AMD: Chartering a Better Patient Experience

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Disclosure

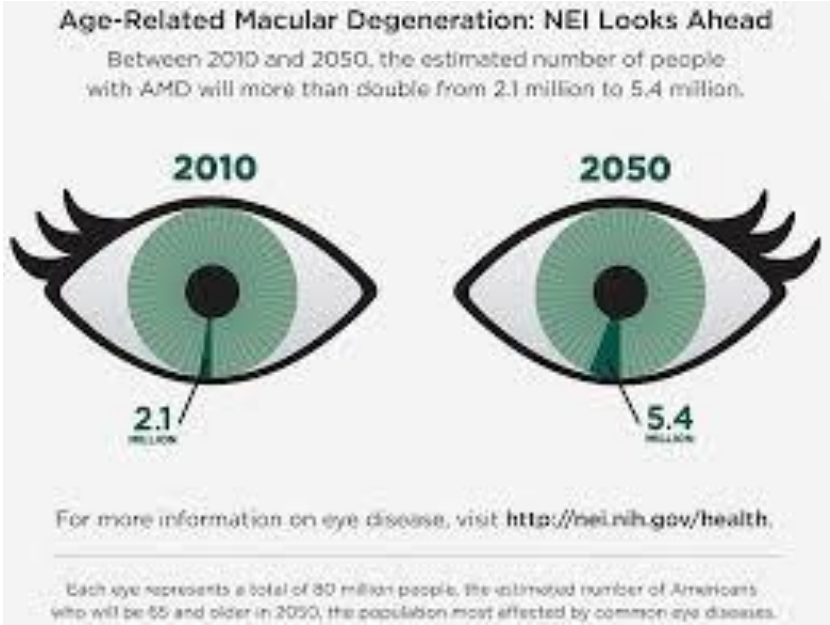
- I have been on advisory boards/a consultant to/received honoraria from/ or been on speakers bureau list of the following:
  - Allergan, Apellis, Astellis, Bausch & Lomb, Essilor, LKC, Luneau Technology, MDA, Notal Vision, Regeneron, Viatris, VSP, ZeaVision

All relevant relationships have been mitigated

"Try this—I just bought a hundred shares."

Conclusion/Take Away

- Prevention and early detection are key to ultimate patient success
  - That's what we do
- Treatment of advanced AMD is not good in the long term
  - We refer for this…



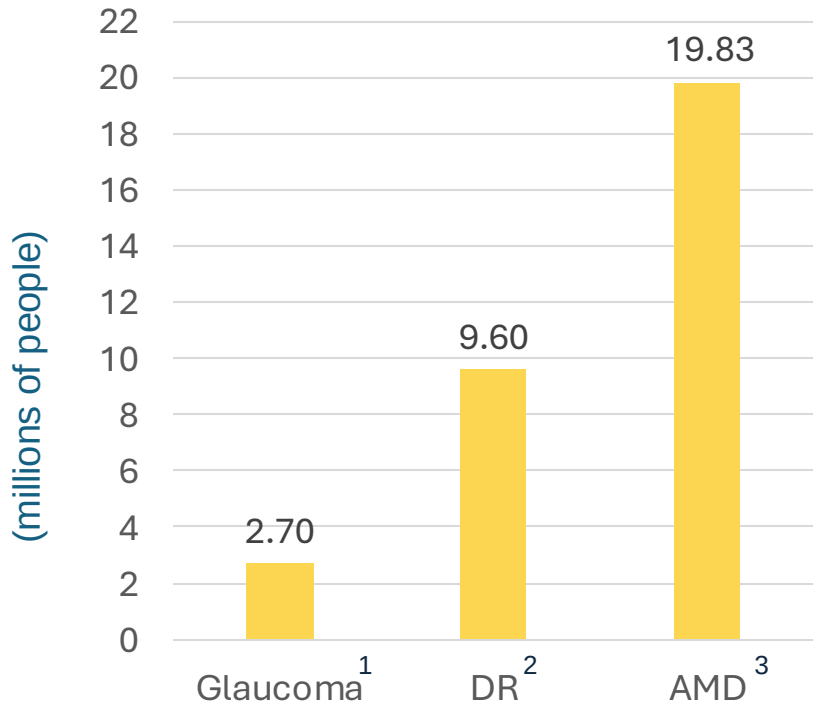
Another important conclusion

- Future Direction: There will be more AMD, less MD's and we will NEED to be more proactive an involved
- We need to be comfortable spending time discussing AMD with our patients
  - More education equals more proactive equals better outcomes
  - We may need to listen some also
    - Take clues to help guide

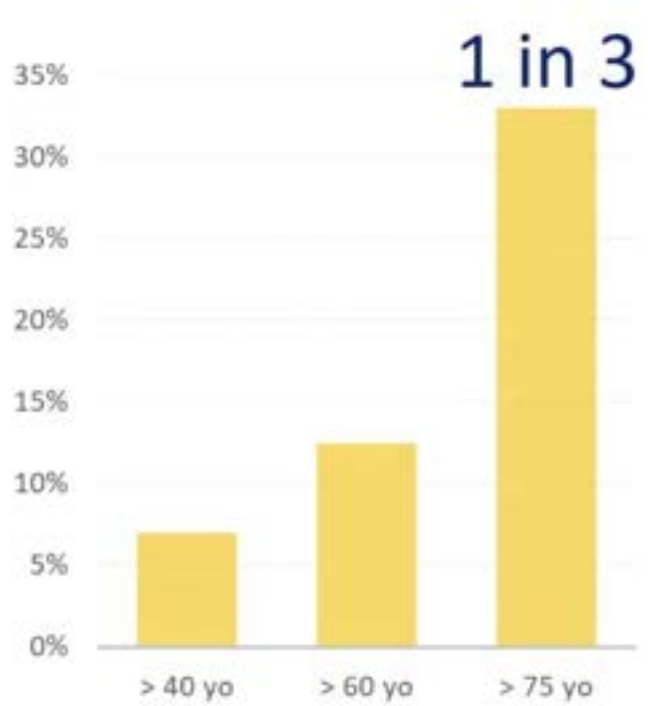
Simply put, why do we need to discuss AMD?

Focusing on age-related macular degeneration (AMD)

Prevalence of Major Eye Diseases in U.S.[1-3]



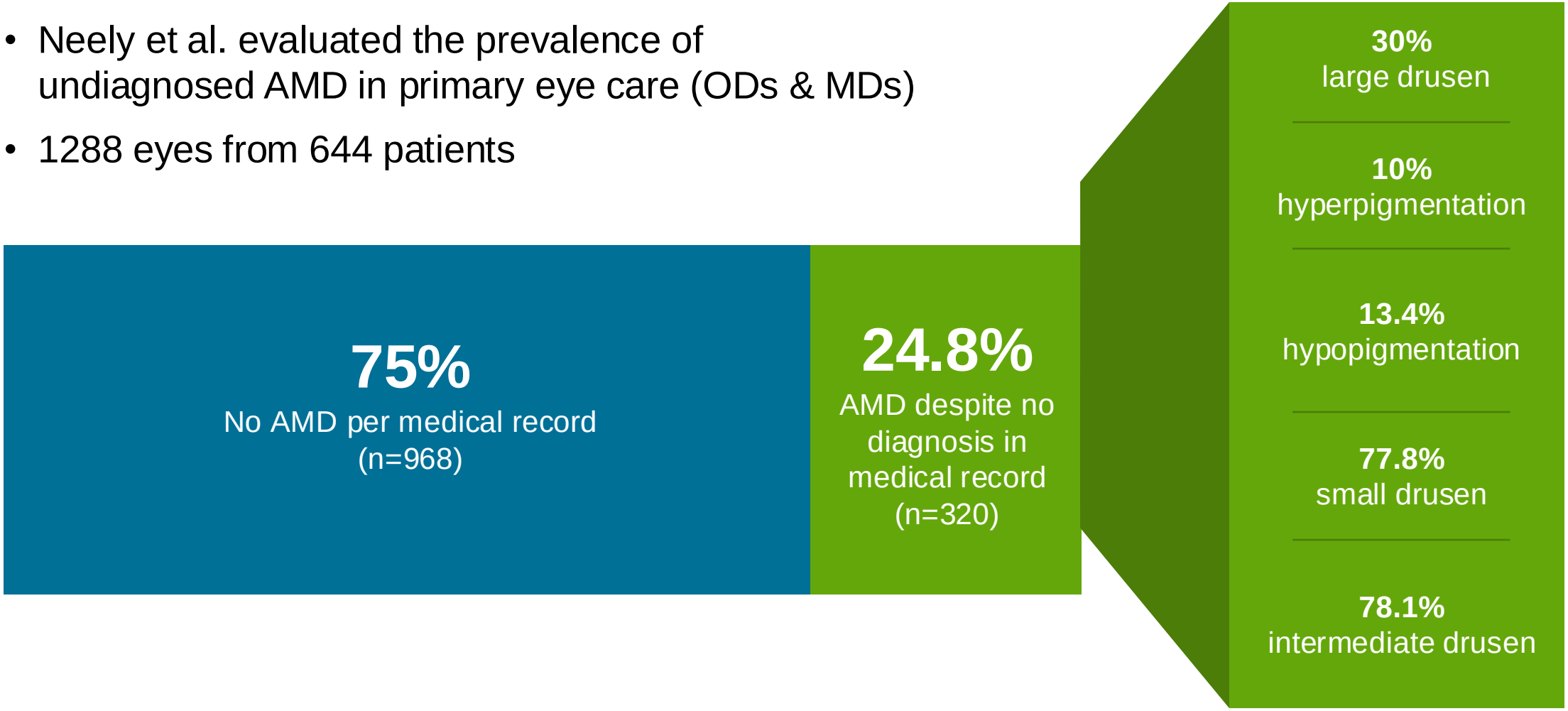
AMD Prevalence by Age in U.S. [4]



1. US Preventive Services Task Force. *JAMA.* 2022;327(20):1992–1997.
2. Lundeen EA, et al. *JAMA Ophthalmol.* 2023;141(8):747–754.
3. Rein DB, et al. *JAMA Ophthalmol.* 2022;140(12):1202–1208.
4. Gupta, et al. *Invest Ophthalmol Vis Sci.* 2016 May; 57(6): 2577-2585.

Intermediate AMD may often go undiagnosed

- Neely et al. evaluated the prevalence of undiagnosed AMD in primary eye care (ODs & MDs)
- 1288 eyes from 644 patients



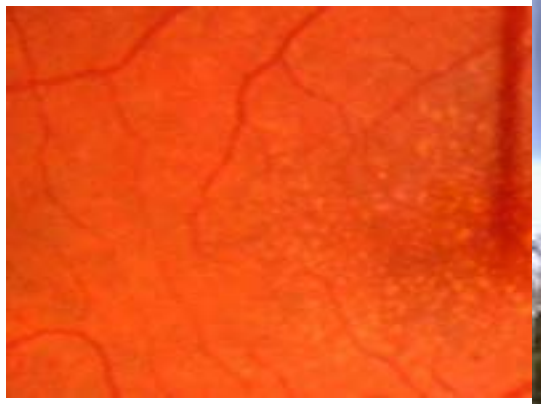
Reference: Neely DC, et al. *JAMA Ophthalmol.* 2017;135(6):570-575.

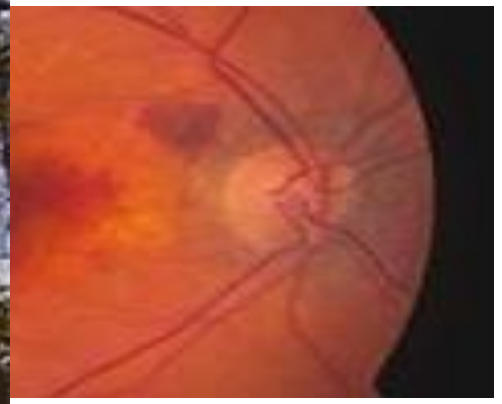
Lets start with a question

- When I say “AMD”, what is the first thing you think of?

- Is it wet vs dry?
- Is it intravitreal injection?
- Is it “Do I need to refer?”

What about this…





- Threat to visio
- Change in outl
- What does it re

Have I changed your outlook?

Impact of AMD on Quality of Life

	Quality of Life Decrement	Comparison
MILD AMD	**17%**	symptomatic HIV moderate cardiac angina
MODERATE AMD	**40%**	permanent renal dialysis severe cardiac angina
SEVERE AMD	**63%**	advanced prostate cancer severe stroke requiring constant nursing care

Note: patients have a perceived impairment that is 96% to 750% greater than the impairment estimated by treating physicians

Brown, Brown, Sharma; Age-related macular degeneration: economic burden and value-based medicine analysis. CJO vlume 40, No.3 / June 2005

What should our first thought really be?

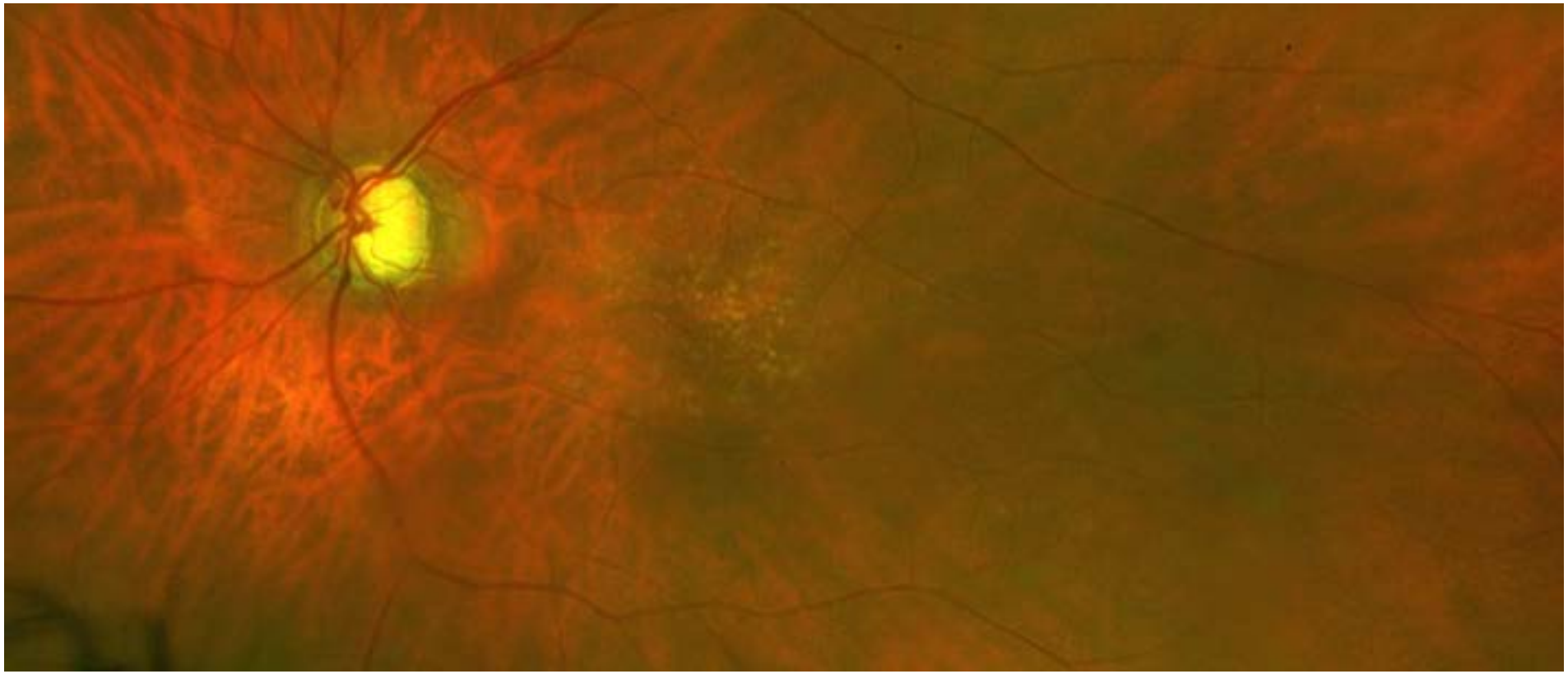
- Our first thoughts should be directed toward the patient
  - The patient experience

Before you get too worried

- Of course I will discuss AMD from the doctors perspective
- What we need to know
- What our patients already or need to know
- What are the steps along the experience/journey
- How we can discuss AMD
  - Treatment options
  - Nutritional options including supplementation

  - NOTE: I COULD TALK ABOUT EACH OF THESE FOR AN HOUR, SO ALTHOUGH NOT RAPID FIRE, THIS WILL BE A “SURVEY” OF THESE TOPICS

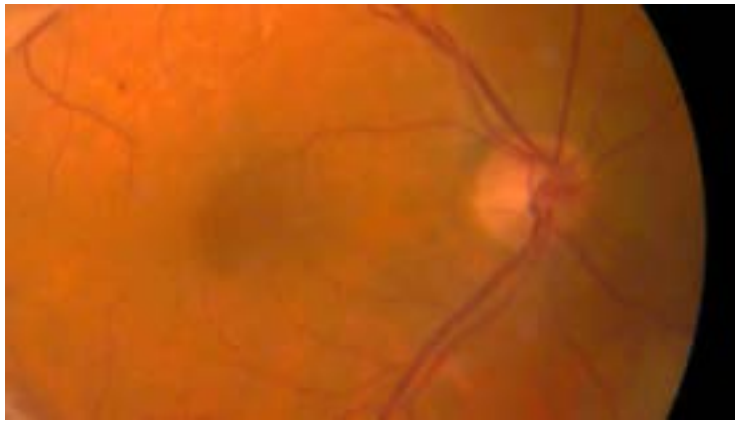
Start with a case…..



- 80 yo (stubborn) male
- Same appearance OU
- 20/25- OU
- What do you want to know?

