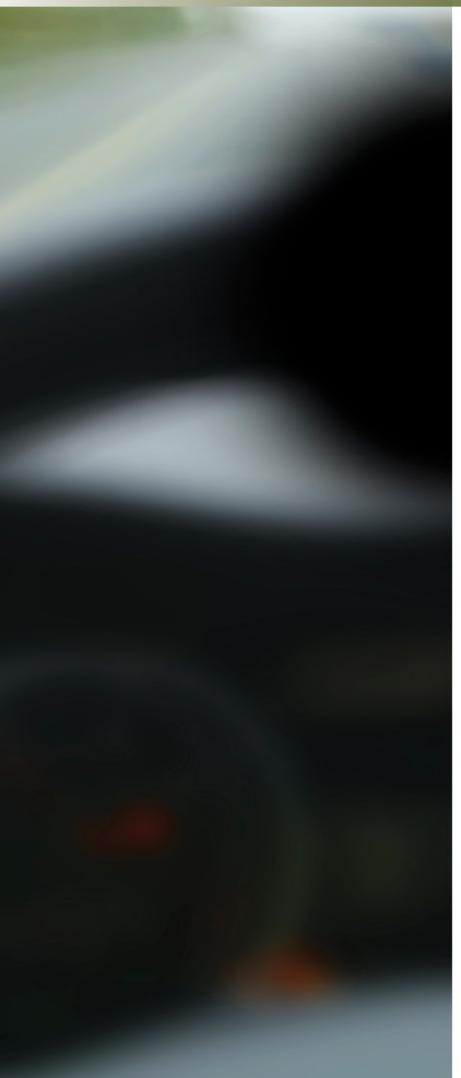
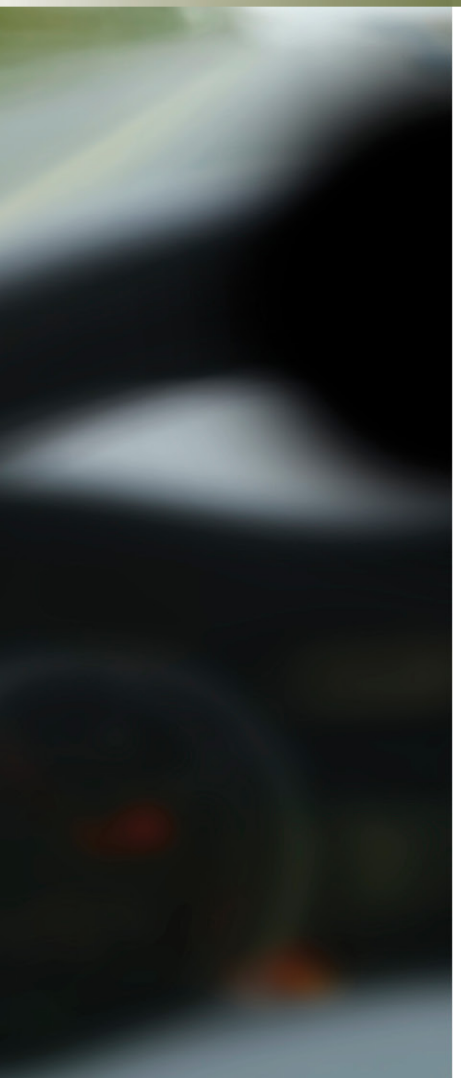
The Dynamic Landscape of Age-Related Macular Degeneration and Diabetic Macular Edema

Real-World Evidence



This educational activity is sponsored by Postgraduate Healthcare Education, LLC and is supported by an educational grant from Genentech.

Faculty



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Adjunct Assistant Professor
University of Michigan College of Pharmacy
Ann Arbor, MI
President
SJR Associates, LLC
Sarasota, FL

Dr. Rich is President of SJR Associates, LLC, a health care consulting company located in Sarasota, FL. He has over 30 years' experience in the pharmacy field, having practiced in hospital, retail, and managed care pharmacy. He is a nationally recognized lecturer and moderator and provides consulting services to managed care organizations, physician practice groups, employers, and pharmaceutical manufacturers. Dr. Rich earned his pharmacy degree from the University of Michigan and holds a Doctorate in Theocentric Business Ethics. He has held the position of Adjunct Assistant Professor at the University of Michigan since 1982 and has had a dual appointment as an Adjunct Assistant Professor with the Eugene Applebaum College of Pharmacy and Health Sciences at Wayne State University since 1994.

Faculty

John W. Kitchens, MD

Ophthalmologist, Vitreoretinal Surgeon & Partner
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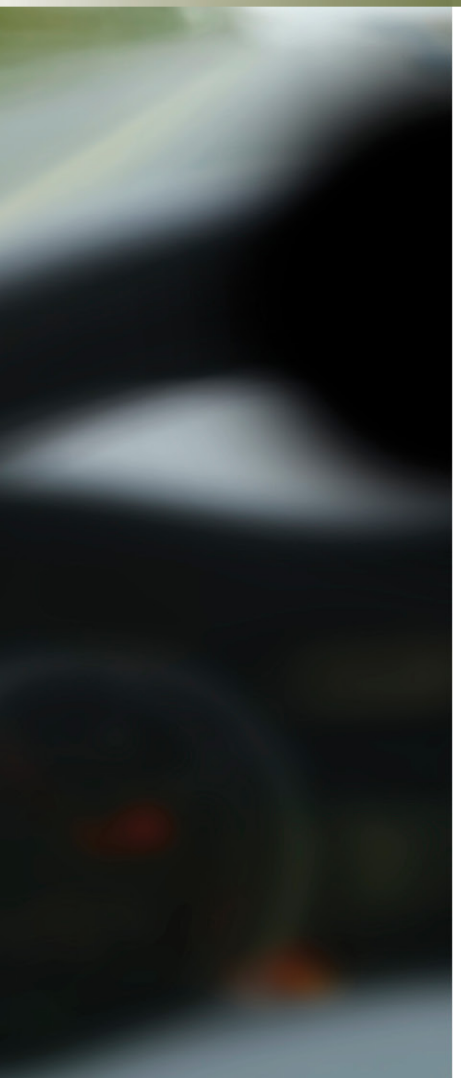
Voluntary Faculty
University of Kentucky
Lexington, KY

Dr. Kitchens is a retina specialist and partner at Retina Associates of Kentucky (RAK) in Lexington. He is a graduate of Indiana University School of Medicine and completed his residency in Ophthalmology at the University of Iowa. He was selected for a Medical Retina Fellowship along with the Chief Resident position at the Bascom Palmer Eye Institute in Miami. RAK shares a retina fellowship training program with the University of Kentucky, participates in numerous clinical trials, and has helped pioneer anti-VEGF therapy for a variety of eye conditions. Dr. Kitchens is past president of the Kentucky Academy of Eye Physicians and Surgeons, a former member of the American Society of Retina Specialists executive board, and a founding member of the Vit-Buckle Society. He also serves as an examiner for the American Board of Ophthalmology.

Disclosures



Dr. Rich has no relevant affiliations or financial relationships with a commercial interest to disclose.

Dr. Kitchens has disclosed that he has received consulting fees from Alcon, Allergan, Bayer, Genentech, Kodiak, Optos, Regeneron, Roche, and Zeiss.

The clinical reviewer, **Alisa Escano, PharmD, BCPS**, has no relevant affiliations or financial relationships with a commercial interest to disclose.

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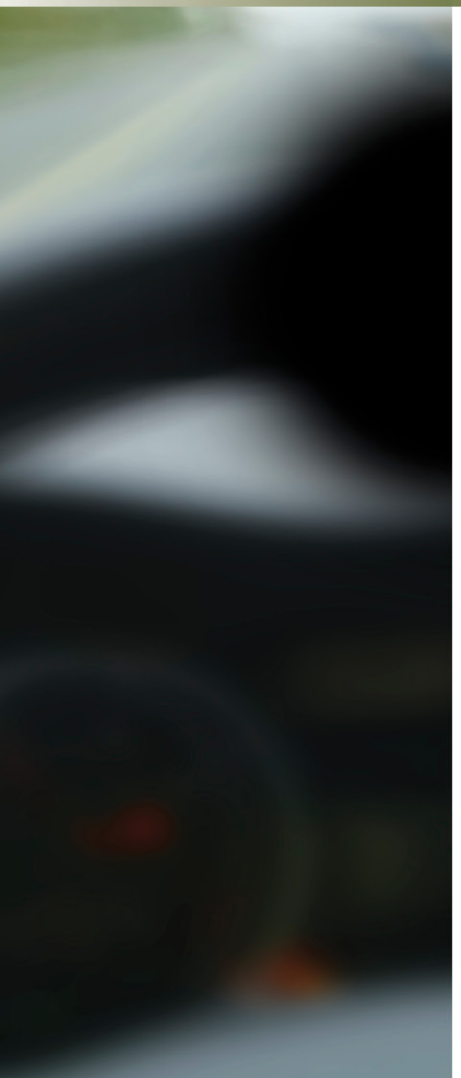
Accreditation



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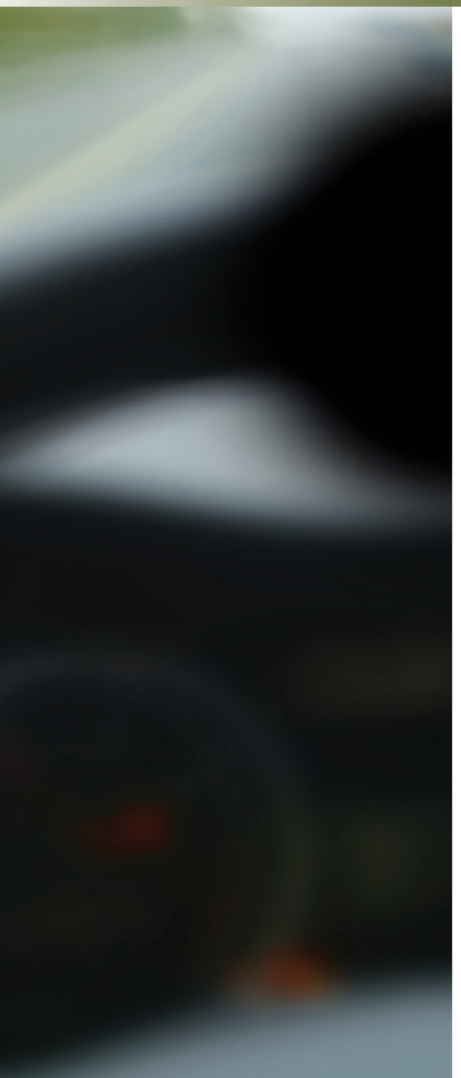
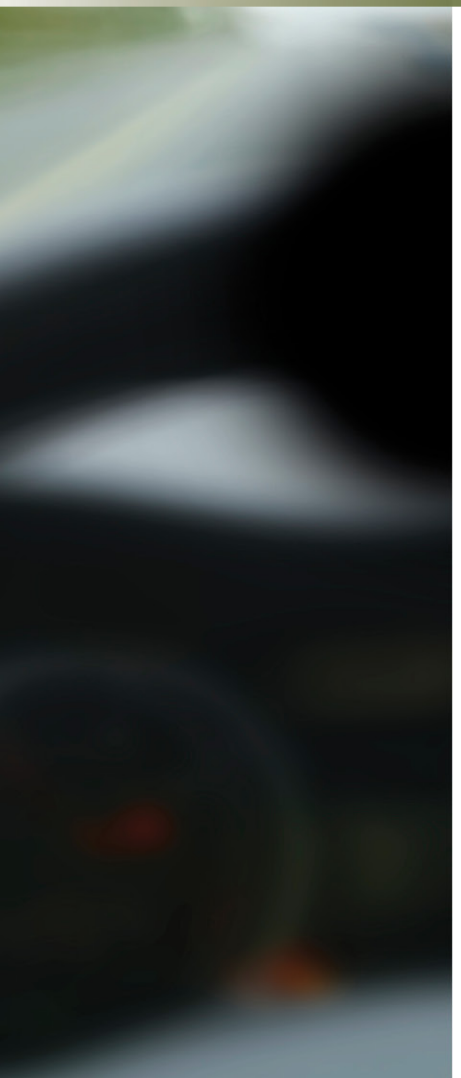
Type of Activity: Application

Learning Objectives



- **Describe** age-related macular degeneration (AMD) and diabetic macular edema (DME) and their impact on patient quality of life
- **Discuss** current and emerging treatment options for AMD and DME, including efficacy, safety, and relevant clinical trial data
- **Interpret** the rationale for using real-world evidence in treatment decision making for AMD and DME to optimize patient quality of life and outcomes
- **Recognize** approaches to assist in improving outcomes in AME and DME

Learning Objective #1



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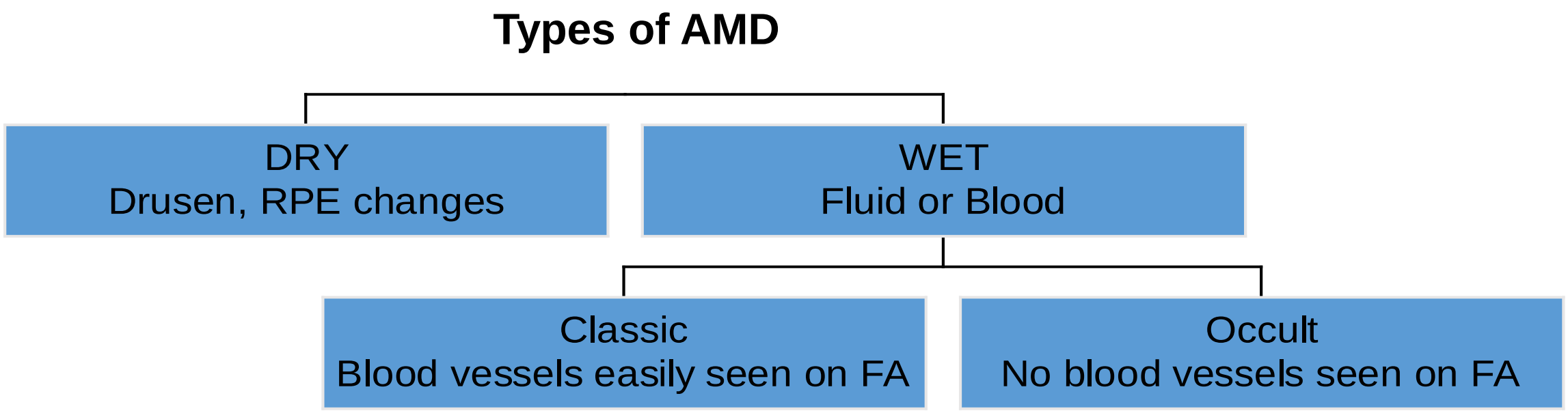
AMD and DME

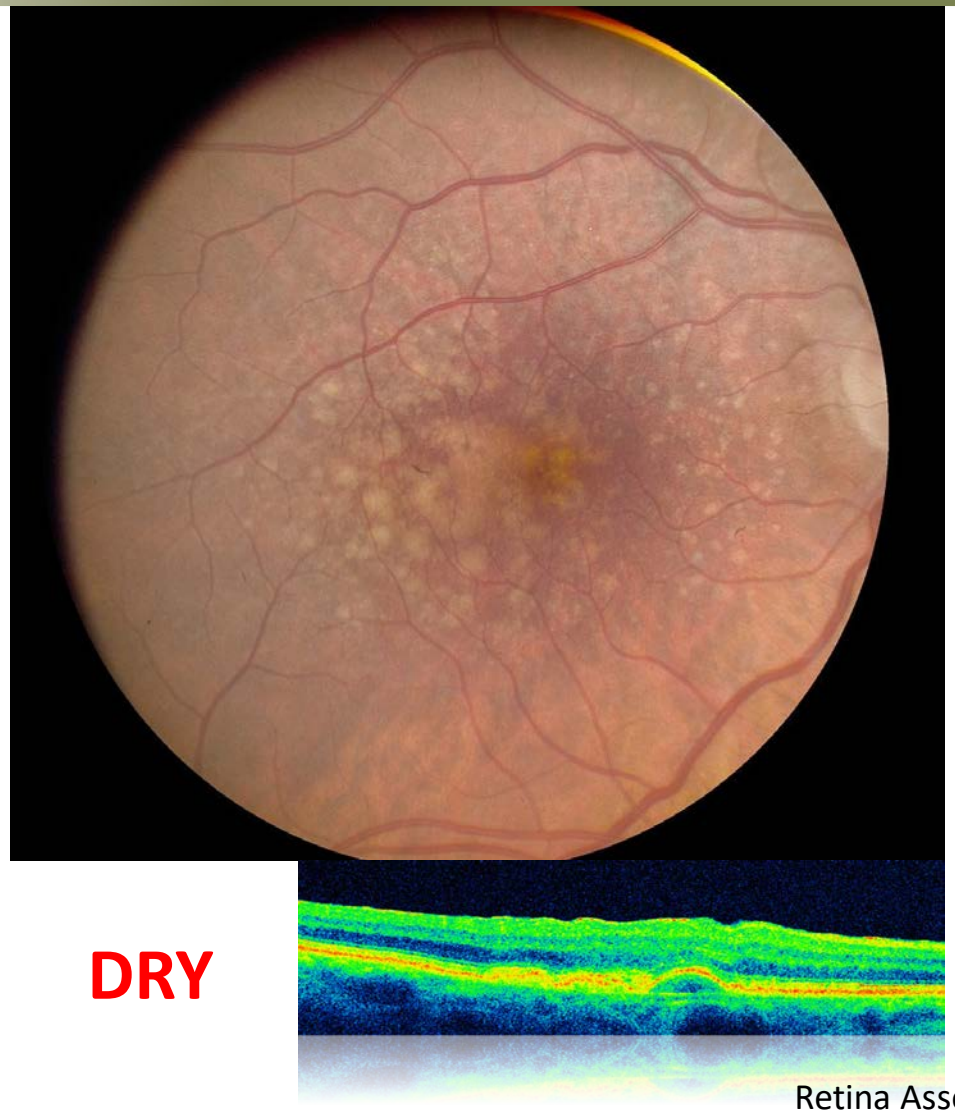
Age-Related Macular Degeneration (AMD)

Age-Related Macular Degeneration (AMD)

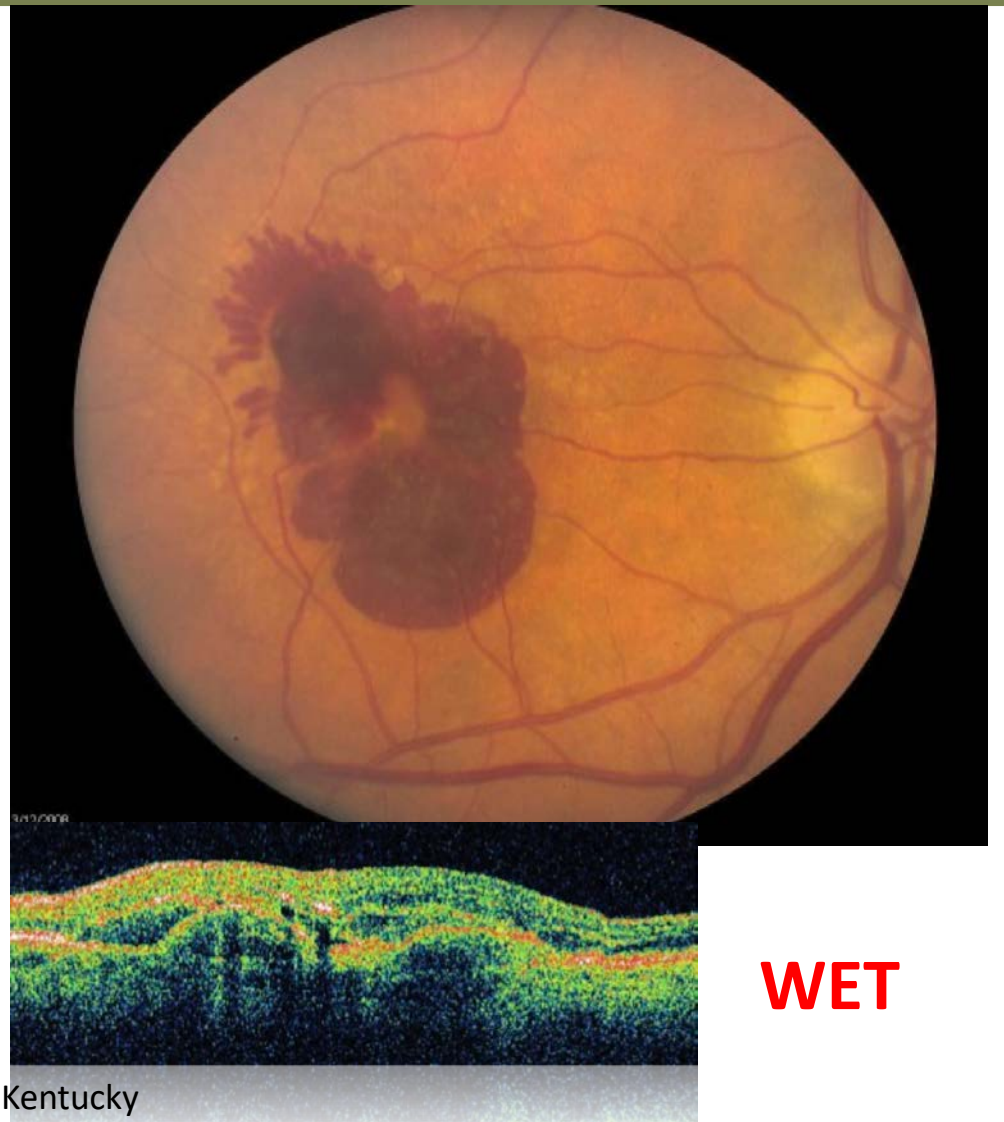


FA, fluorescein angiogram; RPE, retinal pigment epithelium.

