

Age-related macular degeneration and primary care optometry

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Benjamin Franklin's aphorism that "an ounce of prevention is worth a pound of cure" is a succinct description for the role of primary care optometrists in an integrated health care delivery system. Eye doctors diagnose, treat, and manage sight threatening diseases including age-related macular degeneration (AMD), glaucoma, and diabetic retinopathy, among others. Whilst there are many treatments for AMD, there is, regrettably, no cure yet. Consequently, the best approach is early detection followed by a preventative strategy to postpone the onset of the more severe symptoms of the disease.

How big a public health problem is AMD?

According to the Centers for Disease Control and Prevention (CDC) Behavioral Risk Factor Surveillance Survey (BRFSS), AMD in those over 65 years of age ranged from 6.8% in Tennessee to 11.5% in Wyoming, of the states that participated. With increasing age, the prevalence increases dramatically from 4% among those aged 65-69 years to 22% among those aged 85 years or older.¹

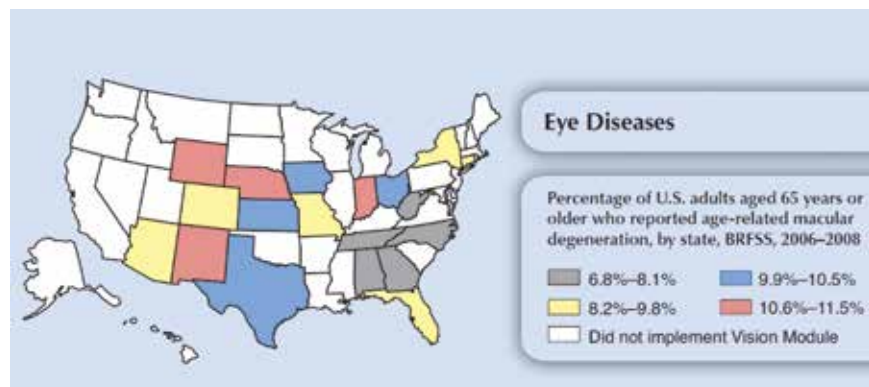


Figure 1: Reprinted from the CDC *The State of Vision, Aging, and Public Health in America*

According to the CDC, **85-90% of AMD cases are dry** or non-exudative. The Eye Disease Prevalence Research Group reported that over 7 million people have drusen greater than 125 μm .² With cases of early AMD expected to double by 2050 to 17.8 million people, it seems that optometrists are on the front line of providing much needed care.³

Evidence-based outcomes and alignment of incentives

One can't improve what isn't measured. This applies in school, business, optometric practice and health care systems. Not surprisingly, the Centers for Medicare and Medicaid Services (CMS) is very interested in improving outcomes on a wide range of quality health measures. One such tool is the Physician Quality Reporting System (PQRS). Incentives in 2013 include a 0.5% bonus calculated from any and all Medicare claims filed by a provider. Penalties in 2015 for non-reporting will be a 1.5% cut in Medicare reimbursement. Rebecca H. Wartman, OD, presented an excellent overview of the relevant PQRS measures for optometry and how to code for them. With regards to AMD specifically, Dr. Wartman reported optometrists' percentage correct coding for AMD at over 90% in 2011.⁴

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The two PQRS national quality measures for those diagnosed with AMD, 50 years of age and older, include 1) measure #14: percentage of patients who have a “dilated macular examination” including documentation AND level of severity within 12 months⁵, and 2) measure #140: percentage of patients/caregivers who receive counseling on the benefits and/or risks of AREDS for delaying the progression of AMD.⁶

“As primary care eye providers, optometrists are expected to see the majority of early AMD and PQRS is the pathway to providing evidence of quality care.

As primary care eye providers, optometrists are expected to see the majority of early AMD and PQRS is the pathway to providing evidence of quality care. Given that early signs of AMD including drusen and retinal pigment epithelium (RPE) may not result in any overt symptoms, the importance of regularly scheduled eye examinations may play a role in early diagnosis.