One more case

- 68yo w T2DM

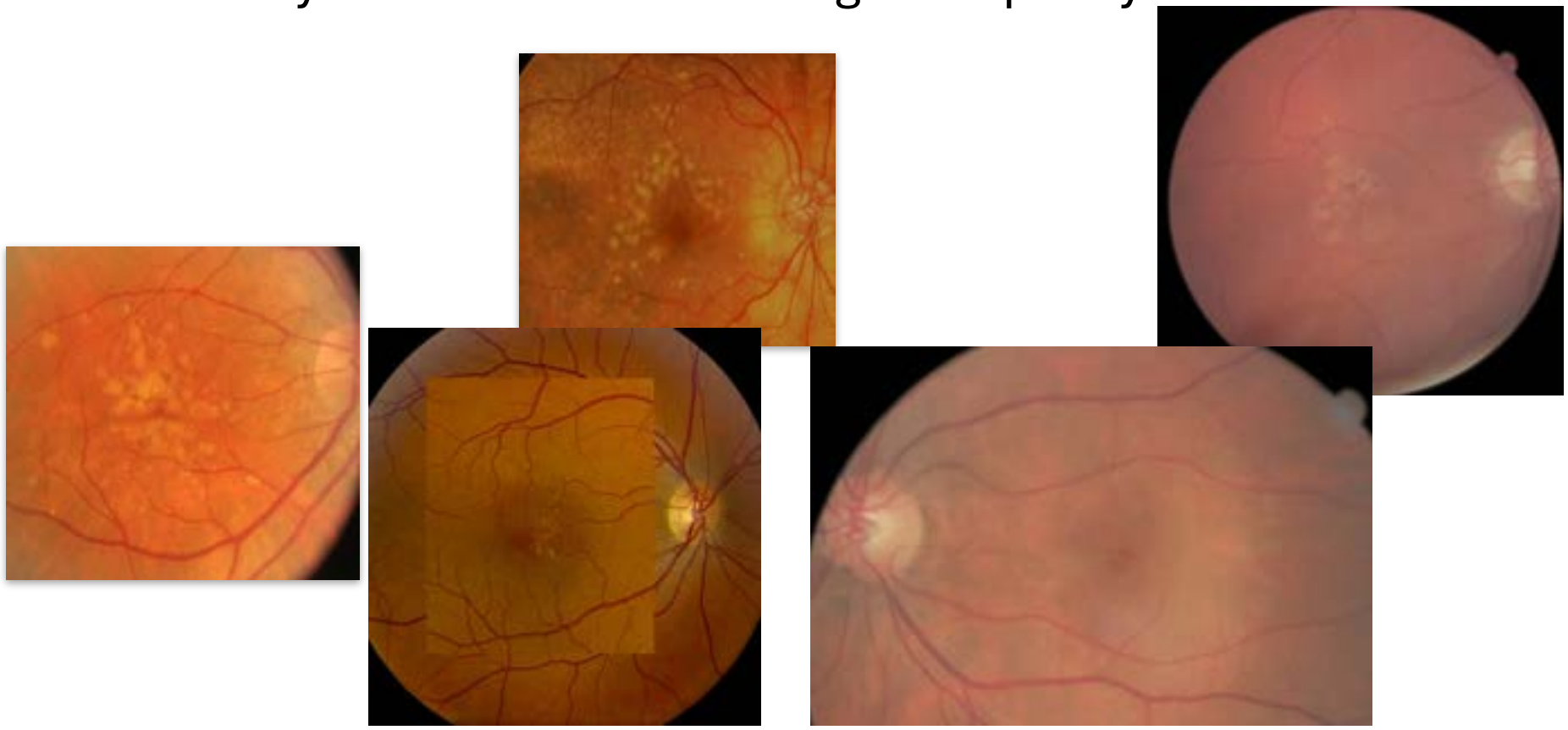


- No real complaints, but ”I don’t like driving at night”
- 20/20, no family history
- What if I told you that they failed their DA screening?

Presenting for routine exam

How do we find AMD?

- Must start with clinical exam
  - What exactly is the minimum findings to “qualify” for AMD?

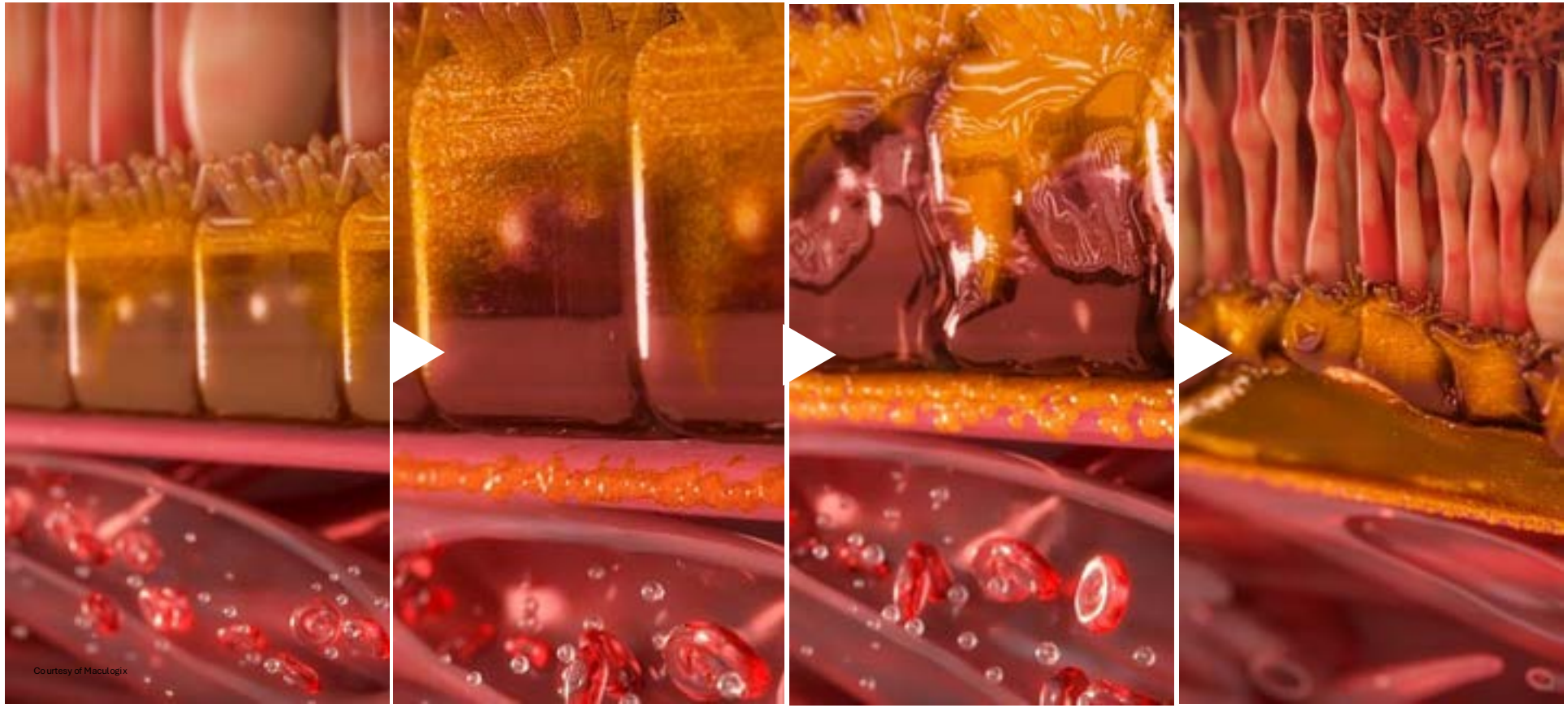


What is “pre-AMD”

- Well defined “pre diabetes” that triggers interventions
- Do we have such a thing with AMD?
  - Should we?
  - Could we?
  - Why would we?

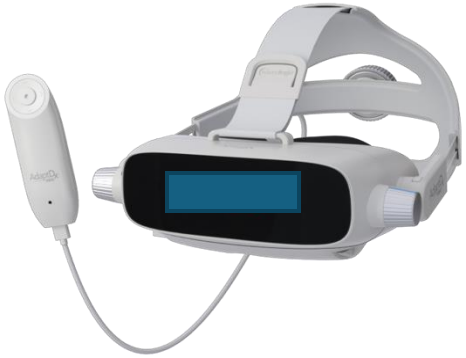
How/where does AMD start

Disease Process of AMD Starts Below the Surface



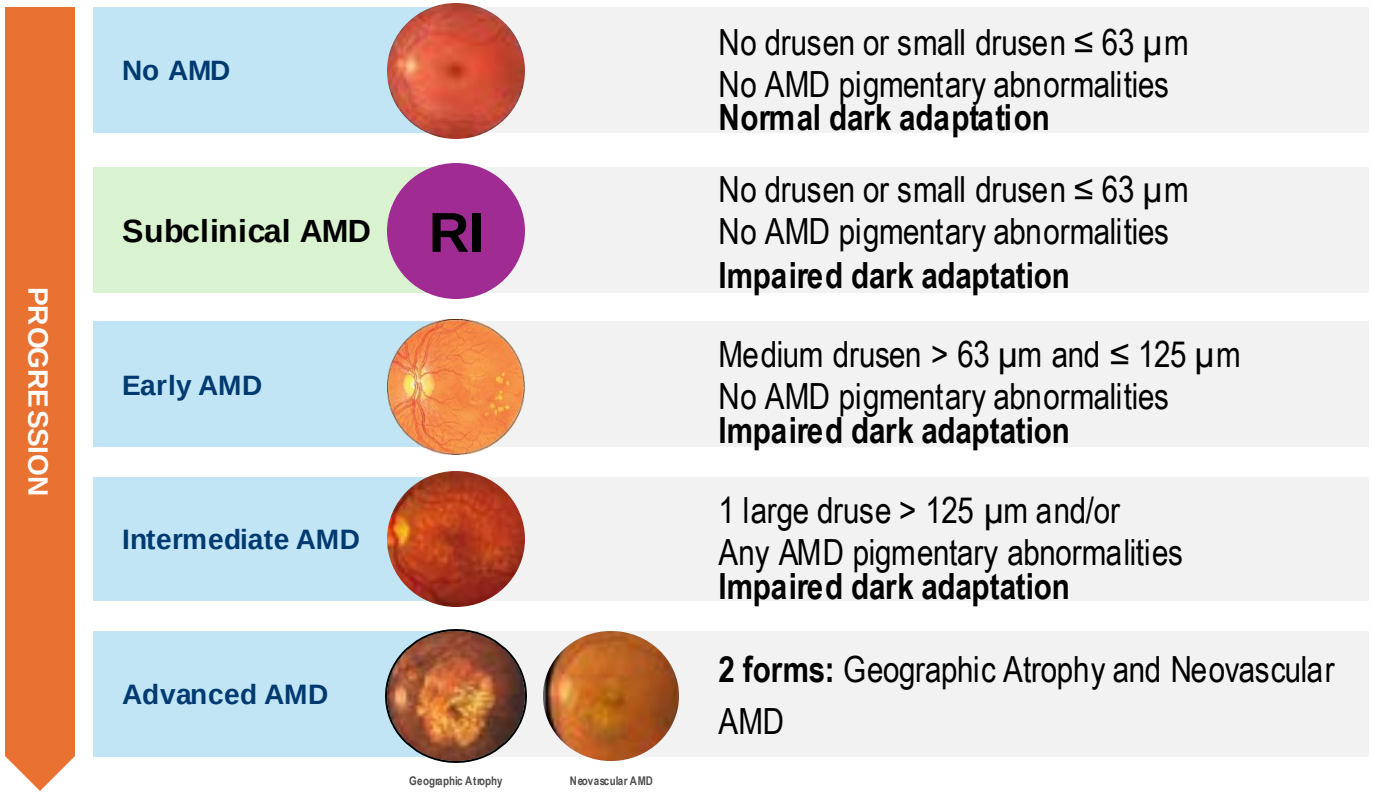
A comparison to visual fields

- In glaucoma, we talk about pre-perimetric glaucoma
  - A recent paper reported on benefits to treating this….
- Is there such thing in AMD?
  - Pre-OCT or Pre-fundus or Pre-FAF AMD
- If there is, what does that mean?
- How do we act?



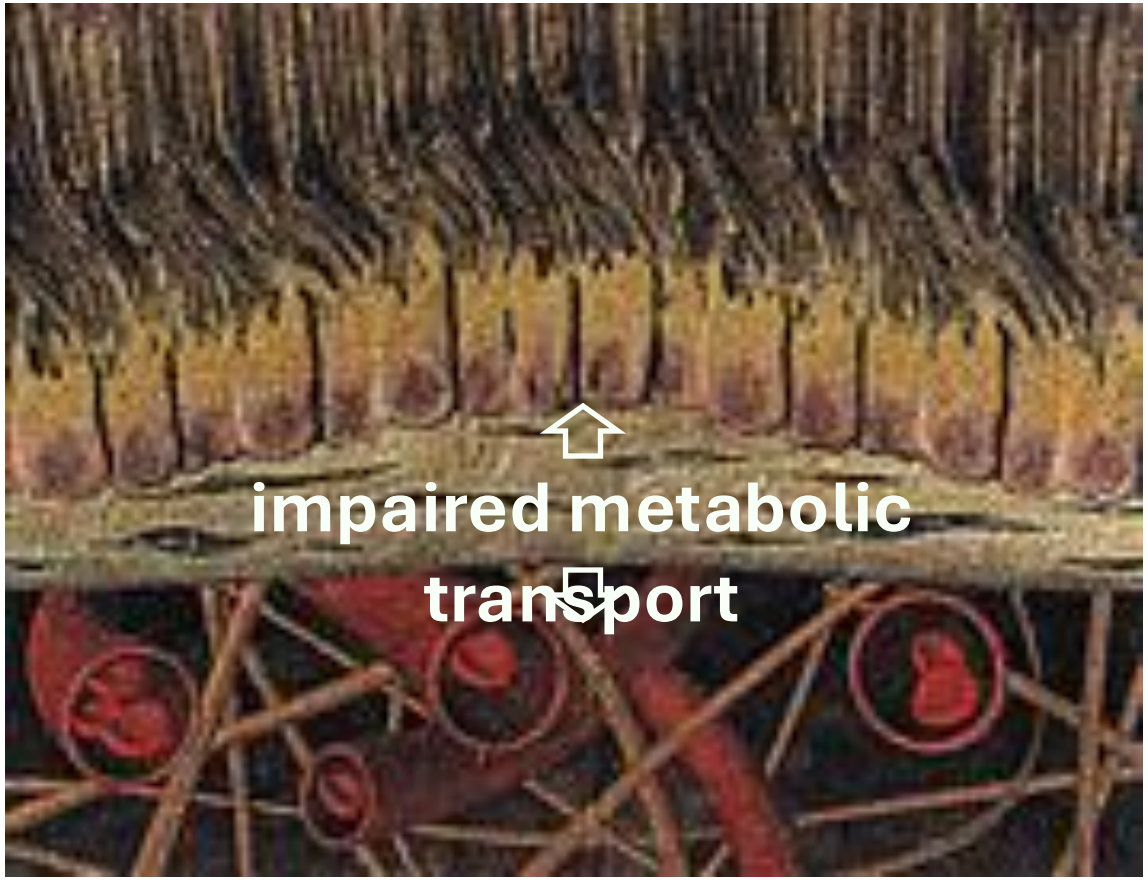
- Not just pre-AMD, but what about…
- SUBCLINICAL AMD

This Leads to a More Comprehensive AMD Classification System: Structure + Function



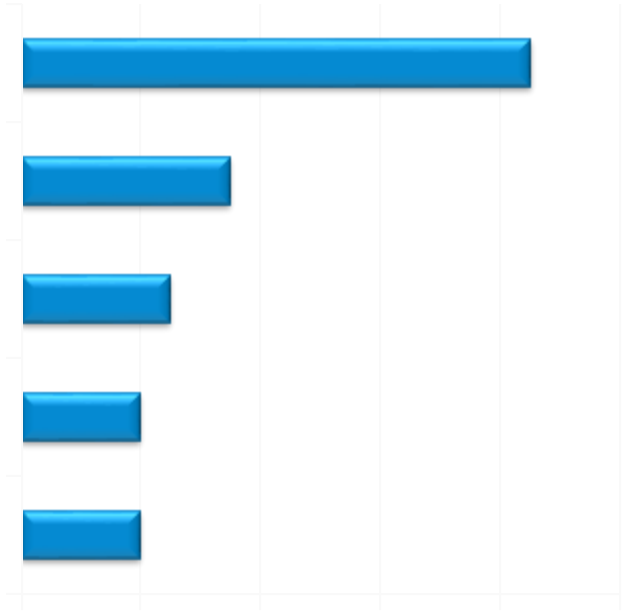
AMD Pathogenesis

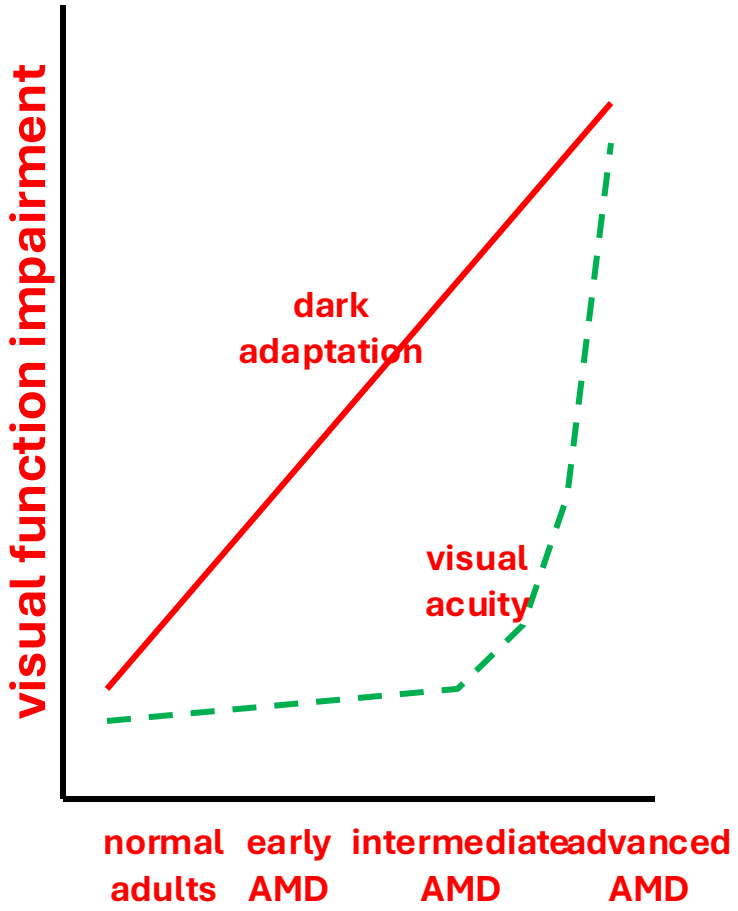
thickened Bruch's membrane & drusen →



Curcio et al. (2000) Investigative Ophthalmology & Visual Science 41:2015

Diagnostic Sensitivity





Akin to stress test in cardiology…rest and then try to perform..

Owsley et al. (2001) Ophthalmology 108:1196

My experience with dark adaptation

- IRB approved, publication pending
- 39/100 “normal” macula patients over age of 60 with impaired dark adaptation.

- The big question with that:
  SO NOW WHAT…..

Dark adaptation has changed how I practice

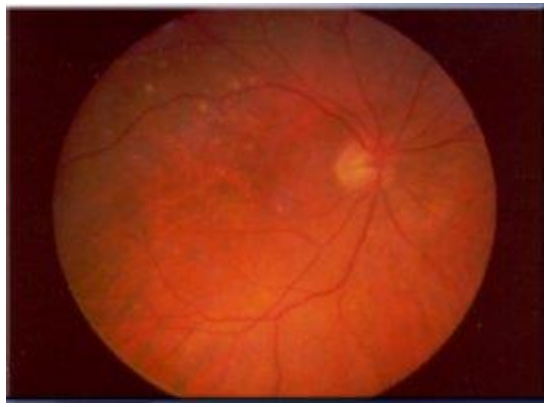
- Likely the first (unrealized) symptom of AMD
  - “I don’t like to drive at night anymore”
- I do it on all patient over age 60
- If fail screening, return for extended testing
- Discussion of pre-emptive measures to take and back to taking care of self…..