Dry and Wet AMD

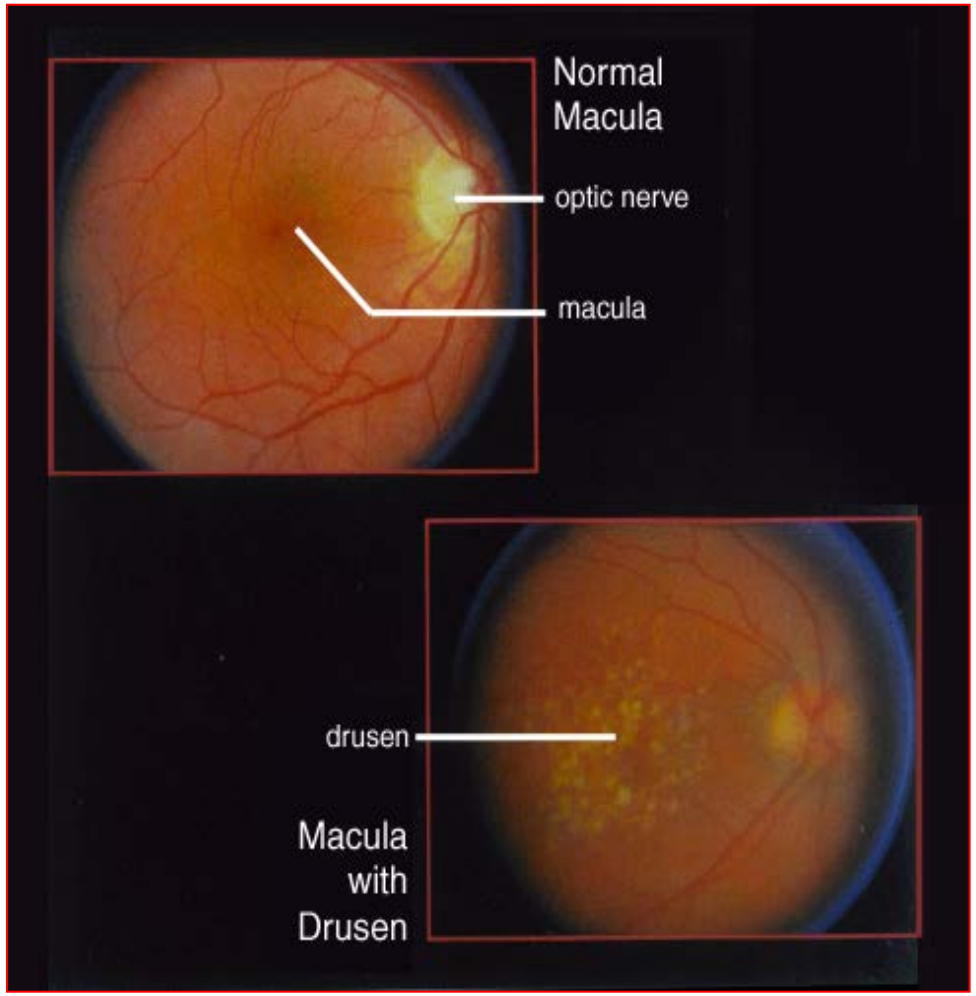


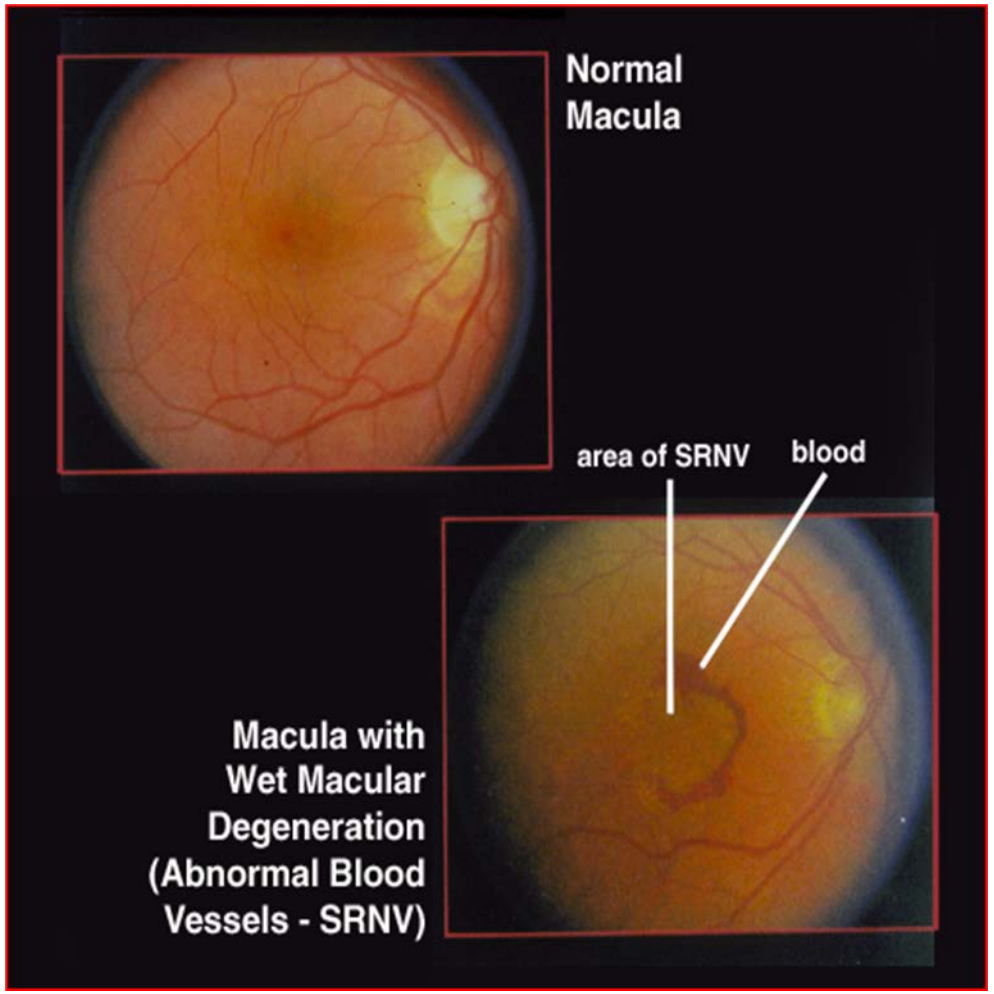
DRY



WET

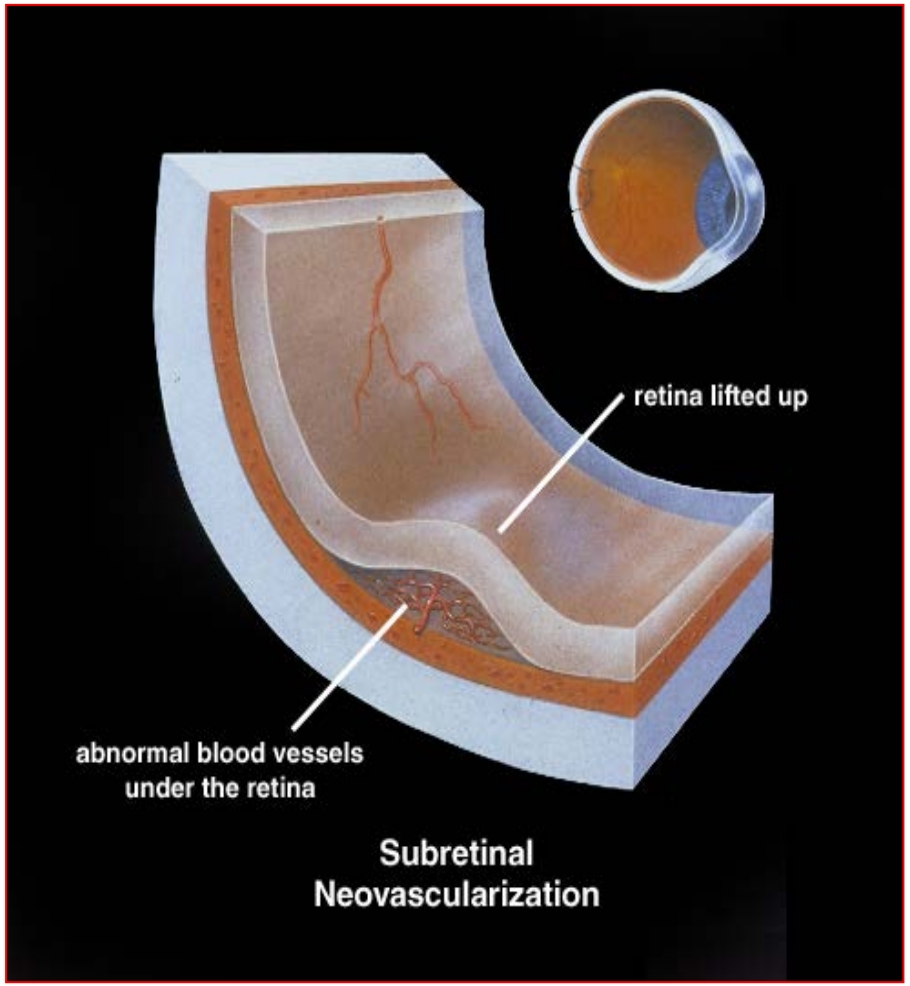
AMD and the Macula



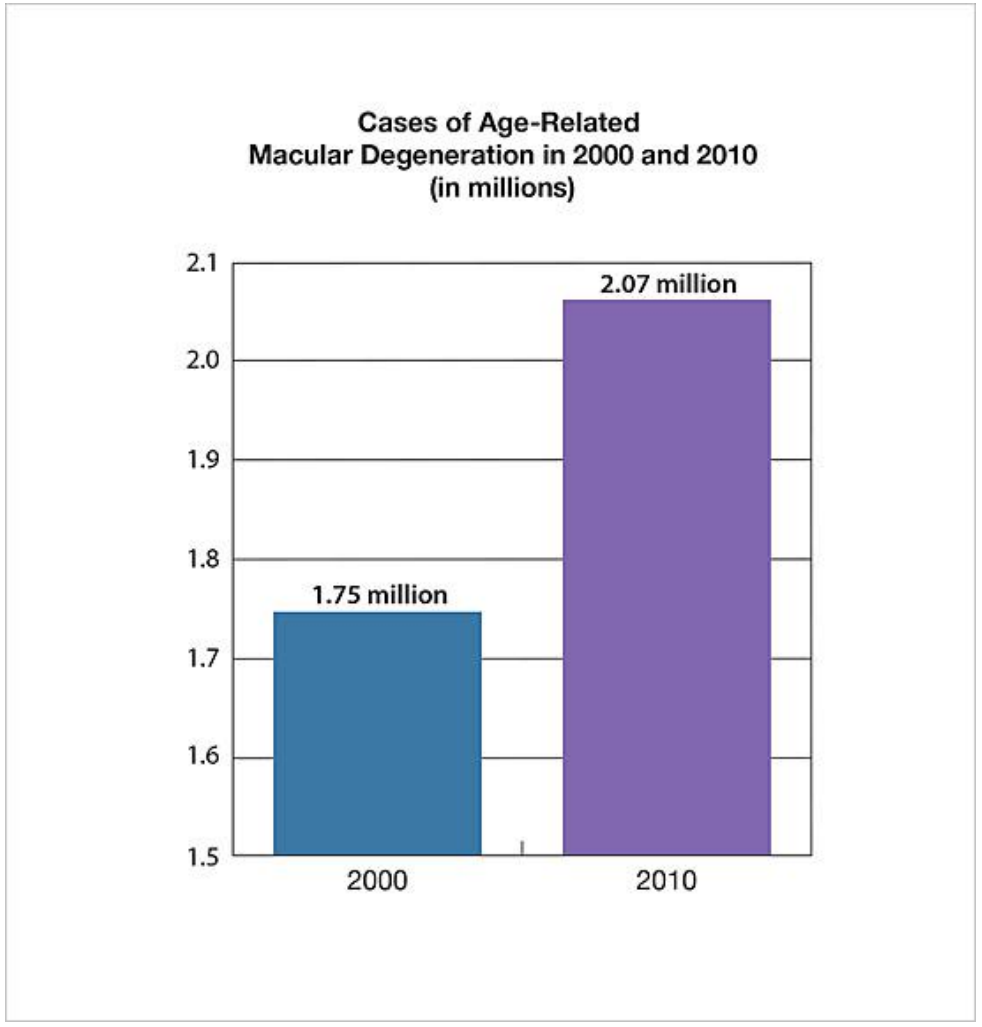


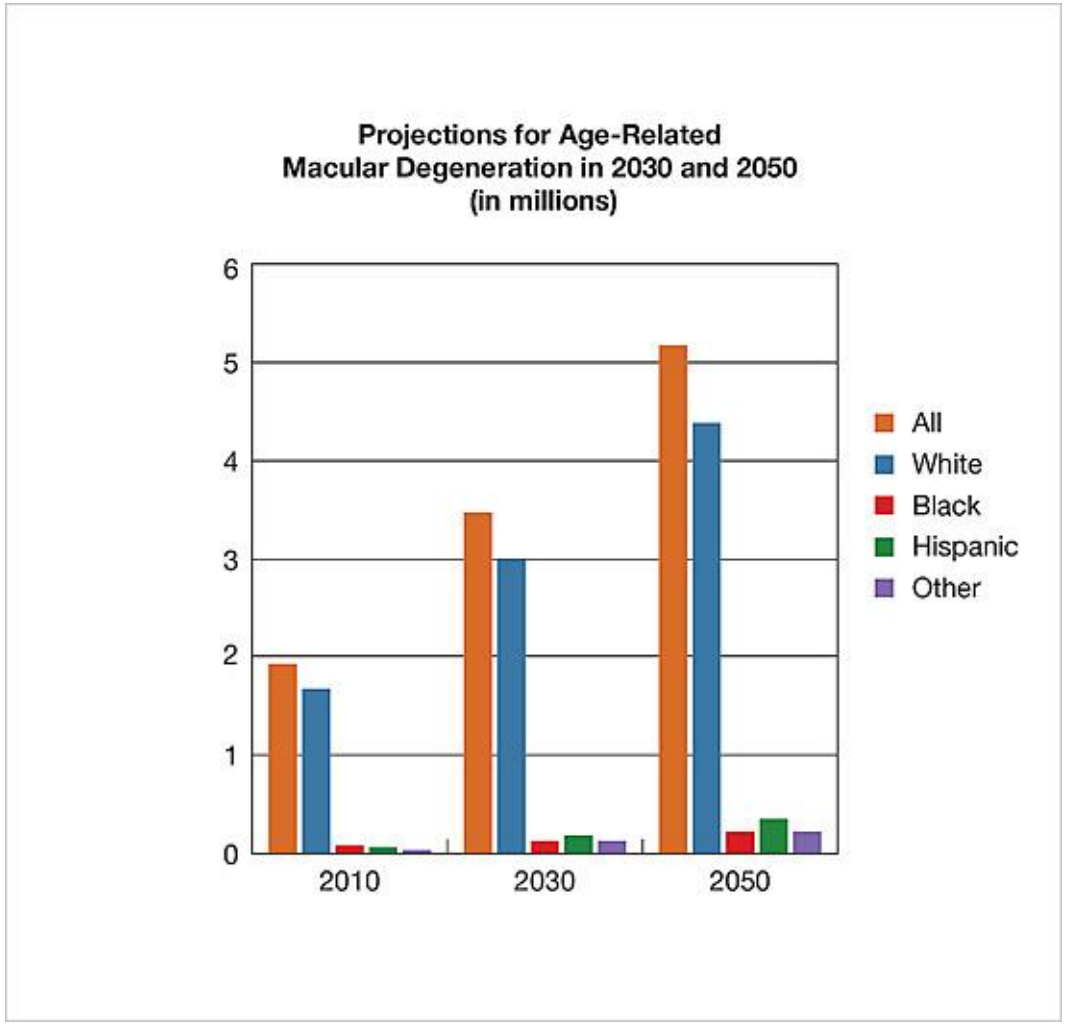
SRVN, subretinal neovascularization.

AMD and Subretinal Neovascularization

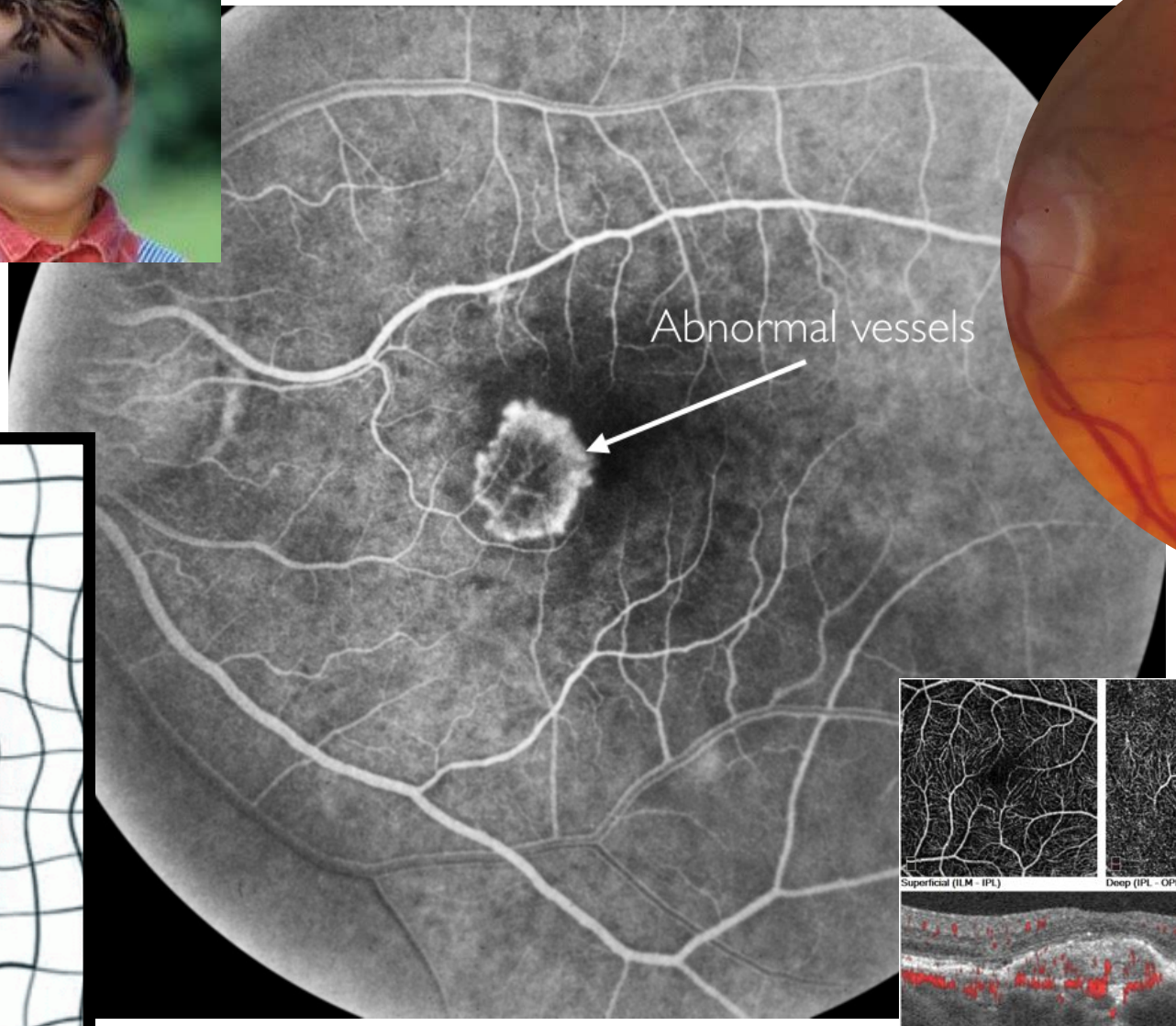


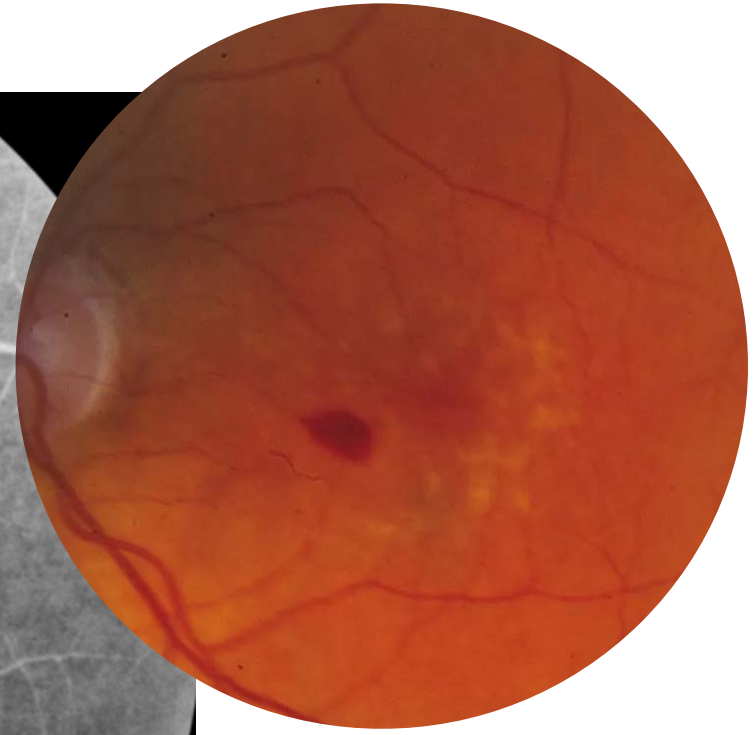
Projections of AMD in the US

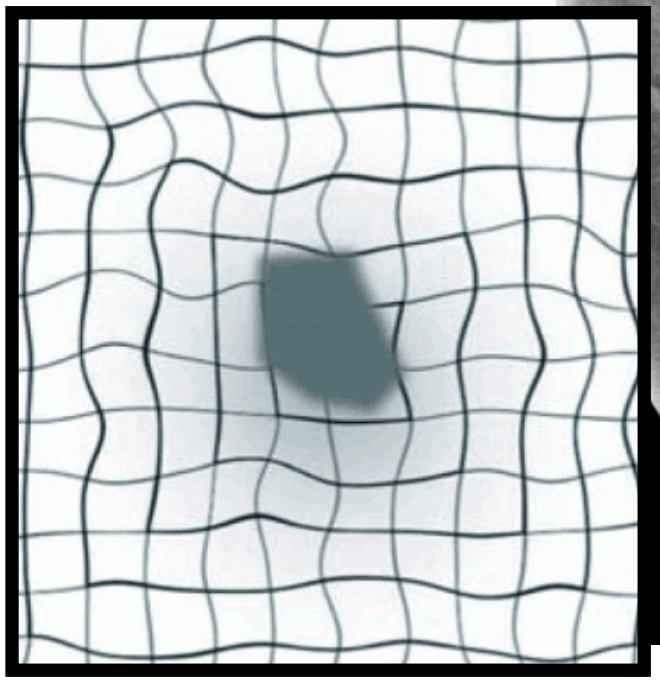


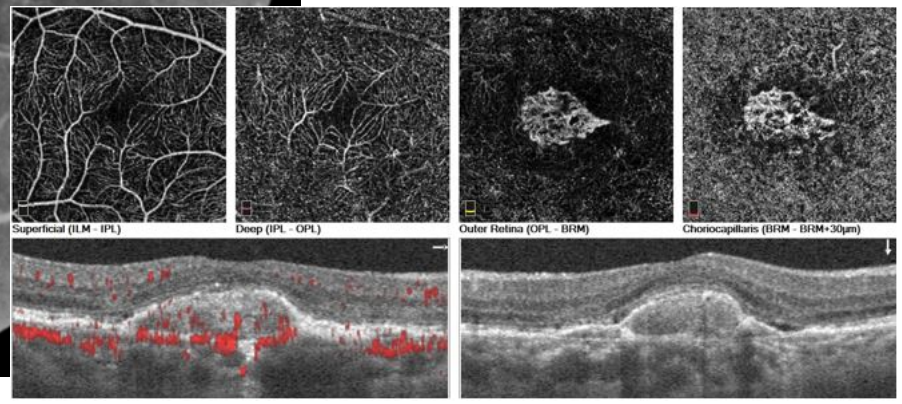


National Eye Institute. https://www.nei.nih.gov/learn-about-eye-health/outreach-campaigns-and-resources/eye-health-data-and-statistics/age-related-macular-degeneration-amd-data-and-statistics

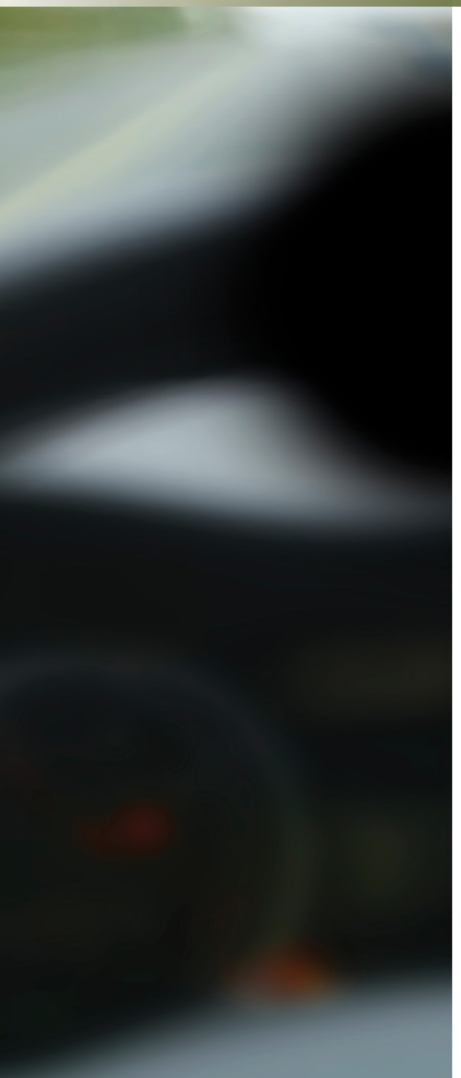

Abnormal vessels






Superficial (ILM - IPL)
Deep (IPL - OPL)
Outer Retina (OPL - BRM)
Choriocapillaris (BRM - BRM+30µm)

