The junction of structure and function: where glaucoma and age-related macular degeneration meet

J. Gerson, OD; P. Lowe, OD
L. Semes, OD

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Disclosures for Jeffry Gerson, OD

- I have been a consultant to/speaker for or otherwise involved with the following during the last 18 months
  - Allergan, AstaReal, Bausch Health, Essilor, Genentech, Macular Degeneration Association, Luneau, Maculogix, Notal Vision, Optos, Regeneron, VSP, Zeavision
- These affiliations will not influence the content of the this talk and are not meant to influence you.

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Financial Disclosures

Leo Semes, OD, FAAO

- Consultant - Maculogix
- Speaker Bureau, Consultant - Regeneron
- Scientific Advisory Board (Consultant) - EyePromise
- Stock options - EyePromise (< 0.01% ownership)

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Glaucoma

A multi-factorial chronic eye disease

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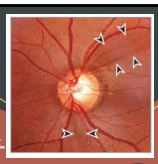
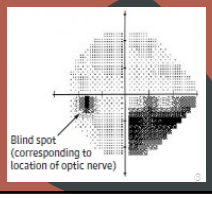
Primary open-angle glaucoma (POAG) definition*

- The open-angle glacuomas are chronic, progressive optic neuropathies that have characteristic pathologic changes of the optic nerve and retinal nerve fiber layer (RNFL) without supervening ocular diseases or congenital anomalies.
- Progressive retinal ganglion-cell death and visual-field depressions are associated with these changes.
- The primary clinically measurable risk factor is elevated intraocular pressure (IOP).





*adapted from AAO PPP

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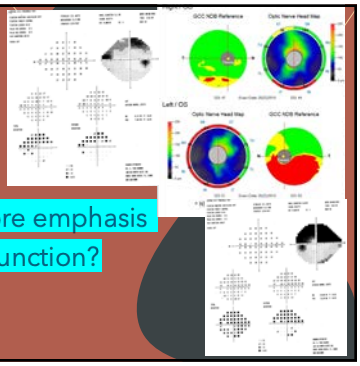
Structure/Function in Glaucoma



Should we place more emphasis on structure or function?

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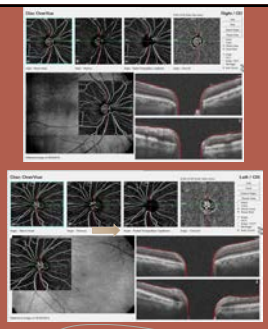
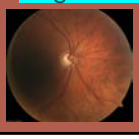
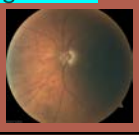
Going forward . . .

What influence will OCT-A have on glaucoma diagnosis/management?







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AMD

Age-related macular degeneration

Also a multi-factorial chronic eye disease

A definition: An eye disease with its onset usually after age 60 that can progressively destroy the macula, the central portion of the retina, impairing central vision.

https://www.medicinenet.com/age-related_macular_degeneration/definition.htm (accessed Novemßber 15, 2021

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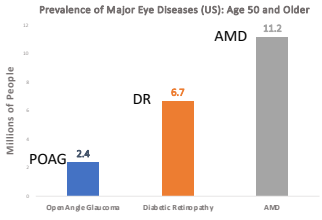
AMD is the Leading Cause of Legal Blindness in the US

Clinical AMD ***is more prevalent*** than glaucoma & diabetic retinopathy combined

(Statistics from the AAOphth)



Sources: https://www.aao.org/newsroom/eye-health-statistics#_edn4; https://www.nei.nih.gov/learn-about-eye-health/resources-for-health-educators/eye-health-data-and-statistics/diabetic-retinopathy-data-and-statistics/diabetic-retinopathy-tables; https://www.nei.nih.gov/learn-about-eye-health/resources-for-health-educators/eye-health-data-and-statistics/glaucoma-data-and-statistics/glaucoma-tables