Diagnosis and imaging in AMD

Optometrists have a number of tools at their disposal to enhance their ability to diagnose and manage AMD. A dilated fundus examination and a slit lamp biomicroscope provide a stereoscopic view of the macula to assist in determining the presence of thickening, hemorrhages, and the presence of drusen. The Age-related Eye Disease Study (AREDS) outlined a color photographic imaging and evaluation procedure to provide guidelines for grading the level of AMD.⁷ Subsequently, AREDS2 validated the grading system using digital imaging technology, which became more widespread in the intervening years.⁸

Table 1: Categories of AMD based on size, area, pigment and diagnosis in the fellow eye⁷

1. Small drusen < 63 μ m, no pigment changes
2. Small or intermediate drusen (63<x<125 μ m) and/or +RPE change
3. Intermediate or large (>125 μ m) drusen between 20-65 in number (1/5 to 1/16 DA) with little or no vision loss
4. Advanced - Drusen and RPE breakdown or hemorrhage, loss of VA, or geographic atrophy + macula in one eye only (other is 1, 2 or 3)

More recent efforts to automate classification of severity of AMD from fundus photographs are being developed with reasonable sensitivity and specificity.⁹ As technology evolves, it can enhance the ability of primary care providers and support efficient diagnoses and management of the patient in the chair.



Figure 2:
Soft drusen in the macula

Optical coherence tomography (OCT)

OCT technology has evolved to provide an effective instrument for the measurement and monitoring of drusen, macular thickness, RPE, and geographic atrophy. Characterizing the drusen volume may provide additional information to augment what is visible in fundus photos.¹⁰

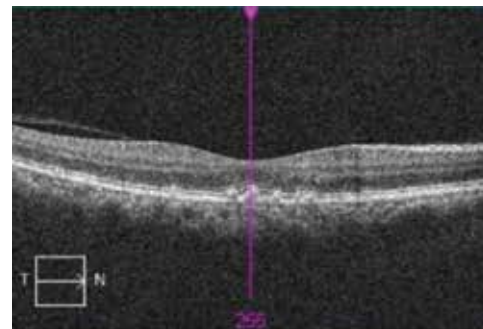


Figure 3:
Optical coherence tomography revealing drusen in cross-section

OCT and RPE analysis

With RPE analysis, one can monitor the elevations of the RPE seen with drusen as well as choroidal neovascular membranes and loss of RPE (sub-RPE illumination) seen in geographic atrophy. Evaluation of scans of the macula will determine the cause of the sub-RPE illuminations as well as the RPE elevations. Advanced RPE analysis is another important piece of the puzzle that helps a clinician decide on rate of progression, rate of follow-ups and effectiveness of current treatment including ocular vitamins and anti-VEGF among others.

Advanced RPE analysis shows multiple areas of RPE elevations from drusen in the central 3mm of the macula. Looking at progression analysis, there is a mild increase in the volume and area of the RPE elevations. Sub-RPE illumination is shown on the RPE profile in yellow, which again indicates an area of RPE

loss. Looking at the current scan, there is actually no sign of sub-RPE illumination which indicates stability or an artifact on the previous scan.

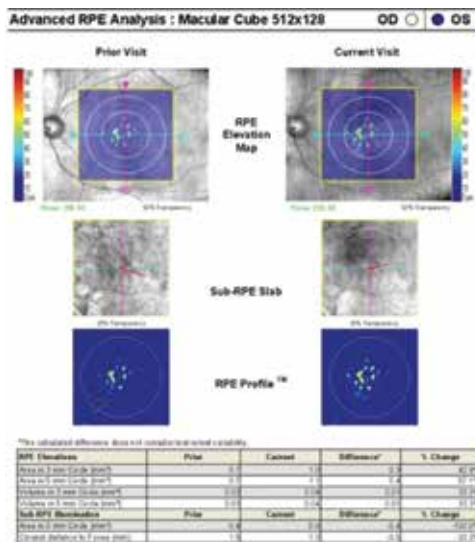


Figure 4:
Advanced RPE
analysis in a
macular cube

Macular Pigment Optical Density (MPOD)

Lutein and zeaxanthin are xanthophyll carotenoids obtained from diet with a predilection for concentration within the macula. Concentration levels and spatial distribution vary in location and by age, but have a putative antioxidant effect believed to be protective against AMD. The optical characteristics arise from a selective attenuation of short wavelength visible light.