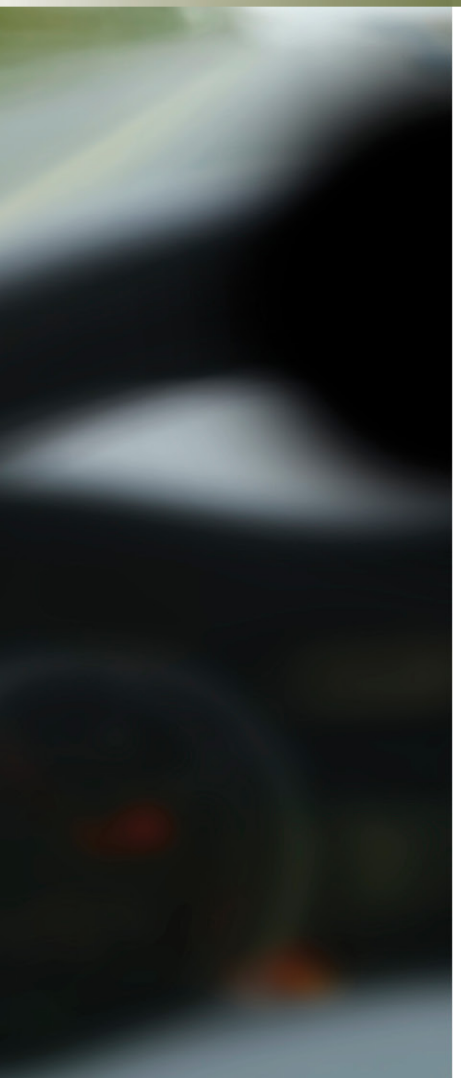
AMD Decreases Quality of Life



- Increased incidence of depression in advanced AMD[1] (depression increases mortality risk)
- Increased mortality risk among individuals with advanced AMD
- Greater need for assistance with activities of daily living versus older adults without AMD[2]

1. Brody BL, et al. *Ophthalmology*. 2001;108(10):1893.
2. Williams RA, et al. *Arch Ophthalmol*. 1998;116(4):514.

AMD Decreases Quality of Life

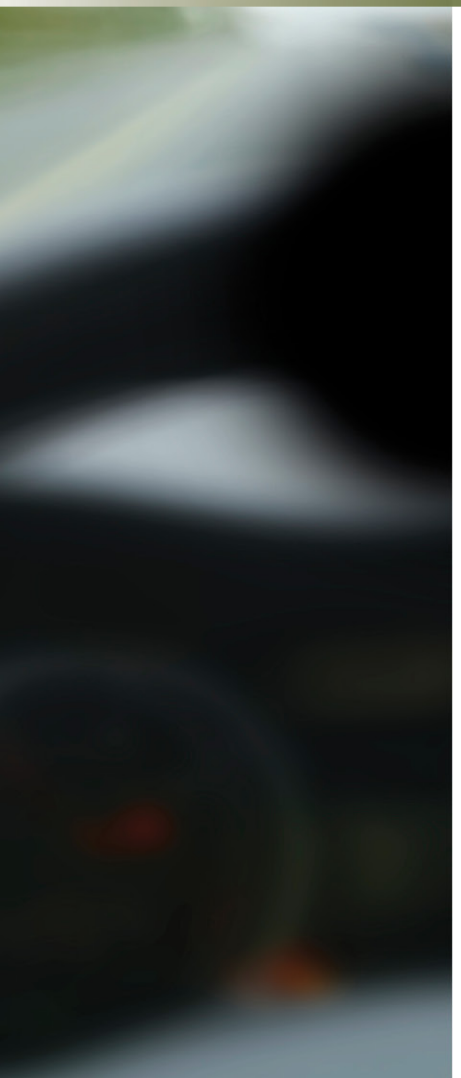


- Both intermediate and advanced AMD negatively impact quality of life[1,2]
  - General vision
  - Near activities
  - Distance vision
  - Driving
  - Mental health
  - Role difficulties
  - Dependency
  - Peripheral vision

1. Berdeaux GH, et al. *Am J Ophthalmol*. 2005;139(2):271.
2. Clemons TE, et al. *Arch Ophthalmol*. 2003;121(2):211.

Diabetic Macular Edema (DME)

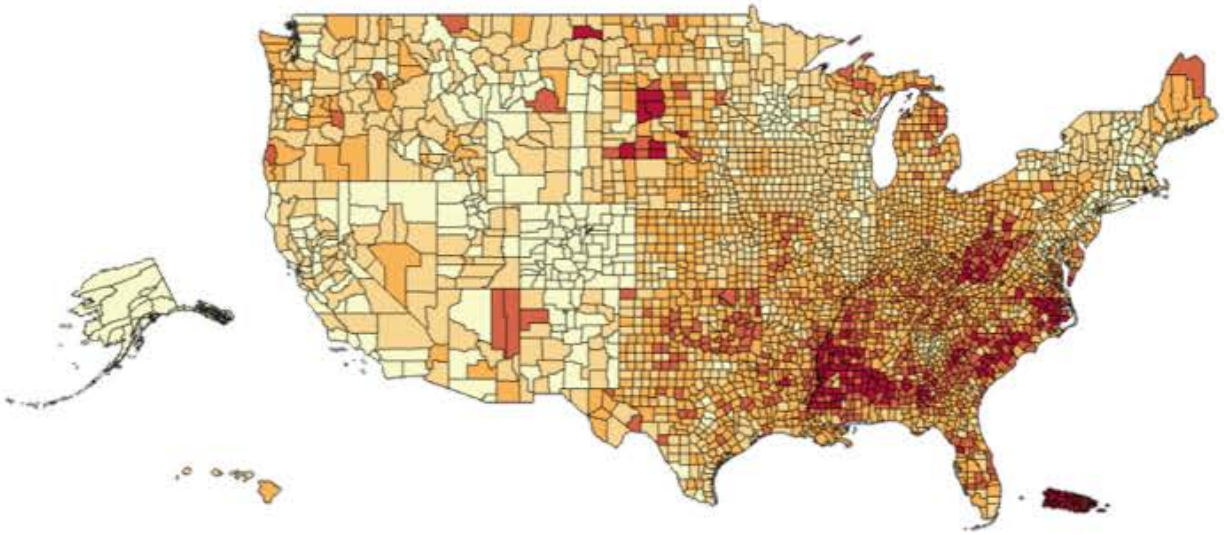
Prevalence of Diabetes in the US



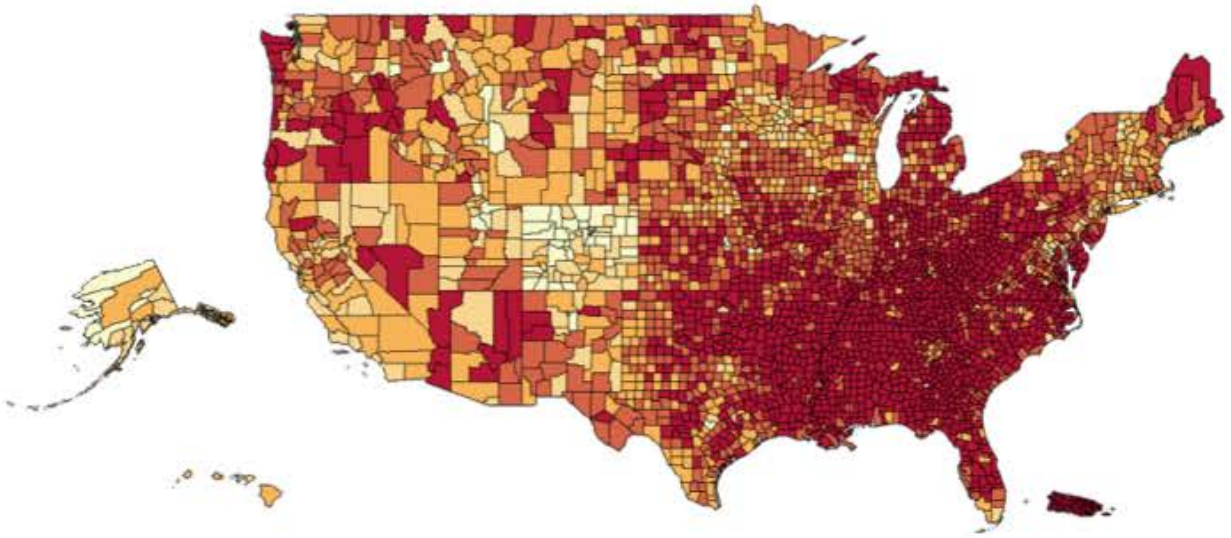
- Approximately 37.3 million people of all ages (11.3% of the US population) had diabetes in 2019
- 8.5 million people have undiagnosed diabetes
- In adults, there are race/ethnicity differences
  - American Indians/Alaska Natives have highest prevalence of diagnosed diabetes (14.5%)
  - Non-Hispanic Blacks (12.1%) and Hispanics (11.8%) have higher prevalence than non-Hispanic Whites (7.4%) and Asians (9.5%)
- Varies based on socioeconomic status and education level
- **ALL** people with diabetes are at risk of developing eye complications
- About 1 in 3 people with diabetes have **diabetic retinopathy (DR)**

CDC. *National Diabetes Statistics Report 2022.* Accessed June 1, 2022. https://www.cdc.gov/diabetes/data/statistics-report/index.html

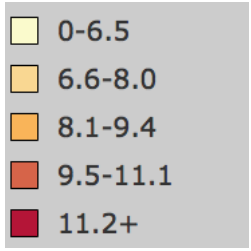
Increasing Prevalence of Diagnosed Diabetes Among Adults 20 Years or Older



2004



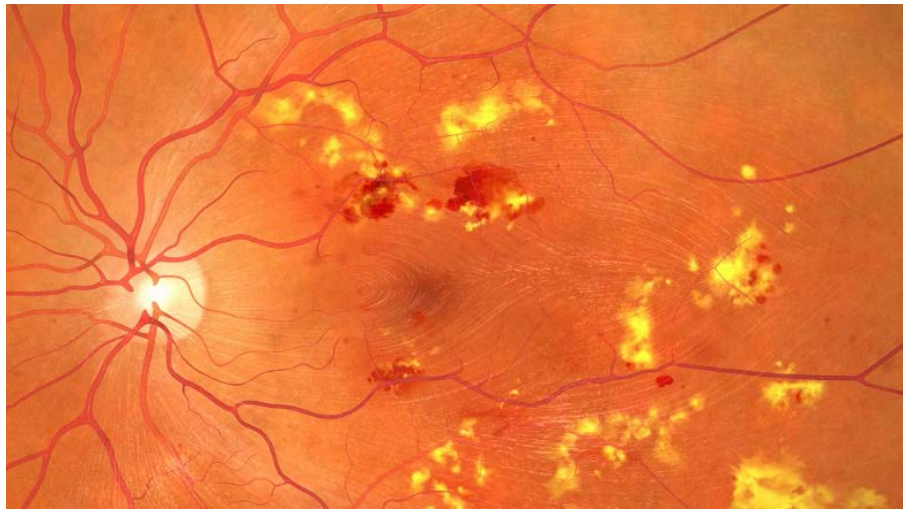
2018

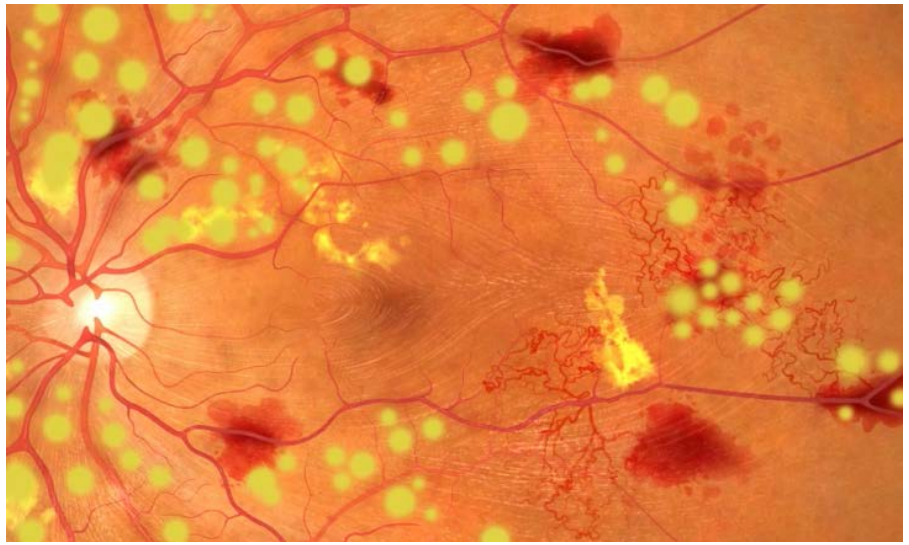


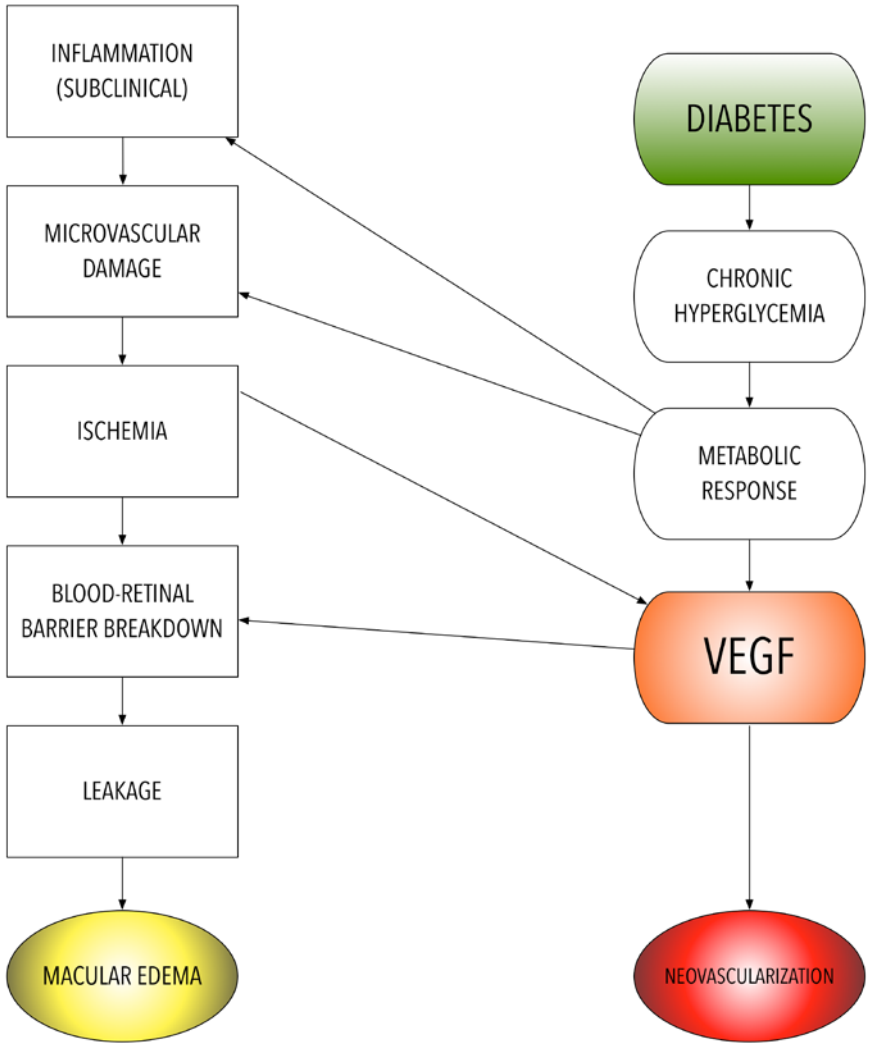
Diagnosed diabetes %

CDC. *National Diabetes Statistics Report 2020*.

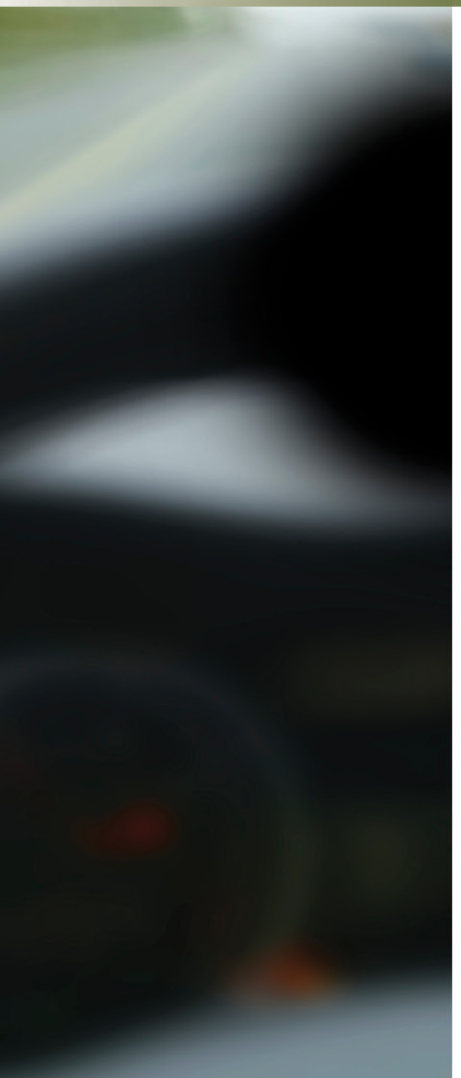
Pathophysiology of Diabetic Retinopathy





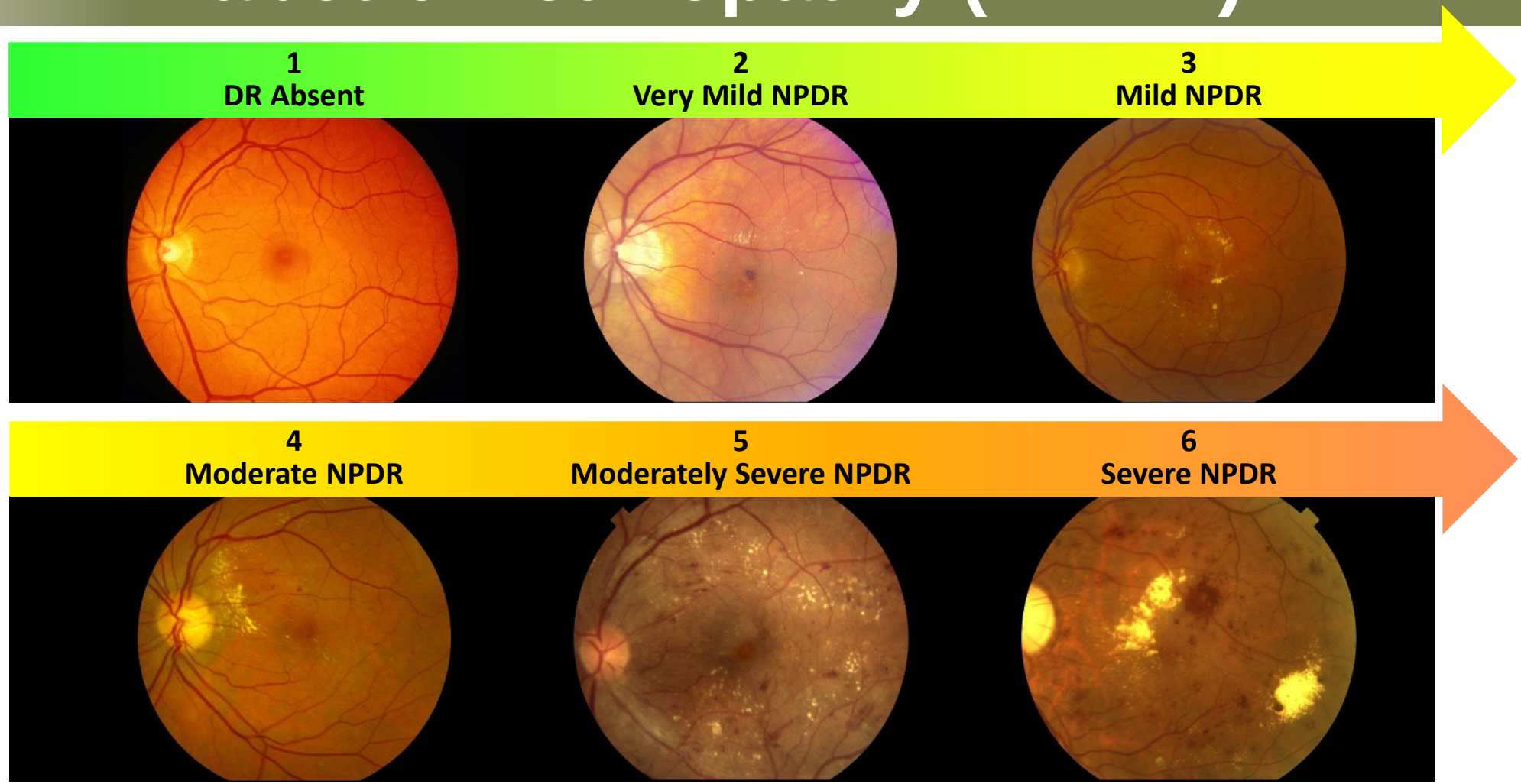


Etiology and Pathogenesis of DR and DME



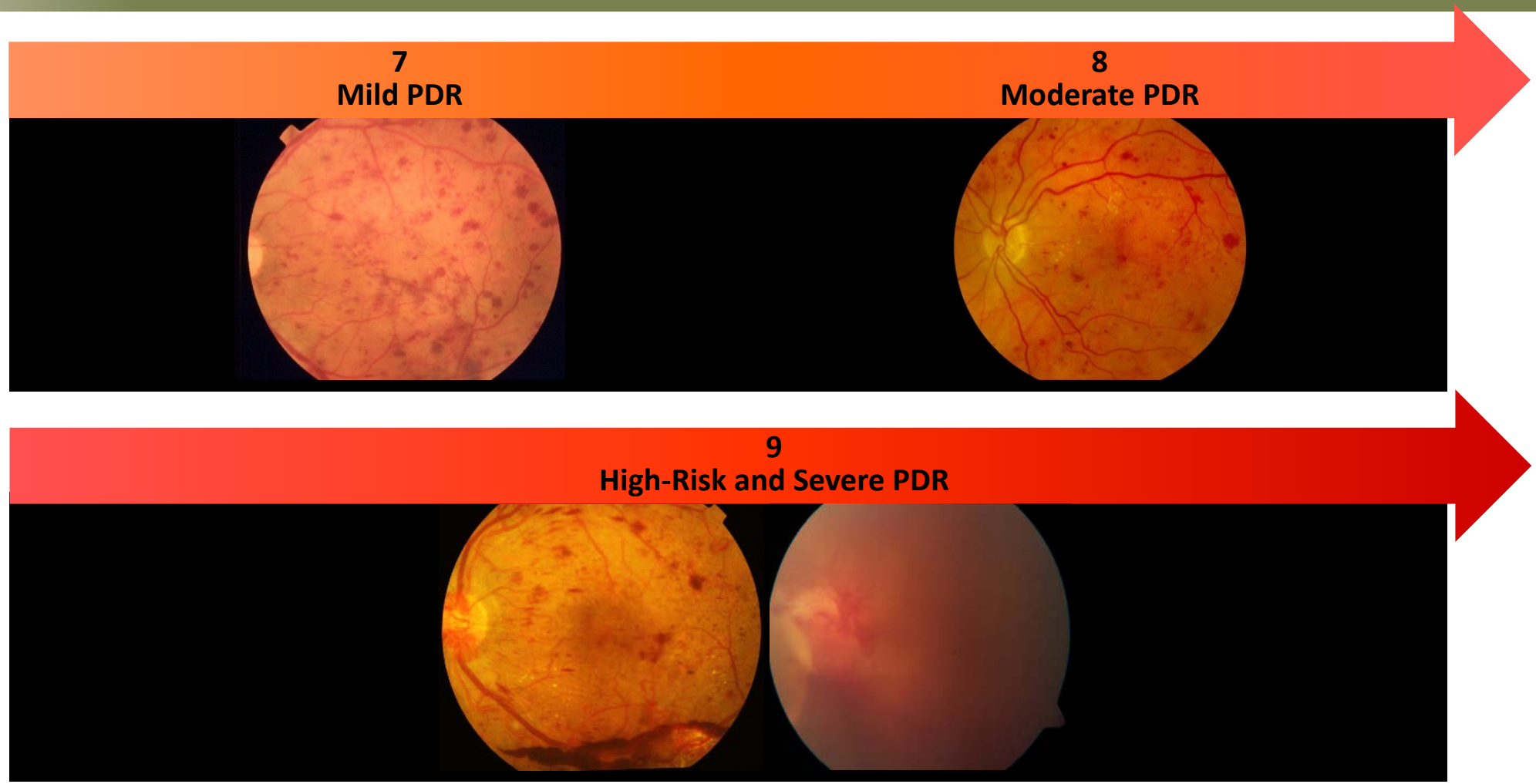
- Chronic exposure to hyperglycemia triggers biochemical and physiological changes, resulting in microvascular damage
- DR is a microvascular complication of diabetes that leads to the development of leaky blood vessels in the retina
- Chemical inflammatory cytokines, including vascular endothelial growth factor (VEGF), play a critical role in the onset of DR and DME
- As DR develops, there may be bleeding (DR) in the retina as well as increased fluid in the macula (DME)
- Patients may have DR and DME without experiencing deficiencies in visual acuity
  - More impairment in central vision with higher permeability in blood vessels
  - Thickening and swelling of macula distorts vision

