

# Current Perspective

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## An Issue Settled ... for Now

Should selected patients with age-related macular degeneration (AMD) routinely have genetic testing? The question has potentially profound medical, scientific, commercial, and payer-coverage implications. Over the past several years, it has pitted clinicians against each other, led to allegations of scientific misconduct, prompted threats from lobbyists, and, finally, resulted in NIH-sponsored independent statistical evaluations. We now have an answer, and it is a clear victory for the scientific process—and for patients.

Prior to 2011, numerous scholarly papers had addressed routine genetic testing in AMD patients, and they had concluded that it was not justified. In the interest of providing guidance on a complicated subject, and given the clinical and public health importance, in 2011 the Academy assembled a blue-ribbon task force of geneticists, clinicians, and methodologists to address the issue of genetic testing. They recommended, “Avoid routine genetic testing for genetically complex disorders like age-related macular degeneration ...”<sup>1</sup>

The following year, a paper was published concluding, “Individuals with moderate AMD could benefit from pharmacogenomic selection of nutritional supplements ... treatment with zinc was associated with increased progression to advanced AMD.”<sup>2</sup> In other words, the paper maintained that patients with “moderate AMD” would benefit from commercial genetic testing because standard nutritional supplements could accelerate the disease in some patients. Scientific methodology aside, 2 of the authors had equity in the company that marketed the genetic test, 2 others were paid consultants, and the company funded the study.

Other investigators, including a scientist at the National Eye Institute (NEI), then rebutted those conclusions. While that individual had no equity interests, the NEI does receive royalties related to a formulation of nutritional supplements. (Federal law not only permits but encourages such royalty arrangements to augment NIH research funding.) Several subsequent independent papers also supported the NEI author. Then the company issued a report in the company’s favor authored by 2 statisticians paid by the company.

Twice between 2012 and 2016, the members of the Academy Task Force re-evaluated the issue, considered recent publications, and found no reason to amend their earlier recom-

mendations. The American Society of Retina Specialists also convened an independent task force that likewise found that routine genetic testing in AMD was not recommended.

Meanwhile, the company marketed the test and paid for referrals. Finally, its leadership contacted the NIH alleging NEI conflict of interest and accused NEI scientists of “misleading charts, inconsistent data across the tables, and incorrect conclusions.”

What to do when faced with such a challenge? After all, this is a complex clinical issue with significant ramifications for patient care that is further complicated by commercial entangle-

ments with hundreds of millions of dollars at stake. One option: Assemble totally independent experts and get all parties to agree in advance to a scientific re-evaluation process.

And that is precisely what the NIH did. All relevant data and analyses were sent by both the company and by the NEI to 3 independent teams of scientists from 3 different scholarly institutions. The 3 reviews took more than 6 months.

Each review concluded that there was no scientifically valid rationale for routine genetic testing in AMD and upheld the methodologic integrity and conclusions of the NEI scientists.

Is this the end of the saga? Hopefully not. Hopefully, our understanding of AMD, its risk factors, and treatment will advance to the point where early AMD testing will lead to personalized, actionable therapies. Until that time, we must applaud the NIH for spending our tax dollars wisely to resolve a complex problem. And we must applaud the dedication of those scientists whose persistence led us to a better understanding of an all-too-common disease. We should hope that this will promote evidence-based patient care and evidence-based health policy and CMS coverage decisions.



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1 Stone EM et al. *Ophthalmology*. 2012;119(11):2408-2410.

2 Awh CC et al. *Ophthalmology*. 2013;120(11):2317-2323.

**Note.** The company involved has issued the following statement: “No provider has received a personal financial inducement for ordering any ArcticDx product.”