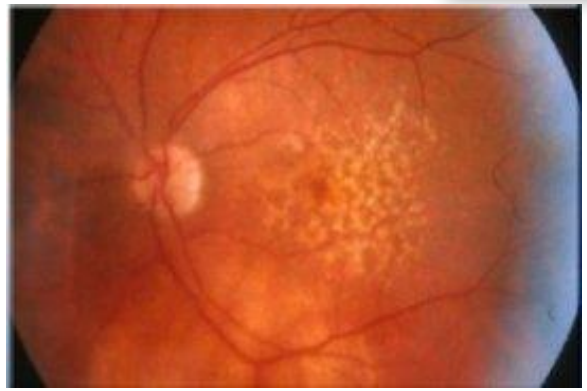
Continuum of AMD similar to Glaucoma

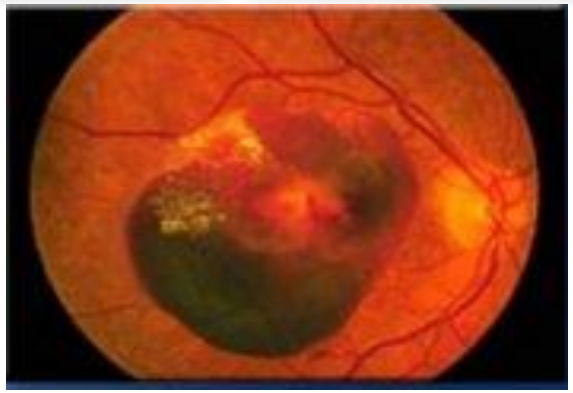
- Never too early to start to “prevent”
- First you must identify the disease with structure and function
- Then you MONITOR the disease with structure and function
- Then you decide when to potentially refer based on structure and function

There Are Three Stages of AMD

- Early AMD
- Intermediate AMD
- Advanced AMD
  - Choroidal Neovascularization (CNV) – 80%
  - Geographic Atrophy (GA) – 20%



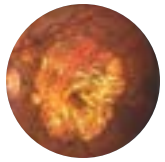




A More Comprehensive Disease Classification System
Structure + Function

PROGRESSION

No AMD	• No drusen • No AMD pigmentary abnormalities • **Normal dark adaptation**
Subclinical AMD	• No drusen or small drusen • No AMD pigmentary abnormalities • **Impaired dark adaptation**
Early AMD	• +/- Small or medium drusen • +/- AMD pigmentary abnormalities • **Impaired dark adaptation**
Intermediate AMD	• 1 large druse > 125 µm • Any AMD pigmentary abnormalities
Advanced AMD	2 forms

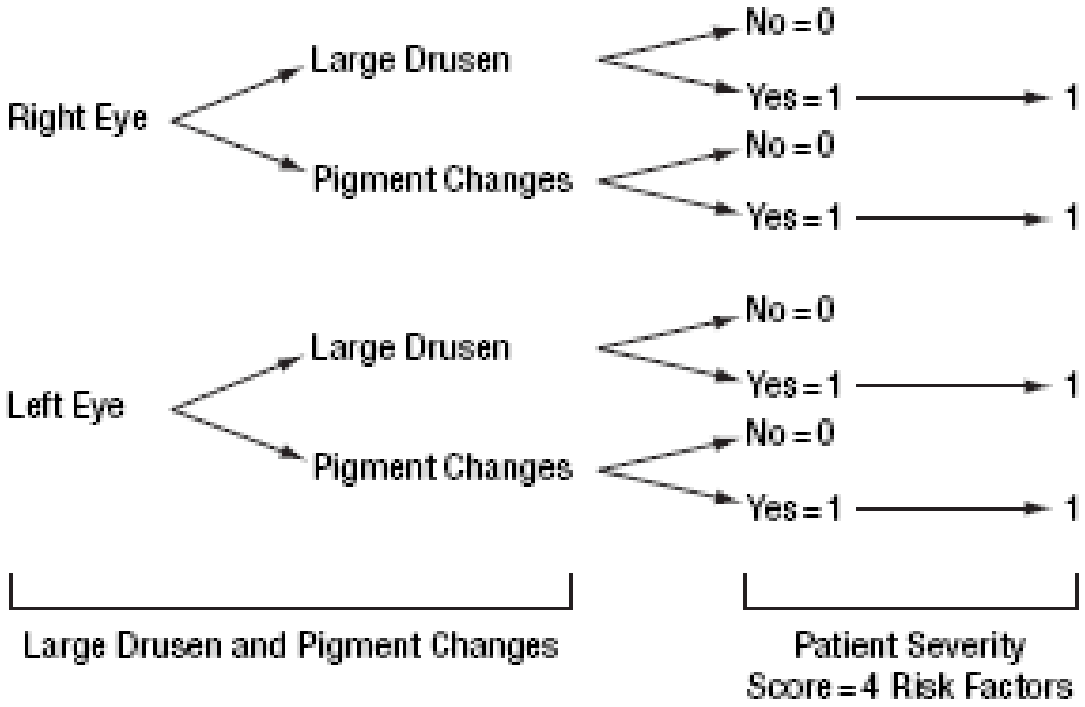


Geographic atrophy

Choroidal Neovascularization

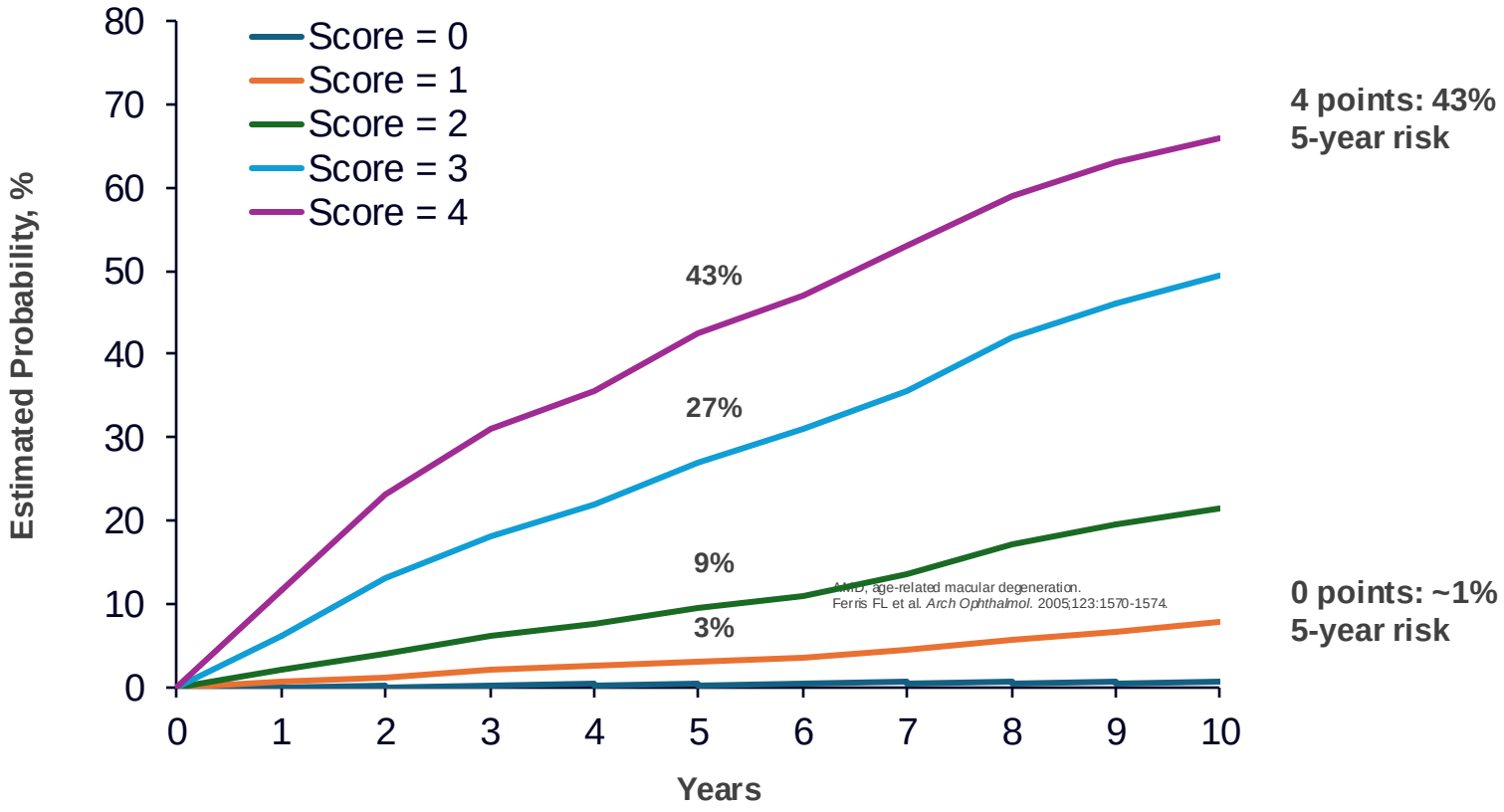
AREDS Simple System 0 to 4 Points

- Treating AMD is important because patients tend to progress with time
- The AREDS study implemented a helpful patient severity scale



NIH Public Access from *Arch Ophthalm*AMD, age-related macular degeneration; AREDS, Age-related Eye Disease Study.
ol. 2005;123:1570–1574.

Risk of Progression to Advanced AMD



AMD, age-related macular degeneration.
Ferris FL et al. *Arch Ophthalmol.* 2005;123:1570-1574.

Updated AREDS Simple scale

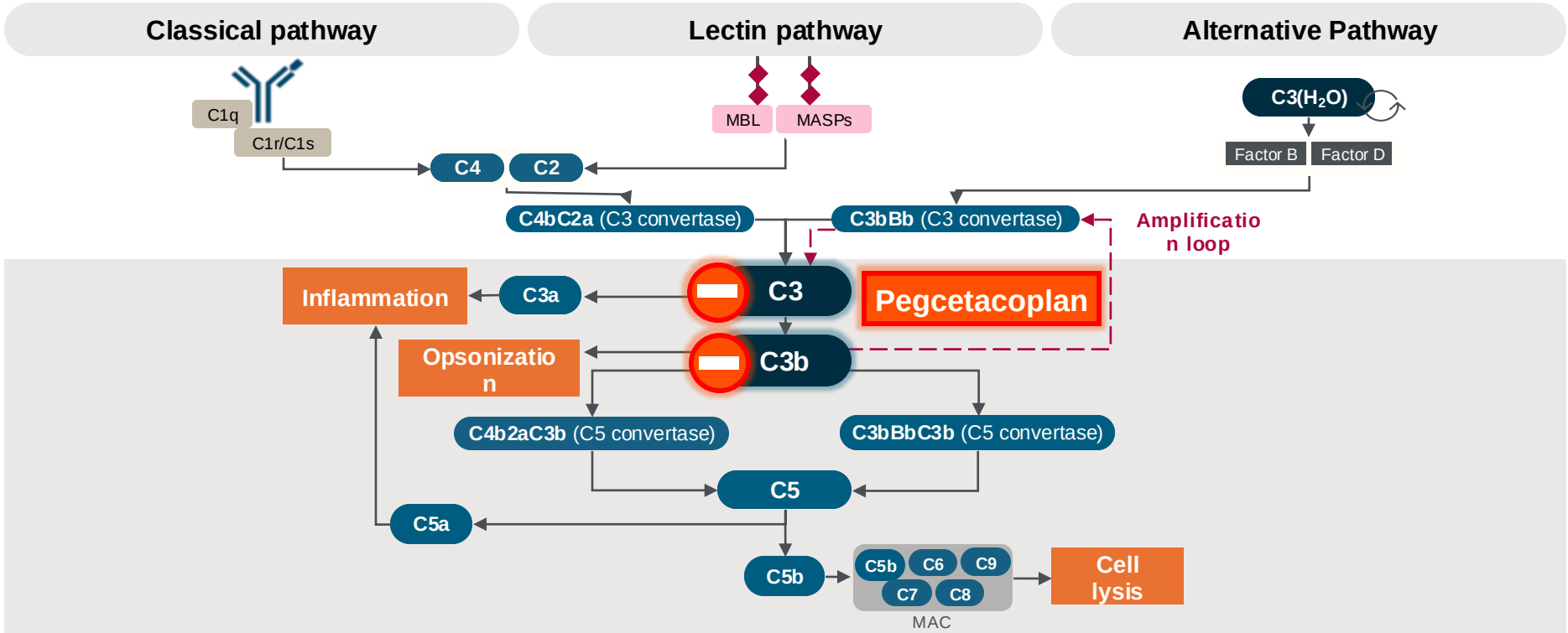
Rate of Progression to Late AMD at Five Years

# of Risk Factors	RPD Absent	RPD Present
0	0.3%	2.8%
1	4.3%	8.0%
2	11.6%	29.0%
3	26.7%	58.7%
4	50.0%	72.2%

Agrón E, Domalpally A, Chen Q, et al. An updated simplified severity scale for age-related macular degeneration, incorporating reticular pseudodrusen: Age-Related Eye Disease Study Report No. 42. Ophthalmology 2024. [Epub ahead of print].

What’s new in AMD

Pegcetacoplan binds to C3 and C3b, inhibiting the downstream effects of the complement pathway and avacincaptad pegol at C5[1–6],



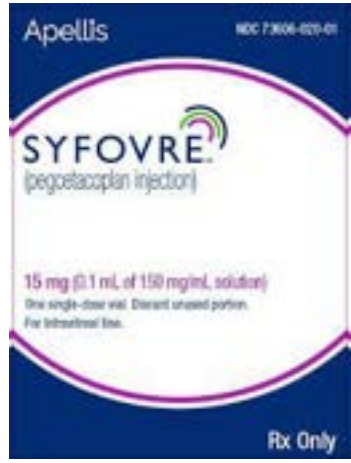
What does all this really mean????

MAC=membrane attack complex; MBL=mannose-binding lectin; MASP=MBL-associated serine protease.

1. Kolev M et al. *Nat Rev Immunol* 2014;14:811–20; 2. Holers VM. *Annu Rev Immunol* 2014;32:433–59; 3. Dunkelberger JR, Song WC. *Cell Res* 2010;20:34–50; 4. Strunz T et al. *Sci Rep* 2020;10:1584; 5. Anderson DH et al. *Am J Ophthalmol* 2002;134:411–31; 6. Boyer DS et al. *Retina* 2017;37:819–35.

There are now 2 approved treatments for GA

- Syfovre (Pegcetacoplan by Apellis Pharmaceuticals)
- Izervay (Avacincaptad pegol by Astellis)
- This has created a whole new conversation and paradigm shift
  - Patients know about this and are asking!
- These do NOT stop progression of GA, but can slow it down
  - Efficacy seems to increase over time



The “Fonz” is helping to create awareness, and so are seniors painting on their faces!

Treatment of Wet AMD

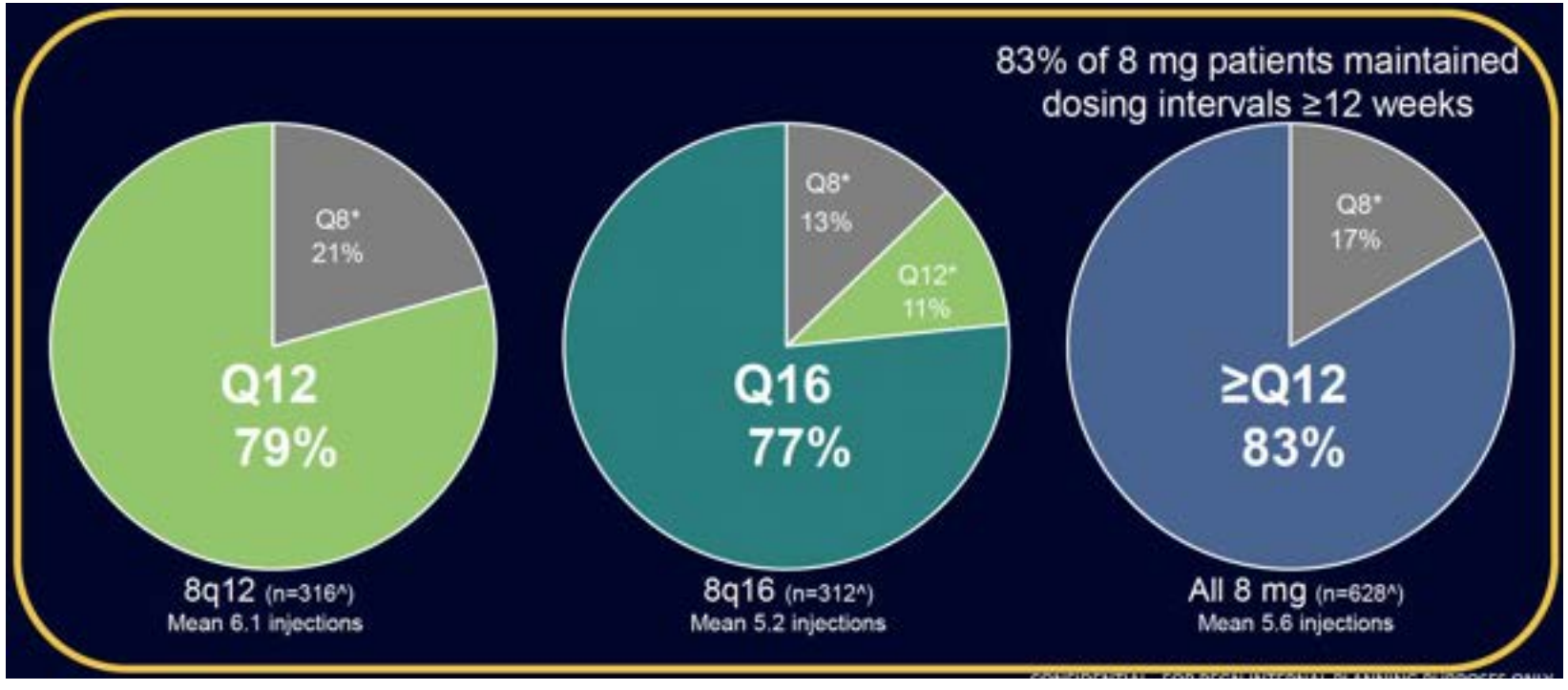
- We all know about the medications for Wet AMD and that they are intravitreal injections
- Differences today from 10 years ago aren’t in efficacy, but in efficiency/patient burden
  - Time between injections much improved vs historic regimens

“New” approval (for wet AMD)

- Vabysmo by Genentech
  - Anti-VEGF and Anti-Ang-2 bi-specific molecule
  - 50% of study participants went 16 weeks between injections
  - Vision and thickness equivalent to monthly injections

Another new “approval”

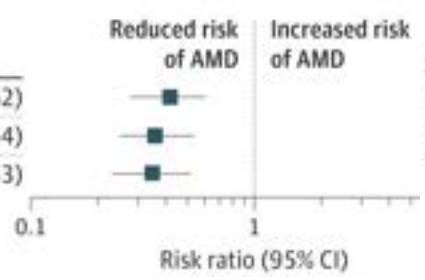
- Aflibercept 8mg
- Pulsar study compared 8mg q12 vs q16 vs 2mg



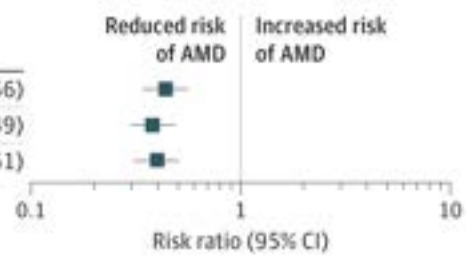
Always new data…

- Melatonin supplementation and AMD
- Melatonin use was associated with a decreased risk of development and progression of AMD.
- Corroborated by a study from China where AMD patients took 3mg and decreased conversion to wet[2]

Age, y	Melatonin Total, No.	Melatonin Events, No. (%)	Control Total, No.	Control Events, No. (%)	Risk ratio (95% CI)
≥50	4150	35 (0.84)	4112	83 (2.02)	0.42 (0.28-0.62)
≥60	3410	33 (0.97)	3349	89 (2.66)	0.36 (0.25-0.54)
≥70	2195	31 (1.41)	2131	86 (4.04)	0.35 (0.23-0.53)



Age, y	Melatonin Total, No.	Melatonin Events, No. (%)	Control Total, No.	Control Events, No. (%)	Risk ratio (95% CI)
≥50	3140	88 (2.80)	3273	211 (6.45)	0.44 (0.34-0.56)
≥60	3094	87 (2.81)	3219	237 (7.36)	0.38 (0.30-0.49)
≥70	2885	86 (2.98)	2979	224 (7.52)	0.40 (0.31-0.51)



1. Jeong et al. Melatonin and Risk of Age-Related Macular Degeneration. *JAMA Ophthalmol.* Published online June 6, 2024. 2. Yi et al. Effects of melatonin in age-related macular degeneration. *Ann N Y Acad Sci*. 2005;1057:384-392.