Nonproliferative Diabetic Retinopathy (NPDR)



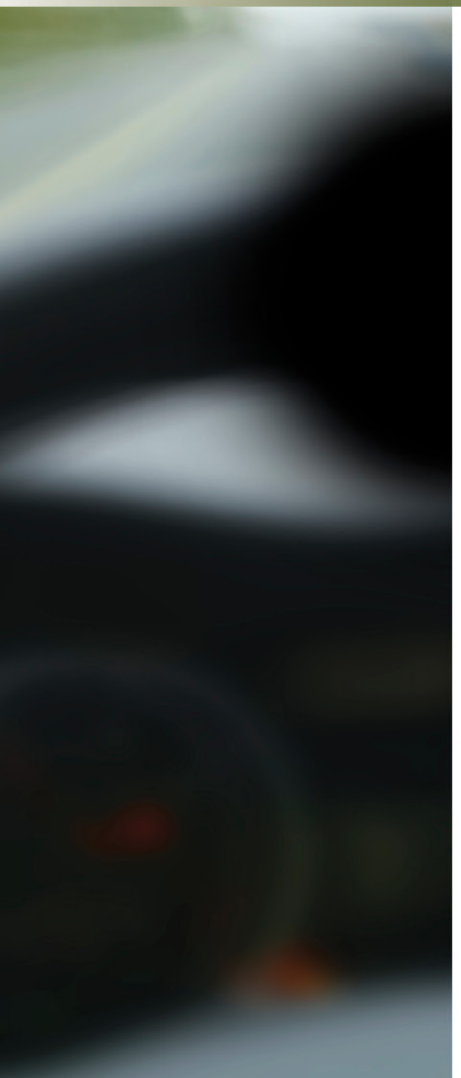
1. ETDRS. *Ophthalmology*. 1991;98(5 suppl):823. 2. Ip MS, et al. *Arch Ophthalmol*. 2012;130(9):1145. 3. Scott IU, et al. *Diabetes and Ocular Disease.* 2nd ed. Oxford University Press; 2010.

Proliferative Diabetic Retinopathy (PDR)



1. ETDRS. *Ophthalmology*. 1991;98(5 suppl):823. 2. Ip MS, et al. *Arch Ophthalmol*. 2012;130(9):1145. 3. Scott IU, et al. *Diabetes and Ocular Disease.* 2nd ed. Oxford University Press; 2010.

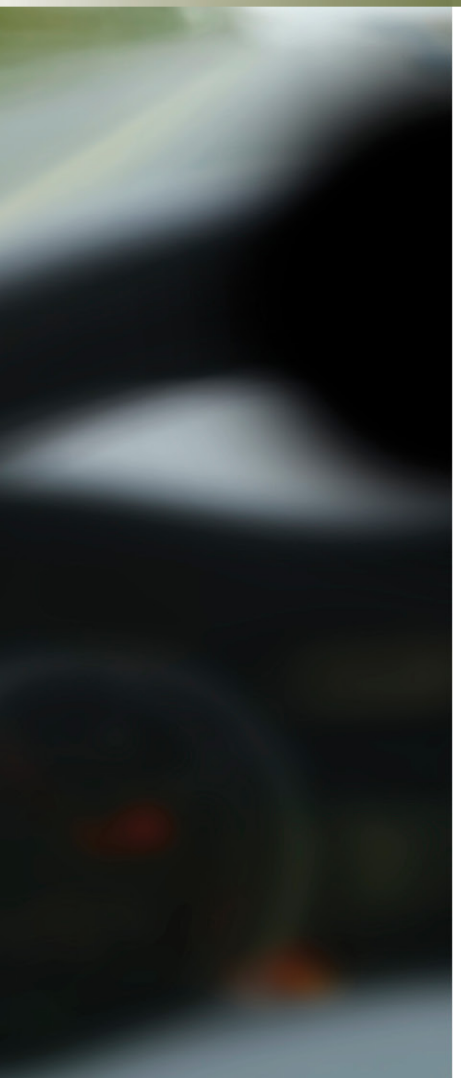
Disease Burden of DR and DME



- Often patients have other chronic diseases as well (eg, depression, cardiovascular disease)
- Vision-related functional burden is high in people with more severe eye disease
  - Approximately 50% have difficulty with at least 1 visual function task (eg, driving, reading, walking)
- Prevention is important to stop progression in this at-risk population
  - As many as 50% of patients are not getting their eyes examined or are diagnosed too late for treatment to be effective

National Center for Chronic Disease Prevention and Health Promotion. CDC. *National Diabetes Statistics Report, 2017*. National Eye Institute. Accessed April 8, 2021. https://nei.nih.gov/health/diabetic/retinopathy

Learning Objective #2



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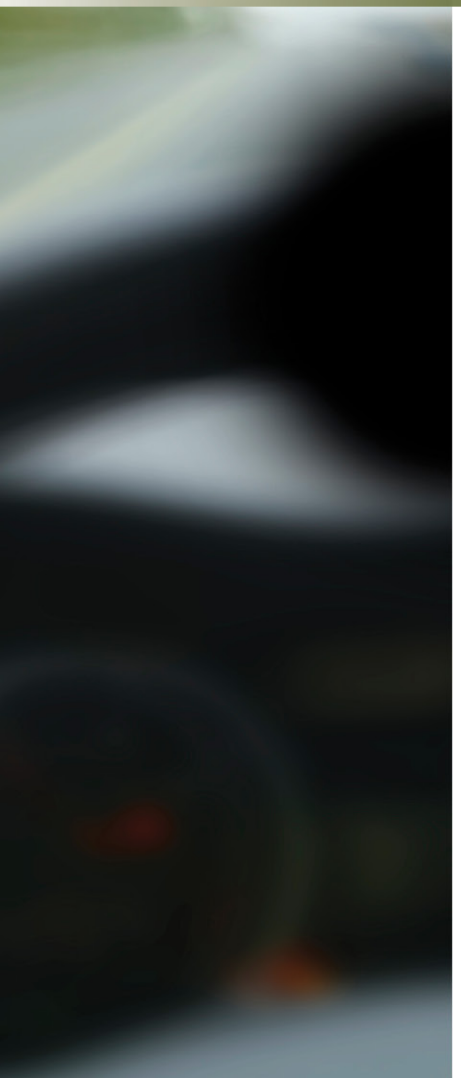
Treatment Options

Wet AMD and DR/DME

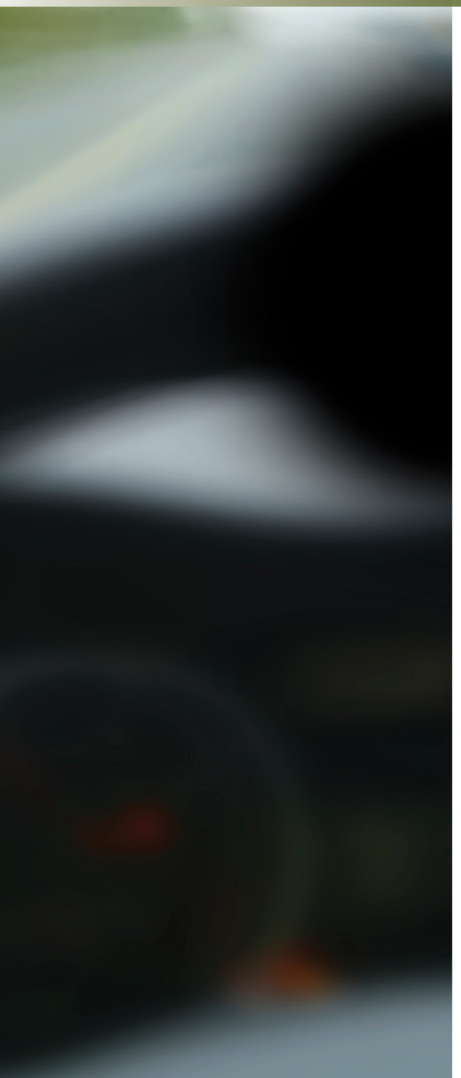
Treatment Options for Wet AMD



- Anti-VEGF therapy
  - Bevacizumab (off-label)
  - Ranibizumab
  - Aflibercept
  - Brolicizumab
  - Faricimab
- Photodynamic therapy
  - Verteporfin
- Thermal laser treatment

VEGF, vascular endothelial growth factor.

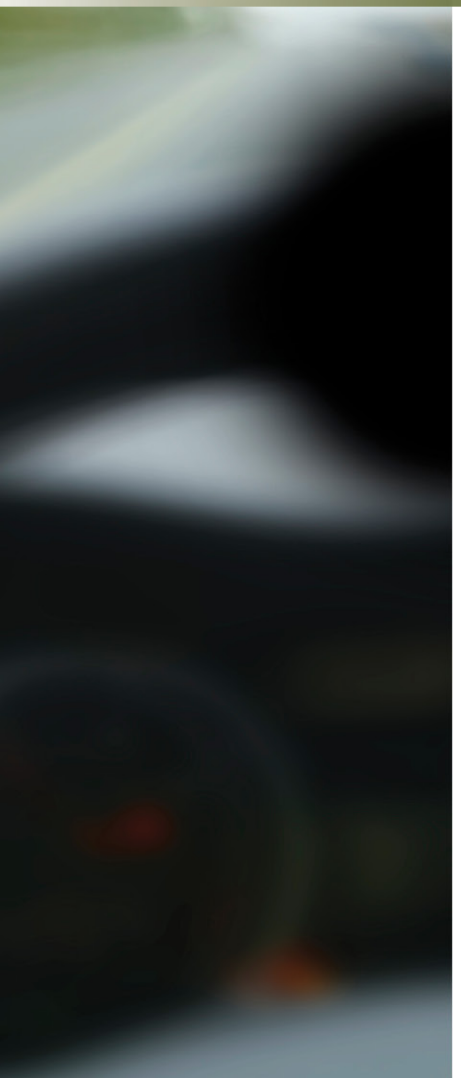
Treatment Options for DR and DME



- Blood glucose control (prevention)
- Laser therapy
  - Focal laser
  - Panretinal laser
- Steroid therapy
  - Intravitreal
  - Sub-Tenon
- Anti-VEGF therapy
  - Bevacizumab (DME)
  - Ranibizumab (DR/DME)
  - Aflibercept (DR/DME)
  - Faricimab (DME)

Intravitreal Anti-VEGF Therapies

Anti-VEGF Current Therapies



- Bevacizumab
- Ranibizumab
  - PDS vs monthly injections
- Aflibercept
- Brolucizumab
- Faricimab
  - Extended interval treatment

PDS, Port Delivery System with ranibizumab.

Bevacizumab (Avastin)

Optical Coherence Tomography Findings After an Intravitreal Injection of Bevacizumab (Avastin®) for Neovascular Age-Related Macular Degeneration

Philip J. Rosenfeld, MD, PhD
Andrew A. Moshfeghi, MD
Carmen A. Puliafito, MD, MBA

Abstract. To determine whether intravitreal bevacizumab could improve optical coherence tomography and visual acuity outcomes in a patient with neovascular age-related macular degeneration who was responding poorly to pegaptanib therapy, an intravitreal injection of bevacizumab (1.0 mg) was given. Within 1 week, optical coherence tomography revealed resolution of the subretinal fluid, resulting in a normal-appearing age-related macular degeneration who are losing vision secondary to macular neovascularization. **[Ophthalmic Surg Lasers Imaging 2005;36:331-335.]**

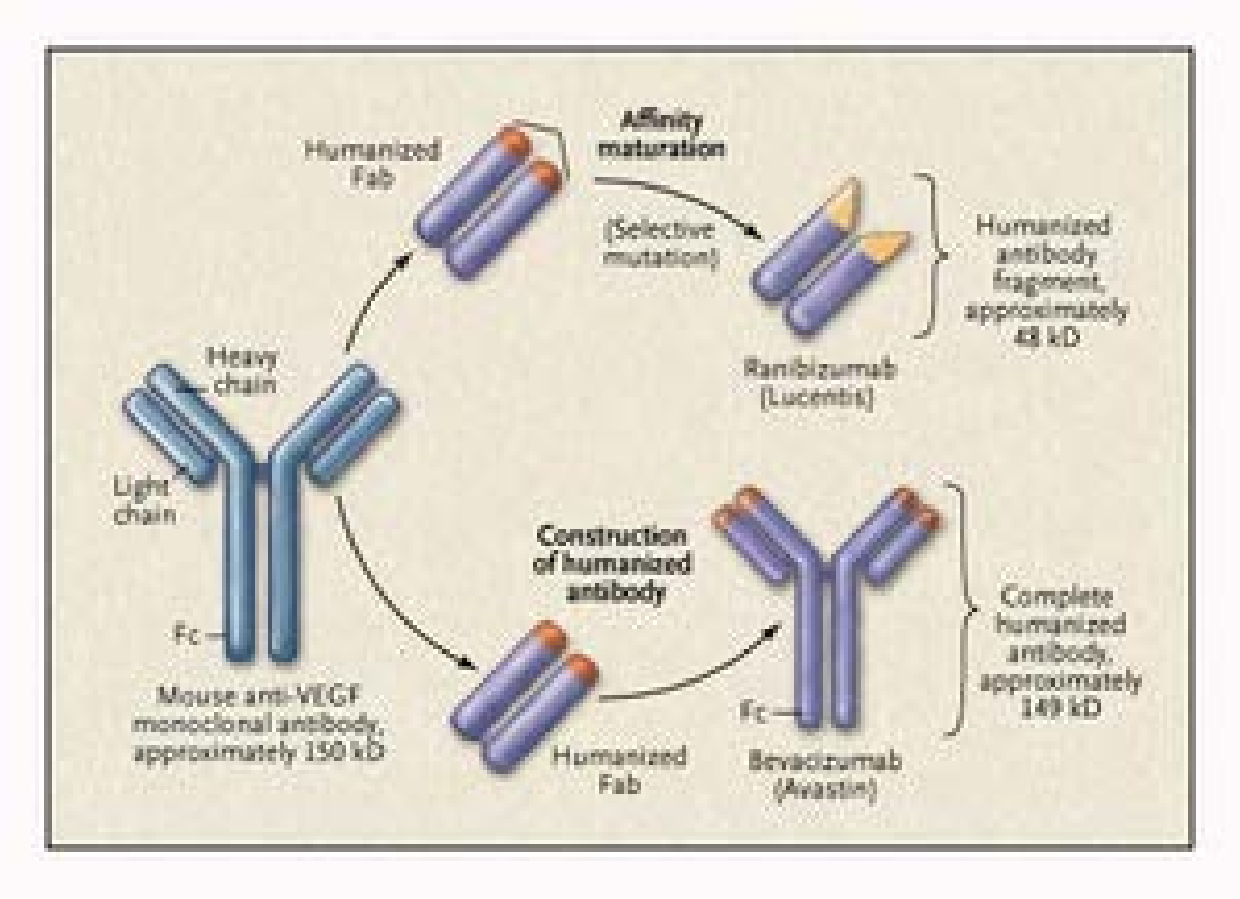
INTRODUCTION

Vascular endothelial growth factor (VEGF) has been implicated as the major angiogenic stimulus responsible for neovascularization in age-related macular degeneration (AMD).[1,2] Inhibition of VEGF using intravitreal injections of pegaptanib sodium (Macugen; Eyetech Pharmaceuticals, Inc., New York, NY) was superior to sham-treated controls in a Phase II/III trial, but the average patient treated with pegaptanib still lost vision.[3] Ranibizumab (Lucentis; Genentech Inc., San Francisco, CA) is another inhibitor of VEGF designed specifically for ophthalmology and is currently in Phase III clinical trials for neovascular AMD.[4] Ranibizumab is derived from a larger molecule known as bevacizumab (Avastin; Genentech Inc.), which was designed as an intravenous anti-angiogenic drug for oncology.[5]

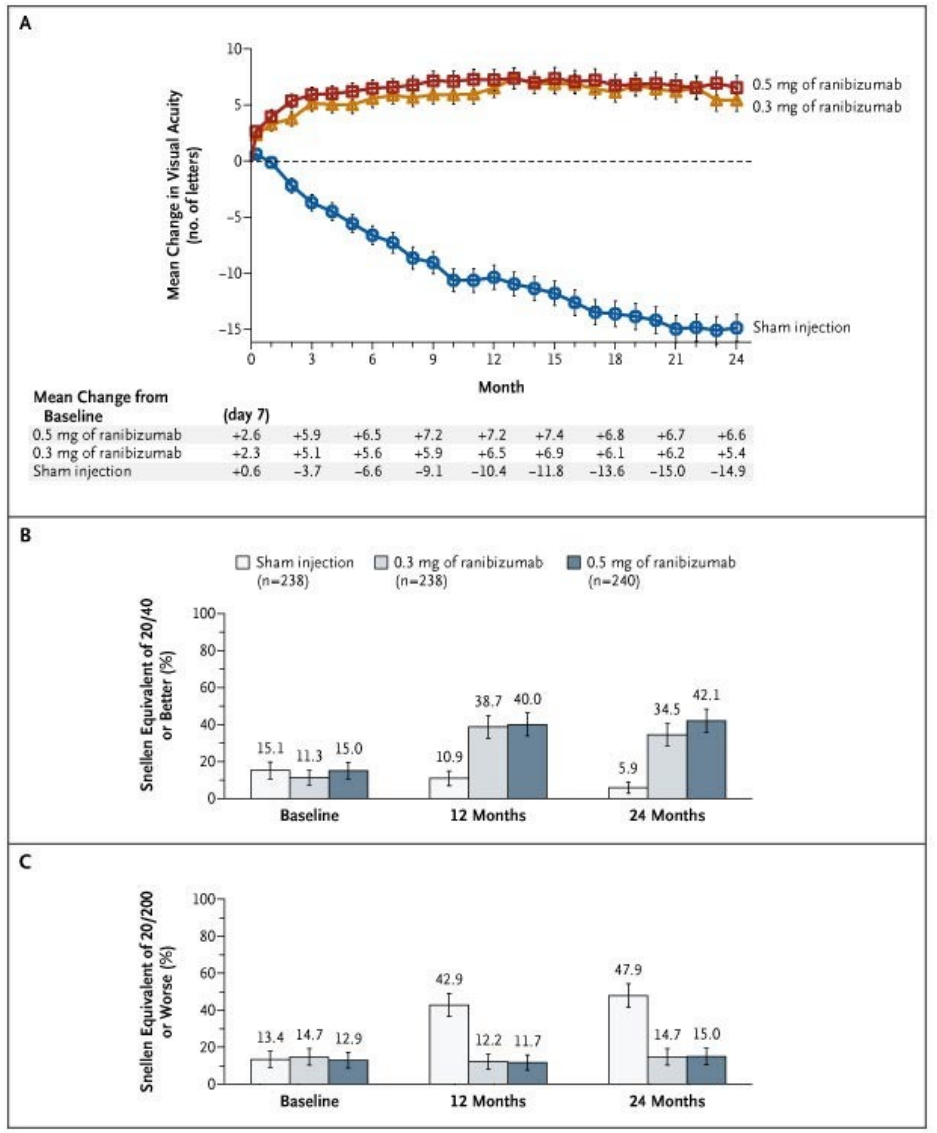
Bevacizumab is approved for the treatment of metastatic colorectal cancer, and a study using off-label intravenous bevacizumab for neovascular AMD showed

Rosenfeld PJ, et al. *Ophthalmic Surg Lasers Imaging*. 2005;36(4):331.

Ranibizumab (Lucentis)



Steinbrock R, et al. *N Engl J Med*. 2006;355(14):1409.