Bernstein et. al., provide an excellent review of the role of macular carotenoid pigments and their impact on MPOD.¹¹ They cite four of the most commonly used techniques including heterochromatic flicker photometry (HFP), fundus reflectometry, resonance Raman spectroscopy (RRS), and autofluorescence imaging. Each of the techniques vary somewhat in approach and sensitivity, but in aggregate form the foundation for better correlating non-invasive assessments with the in-situ gold standard of HPLC.

Fundus Autofluorescence Imaging (FAF)

FAF is an imaging method that complements conventional technology by highlighting the topographical distribution of lipofuscin. Known as the "aging pigment," lipofuscin accumulates in the RPE with excessive production suggestive of active disease processes. Lipofuscin will typically autofluoresce when exposed to short or medium wavelength light with an intensity proportional to its concentration. Increased levels of lipofuscin are visible as hyperfluorescence while a decrease or absence appears as hypofluorescence. In an effort to quantify FAF, Schachar et. al., propose an index of retinal autofluorescence (IRA) based on a "unique horizontally oriented FAF signature composed of vertically averaged gray-scale values." Investiga-

tors found a positive correlation with AREDS score with an ability to distinguish between AREDS grades 3 and 4, which may assist in monitoring progression of AMD.¹²

In early AMD, FAF may reveal more subtle changes than fundus evaluation. A particularly effective use for FAF is to monitor geographic atrophy in patients with dry AMD. The image will reveal patchy, distinct dark areas due to a decrease in autofluorescence from loss of RPE at the site of the lesion. Hyperfluorescence at the junctional zone or borders of the geographic atrophy typically indicates a potential for progression of the atrophy, and thus needs to be monitored closely.¹³

Functional evaluation of AMD progression

The longstanding approach to monitoring progression of AMD is the unilateral observation of the Amsler grid on a daily basis. The theory is that leakage or significant disruption to the RPE in AMD will lead to distortions that are easily visible, and hence a symptom to trigger an urgent evaluation and dilated fundus examination.

Unfortunately, the Amsler grid is woefully inadequate and insensitive because of perceptual filling. Zur and Ullman found perceptual completion across scotomas with a radius of up to 7 degrees. Both gratings and dot arrays were relatively insensitive to detection because of perceptual filling.¹⁴

The Foresee PHP Preferential Hyperacuity Perimeter, based on vernier acuity, is an improvement over the Amsler grid. Similar to an automated field test, it uses a dot array approach to measure the central 14 degrees of visual field. A patient uses a stylus pen to detect the area of a line with the most distortion and compares the findings to a normative database of patients with intermediate-severe dry ARMD and wet ARMD.¹⁵

An alternative psychophysical approach that may be less susceptible to perceptual filling-in uses a stimulus of short line segments of variable orientation to one another. Orientation-discrimination thresholds are predicted to worsen further as the disease process progresses, and the test of orientation discrimination could be converted readily to provide a home-monitoring device such as a cell phone or PDA.¹⁶ More sensitive than the Amsler grid, the technology has the potential to provide a quick, inexpensive and easy to administer test that could lead to better preventative care.

Management, Treatment, Counseling and education — AREDS1 and AREDS2

With dry AMD there is no current treatment to stop progression. However, there are a number of risk factors that have been identified some of which may be modifiable. Most significant among these is smoking, which is a key contributor

to accelerating the progression of AMD to more advanced stages.^{17,18,19} Decreasing HDL, increasing platelet aggregability, and increased oxidative stress were just a few of the adverse physiological changes attributed to smoking. In addition, a complication of increased incidence of lung cancer with use of beta-carotene as an ocular supplement posed an additional hazard to patients diagnosed with AMD.²⁰

Consistent with PQRS measure 140, counseling patients with AMD about the AREDS studies and ocular supplements is essential to good preventive care. The AREDS formulation originally contained beta-carotene, Vitamins C and E, zinc, and copper. Those subjects taking the supplement had a reduced risk of progression by 25% in stages of moderate to advanced ARMD with a reduced probability of vision loss of 19%. Interestingly, use of the AREDS formulation was not found to provide a statistically significant difference in preventing the progression of early AMD to more advanced stages.⁷ The presence of beta-carotene increased risk of lung cancer 24% for smokers.