Lets talk lifestyle...

“Let Thy Food Be Thy Medicine” Hippocrates

A quick tribute to Stuart Richer

- Is this really all that you need?

And to Larry Alexander:
An egg a day keeps Anti-VEGF away

- Increasing diet to 1 egg/d in older adults can increase serum L & Z without affect on serum total cholesterol, HDL, LDL or triglycerides
  - Egg a day and L, Z and HDL/LDL and Cholest. J Nutr. 2006 Oct;136(10):2519-24.
- Increased MPOD w egg consumption: 31% increase w 2 yolks/d. Serum L and Z increased 16% and 36% at 5wks
  - Serum HDL increased 5% and no change in LDL
    - NOTE: These were elderly pts on lipid lowering meds
    - Egg yolks and MPOD. Am J Clin Nutr. 2009 Nov;90(5):1272-9.

Why do we need to discuss?

- What is the leading source of Antioxidants in the average American's diet?[1]
  - Coffee (2nd and 3rd are black tea and bananas)
- What percentage of Americans follow the 4 healthy lifestyle habits?
  - 3%
- What percentage of vege intake in the US is potato + ketchup
  - >50%
    - 2010-2015 F/V consumption down 7% compared to prior period measured
    - Leading "fruit" is OJ and leading "vege" is potato
    - 15% of tomato consumption is ketchup

Vinson et al. Polyphenols and US consumption. American Chem. Society 8/2005.

When does nutrition become important?

- Should everybody pay attention to it?
- Is nutrition preventative or should discussion be reserved for “active” disease?
- At what point in AMD do you start to discuss nutrition?
  - Subclinical disease?
- At what point in DM does nutrition become important?
- When do you discuss nutrition in OSD?

Where is the best place to find nutrition?

- But what's the reality?
- What foods are good for Xanthophyll?
  - Kale (40mg/serving), Spinach (12mg), Romaine lettuce (2.3mg), Broccoli (1.7mg)
- Do you ever ask your patients about f/v consumption?
- What about Mediterranean diet?
  - Approx 47% less Adv AMD
    - More L/Z the better! Hogg. Ophthalmology 11/16.
- An apple a day keeps AMD away!
  - 15% decrease Ophthalmologica 2015: Coimbra Eye Study

But….

- 2022 NHANES analysis shows daily consumption of 100% fruit juice was associated with **a 21-fold** increased risk of advanced AMD after most adjustments!!

- No adjustment for genetics

Front. Nutr., 21 April 2022

Is there a best diet?

The LXXVI Edward Jackson Memorial Lecture 2020 by Dr. Emily Chew

- Re-iterated results of AREDS1 and AREDS2
- Regarding Mediterranean diet: benefits in incident AMD and to late AMD (especially high fish consumption in AREDS 1&2)
- “This would suggest that it is never too early or too late to adopt a healthy diet, such as the Mediterranean diet.”
- Genetics seems to affect efficacy of Med diet to late AMD

AJO 9/2020

Wine consumption

- People in the Mediterranean drink alcohol moderately and regularly. In fact, moderate drinkers outlive nondrinkers!
- 1 to 2 glasses per day with friends and/or with food.
- And no, you cannot save up all week and have 14 drinks on Saturday!

Buettner D, Skemp S. Blue Zones: Lessons From the World's Longest Lived. Am J Lifestyle Med. 2016 Jul 7;10(5):318-321. doi: 10.1177/1559827616637066. PMID: 30202288; PMCID: PMC6125071.

Carotenoids are not just for your eyes!

RESEARCH ARTICLE

Association of Serum Antioxidant Vitamins and Carotenoids With Incident Alzheimer Disease and All-Cause Dementia Among US Adults

May A. Beydoun, PhD, MPH, Hind A. Beydoun, PhD, MPH, Marie T. Fanelli-Kuczmarski, PhD, Jordan Weiss, PhD, Sharmin Hossain, PhD, Jose Atilio Canas, MD, Michele Kim Evans, MD, and Alan B. Zonderman, PhD

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Dr. Beydoun
baydounm@mail.nih.gov

Neurology® 2022;98:e2150-e2162. doi:10.1212/WNL.0000000000200289

NHANES 2022 with over 7k over 26yrs

Dietary carotenoids related to risk of incident Alzheimer dementia (AD) and brain AD neuropathology: a community-based cohort of older adults

Changzheng Yuan,[1,2,3] Hui Chen,[1] Yamin Wang,[4] Julie A Schneider,[5] Walter C Willett,[2,3,6] and Martha Clare Morris[4]

Conclusion: High dietary carotenoid consumption substantially lowers the risk of cognitive decline, dementia & brain neuropathology.

Practical AMD Treatments

Once detected, early treatment can slow disease progression

Proven Treatments

Smoking Cessation

Nutritional Supplementation

Diet & Exercise

Systemic Disease Management

Retinal Light Protection

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

Once Detected, Early Treatment Can Slow Disease Progression

Smoking Cessation is the First Step

- **SMOKING IS THE LARGEST MODIFIABLE RISK FACTOR FOR AMD.**
- Current smokers carry a **2.5 to 34 times** higher risk than non-smokers for late AMD[1].

90% of patients with AMD were not advised to stop smoking[2]

er...

<50% of smokers know that smoking may contribute to blindness[3]

Bottom line: SMOKING IS BAD!!

What Should I Be Eating?

Physical activity and AMD

- 15 year study (Beaver Dam) looking at 5yr intervals[1]
- Active lifestyle lessens risk for exudative AMD w OR of **.3**!!! (active meant regular activity at least 3x/wk)
- ***Walk 1 block per day and cut wet AMD by 50%***
- Regular physical activity may lower risk of developing early AMD and progression of early AMD to late AMD at a level comparable with smoking cessation or dietary supplements.

"You don't need to pump iron or run marathons, just do something[2]"

1. Knudtson et al. Activity and 15yr AMD. BJO 12/2006 2. Subhi et al. Ugeskr Laeger(Danish) 8/2015. 2. Jeffry Gerson, OD

What vitamin should I take?

- We could discuss this for an hour!
- Difference between no AMD vs early AMD vs Intermediate AMD
  - If intermediate, study proven AREDS2 formula
  - If earlier, something with lutein/zeaxanthin

Do you prescribe vitamins?

- Matter of perspective

Is this image a little blurry??

Multi-vitamins

- Are multivitamins worthwhile?
- Are they just a fairy-dust formulation?
- Are they true to label?
  - NY AG investigation of major retailers
- Frame of reference as to AREDS2…

64% of Patients with Moderate to Advanced AMD Are Not Taking an AREDS Formula Vitamin

Key Barriers

Lack of awareness of vitamins based on the AREDS Study

Lack of doctor recommendation

AREDS2

- What did the abstract from AREDS2 tell us?
- What did AREDS2 really tell us?

National Eye Institute Recommended Formula:

Nutrient	Amount (per day)	Percent Daily Value*
Vitamin C	500 mg	840%
Vitamin E	400 IU	1340%
Zinc	80 mg	540%
Copper	2 mg	100%
Lutein	10 mg	**
Zeaxanthin	2 mg	**

*Percent Daily Values (DV) based on a 2,000-calorie diet

**Daily Value (DV) not established

Speak with your doctor to determine if the updated AREDS 2 formula is right for you.

AREDS 2

Age-Related Eye Disease Study 2

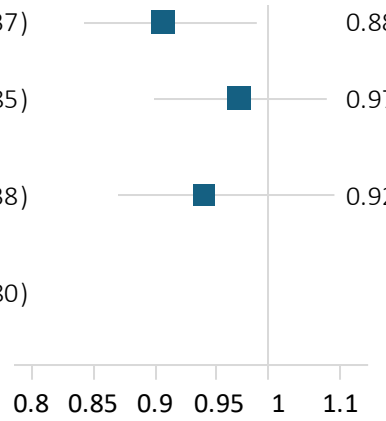
Funded by the National Institutes of Health

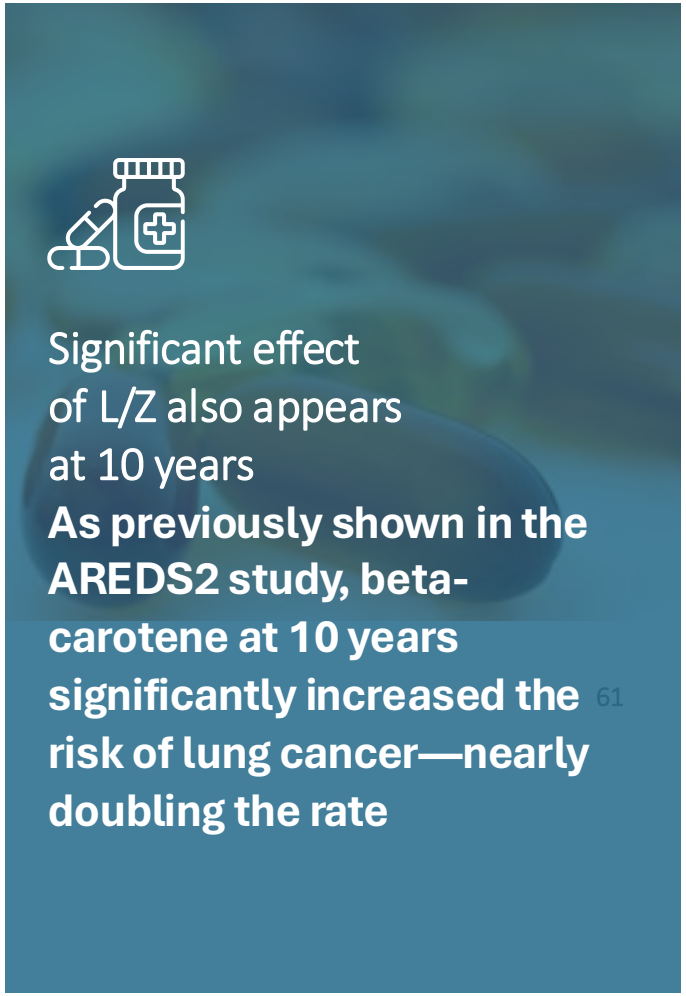
The National Eye Institute Published the AREDS2 10 Year Follow-On Study Results

Published Online June 2, 2022
Jama Ophthalmology

At 10 years, Participants Taking AREDS 2 Supplements with L/Z Had ~10% Reduced Progression to Late AMD

Factorial design by the 4 treatment arms			
Treatment	No. Eyes (No. Events)	Hazard Ratio (95% CI)	P Value
Lutein/Zeaxanthin	1590 (737)	0.88 (0.78-0.99)	0.03
DHA/EPA	1613 (785)	0.97 (0.87-1.09)	0.63
Lutein/Zeaxanthin+DHA/EPA	1590 (738)	0.92 (0.81-1.14)	0.12
Control	1588 (780)		



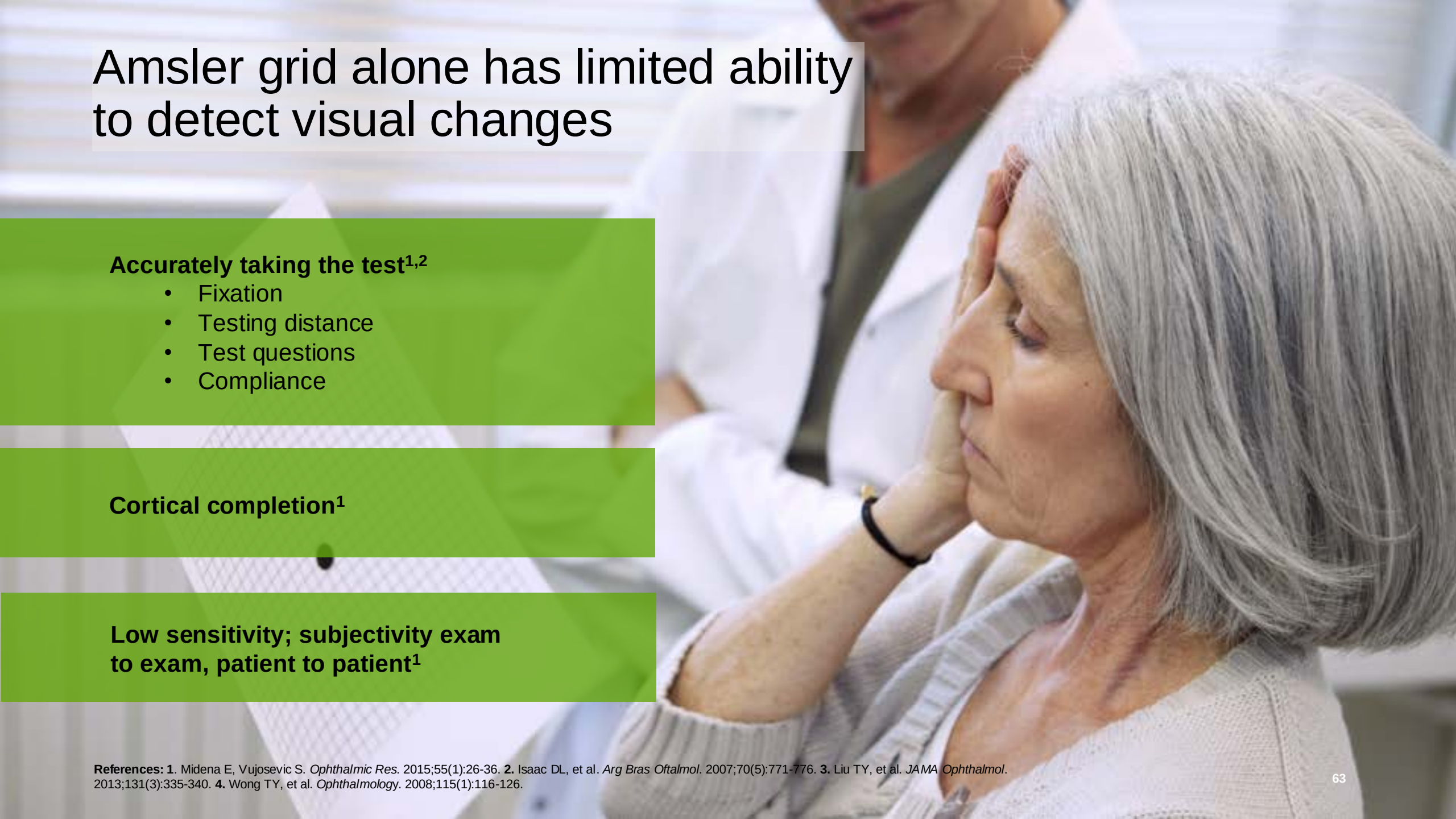


Significant effect of L/Z also appears at 10 years

As previously shown in the AREDS2 study, beta-carotene at 10 years significantly increased the risk of lung cancer—nearly doubling the rate

There is (much) more to AREDS2 than just what vitamin to take

Amsler grid alone has limited ability to detect visual changes



Accurately taking the test[1,2]

- Fixation
- Testing distance
- Test questions
- Compliance

Cortical completion[1]

Low sensitivity; subjectivity exam to exam, patient to patient[1]

References: 1. Midena E, Vujosevic S. *Ophthalmic Res*. 2015;55(1):26-36. **2.** Isaac DL, et al. *Arg Bras Oftalmol*. 2007;70(5):771-776. **3.** Liu TY, et al. *JAMA Ophthalmol*. 2013;131(3):335-340. **4.** Wong TY, et al. *Ophthalmology*. 2008;115(1):116-126.