Accessed October 14, 2021

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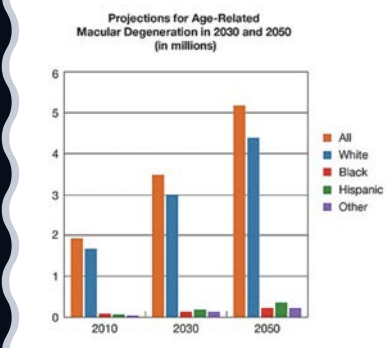
Projections for AMD in 2030 and 2050 (millions)

- https://nei.nih.gov/eyedata/amd
- Accessed October 14, 2021



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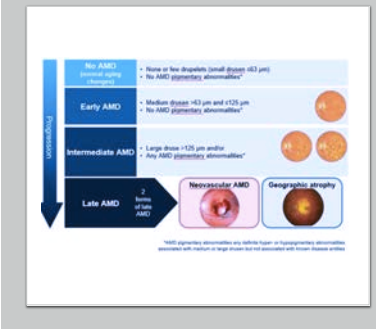
AMD classification from the AREDSs



- Ferris F, et al. Ophthalmology 2013;120:844–851

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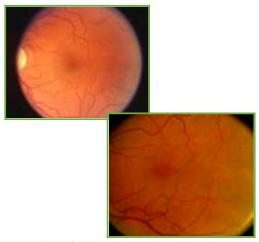
Simplified AREDS Staging (specification)

Category 1
- No or few drusen (<63 microns*), no pigment abnormalities, neither eye Wet
- 0% risk of Wet at 5 yrs

Category 2
- Intermediate drusen (<125 microns*), mild pigment abnormalities, neither eye wet
- <2% risk of Wet at 5 yrs



*Note: Central retinal vein is approximately 125 microns

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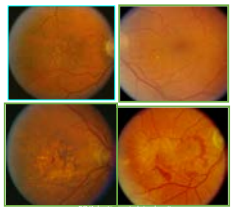
Simplified AREDS Staging (specification)

Note that to be enrolled in AREDS, patients had to have at least moderate AMD and be > 50.

Category 3/Intermediate
- Combo of extensive intermediate or *any* large druse, or GA
- *18% risk of Wet in 5 yrs*

Category 4/Advanced/ High Risk
- One eye with Wet or BCVA worse than 20/32 from Dry



http://www.nei.nih.gov/amd/background.asp

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Trajectory prediction

Ferris F, et al. Ophthalmology 2013;120:844–851.

Validated for 10-year risk:

Liew G, Joachim N, Mitchell P, Burlutsky G, Wang JJ. Validating the AREDS Simplified Severity Scale of Age-Related Macular Degeneration with 5- and 10-Year Incident Data in a Population-Based Sample. Ophthalmology. 2016 Sep;123(9):1874-8.

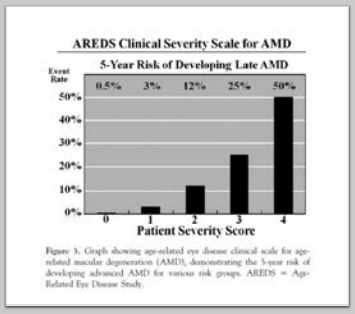

Figure 3. Graph showing age-related eye disease clinical scale for age-related macular degeneration (AMD), demonstrating the 5-year risk of developing advanced AMD for various risk groups. AREDS = Age-Related Eye Disease Study.