AREDS2 looked to add some components that could not be compounded at the time of the original AREDS formulation. Additional components added included Omega 3, lutein, and zeaxanthin.²¹ Omega 3 fatty acid has been found in high concentrations in the retina, and associated with improved vasodilation and anti-inflammatory activity. Lutein and zeaxanthin are carotenoids found in high concentration in the macula often obtained from dietary sources including leafy, green vegetables, eggs, yellow/orange fruit and vegetables.

AREDS2 did not indicate any substantive decrease in the rates of progression with the new formulation as compared to the original. However, substitution of lutein and zeaxanthin for beta-carotene provided a safe alternative for smokers without a loss of efficacy.²²

Other practical primary care considerations in dry AMD — aspirin use and cataract surgery risk

Aspirin is widely used on a chronic, low dose basis for cardioprotective effects. In patients with AMD, 2 recent studies tried to address the perception of elevated risk of progression of AMD with aspirin use. Using subject data from the Beaver Dam Eye Study, Klein et. al., examined data from a 20-year period with the question of whether participants had “regularly used aspirin at least twice a week for more than 3-months.”²³ They utilized the Wisconsin Age-related Maculopathy Grading system, and found that regular aspirin use over a 10-year period was associated with late AMD at a slightly elevated incidence of 1.76% vs. 1.03% who did not use aspirin regularly.

In contrast, Liew et. al., analyzed data from an Australian cohort over a 15-year period who underwent 4 examinations in that time span. This prospective study included a detailed

baseline questionnaire at baseline assessing aspirin use, cardiovascular disease status, and AMD risk factors. Investigators found that regular aspirin users were more likely to present with neovascular AMD, with a cumulative incidence of 9.3% vs. 3.7% in nonusers. Their conclusion was that “regular aspirin use is associated with increased risk of incident neovascular AMD, independent of a history of cardiovascular disease and smoking.”²⁴

Not surprisingly, the variation in results has created some uncertainty in balancing the cardioprotective effects of aspirin with the elevated risk of accelerating the progression to advanced AMD. Whether an association or causal in nature, careful and periodic monitoring may reveal on a case by case basis the rate of change of ocular signs, which can serve as the basis for interprofessional communication about the patient’s health care status and plan.

In low vision rehabilitation centers, cataract surgery seems to precede the increased severity of AMD symptoms of patients with regularity. This anecdotal experience appears to be borne out by several studies, which suggest that the nonphakic eyes had a substantially higher risk for developing either late-stage AMD lesions compared with phakic eyes (non-operated).

Wang et. al., studied two large population cohorts in the Beaver Dam Eye Study (4,926 persons) and the Blue Mountains Eye Study (3,684 persons). Investigators observed that subjects had an elevated risk of developing late stage AMD with an odds ratio of 5.7 compared to phakic eyes. Wang’s conclusion was that “cataract surgery in older persons may be associated with an increased subsequent risk for developing late-stage ARM, particularly neovascular ARM.”^{25, 26}

Proper counseling of risks can be counterbalanced with the advantages of cataract surgery at the appropriate time based on brighter retinal image, improved contrast, and potential improvement in visual acuity. Risk factors for a more guarded prognosis include initial stage of AMD including area and number of confluent drusen and focal RPE hyperpigmentation.

Conclusion

As one of the leading causes of vision loss in the United States, AMD is a significant public health concern. Optometrists as eye doctors are well-trained, accessible, and capable of utilizing existing technology to diagnose, manage, and treat patients with AMD. Early diagnosis and counseling and education about preventative care is beneficial to delaying the onset of more debilitating symptoms. In an attempt to measure quality health care indicators, PQRS measures can be reported in an effort to provide evidence-based quality outcomes directly attributable to optometrists. Aligning good practice habits, consistency and outcome measures can have a direct benefit to patient outcomes and quality of life.