A perfect combination for poor visual acuity at wet AMD diagnosis

Intermediate AMD may go undiagnosed

+

Patients progress between visits

+

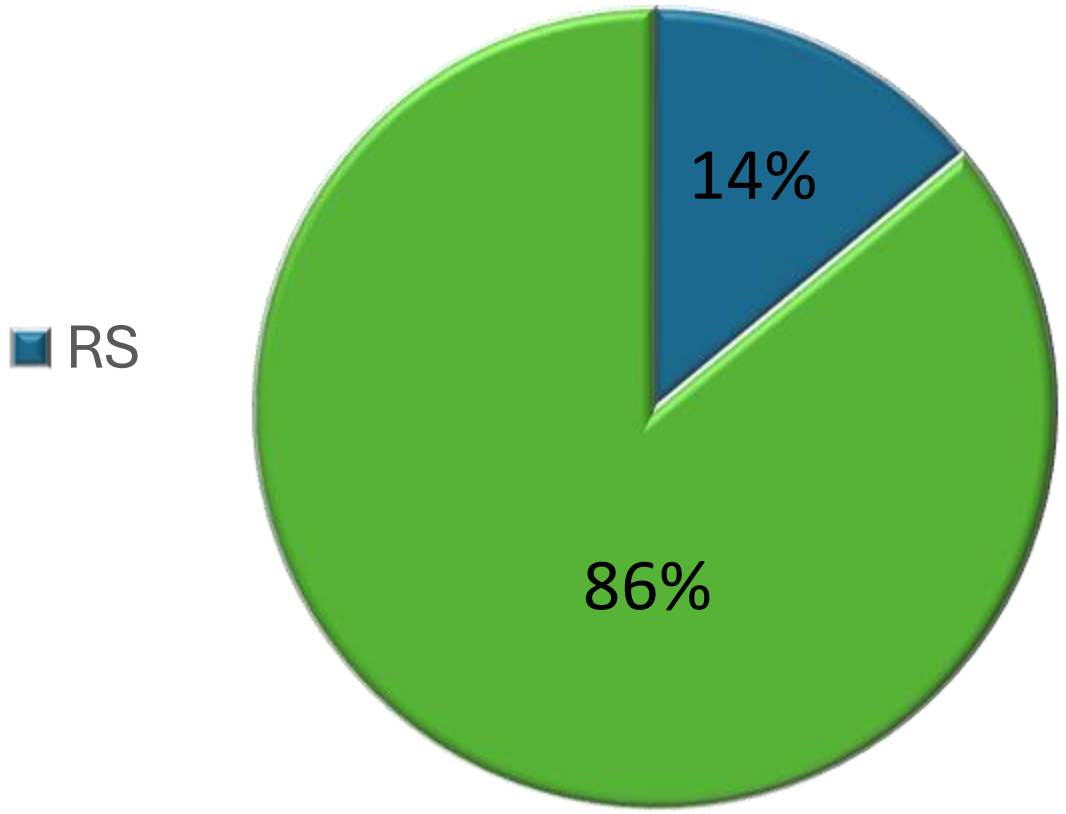
Limitations of Amsler grid

=

Poor VA at wet AMD detection

As the primary eye care professional, ODs can improve vision outcomes for intermediate AMD patients

COs/ODs manage the majority of dry AMD patients



- ~500K intermediate AMD patients are cared for by the **optometric community**
- 5-year risk of progression to wet AMD is up to 50% for high-risk intermediate AMD patients
- When not actively monitored, patients can **lose up to 15 ETDRS*** Letters within one month of developing wet AMD

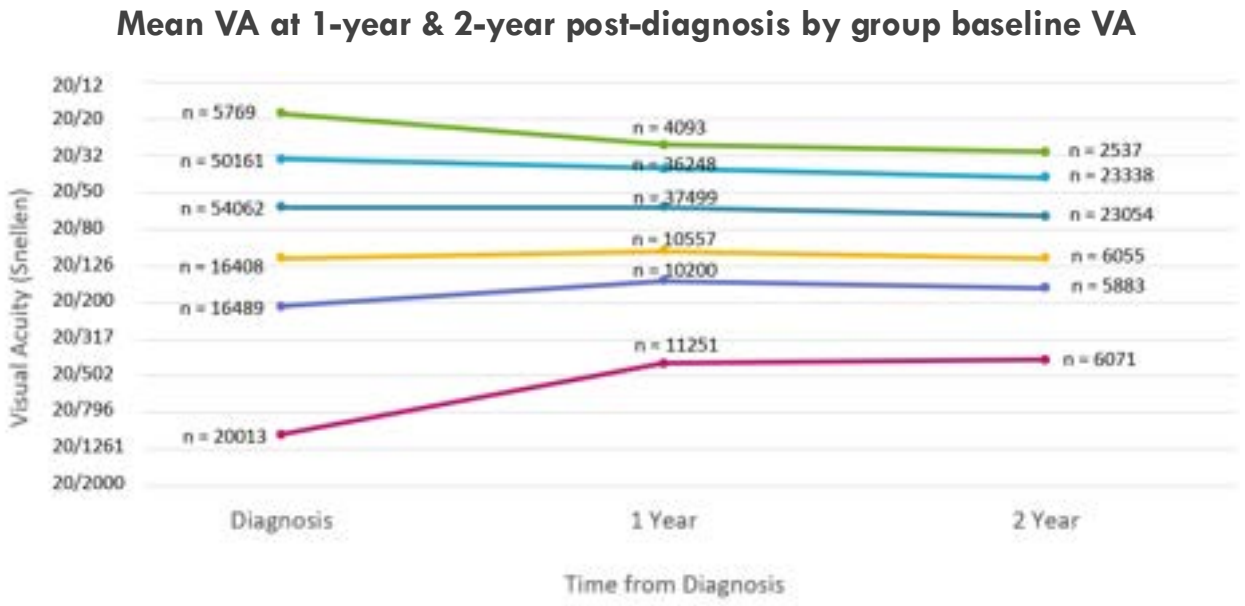
n=3.8M. Source Clearview Mkt Research Aug 2016. Dx'd Intermediate low, high, unilateral GA and wAMD patients.

*Early Treatment Diabetic Retinopathy Study letters

Real-world data supports clinical trial results: early diagnosis with good VA is essential to preserve functional vision with anti-VEGF therapy

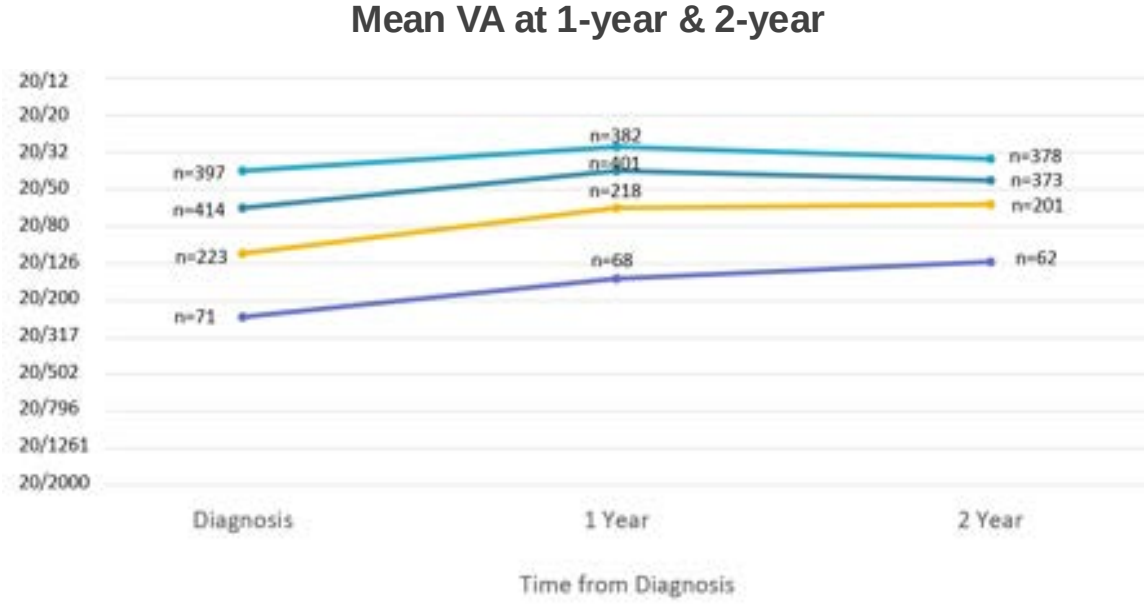
AAO IRIS® Registry Real World Data (US)[1]

January 2013 – June 2017

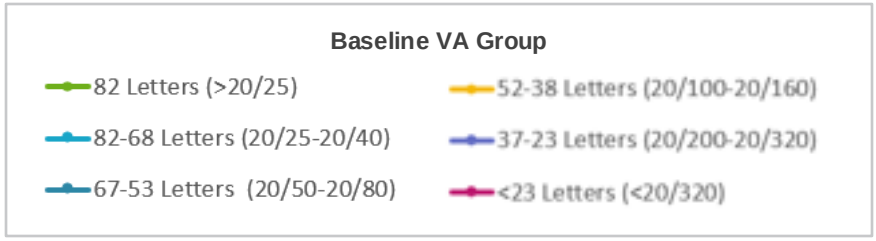


162,902 eyes diagnosed with wet AMD (153,141 patients)

Comparison of Age-related Macular Degeneration Treatment (CATT) Trial (US)[2]



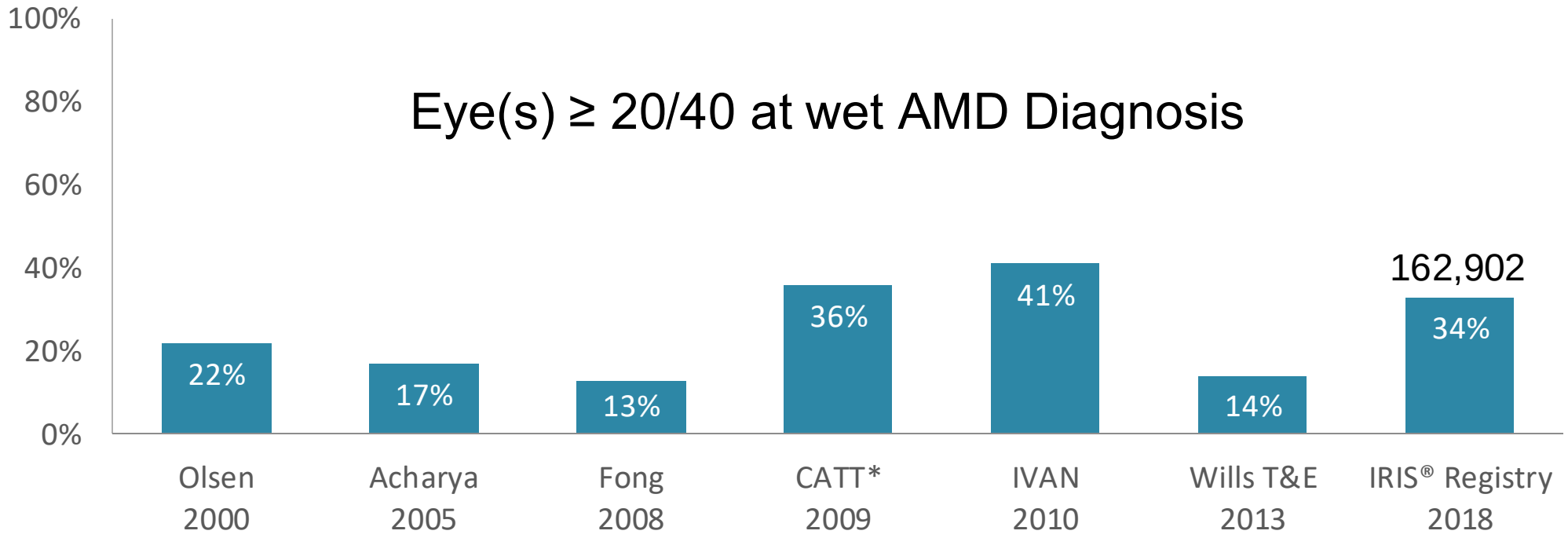
1,185 eyes diagnosed with wet AMD



References: 1. Ho AC, et al. *Ophthalmic Surg Lasers Imaging Retina*. 2020;51:633-639. **2.** Ying GS, et al. *Ophthalmology*. 2015;122(12):2523-2531.

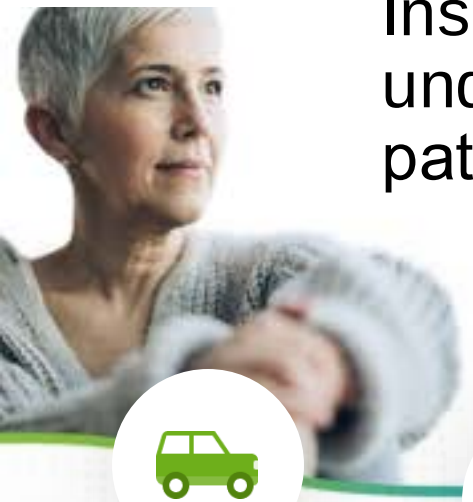
Clinical trial and real-world data show small proportion of patients with good VA at initiation of anti-VEGF therapy

Intermediate AMD patients who convert to wet AMD lose a substantial amount of vision before detection and treatment



Not enough diagnosed wet AMD eyes are detected early

Insights-driven research resulted in a deeper understanding of the intermediate AMD patient's emotional journey



Life Before Symptoms

Noticing Decreased Vision

ANNOYANCE

"The challenge with my eyes has been learning to accept these changes and doing the best I can."

Diagnosis

FEAR, CONFUSION, ANGER

"My doctor gave me no explanation or any additional information of this disease. I was very angry about the way I was brushed off."

Balancing Priorities

SETTLING

"All you can do is wait, which is the worst thing that anyone can do."

Fears Realized
Wet AMD

Taking Control

EMPOWERED

"This would give me peace of mind. I want peace of mind."

Actionable Insights

PATIENT

- Fear and lack of control felt strongest at diagnosis
- Poor AMD awareness leaves no sense of urgency or need
- Desires a better plan, but rarely searches for one
- ECP endorsement is a must
- Doing more is empowering

EYE DOCTOR

- Dry AMD viewed as low risk

Poor vision from late detection can lead to physical injury

54% of patients experienced a fall
30% experienced more than one

35% of patients collided with an object
36% had a laceration

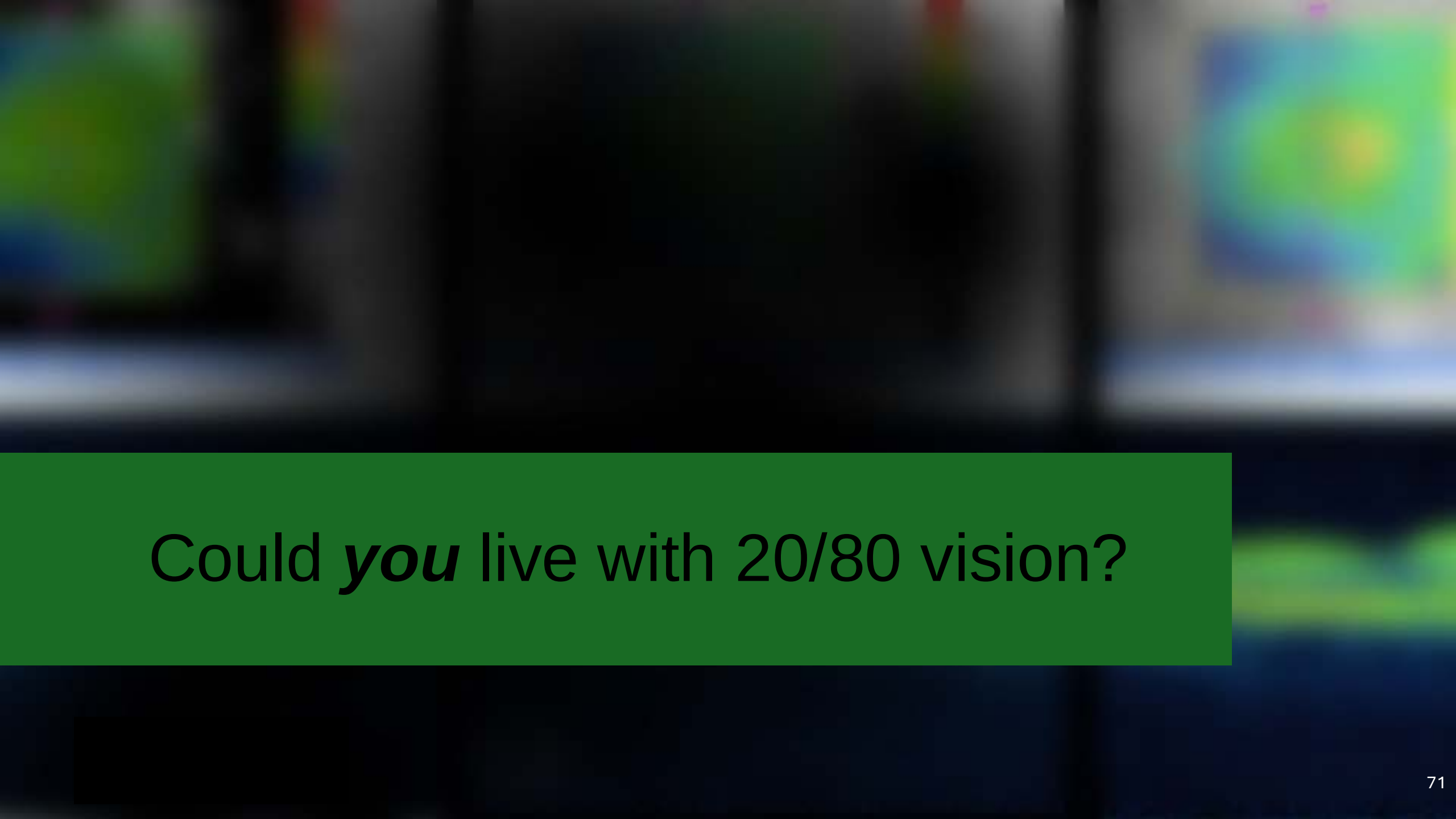
With late detection and poor vision come increased risk of physical injury: falls and non-fall injuries further limit the quality of life for AMD patients.

Poor vision from late wet AMD detection may increase depression and anxiety

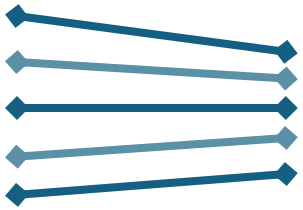
40% of AMD patients are affected by *depression* because of poor vision

10%-30% of AMD patients are affected by *anxiety* because of poor vision

Poor vision from late wet AMD detection can lead to functional disability and subsequent depression and anxiety in AMD patients.


Could ***you*** live with 20/80 vision?

What do we know?



Patients who start with poor vision do not catch up[1]

20/80 mean VA*

*Per IRIS Registry analysis.

34% of patients are ≥ 20/40 at initiation of anti-VEGF treatment[1]

Poor vision increases risk of physical injury, depression, and anxiety[2,3]

VA less than 20/80 can limit:

- Driving
- Reading
- Independence

References: 1. Rao P, et al. *Ophthalmology*. 2018;125(4):522-528. **2.** Wood JM, et al. *Invest Ophthalmol Vis Sci*. 2011;52(8):5088-5092. **3.** Cimarolli VR, et al. *Clin Ophthalmol*. 2015;10:55-63. .