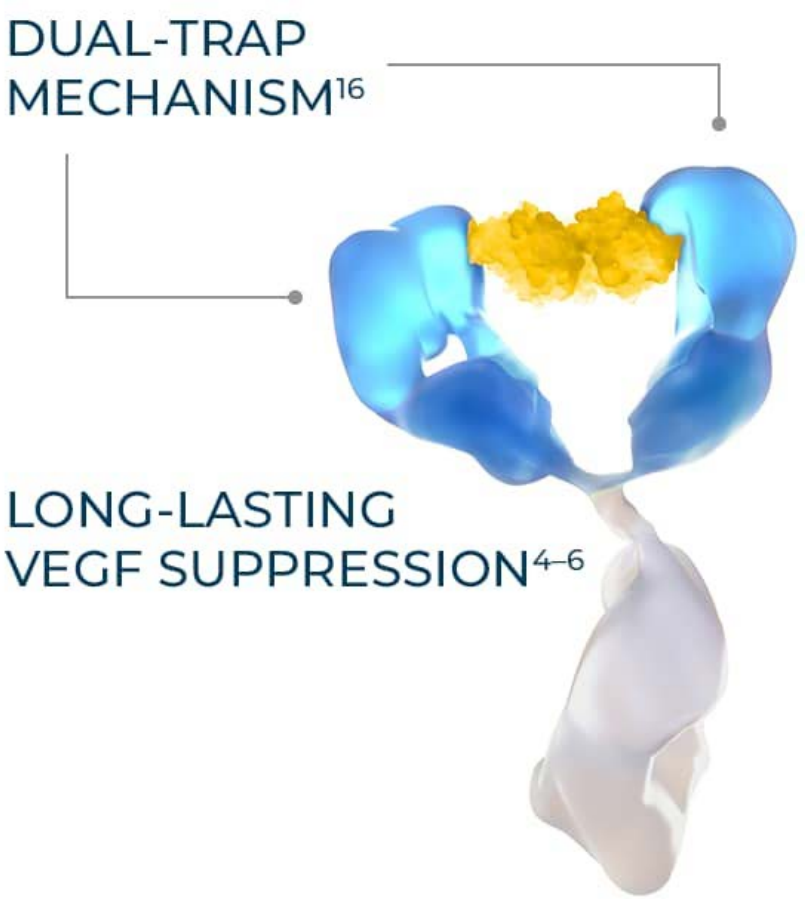


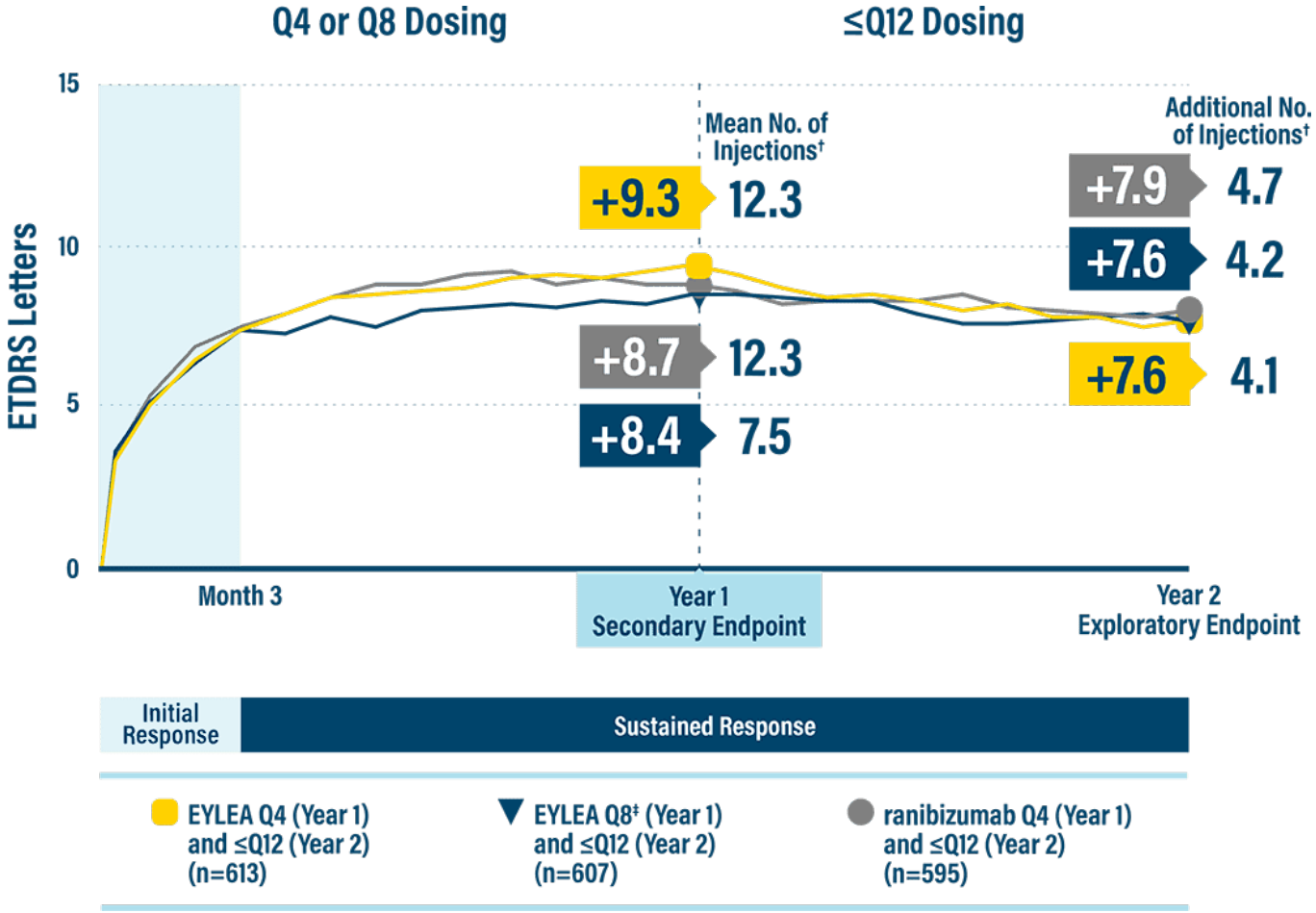
Mean Change from Baseline

	(day 7)								
0.5 mg of ranibizumab	+2.6	+5.9	+6.5	+7.2	+7.2	+7.4	+6.8	+6.7	+6.6
0.3 mg of ranibizumab	+2.3	+5.1	+5.6	+5.9	+6.5	+6.9	+6.1	+6.2	+5.4
Sham injection	+0.6	−3.7	−6.6	−9.1	−10.4	−11.8	−13.6	−15.0	−14.9

Rosenfeld PJ, et al. *N Engl J Med*. 2006;355(14):1419.

Aflibercept (Eylea)

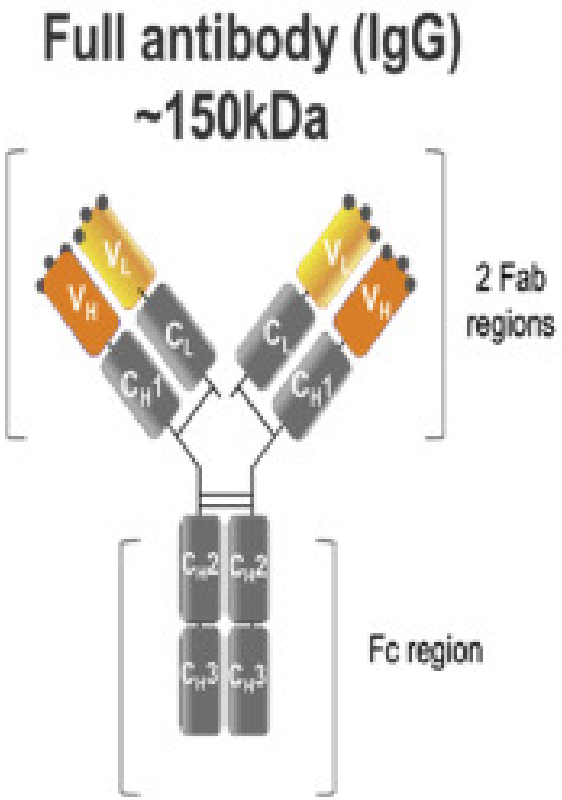




Schimdt-Erfueth U, et al. *Ophthalmology*. 2014;121(1):193.
Khurana RN, et al. *Am J Ophthalmol.* 2019;200:161.

ETDRS, Early Treatment Diabetic Retinopathy Study.

Brolucizumab (Beovu)



Comprises only the antibody variable domains VL and VH that are responsible for binding to its target (joined by a short flexible linker peptide)

Fab, fragment antigen binding; Fc, fragment crystallizable; IgG, immunoglobulin G; kDa, 1000 daltons; scFv, single-chain variable fragment; VH, heavy chain variable domain; VL, light chain variable domain.

Nguyen QD, et al. *Ophthalmology*. 2020;127(7):963.

Brolucizumab (Beovu)

AMERICAN ACADEMY OF OPHTHALMOLOGY®

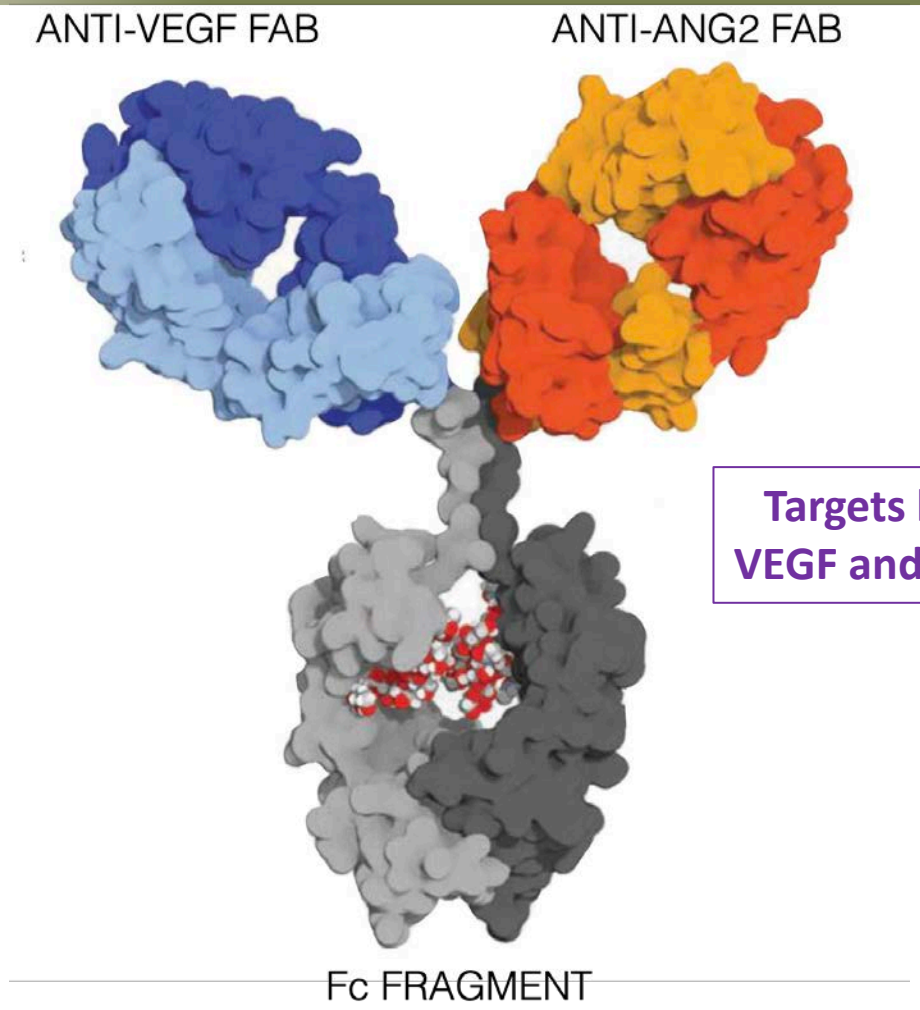
Risk of Inflammation, Retinal Vasculitis, and Retinal Occlusion–Related Events with Brolucizumab

Post Hoc Review of HAWK and HARRIER

Jordi Monés, MD, PhD,[1] Sunil K. Srivastava, MD,[2] Glenn J. Jaffe, MD,[3] Ramin Tadayoni, MD, PhD,[4,5] Thomas A. Albini, MD,[6] Peter K. Kaiser, MD,[2] Frank G. Holz, MD,[7] Jean-Francois Korobelnik, MD,[8,9] Ivana K. Kim, MD,[10] Christian Pruente, MD,[11,12,13] Timothy G. Murray, MD, MBA,[14] Jeffrey S. Heier, MD[15]

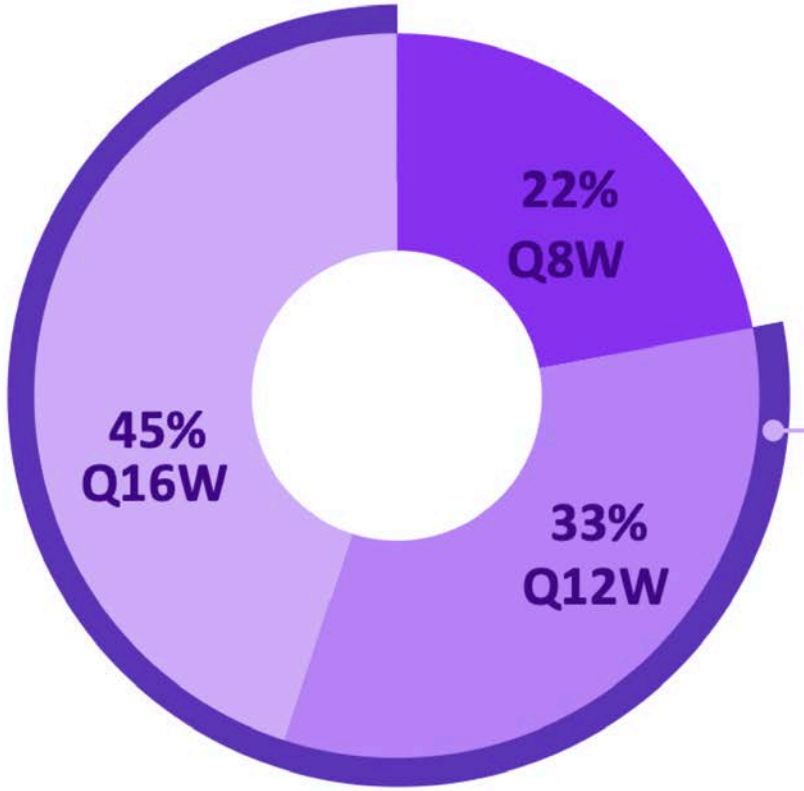
Monés J, et al. *Ophthalmology*. 2020;128(7):1050.

Faricimab (Vabysmo)



Targets both VEGF and Ang-2

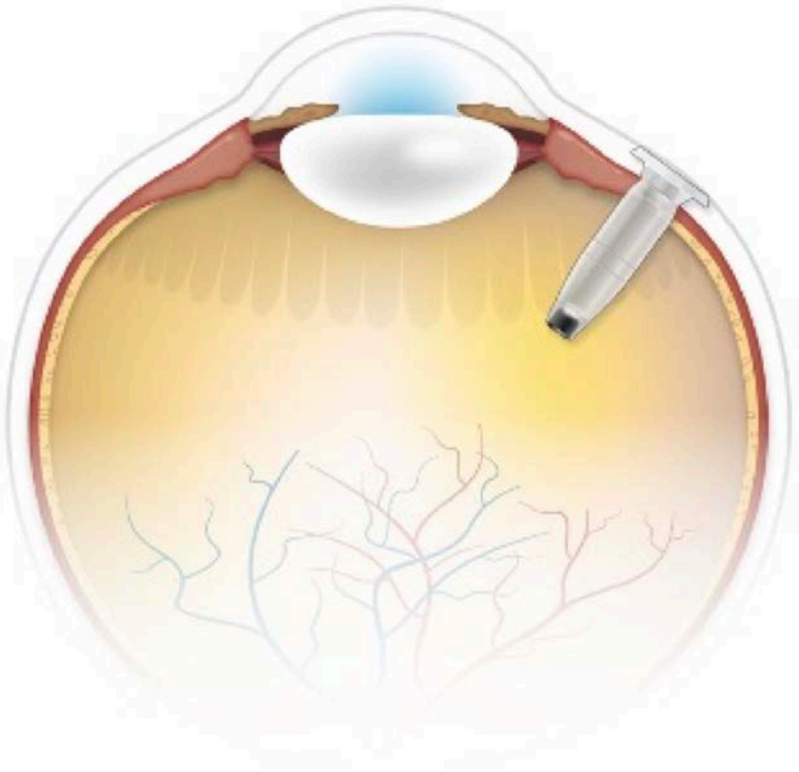
TENAYA/LUCERNE Pooled (n = 655)[1,2,a]

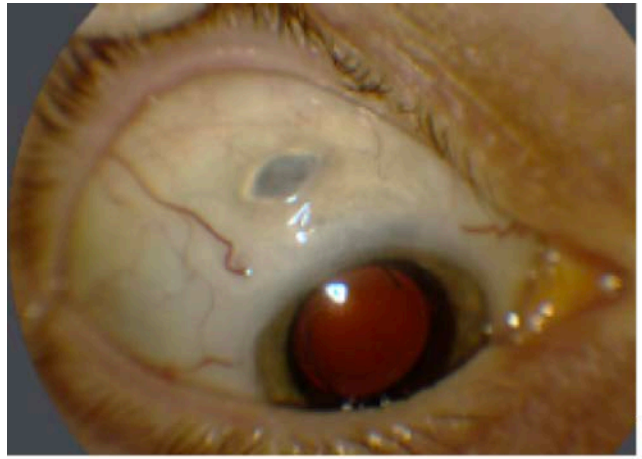


Huang N, et al. *Retina Today*. 2019;14(4):20.

Heier JS, et al. *Lancet*. 2022;339(10326);729.

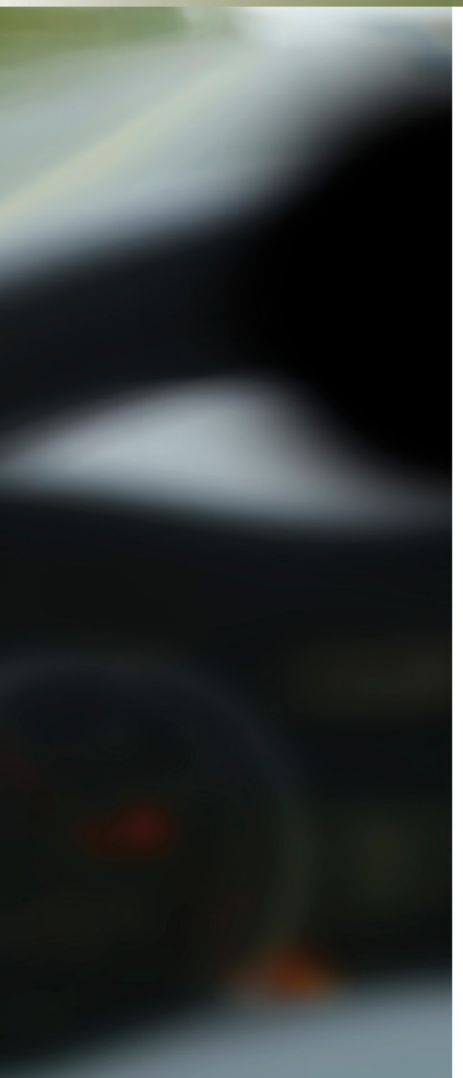
Port Delivery System With Ranibizumab (Susvimo)





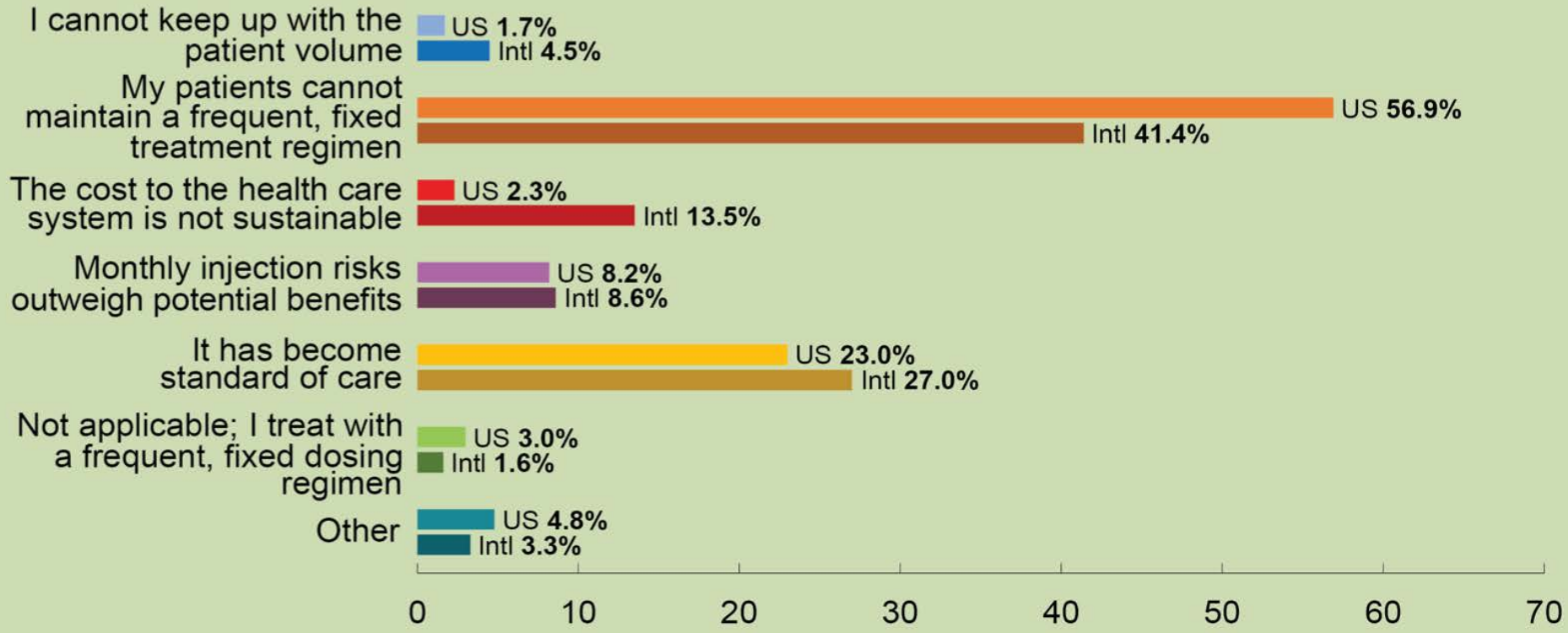
Holekamp MN, et al. *Ophthalmology*. 2022;129(3):295.

Dosing Strategies



- As needed (PRN)
  - With monthly follow-up
- Monthly
- Every other month
- Treat and Extend (T&E)

Despite most pivotal anti-VEGF trials studying monthly dosing, why do you favor T&E or PRN?



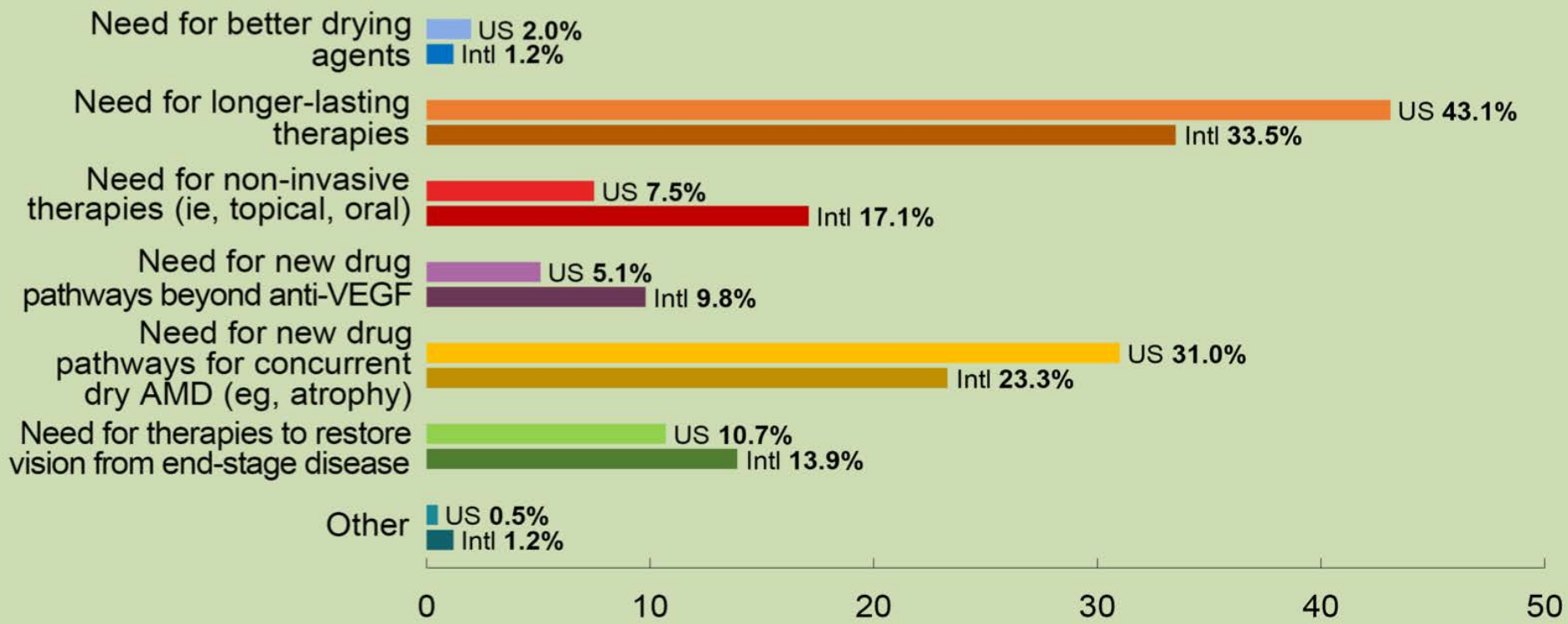
36. Despite most pivotal anti-VEGF trials studying monthly dosing, what is the main reason you favor a treat-and-extend (T&E) or pro re nata (PRN, ie, as-needed) approach?

n = 987

36

Hahn P, ed. *ASRS 2021 Preferences and Trends Membership Survey*. Chicago, IL. American Society of Retina Specialists; 2021.