REFERENCES:

1. Centers for Disease Control and Prevention. The State of Vision, Aging, and Public Health in America. Atlanta: U.S. Department of Health and Human Services; 2011.
2. Eye Disease Prevalence Research Group. Prevalence of age-related macular degeneration in the United States. *Arch Ophthalmol* 2004;122(4):564-72.
3. Rein DB, Wittenborn JS, Zhang X, Honeycutt AA, Lesesne SB, Saadine J. Forecasting age-related macular degeneration through the year 2050: the potential impact of new treatments. *Arch Ophthalmol* 2009;127(4):533-540.
4. AOA news Rebecca H. Wartman, O.D. "Optometrists enter crucial years with PQRS: 2013"; March 11, 2013. <http://newsfromaoa.org/2013/03/11/optometrists-enter-crucial-year-with-pqrs-2013/>
5. AHRQ link <http://www.qualitymeasures.ahrq.gov/content.aspx?id=28115&search=age+related+macular+degeneration>
6. AHRQ link <http://www.qualitymeasures.ahrq.gov/content.aspx?id=27984&search=age+related+macular+degeneration>
7. Age-related Eye Disease Study Research Group. The Age-related Eye Disease Study system for classifying age-related macular degeneration from stereoscopic color fundus photographs: the Age-Related Eye Disease Study Report Number 6. *Am J Ophthalmol* 2001;132(5):668-81.
8. Danis RP, Domalpally A, Chew EY, Clemons TE, Armstrong J, Sangiovanni JP, Ferris FL 3rd; AREDS2 Study Group. Methods and reproducibility of grading optimized digital color fundus photographs in the age-related eye disease study 2 (AREDS2 Report Number 2). *Invest Ophthalmol Vis Sci* 2013;54(7):4548-54.
9. Kankanahalli S, Burlina PM, Wolfson Y, Freund DE, Bressler NM. Automated classification of severity of age-related macular degeneration from fundus photographs. *Invest Ophthalmol Vis Sci* 2013;54(3):1789-96.
10. Freeman SR, Kozak I, Cheng L, Bartsch DU, Mojana F, Nigram N, Brar M, Yuson R, Freeman WR. Optical coherence tomography-raster scanning and manual segmentation in determining drusen volume in age-related macular degeneration. *Retina* 2010;30(3):431-5.
11. Bernstein PS, Delori FC, Richer S, van Kuijk FJ, Wenzel AJ. The value of measurement of macular carotenoid pigment optical densities and distributions in age-related macular degeneration and other retinal disorders. *Vision Res* 2010;50(7):716-28.
12. Schachar IH, Zahid S, Comer GM, Stern M, Schachar AG, Saxe SJ, Gardner TW, Elnor VM, Jayasundera T. Quantification of fundus autofluorescence to detect disease severity in nonexudative age-related macular degeneration. *JAMA Ophthalmol* 2013 Jun20:1-7.
13. Schmitz-Valckenberg S, Fleckenstein M, Scholl HP, Holz FG. Fundus autofluorescence and progression of age-related macular degeneration. *Surv Ophthalmol* 2009;54(1):96-117.
14. Zur D, Ullman S. Filling-in of retinal scotomas. *Vision Research* 2003;43(3):971-82.
15. Alster Y, Bressler NM, Bressler SB, Brimacombe JA, Crompton RM, Duh YJ, Gabel VP, Heier JS, Ip MS, Loewenstein A, Packo KH, Stur M, Toaff T; Preferential Hyperacuity Perimetry Research Group. Preferential Hyperacuity Perimeter (PreView PHP) for detecting choroidal neovascularization study. *Ophthalmology* 2005;112(10):1758-65.
16. Bedell HE, Tong J, Woo SY, House JR, Nguyen T. Orientation discrimination with macular changes associated with early AMD. *Optom Vis Sci* 2009;86(5):485-91.
17. Thornton J, Edwards R, Mitchell P, Harrison RA, Buchan I, Kelly SP. Smoking and age-related macular degeneration: a review of association. *Eye* 2005;19(9):935-44.
18. Mitchell P, Wang JJ, Smith W, Leeder SR. Smoking and the 5-year incidence of age-related maculopathy: the Blue Mountains Eye Study. *Arch Ophthalmol* 2002;120(10):1357-63.
19. Klein R, Klein BE, Tomany SC, Moss SE. Ten-year incidence of age-related maculopathy and smoking and drinking: the Beaver Dam Eye Study. *Am J Epidemiol* 2002;156(7):589-98.
20. Omenn GS, Goodman GE, Thornquist MD, Balmes J, Cullen MR, Glass A, Keogh JP, Meyskens FL, Valanis B, Williams JH, Barnhart S, Hammar S. Effects of a combination of beta carotene and vitamin A on lung cancer and cardiovascular disease. *N Engl J Med* 1996;334(18):1150-5.
21. AREDS2 Research Group, Chew EY, Clemons T, Sangiovanni JP, Danis R, Domalpally A, McBee W, Sperduto R, Ferris FL. The Age-related eye disease study 2 (AREDSa2): study design and baseline characteristics (AREDS2 report number 1). *Ophthalmology* 2012;119(11):2282-9.
22. The Age-Related Eye Disease Study 2 Research Group. Lutein + zeaxanthin and omega-3 fatty acids for age-related macular degeneration: The Age-Related Eye Disease Study 2 (AREDS2) randomized clinical trial. *JAMA*. 2013 15;309(19):2005-15.
23. Klein BE, Howard KP, Gangnon RE, Dreyer JO, Lee KE, Klein R. Long-term use of aspirin and age-related macular degeneration. *JAMA* 2012;308(23):2469-78.
24. Liew G, Mitchell P, Wong TY, Rochtchina E, Wang JJ. The association of aspirin use with age-related macular degeneration. *JAMA Intern Med* 2013;173(4):258-64.
25. Wang JJ, Klein R, Smith W, Klein BE, Tomany S, Mitchell P. Cataract surgery and the 5-year incidence of late-stage age-related maculopathy: pooled findings from the Beaver Dam and Blue Mountains eye studies. *Ophthalmology*. 2003;110(10):1960-7
26. Cugati S, Mitchell P, Rochtchina E, Tan AG, Smith W, Wang JJ. Cataract surgery and the 10-year incidence of age-related maculopathy: the Blue Mountains Eye Study. *Ophthalmology* 2006;113(11):2020-5.