Product and Network Provider Overview

Uses **Preferential Hyperacuity Perimetry (PHP),** proven with Level 1 Evidence

Medicare covered & No Cost to Your Practice

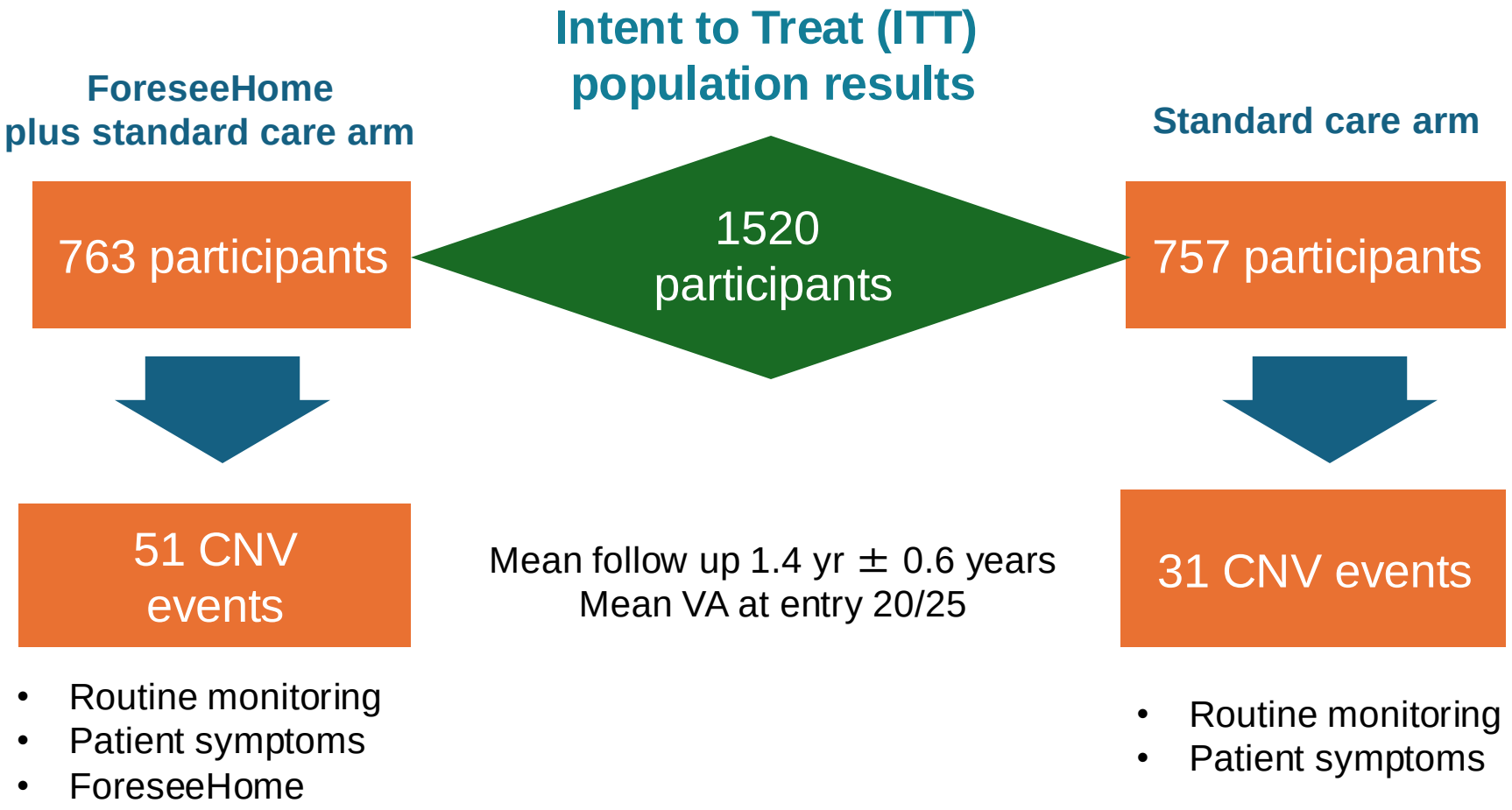
3,300+ referring physicians
- 1,120 Optometrists
- 2,076 Ophthalmologists

35,500+ patients served with **8,000+** actively testing patients

Proven efficacy with level 1 evidence

Nationwide service for remote patient care

AREDS2-HOME Study



***Primary outcome:** Change in BCVA from baseline to CNV detection*

Reference: AREDS2-HOME Study Research Group. *Ophthalmology*. 2014;121(2):535-544.

ForeseeHome Arm

Intent to Treat (ITT)

Per Protocol 1 (PP1)

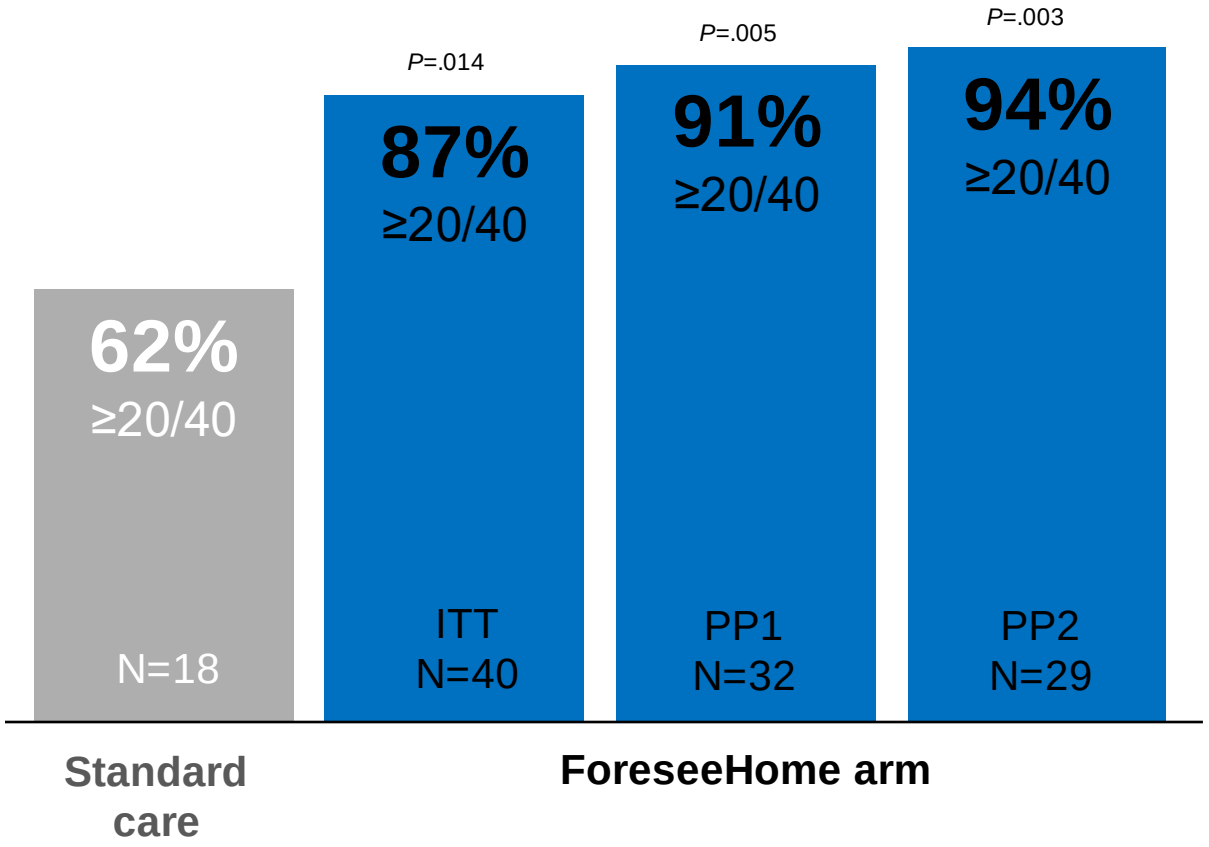
at least 1 test throughout the study

Per Protocol 2 (PP2)

≥ 2x per week (8x per month)

Reference: AREDS2-HOME Study Research Group. *Ophthalmology*. 2014;121(2):535-544.

More patients who used ForeseeHome maintained ≥20/40 VA



50% MORE
patients maintained 20/40 or better when using ForeseeHome vs standard of care alone

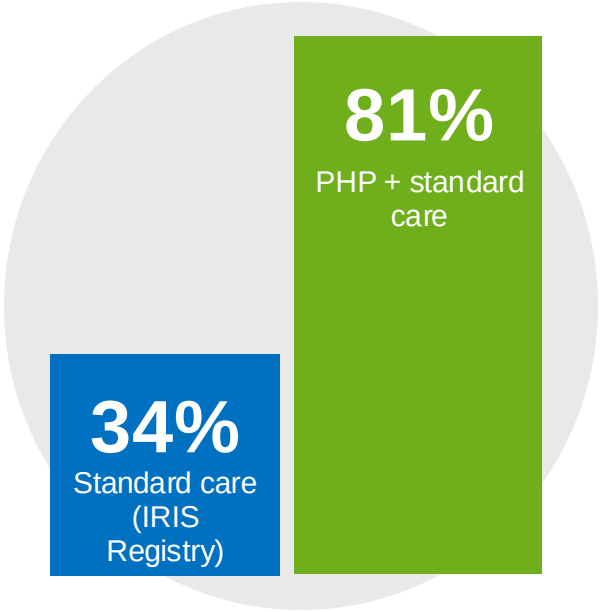
94% of patients maintained 20/40 or better visual acuity at time of wet AMD diagnosis; Absolute visual acuity at time of wet AMD diagnosis is critical to visual acuity outcomes

Reference: AREDS2-HOME Study Research Group. *Ophthalmology*. 2014;121(2):535-544.

ForeseeHome real-world performance resembles pivotal trial results

Real-World Data Analysis[1,2]

October 2009 – September 2018

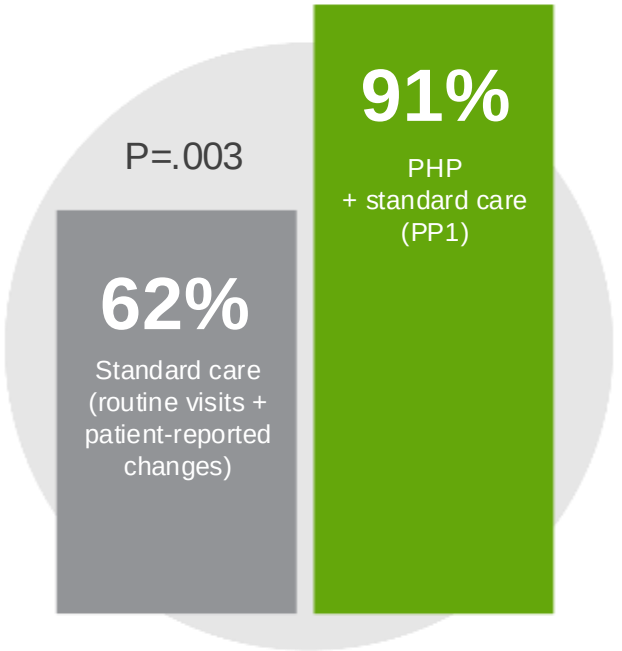


5.6±3.2

Percentage of patients **maintaining functional vision** (20/40 or better) with **ForeseeHome** at time of wet AMD diagnosis

Patients testing compliance
Number of tests per week

AREDS2-HOME Study[3]



4.4±1.7

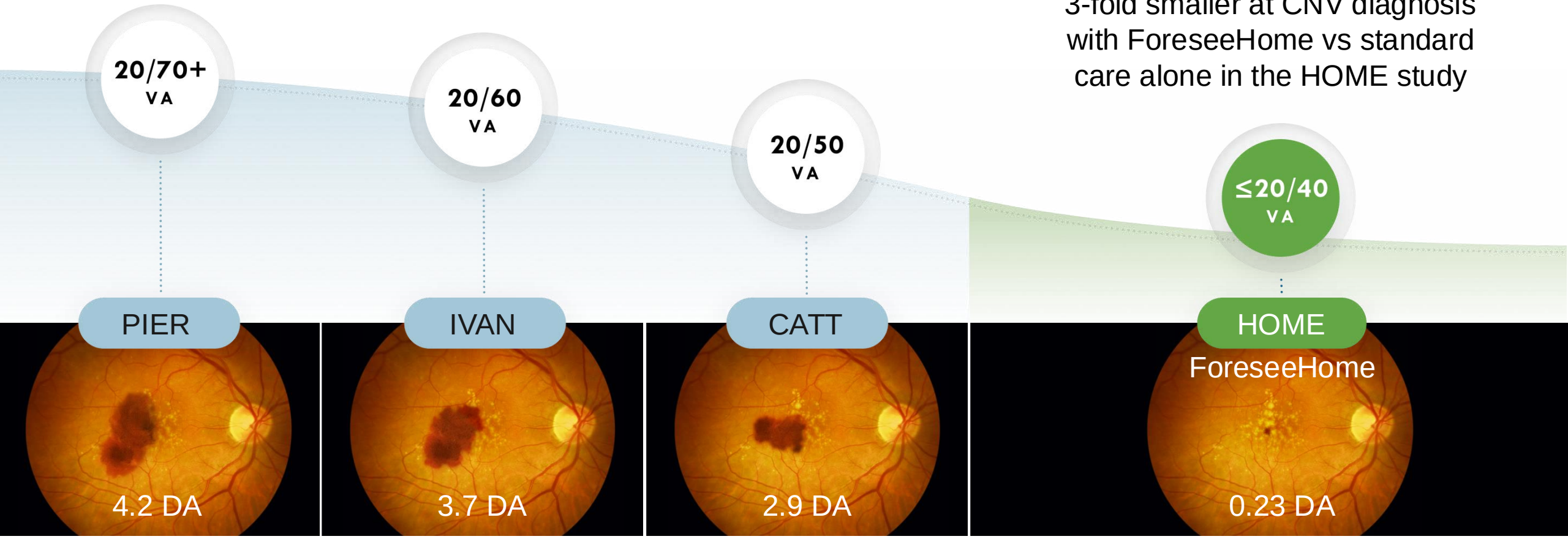
IRIS Registry demonstrates few newly diagnosed CNV eyes are detected early

Visual Acuity and Lesion Size at diagnosis of wet AMD

REAL WORLD ACUITY IN CLINICAL TRIALS

HOME STUDY

Lesions were approximately 3-fold smaller at CNV diagnosis with ForeseeHome vs standard care alone in the HOME study

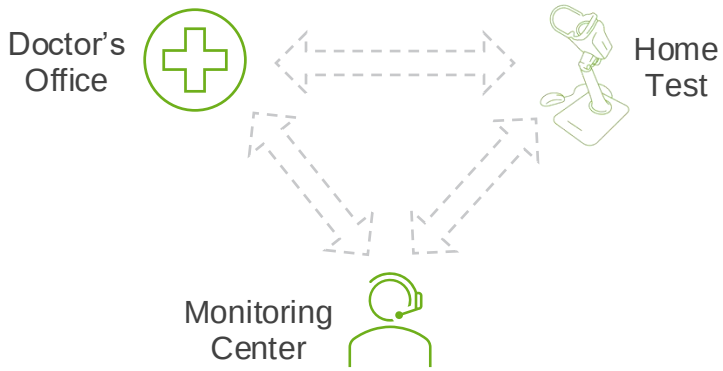


HOME Study: AREDS2-HOME Study Research Group. Ophthalmology. 2014;121(2):535-544. **CATT Study:** Ying GS, et al. Ophthalmology. 2015;122(12):2523-2531 **IVAN Study:** Chakravarthy U, et al; IVAN Study Investigators. Ophthalmology. 2012;119(7):1399-1411 **PIER Study**: Regillo CD, et al. Am J Ophthalmol. 2008 Feb;145(2):239-248

10-year ALOFT Study: Impact of the Model on Treatment Outcomes

Mathai et al., *Ophthalmology Retina*, April 2022

HOME MONITORING MODEL



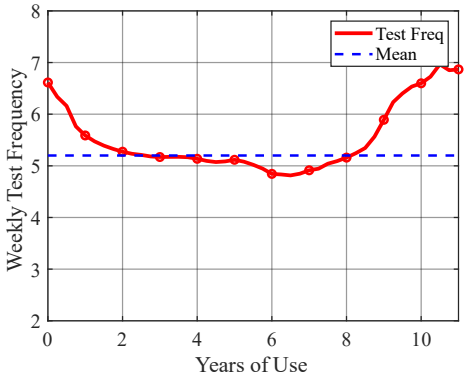
STUDY DESIGN

2,123 patients	3,334 eyes	5 clinics	10 years

Large retrospective study involving **all referred patients** at 5 clinics

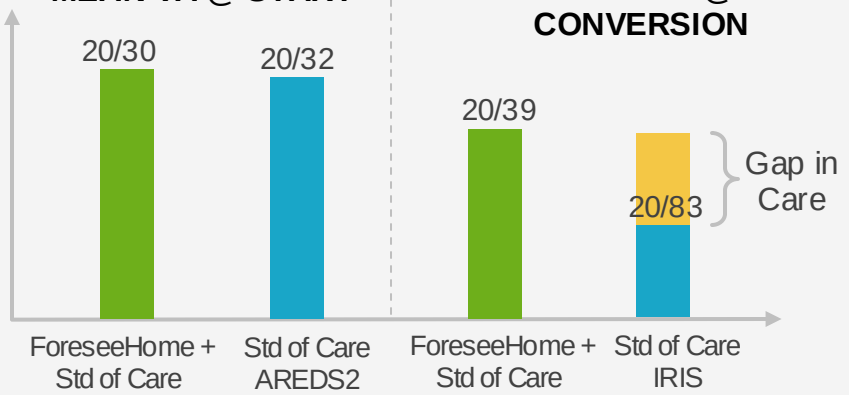
RESULTS

AVERAGE TEST FREQUENCY



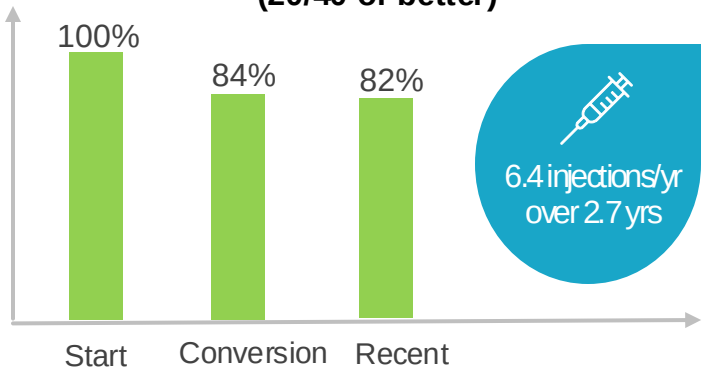
5.2 tests/week maintained over 10 years!

MEAN VA @ START / MEAN VA @ CONVERSION



Same starting point ... … but substantially better VA

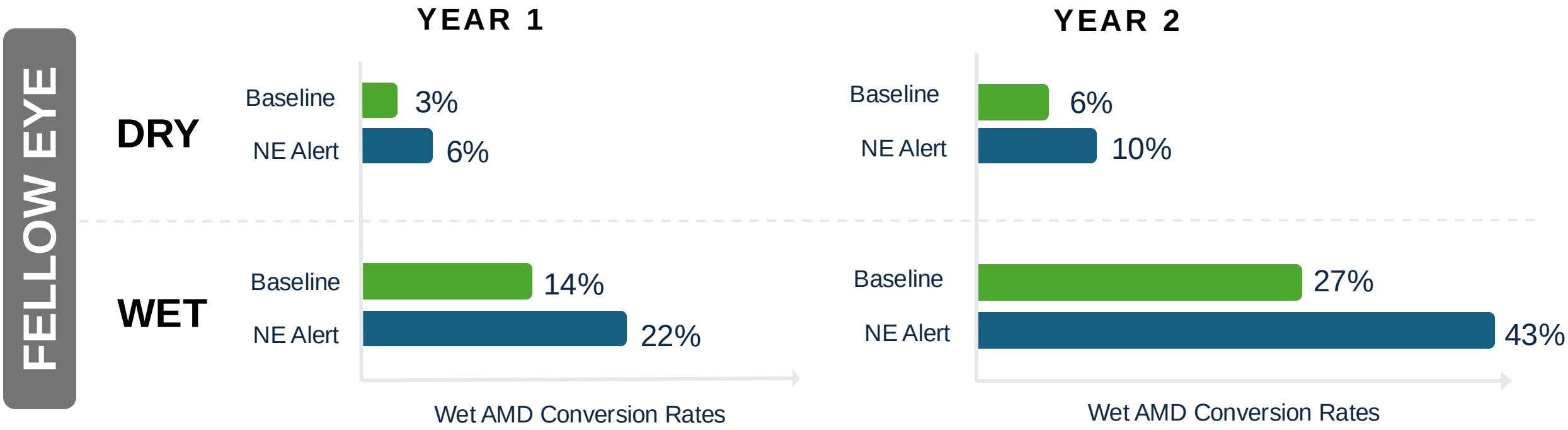
MAINTAINING FUNCTIONAL VISION (20/40 or better)



Over 80% maintained functional vision!

