer's Foundation of America Medical, Scientific and Memory Screening Advisory Board to identify three critical areas for attention: 1) ensure consumer understanding of test results; 2) address and limit potential negative

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consequences of acquiring this information; and 3) support linking results with positive health behaviors, including potential clinical trial participation. Improving access to appropriate sources of genetic counseling as part of the testing process is critical and requires action from clinicians and the genetic testing industry. Standardizing information and resources across the industry should start now, with the input of consumers and experts in genetic risk and health information disclosure. Direct-to-consumer testing companies and clinicians should assist consumers by facilitating consultation with genetic counselors and facilitating pursuit of accurate information about testing.

Keywords: APOE, genetic risk, genetic testing, late-onset Alzheimer's disease

Commercially available direct-to-consumer genetic testing is now a reality, and as of April 2017 consumers could learn their apolipoprotein E4 (APOE4) genotype, which is an established risk factor for Alzheimer's disease and one of the strongest genetic factors linked with a disease process. With this newly available testing, consumers get information about risk, a probability about future outcome. However, consumer understanding of the meaning and implications of genetic test results is limited, as is the understanding by many physicians, largely due to lack of attention to this vital area in medical school curricula. Nonetheless, the genetic genie is out of the bottle, preempting debates about advisability and making identification of ways to address the very real needs associated with direct-to-consumer testing paramount.

Historical examples of disease disclosure offer a brief course in medical paternalism, from debates about sharing cancer diagnoses in the 1960s, to concerns about disclosure of HIV infection in the 1990s and later home testing and controversies about disclosure of genetic predisposition for disorders such as Huntington's disease in which disease development is more specifically determinable than late-onset Alzheimer's disease (LOAD) [1–3]. Patient and consumer access to health-related information about themselves is expected to increase, and such access is consistent with increased emphasis on patient-empowerment and shared medical decision-making [4, 5]. Clinical wisdom is required as a guide to medical decisions, but the patient role is now understood as appropriately primary and autonomous.

Given increasing availability of genetic testing for risk of LOAD, there are three goals for optimizing this type of genetic testing (see https://alzfdn.org/genetesting/).

The first goal is to ensure that consumers understand the meaning of test results. For APOE genes, understanding that a measure of risk is not a clinical diagnosis is a crucial point. As important is conveying that "negative" results do not confer protection against development of the disorder at a later time. Beyond APOE, there are at least 20 other genetic factors which have been shown to have a small but significant role in determining Alzheimer risk. Such information can and should be used by individuals and families in making plans for their future lives. Understanding of genetic test results also requires attention to the potential for inaccurate results.

The second goal is to limit negative consequences that result from acquiring new genetic information. Stories continue to appear in the popular press and social media about individuals who learn details about themselves and their families from genetic testing that cause upset or harm—surprises about true paternity, for example. Disclosure of information about risk of LOAD may have negative consequences [6]. Given the current limitations in disease modification, the absence of effective treatments, and the distressing outcomes for individuals with dementia and their families—concerns about negative consequences following a test result are not unfounded and should be taken seriously and addressed.

The third goal is that, at both the individual- and the population-level, results should be used to inform and support adoption and maintenance of lifestyle modifications that may reduce overall risk for LOAD. Evidence is suggestive, but not definitive, that these interventions can alter the age of dementia onset by several years (e.g., [7]). Increased participation in relevant clinical research studies is another public health outcome that can be supported through provision of information about risk.

With these goals in mind, what is the best setting and what are optimal methods to support appropriate understanding and use of genetic information, including mitigating the potential negative emotional impact?

Some suggest that the physician's office is the only appropriate venue for learning these results. While physicians certainly could provide appropriate guidance about risk and offer insights into treatment

options, the reality is that most clinicians lack the training and report feeling ill equipped to address genetic test results [8]. Limited training may result in a wide variation in the information and counseling provided, further reducing the value of the office consultation. Given the rapidly growing use of genetic testing, training in conveying and explaining the genetic test results should be included in the education of health professionals. This training can address when referral to genetic counseling is appropriate.

Consumers are receiving results at home, with the information provided by commercial entities offering the testing reviewed in the US by the FDA under regulation of medical devices. The value of the information to meet the goals described above has yet to be determined. There are viable paths for consumers to optimize their own experience without a visit to a clinician, or in addition to such a visit. Increasingly, consumer-led online communities are available as a source of support and some guidance to those learning of a risk of younger onset of LOAD. Inclusion of clinicians and genetic counselors in these forums can enhance the quality of the guidance provided and improve understanding of the meaning of increased risk.

As more biomarkers associated with dementia and other diseases and conditions are identified, ongoing research will be increasingly needed to inform improvements in how consumers obtain and use information about risk, as well as the benefits and harms of learning personal genetic information. The priority now is to ensure the availability of resources for understanding genetic risk information, reduce avoidable negative impacts of this information and advance ways that the information can be used to support individual and population health. Improving access to appropriate sources of genetic counseling as part of the testing process is critical, as is avoiding inappropriate disclosure of confidential information. Protections for consumers who learn their genetic risk, including with health insurance, long term care insurance, and life insurance, must be clear. Developing and standardizing systems for information and resource management across the industry should start now, with the input of consumers and experts in genetic risk and health information disclosure. Consumers should be encouraged to consult with genetic counselors as part of their decision to discover their genetic make-up, by clinicians they may consult prior to testing, and by the direct-to-consumer testing companies themselves. The genie is out of the bottle; with the right information consumers can be the recipients of the benefit.

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DISCLAIMERS

This viewpoint is based on the Alzheimer's Foundation of America Medical, Scientific and Memory Screening Advisory Board statement on genetic screening. All authors are members of the AFA Advisory Board. The views expressed in this article are the authors' and do not represent an official position of the authors' institutions.

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