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Underdiagnosis of early AMD

RESULTS The sample consisted of 1288 eyes from 644 participants (231 [35.9%] male and 413 [64.1%] female; mean [SD] age, 69.4 [6.1] years; 611 white [94.9%]) seen by 31 primary eye care ophthalmologists or optometrists. A total of 968 eyes (75.2%) had no AMD, in agreement with their medical record. 320 (24.8%) had AMD despite no diagnosis of AMD in the medical record. Among eyes with undiagnosed AMD, 32 (10.0%) had hyperpigmentation, 43 (13.4%) had hypopigmentation, 249 (77.8%) had small drusen, 250 (78.1%) had intermediate drusen, and 96 (30.0%) had large drusen. Undiagnosed AMD was associated with older patient age (odds ratio [OR], 1.06; 95% CI, 1.04-1.09; $P < .001$), male sex (age-adjusted OR, 1.39; 95% CI, 1.02-1.91; $P = .04$), and less than a high school education (age-adjusted OR, 2.40; 95% CI, 1.03-5.62; $P = .04$). Prevalence of undiagnosed AMD was not different for ophthalmologists and optometrists (age adjusted OR, 0.99; 95% CI, 0.71-1.36; $P = .94$).

JAMA Ophthalmology | Original Investigation
Prevalence of Undiagnosed Age-Related Macular Degeneration in Primary Eye Care

Should we rely on stereoscopic observation and CFP or is sophisticated imaging needed?

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M3-global quiz

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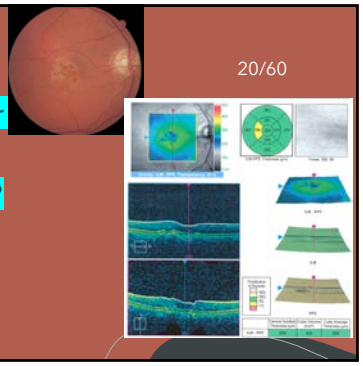
When do you order OCT among patients with AMD?



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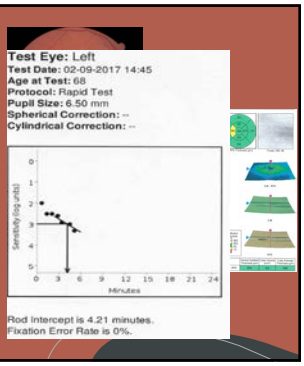
For AMD, do you place more emphasis on functional or structure measurements?

What is the value of dark-adaptation measurement?



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Are macular pigment density measurements valuable?

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Given the multiple burdens of AMD, do you foresee it as an area ripe for screening in non-ophthalmic settings?

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HHS Public Access
Author manuscript
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Combined automated screening for age-related macular degeneration and diabetic retinopathy in primary care settings

Alauddin Bhuiyan[1,2], **Arun Govindaiah**[1], **Sharmina Alauddin**[2], **Oscar Otero-Marquez**[2], **R. Theodore Smith**[2]

[1]Research & Development Department, iHealthScreen Inc., Richmond Hill, USA

[2]Department of Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, USA

Abstract

Background: Age-related macular degeneration (AMD) and diabetic retinopathy (DR) are among the leading causes of blindness in the United States and other developed countries. Early detection is the key to prevention and effective treatment. We have built an artificial intelligence-based screening system which utilizes a cloud-based platform for combined large scale screening through primary care settings for early diagnosis of these diseases.

For AMD

Sensitivity: 86.6%
Specificity: 92.1%
Accuracy: 90.7%
kappa score: 0.76

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EARLY DIAGNOSIS – SO WHAT?

Preventive care & careful monitoring & are the keys to vision preservation

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Aren't the anti-VEGF agents the saving grace for nAMD?

Visual Acuity Outcomes and Anti–Vascular Endothelial Growth Factor Therapy Intensity in Neovascular Age-Related Macular Degeneration Patients

A Real-World Analysis of 49 485 Eyes

Conclusions: Real-world nAMD patients receive fewer anti-VEGF injections and experience worse visual outcomes compared with patients receiving fixed, frequent therapy in randomized controlled trials. Mean change in VA correlates with treatment intensity at 1 year, but with ceiling effects related to treatment intensity and baseline VA. Older patients and those with poor baseline VA may be particularly prone to undertreatment. *Ophthalmology Retina 2020;4:19-30* © *2019 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

Mmmmm. No. But that was 2020.