Non-exudative (NE) Alerts **Predict Increased Risk** of Future Conversion to Wet AMD

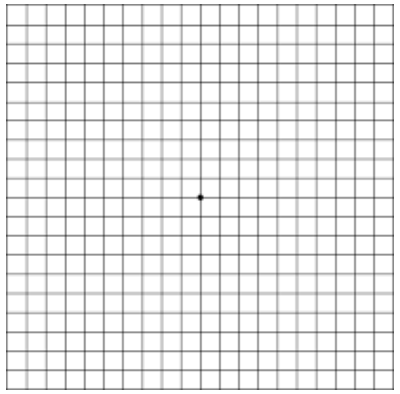
Rate of conversion starting from baseline and NE alert[2]



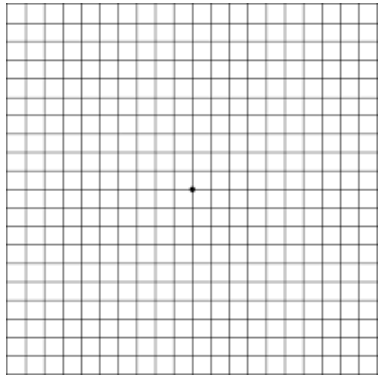
Patients with non-exudative (NE) alert:

- ✓ 2x as likely to convert
- ✓ Require additional vigilance

Amsler Grid

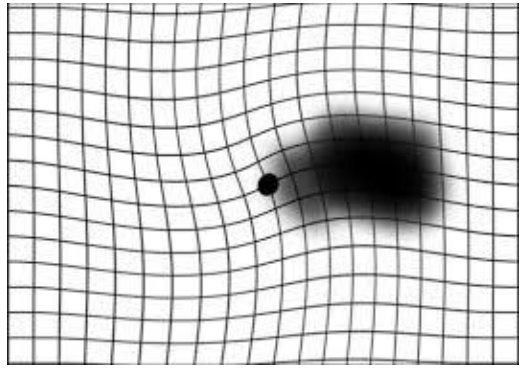


Normal Amsler



“Abnormal” Amsler

May have CNVM but performed incorrectly



Abnormal Amsler

Who thinks that this is truly adequate for our patients?

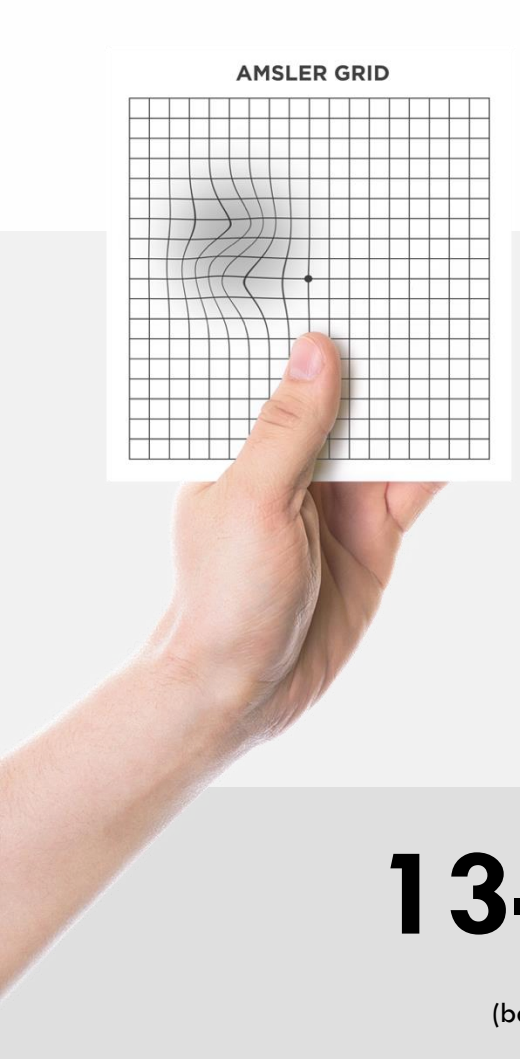
Can/Should there be better

- Recent publication reviewed 3 readily available vision testing apps
- This study looked at the KeepSight Journal (paper), MyVision Track App and MultiBit App in 297 patients
- Compared to in office visit for detection of CNVM

CONCLUSIONS AND RELEVANCE Results suggest that no home-monitoring vision test evaluated provided satisfactory diagnostic accuracy to identify active nAMD diagnosed in hospital eye service follow-up clinics. Implementing any of these evaluated tests, with ophthalmologists only reviewing test positives, would mean most active lesions were missed, risking unnecessary sight loss.

Hogg et al. Home-Monitoring Vision Tests to Detect Active Neovascular Age-Related Macular Degeneration JAMA Ophthalmology June 2024 Volume 142, Number 6

At-home monitoring for conversion to wet AMD



1940s

vs

2024

Standard of Care

ForeseeHome® AMD Monitoring Program

13-41%

standard of care alone
(based on anti-VEGF trials)

Maintained driving vision at time of diagnosis

(20/40 or better)

94%

when ForeseeHome was added to standard of care (AREDS2-HOME Study PP2)

This just in

- If a patient has wet AMD, there is a new way to monitor from home
- Same technology as your office!
- Individual based retreatment protocols
  - Think TXE but personalized!

SCANLY Home OCT Device

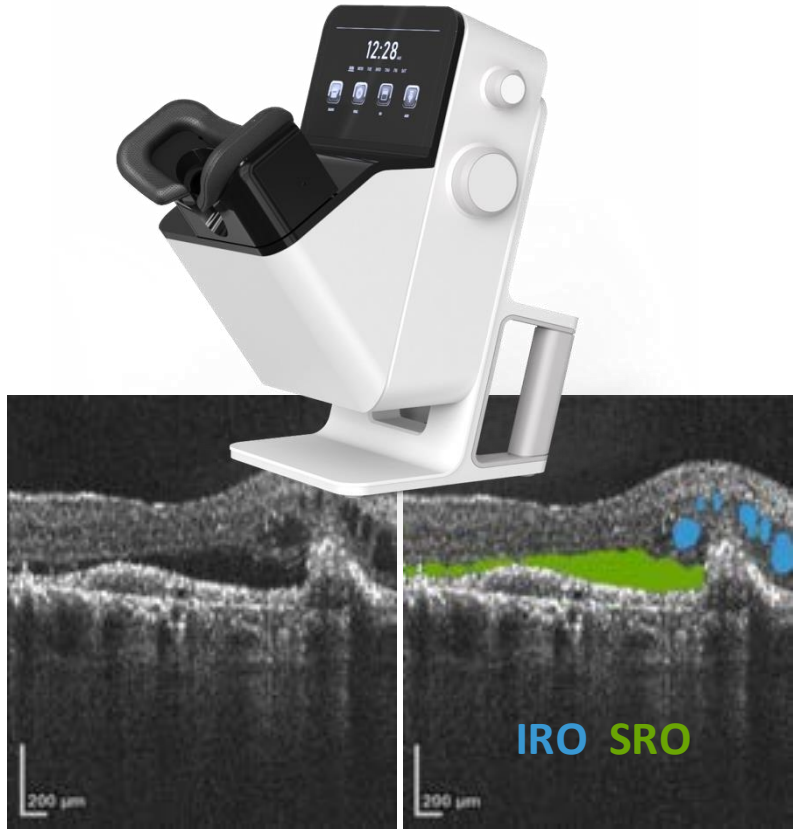
EASY-TO-USE PATIENT SELF-OPERATED CONNECTED DEVICE

Key Features

- Portable device: size 14”x11”x14” (WxDxH), weight <16 lbs.
- Patient self-setup and self-operation
- Automatic data transmission via built-in wireless connection
- AI-enabled estimation of hypo-reflective spaces

Imaging System Specifications

- Spectral-domain optical coherence tomography (SD-OCT)
- Scan area: 10 x 10 degree (3mm x 3mm)
- High density volume scan with up to 88 B-scans and 34 µm spacing
- Self-imaging time < 1 minute per eye[1]

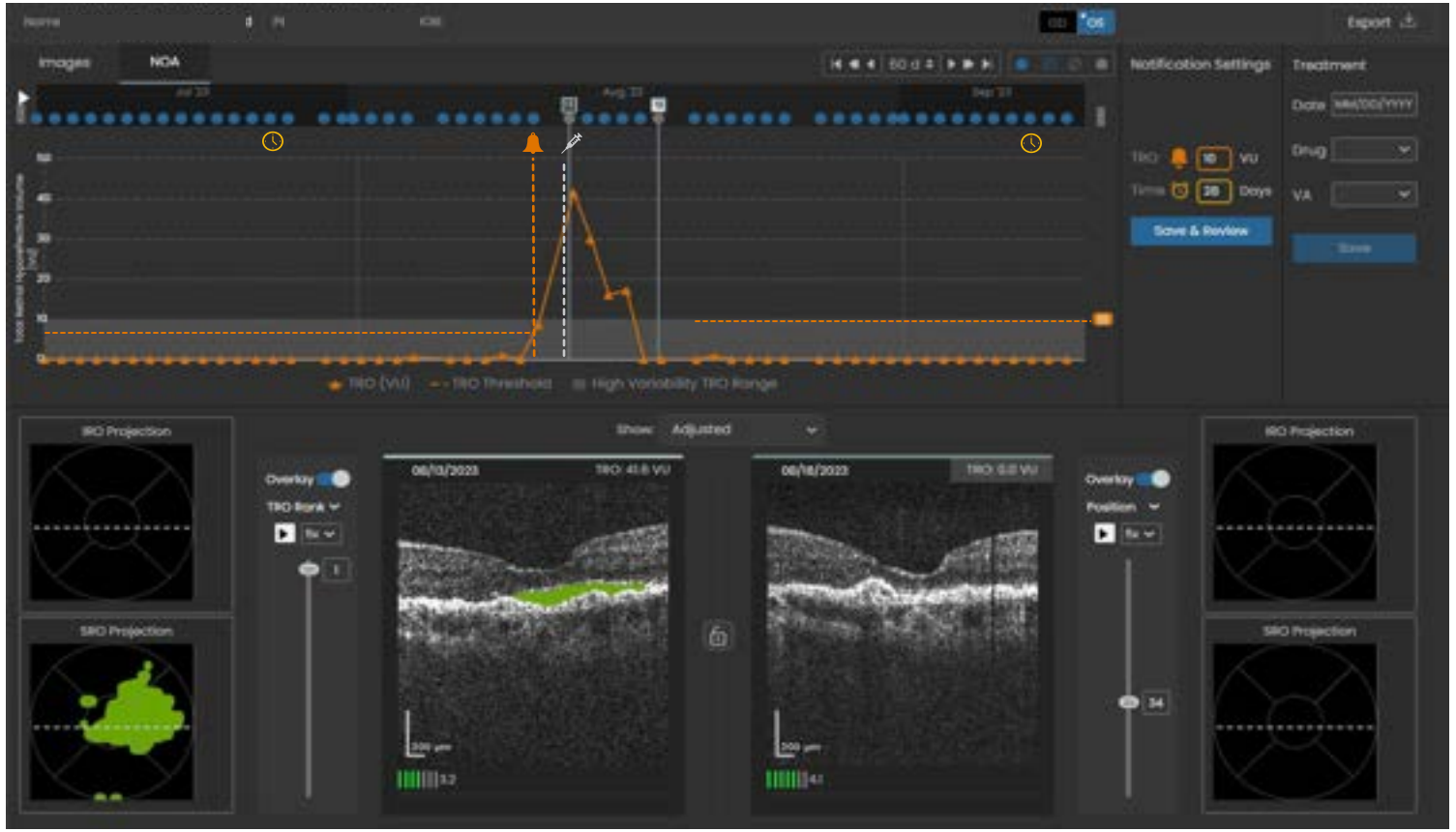


1. https://clinicaltrials.gov/study/NCT04907409

IRO: Intra-retinal hypo-reflective spaces | **SRO**: Sub-retinal hypo-reflective spaces

SCANLY Home OCT Portal

Physician-led Patient Management Via Remote Access to OCT Images and AI-based Analyses



- ✓ Order program for patients
- ✓ Review images and analyses
- ✓ Set notification criteria
- ✓ Review notifications
- ✓ Report patient management decisions and treatments

Imaging / Analysis / Tracking

- OCT images with and without IRO and SRO segmentation overlay
- TRO area ranked B-scans
- IRO and SRO projection
- TRO volume trajectories

IRO: Intra-retinal hypo-reflective spaces | **SRO**: Sub-retinal hypo-reflective spaces | **TRO**: Total retinal hypo-reflective spaces

AI-powered SCANLY safe and effective for wet AMD home monitoring

Service has been used by patients to self-image over 1,500 eyes in clinical trial settings!

Imageability At Home

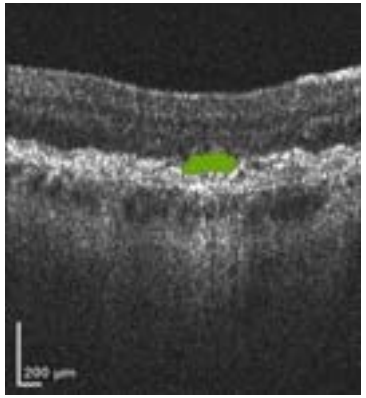
- Self-imaging time: 48 seconds (mean)[1]
- Patients able to successfully activate: 97%[1]
- Self-imaging success attempts: 97%[1]
- In patients with BCVA of 20/320 or better[1]

AI Capability of Notal OCT Analyzer

- Image gradeability rate: 88%[2]
- AI agreement with human graders nearly as high as agreement between graders[2]

Longitudinal Performance

- Adherence: 5.9 scans/week[1]



VU: Volume Units | **SRO**: Sub-retinal hypo-reflective spaces | **TRO**: Total retinal hypo-reflective spaces

1. https://clinicaltrials.gov/study/NCT04907409
2 https://clinicaltrials.gov/study/NCT05202587

What does this mean to patients

- This improves the overall experience by creating a personalized plan for return visits/treatments
- Can create peace of mind in patients knowing they are not being undertreated
  - Like having a daily or several times a week high tech exam monitored by a reading center and their doctor

Genetic testing: Another means of personalizing care

- Can this be used to improve patient experience?

- Knowing can decrease anxiety if low risk
- Knowing could be impetus to take more seriously
- The unknown is often the greatest source of anxiety!
- 2 companies with patient-pay model

Geographic Atrophy Is an Advanced Form of Age-Related Macular Degeneration

- Globally, AMD is among the **leading causes of blindness** in adults aged ≥50 years[1]
- GA is a **progressive, advanced form** of dry AMD characterized by loss of the RPE, photoreceptors, and choriocapillaris leading to **significant, irreversible loss of visual function**[2]

GA affects more than
5 million
people worldwide[2,3]

~973,000
people in the United States
have GA in ≥1 eye[4]

4×

After age 50, **prevalence of GA approximately**
quadruples
every 10 years[5]

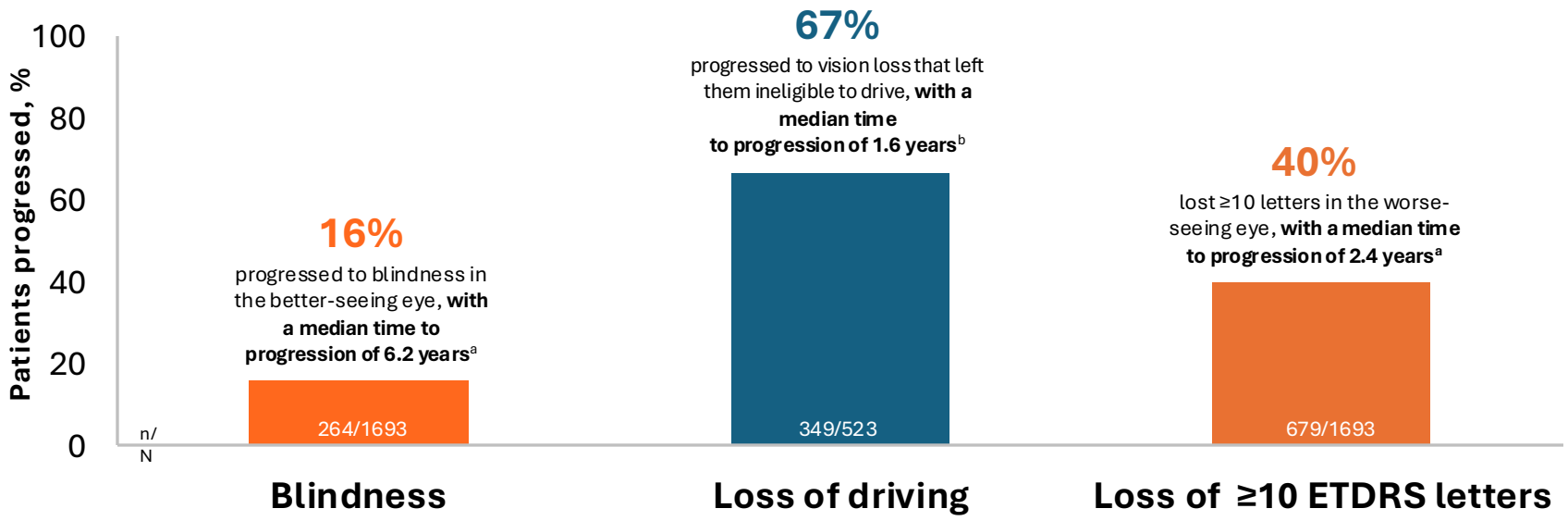
GA accounts for
20% **of all legal blindness**
attributed to AMD[6,7]

AMD, age-related macular degeneration; GA, geographic atrophy; RPE, retinal pigment epithelium.

1. GBD 2019 Blindness and Vision Impairment Collaborators; Vision Loss Expert Group of the Global Burden of Disease Study. *Lancet Glob Health*. 2021;9(2):e144-e160.
2. Fleckenstein et al. *Ophthalmology*. 2018;125(3):369-390. 3. Wong et al *Lancet Glob Health*. 2014;2(2):e106-e116. 4. Friedman et al. *Arch Ophthalmol*. 2004;122(4):564-572.
5. Rudnicka et al. *Ophthalmology*. 2012;119:571-580. 6. Biarnés et al. *Optom Vis Sci*. 2011;88(7):881-889. 7. Ferris et al. *Arch Ophthalmol*. 1984;102:1640-1642.

Vision Loss in GA Can Progress Quickly and Can Have Profound Impacts

Retrospective cohort analysis of a 10-center EMR database across the UK in patients aged ≥50 years with bilateral GA



[a]Of patients with bilateral GA who had VA follow-up and who did not meet the UK definition of blindness at baseline. [b]Of patients who had VA follow-up and a level of VA in their better-seeing eye that would have placed them in a category of eligible to drive at baseline.

EMR, electronic medical record; ETDRS, Early Treatment Diabetic Retinopathy Study; GA, geographic atrophy; VA, visual acuity.