What do you think is the biggest unmet need in wet-AMD therapeutics?



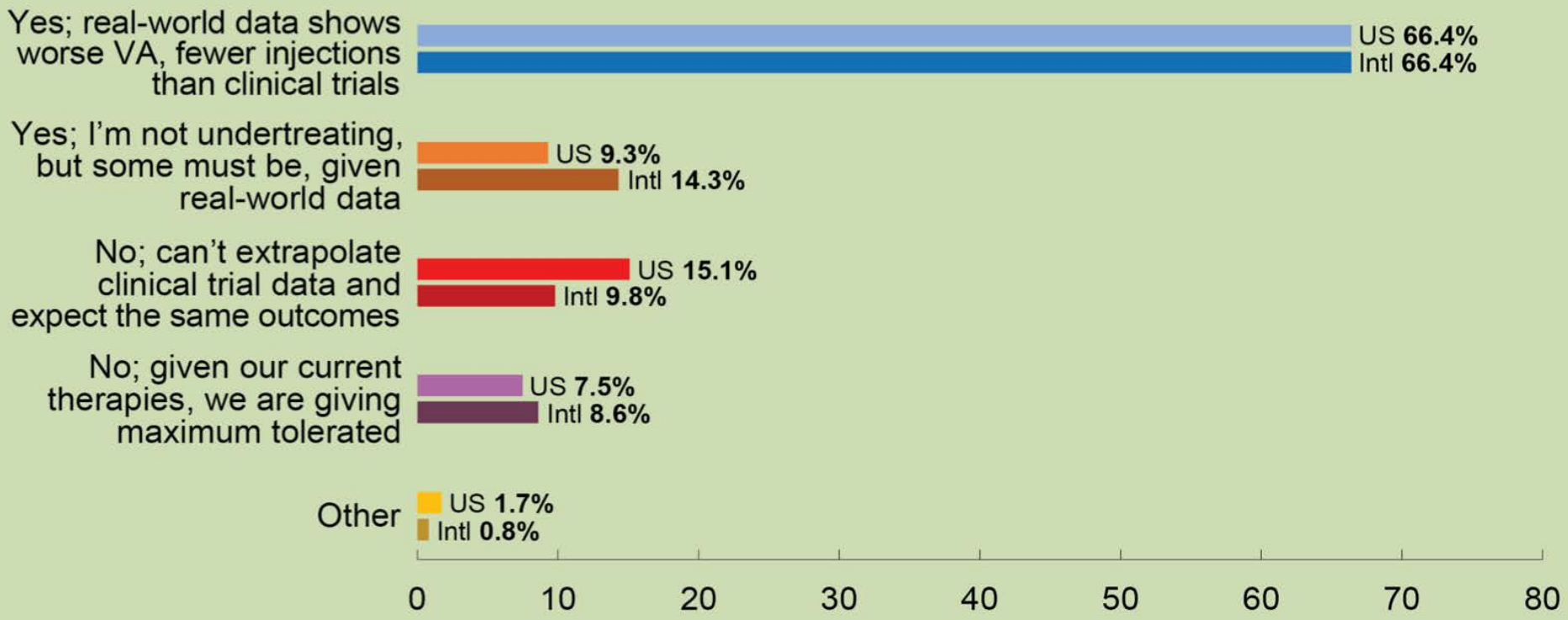
33. What do you think is the biggest unmet need in wet-AMD therapeutics?

n = 990

ASRS American Society of Retina Specialists

Hahn P, ed. *ASRS 2021 Preferences and Trends Membership Survey.* Chicago, IL. American Society of Retina Specialists; 2021.

Do you believe patients with wet AMD are being undertreated?

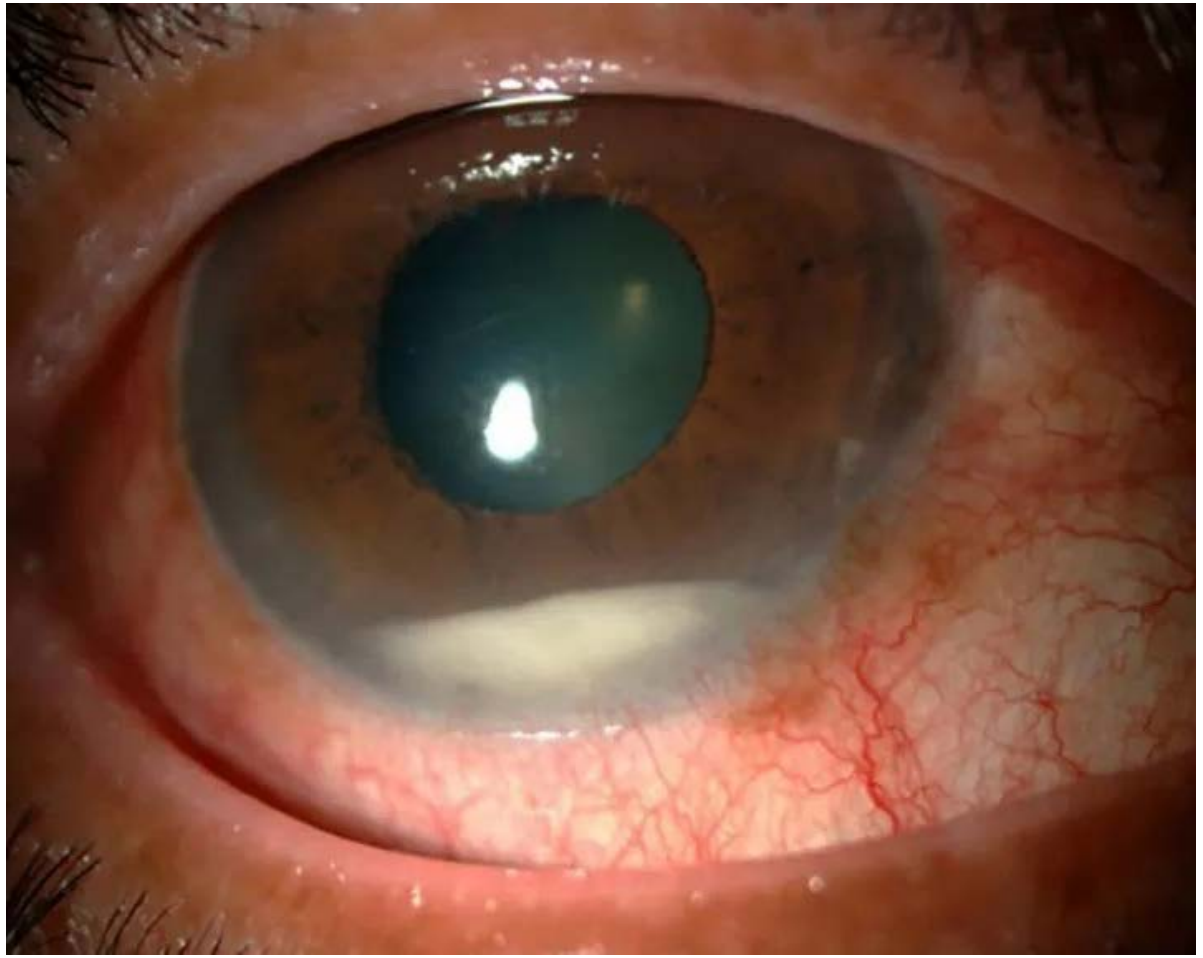


35. Do you believe patients with wet AMD are being undertreated? *n = 988*

Hahn P, ed. *ASRS 2021 Preferences and Trends Membership Survey.* Chicago, IL. American Society of Retina Specialists; 2021.

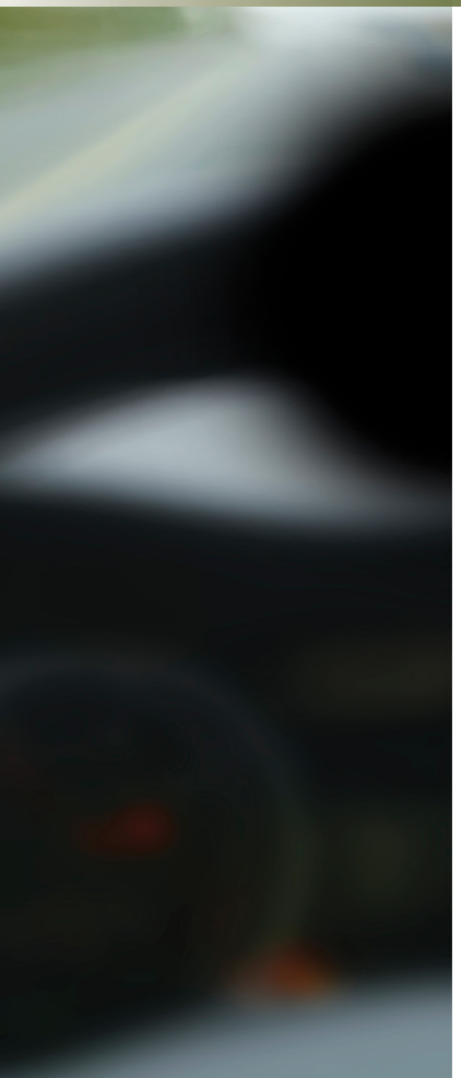
Intravitreal Injections: Risks

- Endophthalmitis
  - 1% in clinical trials but far less in reality (1 in 3500 RAK)
- Cataract formation (rare)
- Retinal detachment (rare)
- IOP increase (transient)
- Inflammation (rare, drug dependent)
- Vitreous hemorrhage
- Subconjunctival hemorrhage (5-10%)
- Pain
  - Typically, due to topical anesthetic/betadine



IOP, intraocular pressure. RAK, Retina Associates of Kentucky

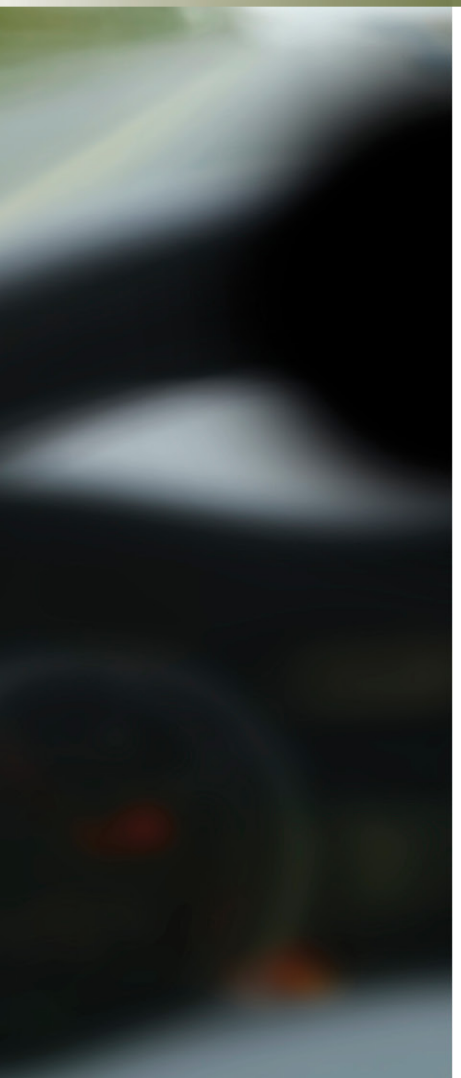
Emerging Therapies



- Gene therapy for AMD and diabetic eye disease
- Port delivery system for diabetic eye disease

Khanani AM, et al. *Eye*. 2022;36:301.
ClinicalTrials.gov Identifier: NCT04503551.

Learning Objective #3



- **Describe** age-related macular degeneration (AMD) and diabetic macular edema (DME) and their impact on patient quality of life
- **Discuss** current and emerging treatment options for AMD and DME, including efficacy, safety, and relevant clinical trial data
- **Interpret** the rationale for using real-world evidence in treatment decision making for AMD and DME to optimize patient quality of life and outcomes
- **Recognize** approaches to assist in improving outcomes in AME and DME

Real-World Evidence (RWE)

Real-World Data and Evidence

Real-World Data (RWD)

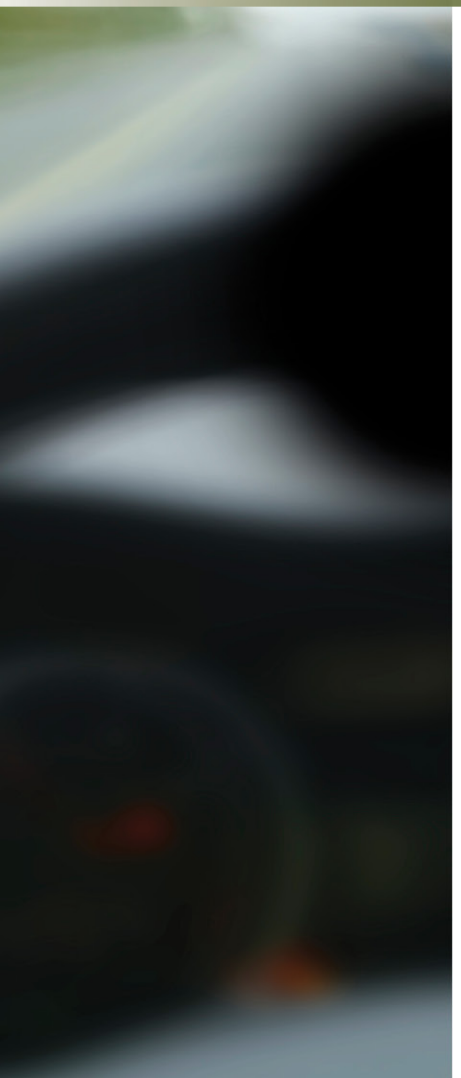
- RWD are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources
- Example sources:
  - Claims and billing data
  - Electronic health records (EHRs)
  - Clinical registries
  - Digital health data

Real-World Evidence (RWE)

- The clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD
- Example study designs:
  - Case control
  - Retrospective cohort
  - Prospective cohort
  - Pragmatic trials

Framework for FDA's Real-World Evidence Program. Accessed April 12, 2022. https://www.fda.gov/media/120060/download

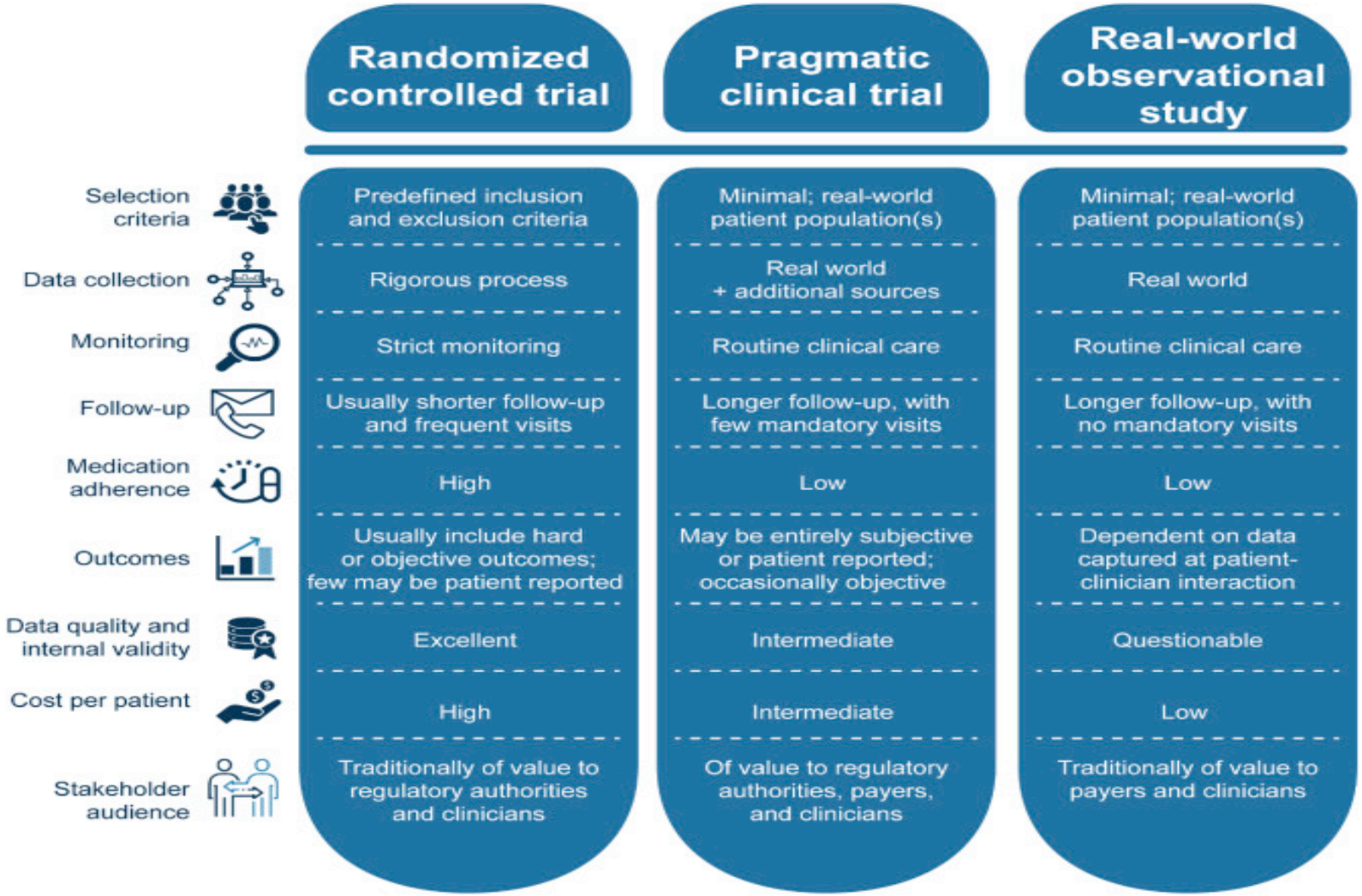
How Can RWE Be Used in Medicine Development?



- Understanding “real-world” settings, such as treatment populations, patterns of care, and the burden of disease
- Assessing the effectiveness of current therapies using existing data
- Refining or supplementing evidence from conventional trials of new medicines
- Providing new evidence of relative effectiveness of novel medications

RWE Navigator EU. Accessed April 12, 2022. https://rwe-navigator.eu/

Comparison of a RCT, PCT, and Real-World Observational Study



Accessed April 12, 2022. https://www.sciencedirect.com/science/article/pii/S2590143520300038

Limitations of RWE

- RWE is subject to numerous biases:
  - Bias is prejudice in favor of or against 1 thing, person, or group compared with another, usually in a way considered to be unfair
    - Selection bias (where patient groups are not comparable)
    - Performance bias (where patients are exposed to different interventions)
    - Exclusion bias (when patients are lost to follow-up because of sickness)
    - Detection bias (where patients are assessed at different points in time)
- Confounding
  - When the measured association between an exposure and disease occurrence is distorted by an imbalance between exposed and nonexposed persons with regards to 1 or more risk factors for the disease
- Observational studies potentially have high external and low internal validity
  - Reduction of bias can enhance internal validity

Dreyer NA, et al. *Am J Manag C*are. 2010;16(6):467.

RWE: The Limits of Emulating RCTs

- Only about half of a select group of clinical trials could be well-emulated with available RWE, according to the newly discussed results of an FDA pilot program
- The FDA-funded program (RCT-DUPLICATE) helped researchers from the Brigham and Women's Hospital in Boston evaluate whether RCTs can be duplicated with RWE across a range of therapeutic areas
- The initiative is part of the FDA's work, mandated by Congress in the 21st Century Cures Act, on how it plans to evaluate the use of RWE to assess the effectiveness of medical products
- Researchers found that 50% of the selected RCTs could be emulated closely regarding design and analysis, and they saw comparable treatment effects. But RCT and RWE findings were more likely to diverge when there were substantive emulation challenges, which could be because the database and RCTs are targeting different questions, or due to bias, or both

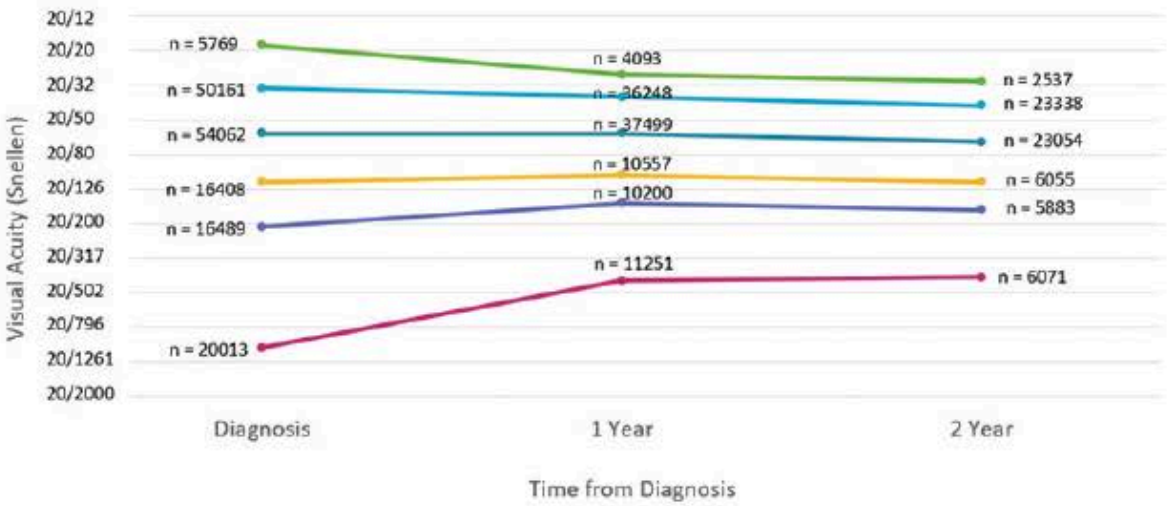
FDA, Food and Drug Administration; RCT, randomized controlled trial; RWE, real-world evidence.

Endpoints News. May 16, 2022.