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Published March 21, 2021

Intravitreal Aflibercept Injection vs Sham as Prophylaxis Against Conversion to Exudative Age-Related Macular Degeneration in High-risk Eyes
A Randomized Clinical Trial

Do the anti-VEGF agents protect against nAMD?

CONCLUSIONS AND RELEVANCE In this evaluation of quarterly anti-VEGF exposure as prophylaxis to reduce conversion of eyes with high-risk dry AMD to eAMD, the rates of conversion were not lower in the IAI group compared with the sham treatment group at month 24. Understanding the mechanism of conversion to eAMD and therapies that could prevent this event remains an important unmet need.

Well, no.

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Bottom line: 4/5 of eyes experienced reactivation

Five-Year Reactivation After Ranibizumab or Aflibercept Treatment for Neovascular Age-Related Macular Degeneration and Polypoidal Choroidal Vasculopathy

November 11, 2021

Abstract

Purpose: To evaluate 5-year reactivation after ranibizumab or aflibercept treatment for neovascular age-related macular degeneration (AMD) and polypoidal choroidal vasculopathy (PCV).
Methods: This retrospective study included 192 patients (192 eyes) who had been diagnosed with neovascular AMD or PCV and treated with ranibizumab or aflibercept. The incidence and timing of lesion reactivation during the 5-year follow-up period were evaluated, and the factors associated with reactivation were also investigated.
Results: During the follow-up period, lesion reactivation was noted in 156 patients (81.3%) at a mean of 9.5 ± 10.5 months after the third antivascular endothelial growth factor injection. The incidence of reactivation was 59.9% during the first 12 months, 33.7% during ≥12 and <24 months, 11.8% during >24 and ≤36 months, 15.5% during >36 and ≤48 months, and 5.3% during >48 and ≤60 months. There was a significant difference in the incidence among the 5 periods ($P < 0.001$). The proportion of PCV was significantly higher in patients experiencing reactivation (51.9%) than in those who did not (30.6%) ($P = 0.021$).
Conclusions: During the 5-year follow-up, lesion reactivation was noted in approximately four-fifths of the patients. The incidence of lesion reactivation was highest during the first 12 months and decreased thereafter. The incidence was higher in patients with PCV than in those with neovascular AMD, especially after 12 months.

- Kim JH, Kim JW, Kim CG. Five-Year Reactivation After Ranibizumab or Aflibercept Treatment for Neovascular Age-Related Macular Degeneration and Polypoidal Choroidal Vasculopathy. J Ocul Pharmacol Ther. 2021 Nov;37(9):525-533. doi: 10.1089/jop.2021.0051. Epub 2021 Sep 14.

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Some Practical dry AMD management recommendations

Once detected, early interventions can slow disease progression

Five proven approaches to modifiable risk factors (preventive care)

Smoking Cessation | Diet & Exercise | Nutritional Supplementation | Systemic Disease Management | Retinal Light Protection

Leading optometrists agree: Practical treatments should be used for **ALL STAGES OF AMD** to slow progression and improve outcomes.

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How do you view Amsler grid for self-monitoring in patients with AMD?

20/60

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AMERICAN ACADEMY OF OPHTHALMOLOGY

Ophthalmology Science 2021;1:100034

Prospective, Longitudinal Pilot Study

Careful monitoring

Daily Self-Imaging with Patient-Operated Home OCT in Neovascular Age-Related Macular Degeneration

Tiarnan D.L. Keenan, BM BCh, PhD,[1] Michaella Goldstein, MD,[2,3] Dafna Goldenberg, MD,[2,3,4] Eliah Zur, MD,[2,3] Shlomi Shulman, MD,[4] Anat Loewenstein, MD[2,3]

Results (n = 211/240 scans; good adherence/4 pts., 1 mo.)

- Notal OCT analyzer (NOA) vs. human graders (retina specialists) : Fluid presence 94.7% agreement.
- "Daily self-imaging with automated OCT analysis permitted detailed characterization of the dynamics of fluid exudation and revealed wide variation among eyes."

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Thank you

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