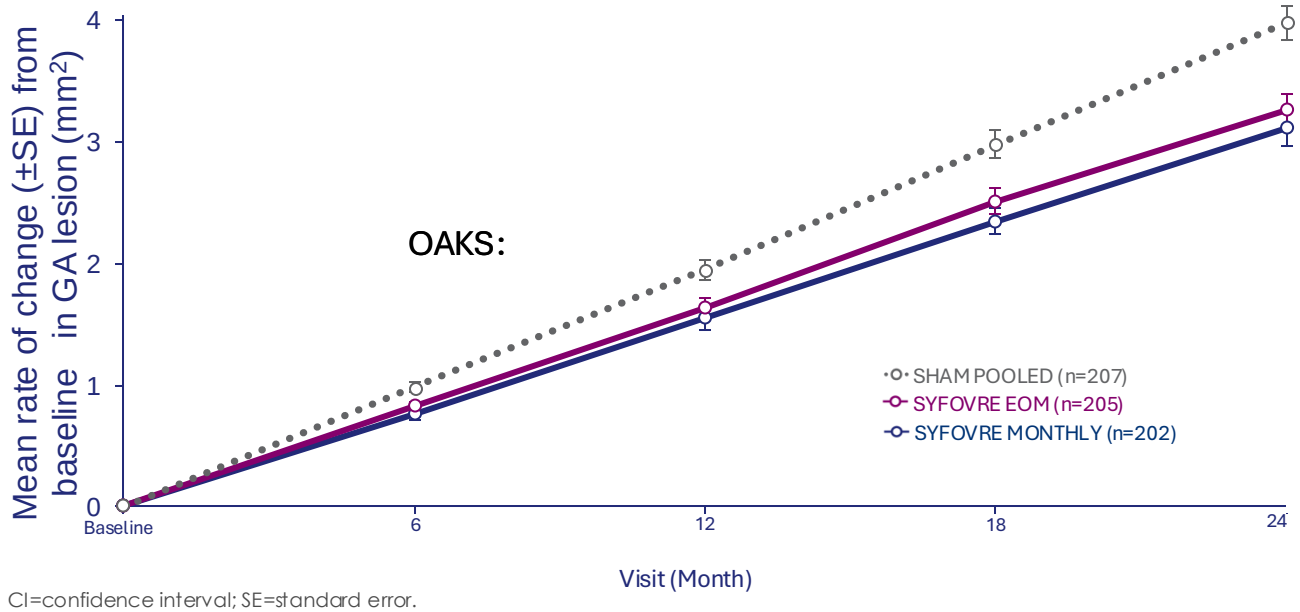
Chakravarthy et al. *Ophthalmology*. 2018;125(6):842-849.

GA is treatable

- Approximately 20% decrease in lesion growth
- Some increase in likelihood of CNVM
- Is it for everybody?
  - Is it for every retina specialist?

SYFOVRE Achieved Continuous Reductions in Lesion Growth Rate Through Month 24[1,2] (OAKS)

REDUCTION IN LESION GROWTH RATE WITH SYFOVRE VS SHAM POOLED[1*†]



Reduction vs sham
Baseline - Month 24‡

18 % -0.72 mm^2 (95% CI: -1.10 to -0.33)

22 % -0.87 mm^2 (95% CI: -1.27 to -0.47)

CI=confidence interval; SE=standard error.

*Based on a mixed effects model for repeated measures assuming a piecewise linear trend in time with knots at Month 6, Month 12, and Month 18.[1]

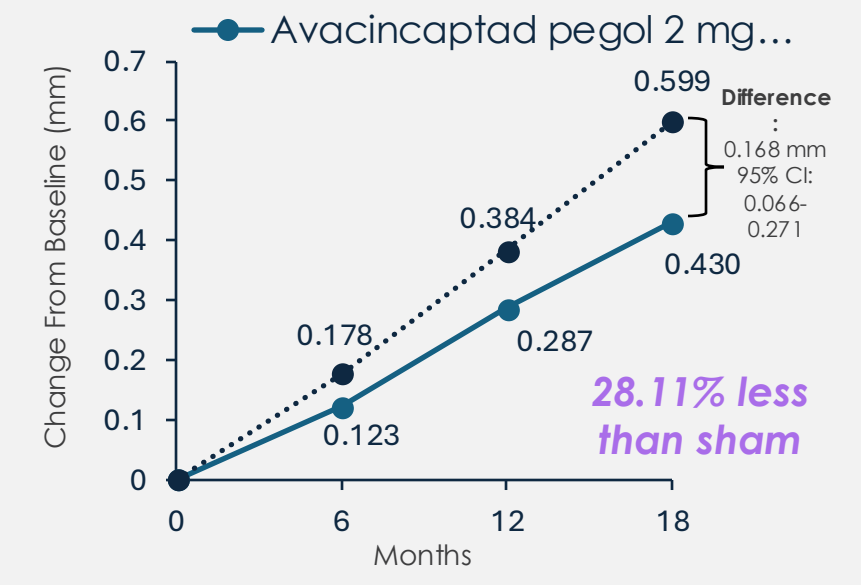
†SHAM EOM and SHAM Monthly were pooled for analysis.[2]

‡Slope for baseline to Month 24 is an average of slope of baseline to Month 6, Month 6 to Month 12, Month 12 to Month 18, and Month 18 to Month 24.[1]

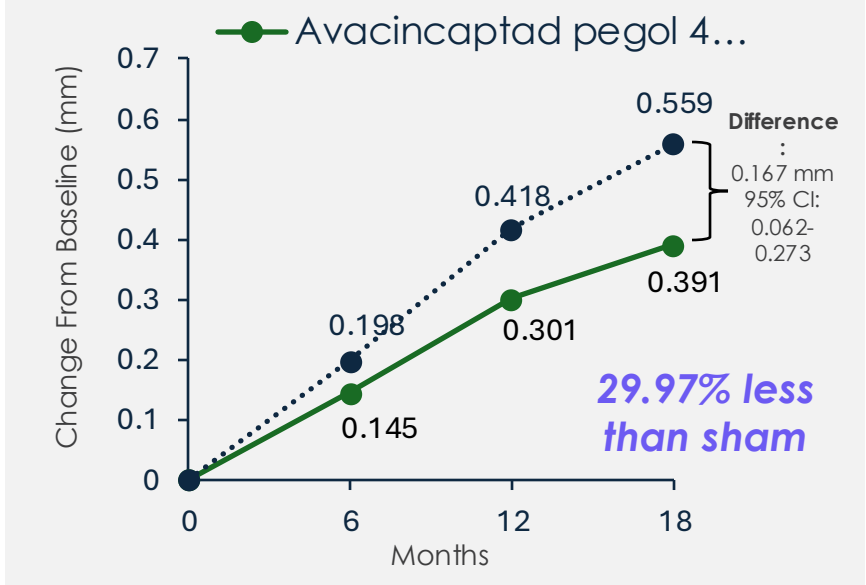
1. SYFOVRE (pegcetacoplan injection) [package insert]. Waltham, MA: Apellis Pharmaceuticals, Inc; 2023. 2. Data on file. Apellis Pharmaceuticals, Inc.

Continuous treatment effect and separation from sham observed over 18 months (square root transformation)

Avacincaptad pegol 2 mg vs sham



Avacincaptad pegol 4 mg vs sham



Note: Based on LS means from MRM; for ITT population, Hochberg procedure was used for significance testing; prespecified and descriptive analysis. These LS means are estimates of the MRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data.
CI, confidence interval; GA, geographic atrophy; ITT, intent-to-treat; LS, least square; MRM, mixed-regression model.
Data on file. IVERIC Bio.

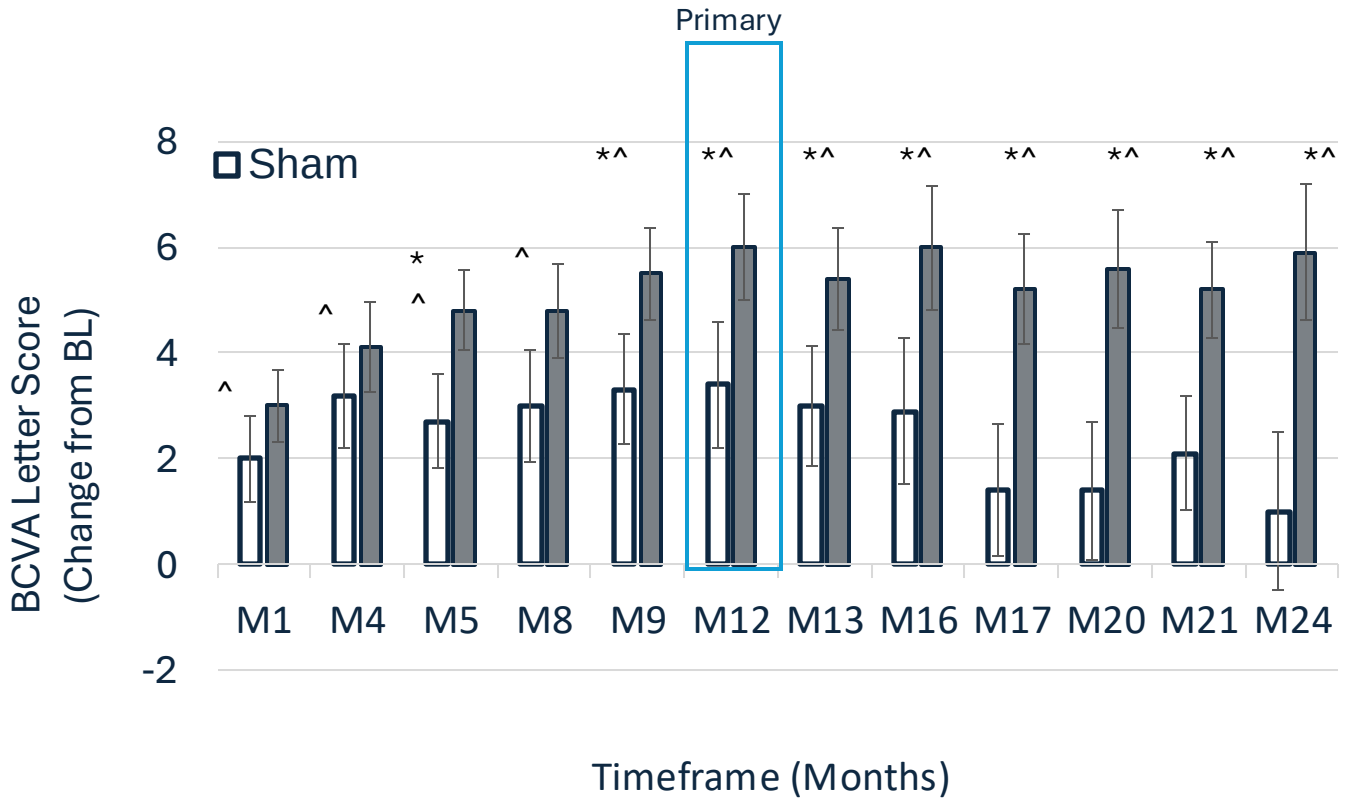
Can light help AMD?

- Photobiomodulation (using light to induce chemical reactions in biological systems)
- Lightsite III: Prospective, double blind, controlled treating q4m for 24 mos
- 5.5 letter improvement at 13 mos in Dry AMD patients (intermediate)

US LIGHTSITE III Pivotal Study Design – 13M Primary Vision Efficacy Met and Sustained

Trial Design

- 100 subjects (148 eyes) from 10 leading retinal centers throughout the US
- Topline data showed a statistically significantly difference between the PBM and Sham groups at month 13 ($p = 0.02$) and Month 24 ($p = 0.0015$)
- PBM provided a sustained and improved BCVA with a mean 5.5 letter change from BL gain at month 13 ($p < 0.0001$) and mean 5.9 letter change from BL at month 24



LIGHTSITE III Summary

LIGHTSITE III met the predetermined primary efficacy BCVA endpoint with a statistically significant difference between the PBM group versus the Sham group at M13 ($p = 0.02$) and M24 ($p = 0.0015$)

An improved BCVA with a mean > 5 letter gain in PBM eyes from BL values at M13 and M24 was seen ($p < 0.0001$). At Month 24:

- 58.2% of PBM eyes responded with a >5 letter gain with a mean of 8.5 + 0.5 letters
- 18.7% of PBM eyes responded with a >10 letter gain with a mean of 13.4 + 0.6 letters
- 5.5% of PBM eyes responded with a >15 letter gain with a mean of 16.6 + 0.8 letters

Approximate 2x decrease in patients with lost BCVA letter scores in the PBM-treated eyes versus the Sham eyes at 13 months and significant loss in vision at 24 months in the Sham group

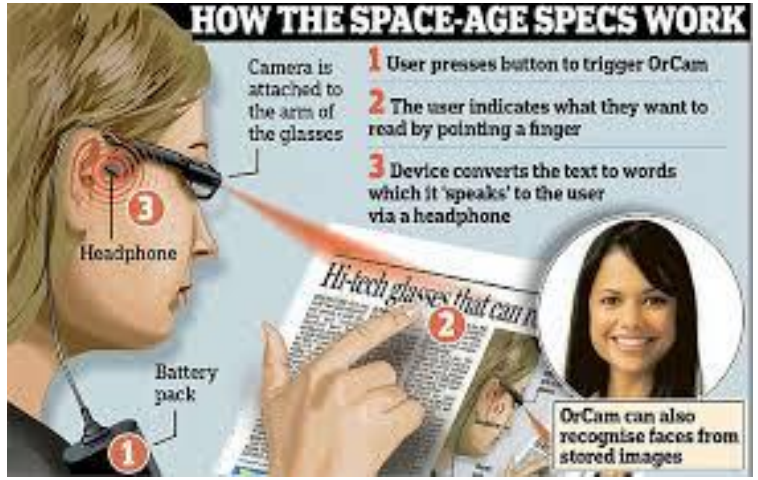
A non-significant numerical increase in central drusen volume was observed in the Sham group, vs no increase in central drusen volume in the PBM group at M13 and M24 (~4-fold over PBM) consistent with LT I and II, suggesting a disease modifying benefit

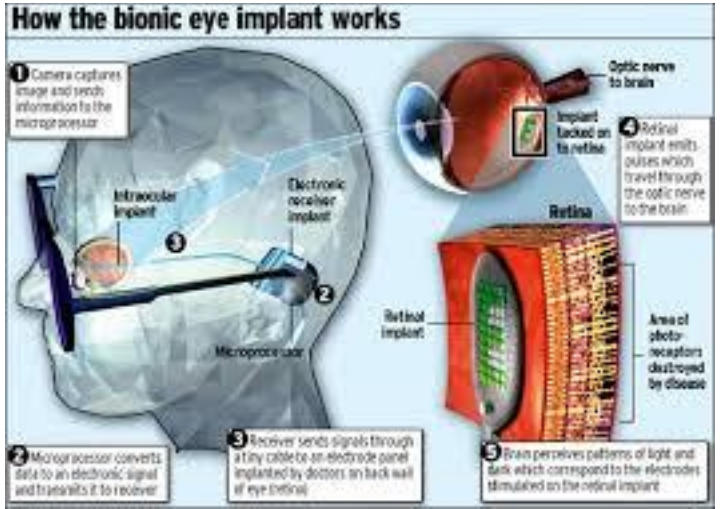
PBM treatment with Valeda shows an excellent safety profile

Occurrence of later stage, new GA observed in 24.0% of Sham vs 6.8% of PBM eyes. Occurrence of new GA was significantly higher in the Sham group than in the PBM group ($p = 0.007$, Fisher exact test, odds ratio 4.2) demonstrating slowing of disease progression.

When Medical treatment fails…

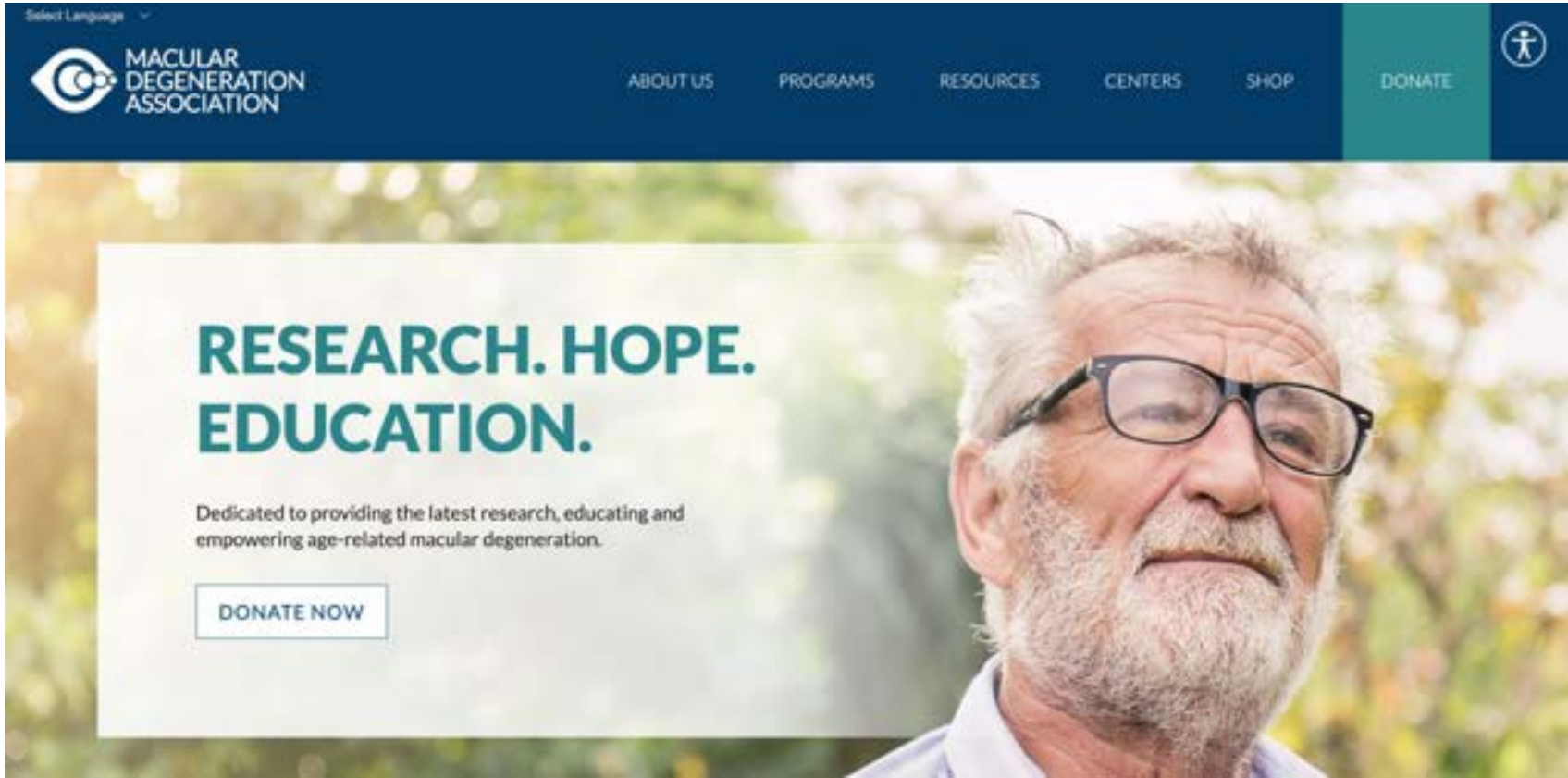
- Low vision is an important option
  - Traditional and newer / digital devices
    - Too many to really discuss, but something to help nearly all patients needing help
  - Surgical options on the horizon
  - Associations and support groups
    - State and other non-profit agencies





A shameless pitch

- For a non-profit organization
- Macular Degeneration Association
- Macularhope.org



Thank You!

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