Characteristics Associated With Better Outcomes

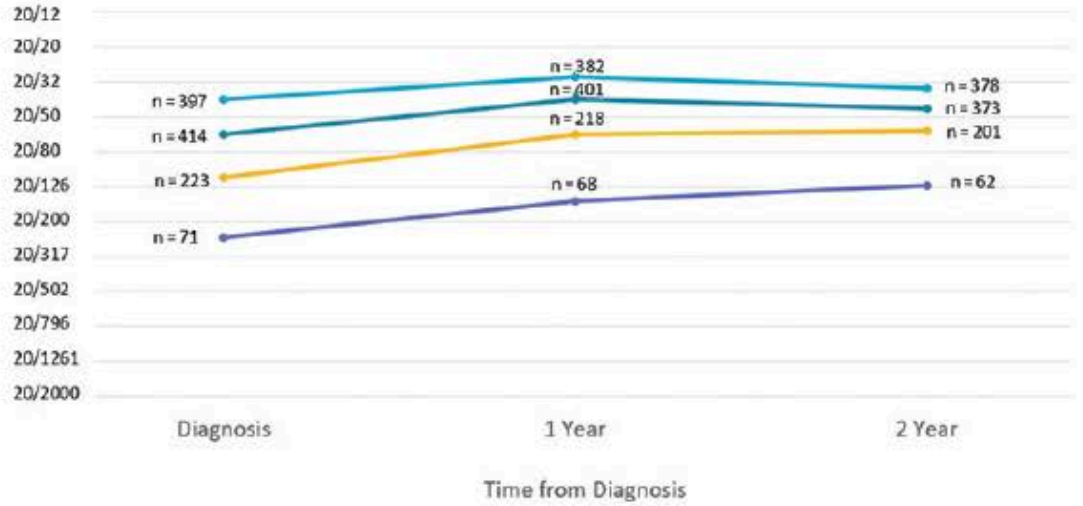
AAO IRIS® Registry Real World Data (US)
January 2013 – June 2017

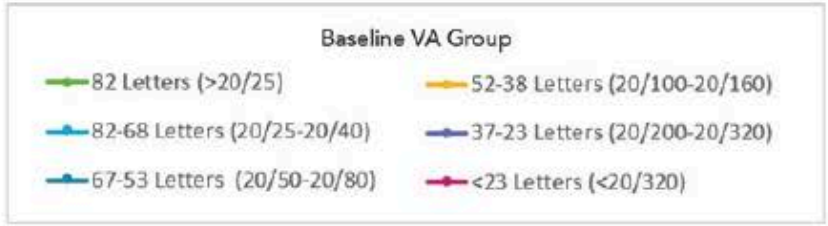
Mean VA at 1-year & 2-year post-diagnosis by group baseline VA



Comparison of Age-related Macular Degeneration Treatment Trials (CATT) (US)

Mean VA at 1-year & 2-year





VA, visual acuity.

Ho AC, et al. *Ophthalmic Surg Lasers Imaging Retina*. 2020;51(11):633.
Ying G, et al. *Ophthalmology*. 2015;122(12):2523.e1.

ETOILE: RWE of Ranibizumab in Patients With Visual Impairment Due to DME

- **PURPOSE:** To evaluate the real-world effectiveness of intravitreal ranibizumab 0.5 mg in improving VA in adults with decreased VA due to DME.

- **PATIENTS AND METHODS:** Real-world prospective observational 24-month study. Ranibizumab-naïve patients (n = 116) were enrolled, treated, and followed up according to investigators' usual procedures. Outcomes included change from baseline to month 24 in BCVA (primary outcome), CRT, treatment exposure, and safety.

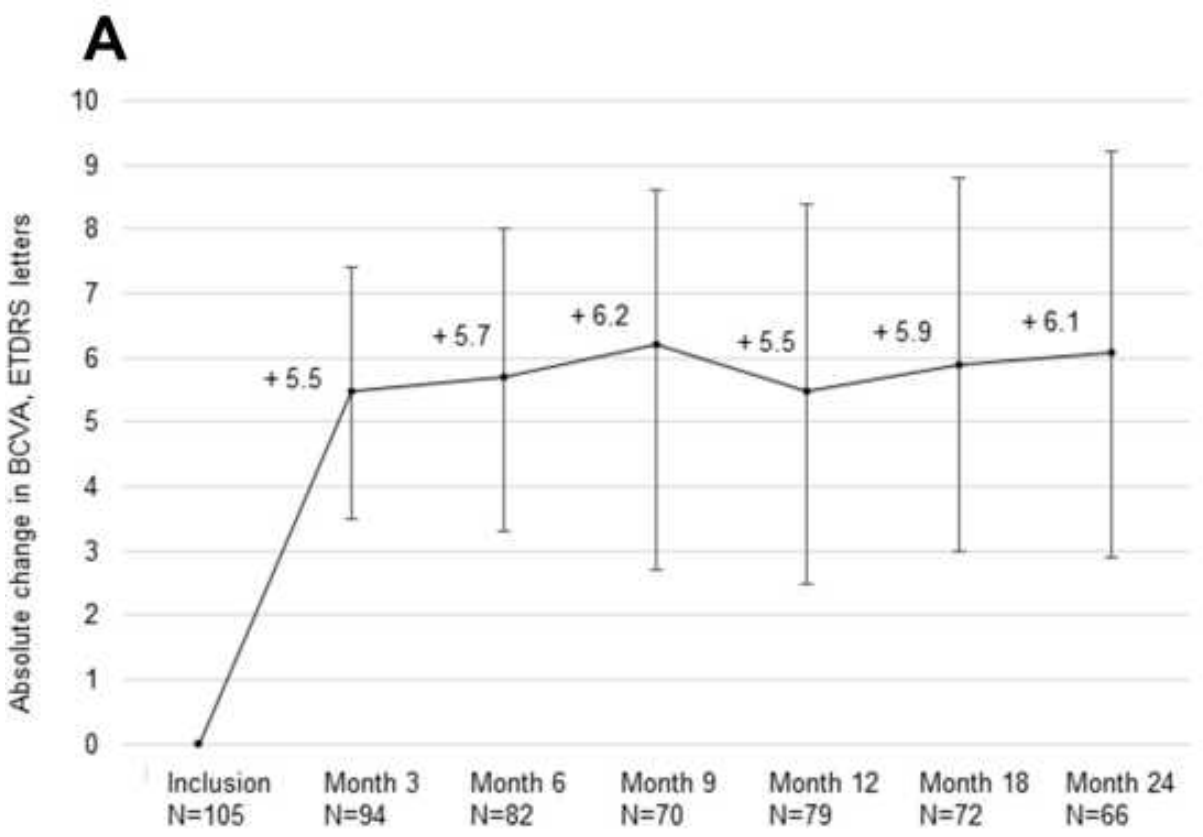
- **RESULTS:** Overall, 62.9% of patients completed the study per protocol, 68.6% completed the induction phase (first 3 injections 1 month apart). On average, patients had 12.5 ophthalmologist visits and 5.74 injections in year 1, decreasing to 4.6 visits and 1.94 injections in year 2. Mean baseline BCVA was 58.4 letters, mean gain at M24 was +6.08 letters (95% CI: 2.95, 9.21). Gains were higher for patients who completed induction and for those who did not switch treatment. Mean CRT improved by 149.17 µm at M24. There were no new safety signals. BCVA variation of ≥6 letters by M3 was predictive of BCVA gains at M24 (*P* = .007), as was hypertension medication at baseline (*P* = .022).

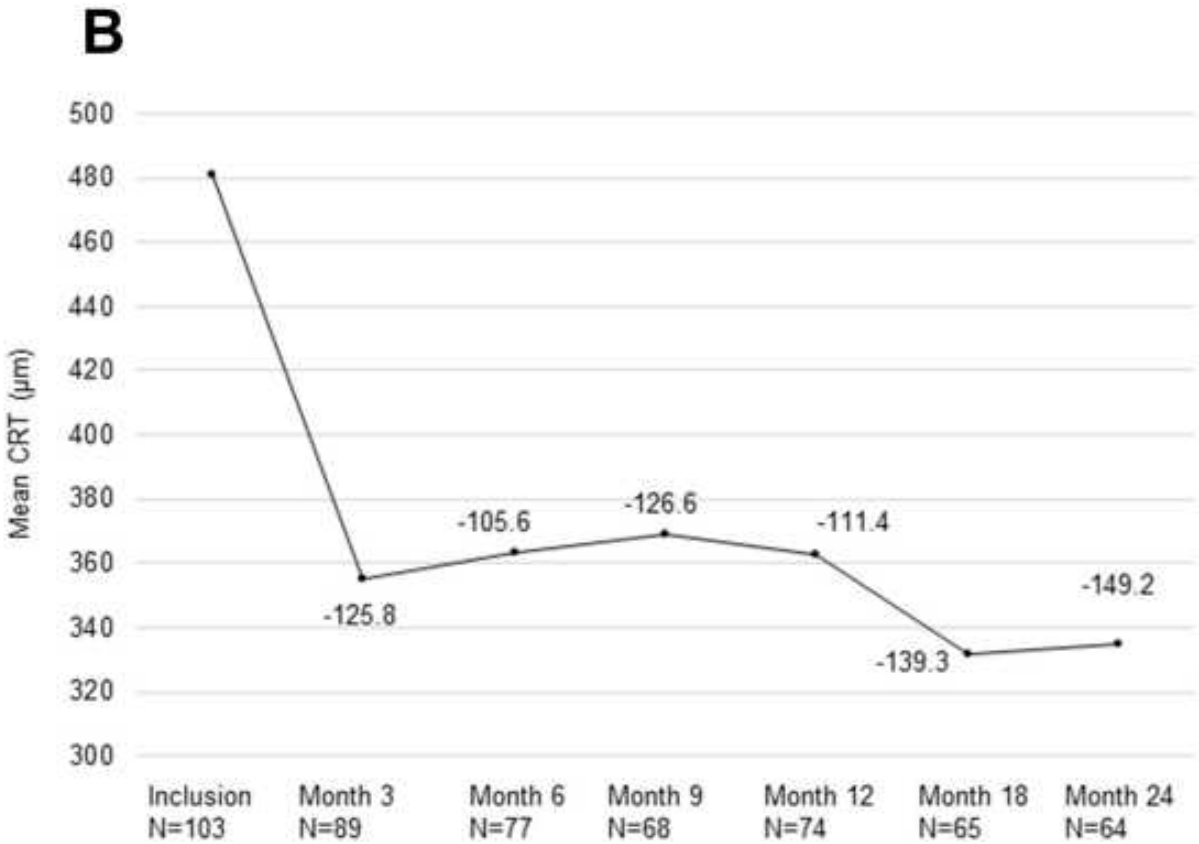
- **CONCLUSION:** Real-world ranibizumab treatment improved VA in DME patients, despite fewer injections than recommended.

BCVA, best-corrected visual acuity; CRT, central retinal thickness; VA, visual acuity.

Kodjikian L, et al. *Clin Ophthalmol*. 2021;15:2307.

ETOILE: Change From Baseline in (A) VA and (B) CRT

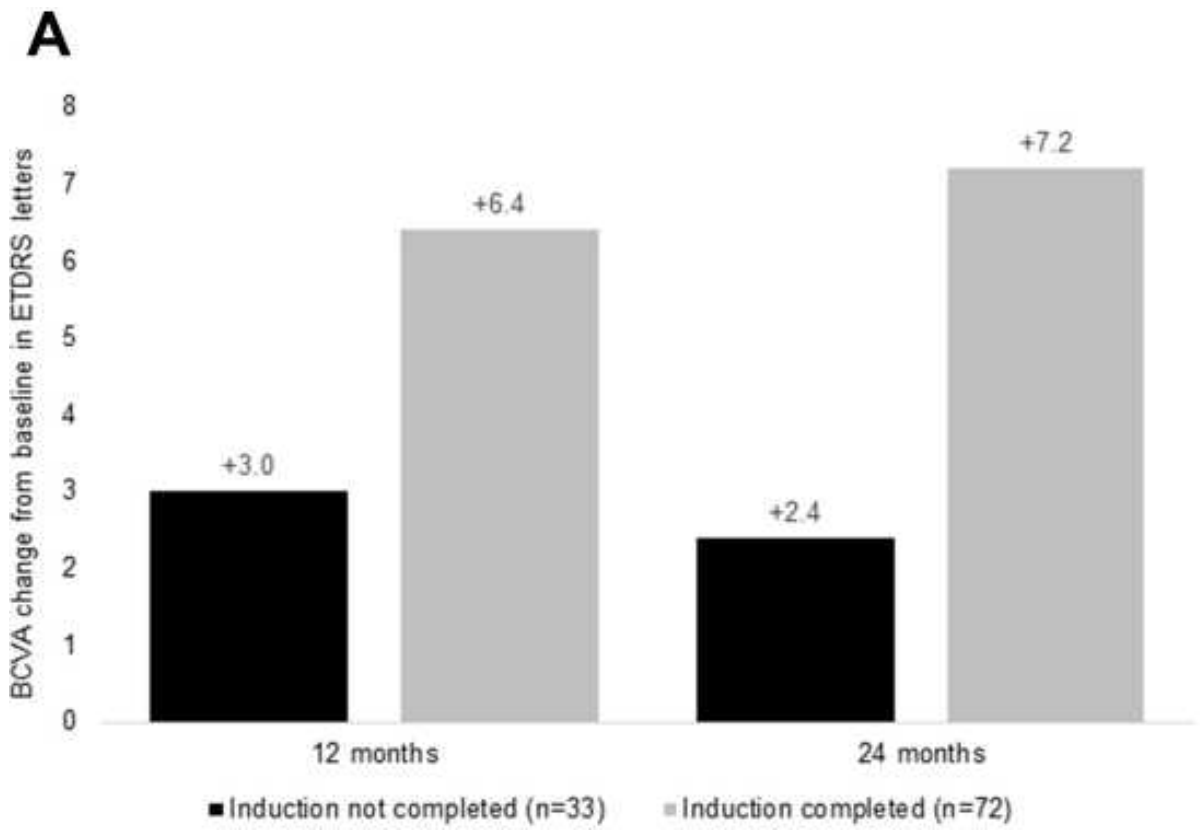


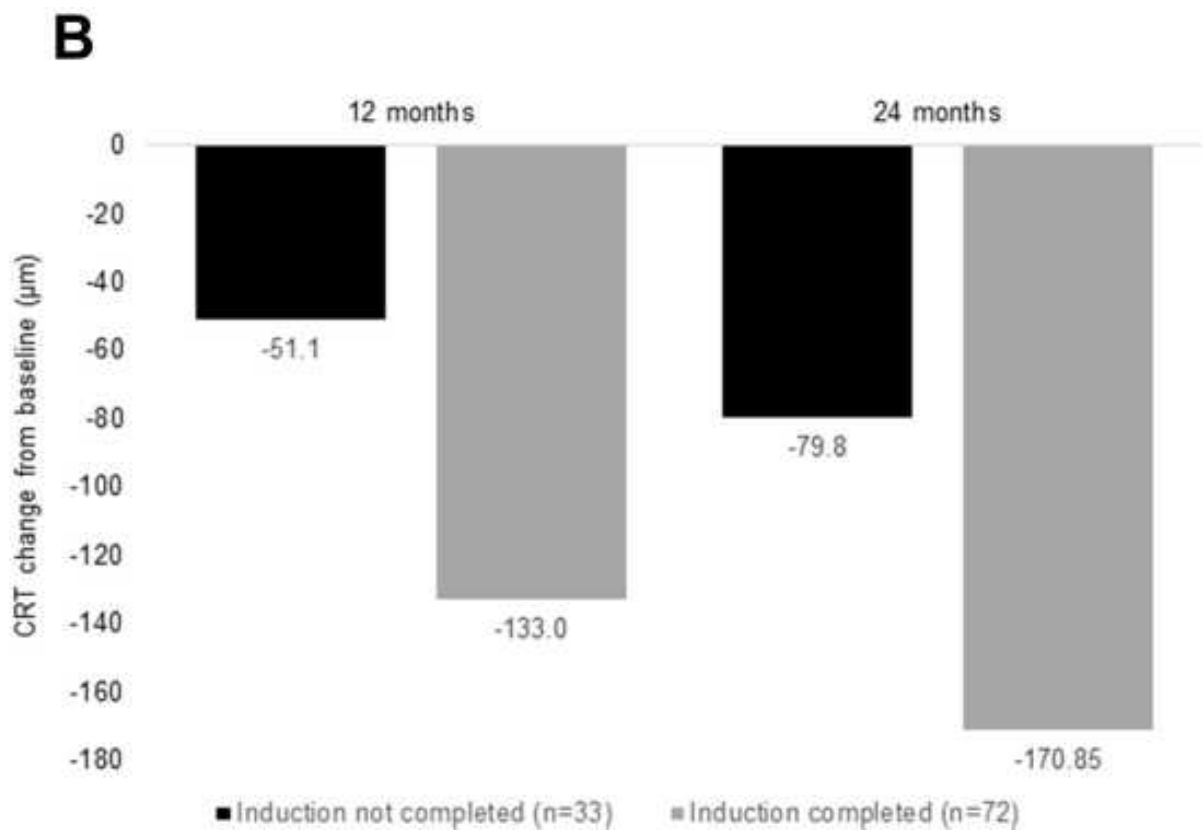


BCVA, best-corrected visual acuity; CRT, central retinal thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; VA, visual acuity.

Kodjikian L, et al. *Clin Ophthalmol*. 2021;15:2307.

ETOILE: Change From Baseline in (A) VA and (B) CRT (Induction Phase)

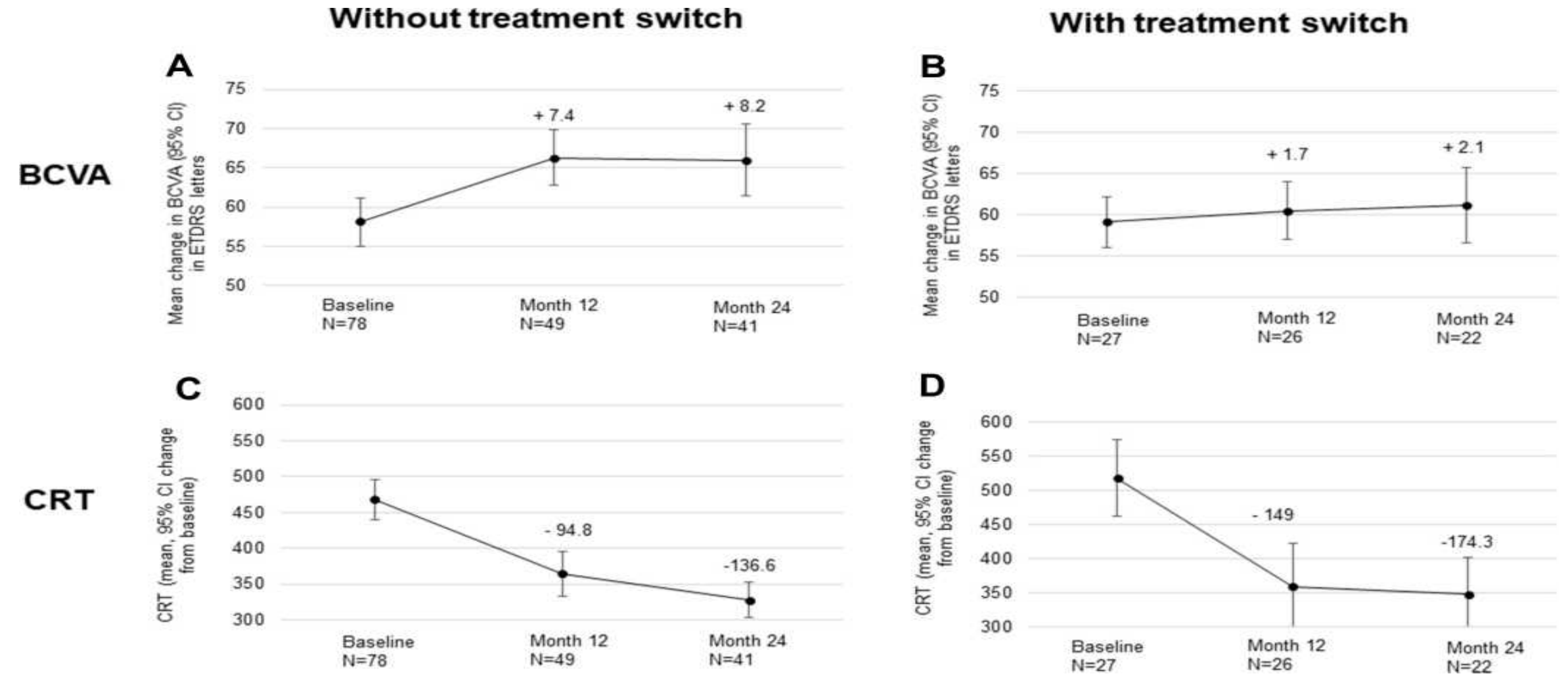




BCVA, best-corrected visual acuity; CRT, central retinal thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; VA, visual acuity.

Kodjikian L, et al. *Clin Ophthalmol*. 2021;15:2307.

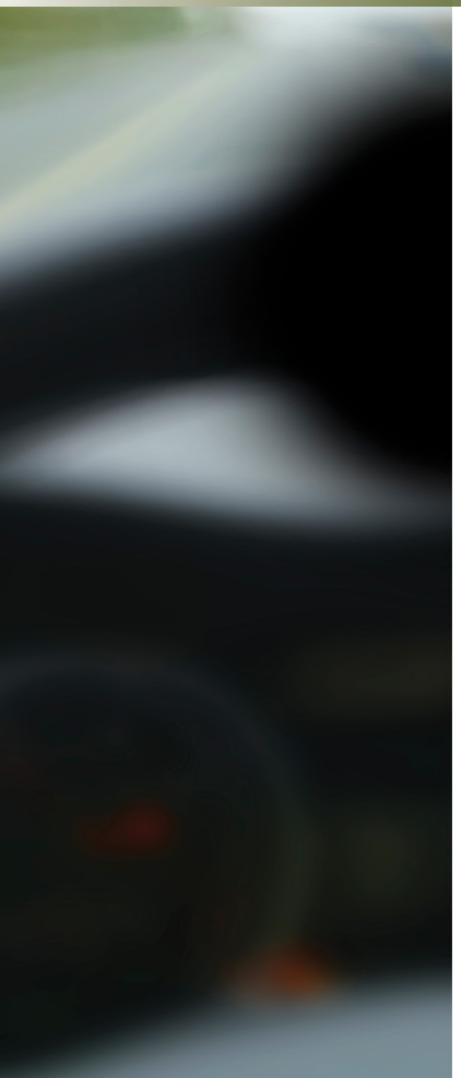
ETOILE: Change From Baseline in VA and CRT Without and With Treatment Switch



BCVA, best-corrected visual acuity; CRT, central retinal thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; VA, visual acuity.

Kodjikian L, et al. *Clin Ophthalmol*. 2021;15:2307.

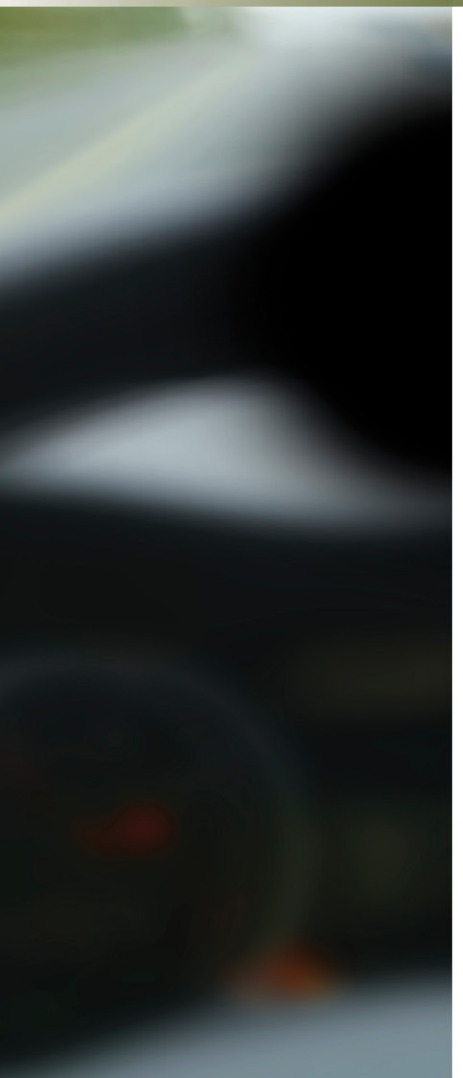
What Is Driving the Undertreatment of Patients?



