

## Susceptibility testing for Alzheimer's disease: race for the future

Alzheimer's disease (AD) is at the centre of the revolution in personalised genetic medicine. As expectations for preventative therapies grow, tests for genetic mutations and alleles will be ever more important indicators of an individual's risk of developing the disease. Scientific data that describe how genetics influences the risk of developing AD will also be incorporated into conversations between individuals and their health-care providers; between patients and their families; within the medical community; between medicine and industry; and among politicians and their constituents.

It is well established that the presence of an apolipoprotein  $\epsilon 4$  (*APOE*  $\epsilon 4$ ) allele, particularly in the homozygous state, increases risk of dementia in various populations.<sup>1,2</sup> However, the degree of risk among African Americans who have one or two copies of the *APOE*  $\epsilon 4$  allele is controversial.<sup>3,4</sup> A recent report from the MIRAGE (Multi-Institutional Research in Alzheimer's Genetic Epidemiology) study suggests that first-degree relatives of African-American patients with AD have a greater risk of developing dementia than do their European-American counterparts.<sup>5</sup> However, this report also suggests that the additional risk associated with being a first-degree relative, being female, or the probability of having an *APOE*  $\epsilon 4$  allele, is not different between African Americans and European Americans. Since race is a socially constructed concept and does not map well onto particular patterns of genetic variability, the self-identified status of being African American may be uninformative.

We participate in REVEAL (Risk Evaluation and Education in Alzheimer's disease), a randomised controlled study, funded by the US National Institutes of Health, of genetic testing and counseling in individuals known to be at risk of developing AD because one of their parents has been diagnosed with the disease. In REVEAL, we randomise participants into two groups, both of

which receive counselling on the genetic-risk assessment for AD. The risk estimates for individuals in the intervention group are calculated based on age, gender, family history, and *APOE* status. For those in the control group, *APOE* genotype is not



A focus group REVEALS what's needed.

included in the calculations. For statistical reasons the risk calculations used in REVEAL were based on the European-American subset of MIRAGE participants. A major dilemma during this project has been to decide what risk information to provide to participants who identify themselves as African American, as we recognise that the link between *APOE* status and AD risk is controversial in this population, and that our own original data sets are limited.

We organised focus groups with African Americans who had a parent with AD. Although this was only the first step in learning how to communicate the difficult concept of risk, we were able to learn valuable information from the participants in these groups.

The first focus group considered the diversity of individuals who label themselves as African American; in particular how it is difficult, and perhaps inappropriate, for any one individual or group of individuals to speak for the larger group as a whole. The second focus group emphasised the importance of inclusion and communication in research studies. Individuals in this group said that they expected to be told about the derivations of the risk estimates, and any concerns we had about the relevance of those estimates to them, but that our concerns about the data

should not keep us from enrolling African-American participants into the REVEAL study. The importance of inclusion is also emphasised by a report titled "NIH policy and guidelines on the inclusion of women and minorities as subjects in clinical research", which was released in October, 2001. The report includes categories that distinguish five racial and two ethnic groups, and strongly encourages enrolling participants from all backgrounds.

Ultimately, the challenge for the health-care profession will be to integrate genetic information into individualised health-care decisions. As we enter the era of personalised medicine, an understanding of our individual genetic make-up may allow us to adjust our lifestyle in response to known susceptibilities to disease. However, we need to examine carefully the costs of such genetic information, to both the individual and to society. We are just beginning to understand how broadly the knowledge of our genetic status can affect our self-image, lifestyle and medical decisions, family dynamics, conceptions of health and justice, and societal economics. Moreover, we need to ensure that we do not focus so much attention on individual genetic risk and personalised medicine that we ignore the larger health-care consequences of the influence of environmental conditions on public health around the world.

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### Acknowledgments

We would like to acknowledge the REVEAL study group.

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