CE Questions

- Which of the following is **FALSE** regarding the results from the AREDS2 study?
 - Omega 3s were not shown to provide any added benefit to the original AREDS1 formulation
 - Lutein and zeaxanthin can be used instead of beta-carotene in the AREDS1 formulation with added benefit
 - Beta-carotene was not shown to increase the risk of lung cancer in former smokers
 - Lutein and zeaxanthin were not shown to provide any added benefit to the original AREDS1 formulation
- Which of the following components was **NOT** part of the original AREDS1 formula?
 - Beta carotene
 - Lutein
 - Vitamin C
 - Copper
- Which of the following typically show a decrease in auto-fluorescence on FAF?
 - Geographic atrophy
 - Pseudo-drusen
 - RPE dropout
 - All of the above
- The Foresee PHP has been shown to be more beneficial than an Amsler grid in detecting changes in AMD.
 - True
 - False
- Which component of the AREDS1/2 formula is associated with an increased risk of lung cancer in smokers?
 - Vitamin C
 - Vitamin E
 - Beta-Carotene
 - Zinc
- The Physician Quality Reporting System (PQRS) rewards optometrists for participation in 2013.
 - True
 - False
- PQRS measure 140 may include which of the following counseling and education elements?
 - AREDS
 - Patient
 - Caregiver
 - All of the above
- Chronic, long-term aspirin use may be associated with an increased incidence of AMD?
 - True
 - False
- Cataract surgery is associated with an increased incidence of AMD?
 - True
 - False
- Which of the following phenomenon contribute to the poor sensitivity and reliability of the Amsler grid?
 - Pulfrich
 - Perceptual filling
 - Afterimage
 - Anomalous retinal correspondence

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