- Treating physician causes
  - Increased clinical volumes
  - Patient input
  - Concern for health care cost
- Poor patient adherence
  - One prior study showed 22.2% lost to follow-up at 12 months
    - Older age, lower income, travel distance
- Effect of treatment breaks
  - One prior study showed that in patients who had a treatment break for >6 months, they did not return to pretreatment break VA even with reinitiating of anti-VEGF therapy

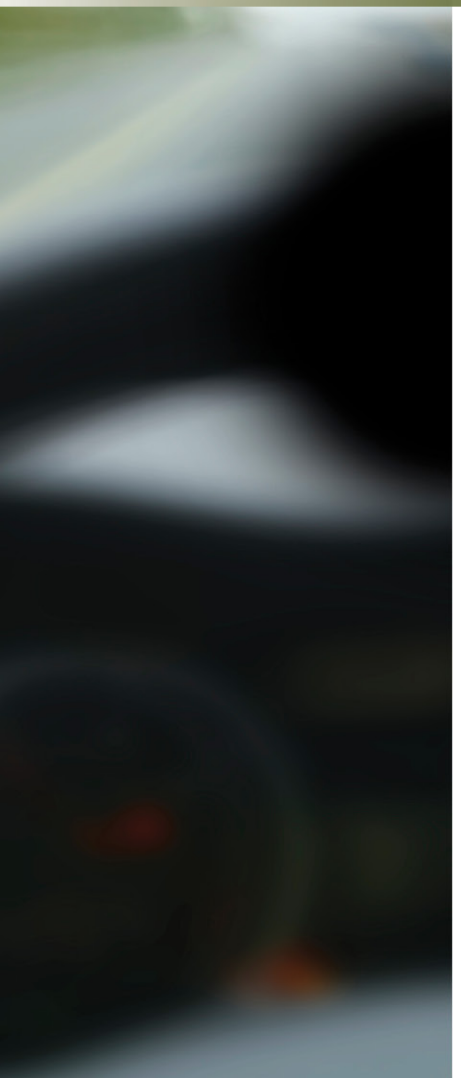
Hsu J, et al. *Ophthalmology*. 2020;127(9):1189.

Better Outcomes Through Patient Education and Compliance Improvement



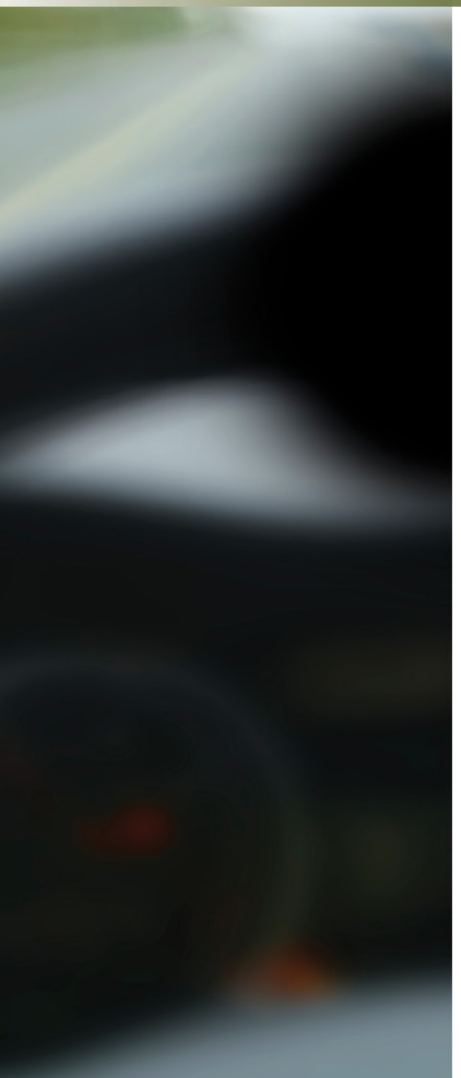
- Explain therapy requirements (frequent visits), cost, and possible adverse effects
- Monitor therapy safety and efficacy
- Describe what to expect with therapy
- Stopping vision loss
- Vision improvement expectations

Monitoring and Importance of Treatment Adherence



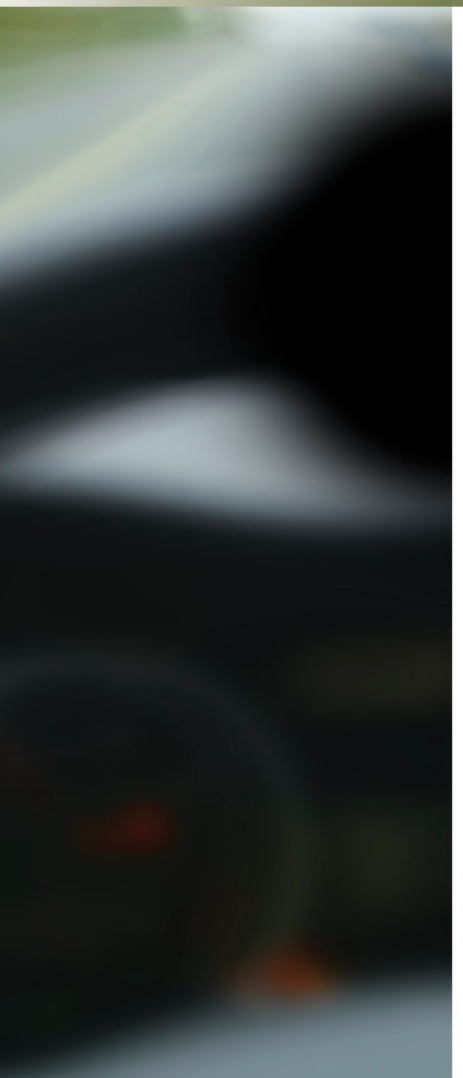
- Slow progression of DME
- Prevent vision loss or blindness
- Emphasize importance of ongoing treatment
- Follow up with patients to ensure they are adhering to therapy
  - If they are not, find out why and try to help address the issue
- Possibly offer less expensive alternatives or less complicated treatment regimens
- Provide assistance with cost of care whenever possible

Treatment Decisions: New Patient Variables



- What is the diagnosis?
- What drug is available to the patient?
- Can the patient receive treatment today?
- What are the cost considerations for the patient?
- What are the travel limitations to the patient?
- *Educating the patient and their family, answering questions, corresponding with their referring and primary care physicians, diagnosing and treating other ocular disorders, etc.*

Treatment Decisions: Return Patient Variables



- Are there any new problems (eg, fellow eye)?
- Is the drug working? Patient perception vs clinical evaluation
- Should we change the dosing interval of the drug?
- Should we change the drug?
- *Educating the patient and their family, answering questions, corresponding with their referring and primary care physicians, diagnosing and treating other ocular disorders, etc.*

Case #1

Presentation

64-YEAR-OLD FEMALE

- Decreased vision OS
- BCVA: 20/400
- PDT × 1
- Bevacizumab (BEV) × 16
- Ranibizumab (RAN) × 12
- Aflibercept (AFL) × 4

BCVA, best-corrected visual acuity; OS, oculus sinister (left eye); PDT, photodynamic therapy.

2008

2008	**2012**	**2015**	**2020**
MULTIPLE THERAPIES	AFL MONTHLY	AFL BIMONTHLY	AFL Q10W
20/400	20/70	20/80	20/100

Fellow Eye

4 YEARS LATER…

- Decreased vision OD
- BCVA: 20/80
- AFL therapy initiated

- BCVA (OS): 20/70
- AFL therapy maintained

AFL, aflibercept; BCVA, best-corrected visual acuity; OD, oculus dexter (right eye); OS, oculus sinister (left eye).

2012

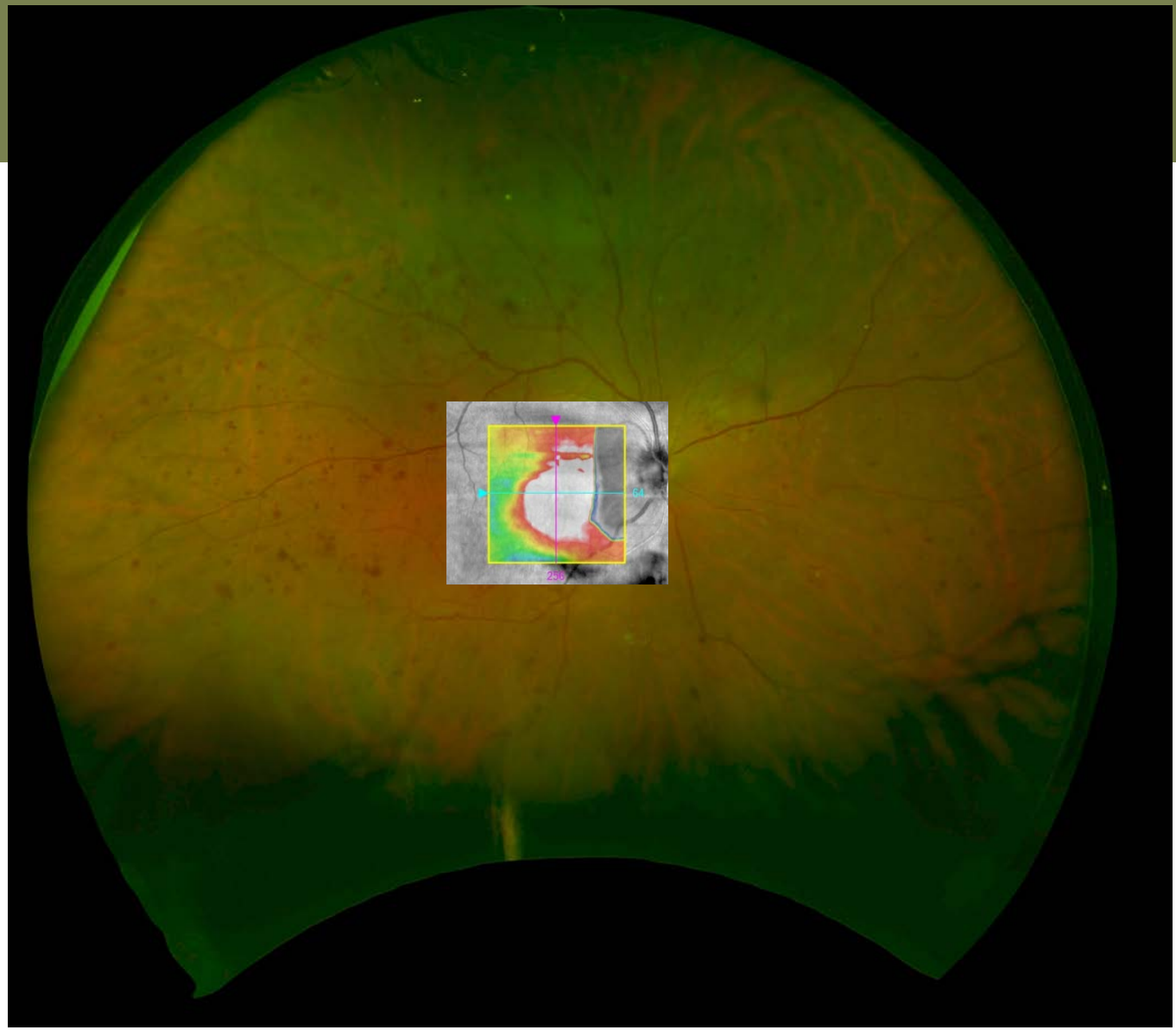
2008	**2012**	**2015**	**2020**
NO TREATMENT	AFL MONTHLY	AFL BIMONTHLY	AFL Q10W
20/25	20/80	20/30	20/40

Case #2

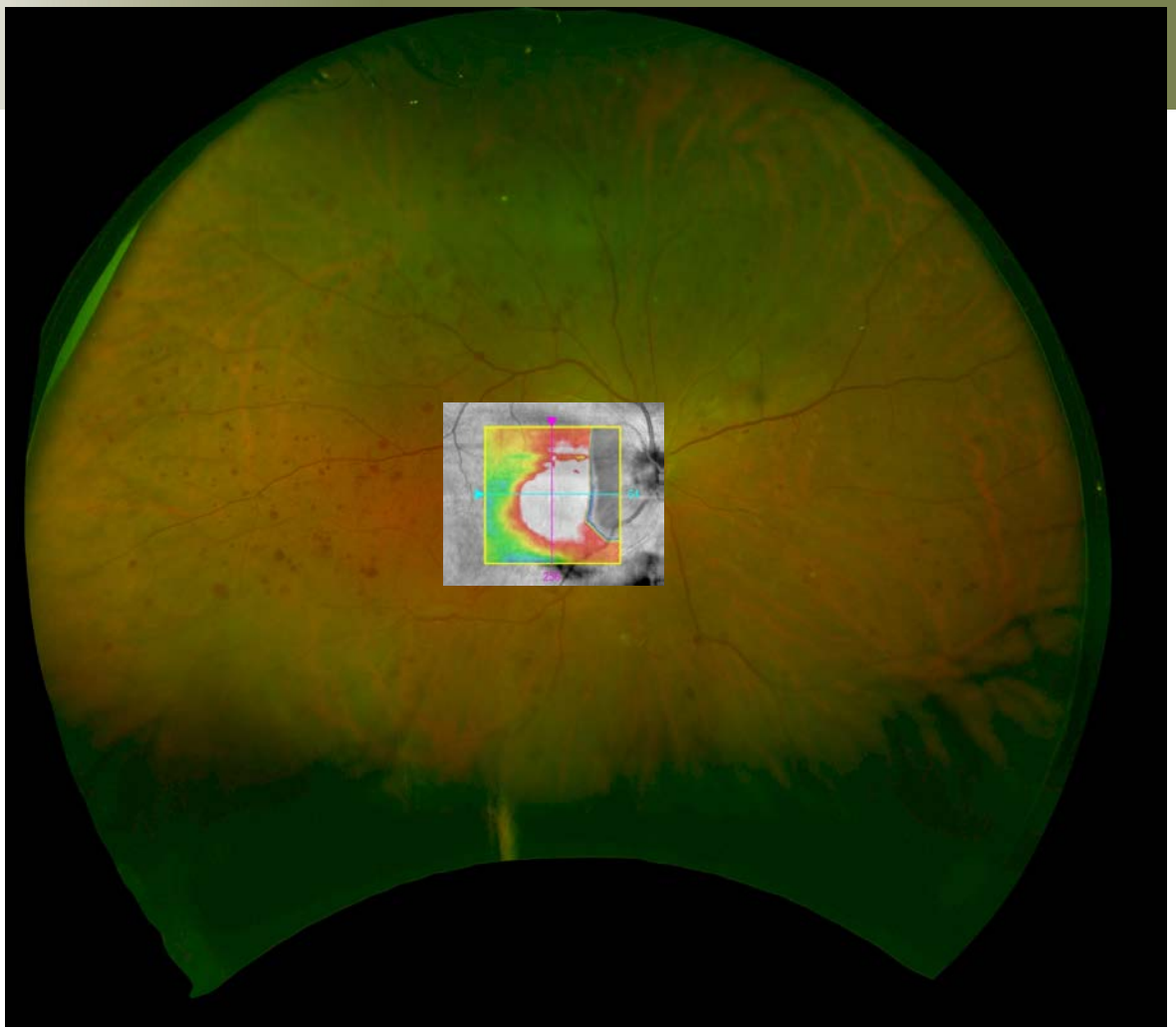
Presentation

41-YEAR-OLD FEMALE

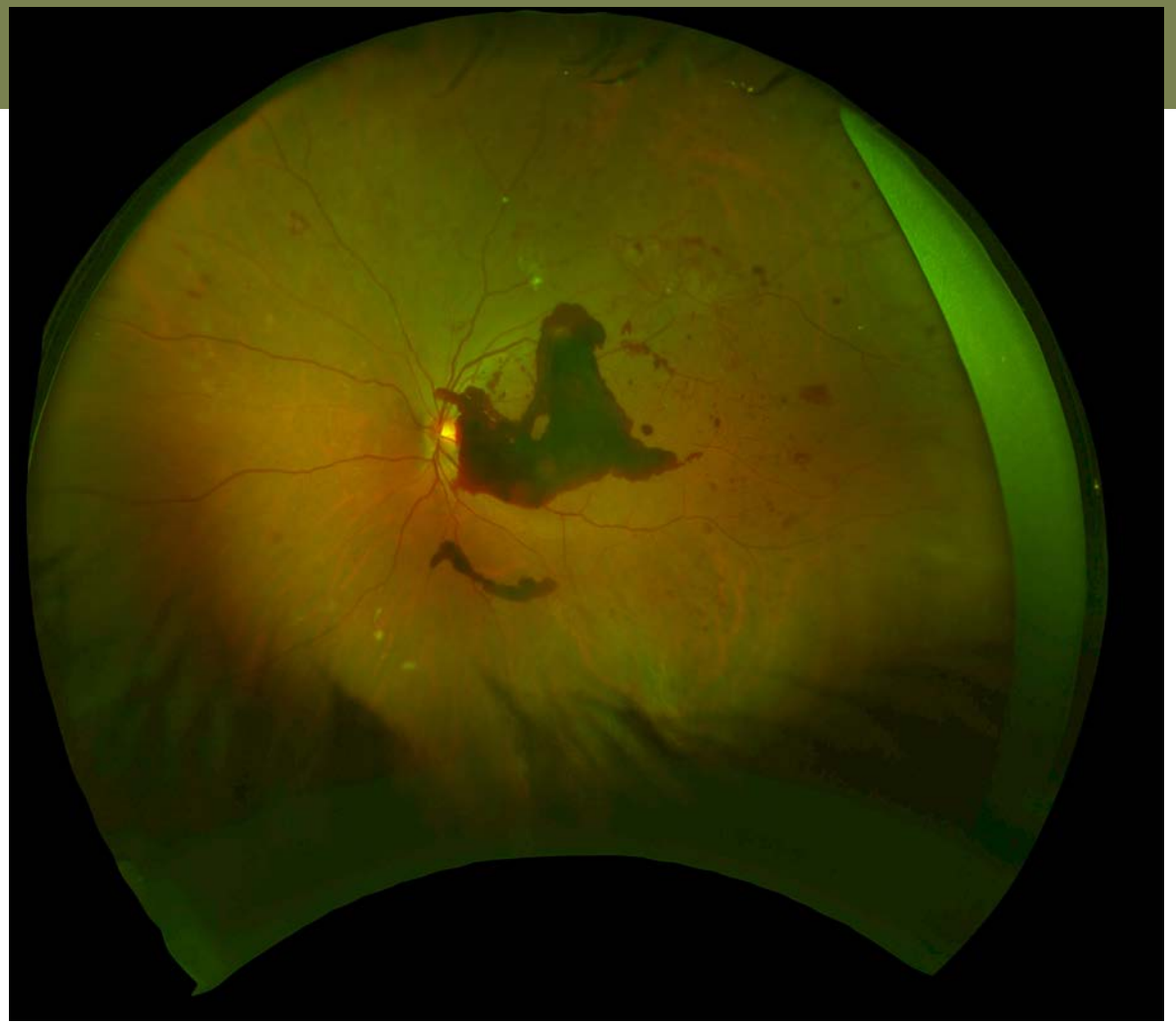
- Decreased vision OU
- BCVA OD: 20/200
- BCVA OS: 20/400



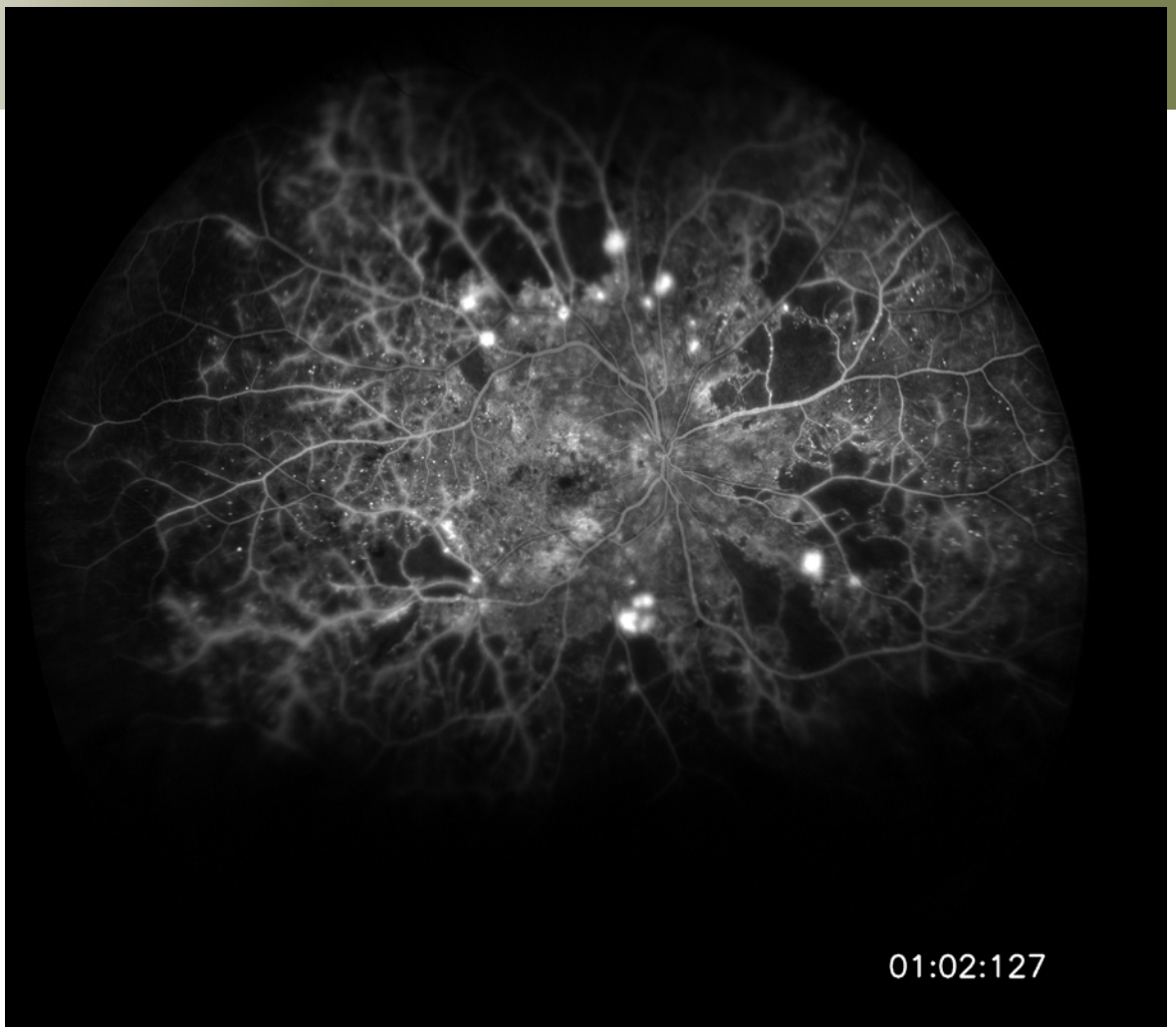
BCVA, best-corrected visual acuity; OD, oculus dexter (right eye); OS, oculus sinister (left eye); OU, oculus uterque (both eyes).



20/200



20/400



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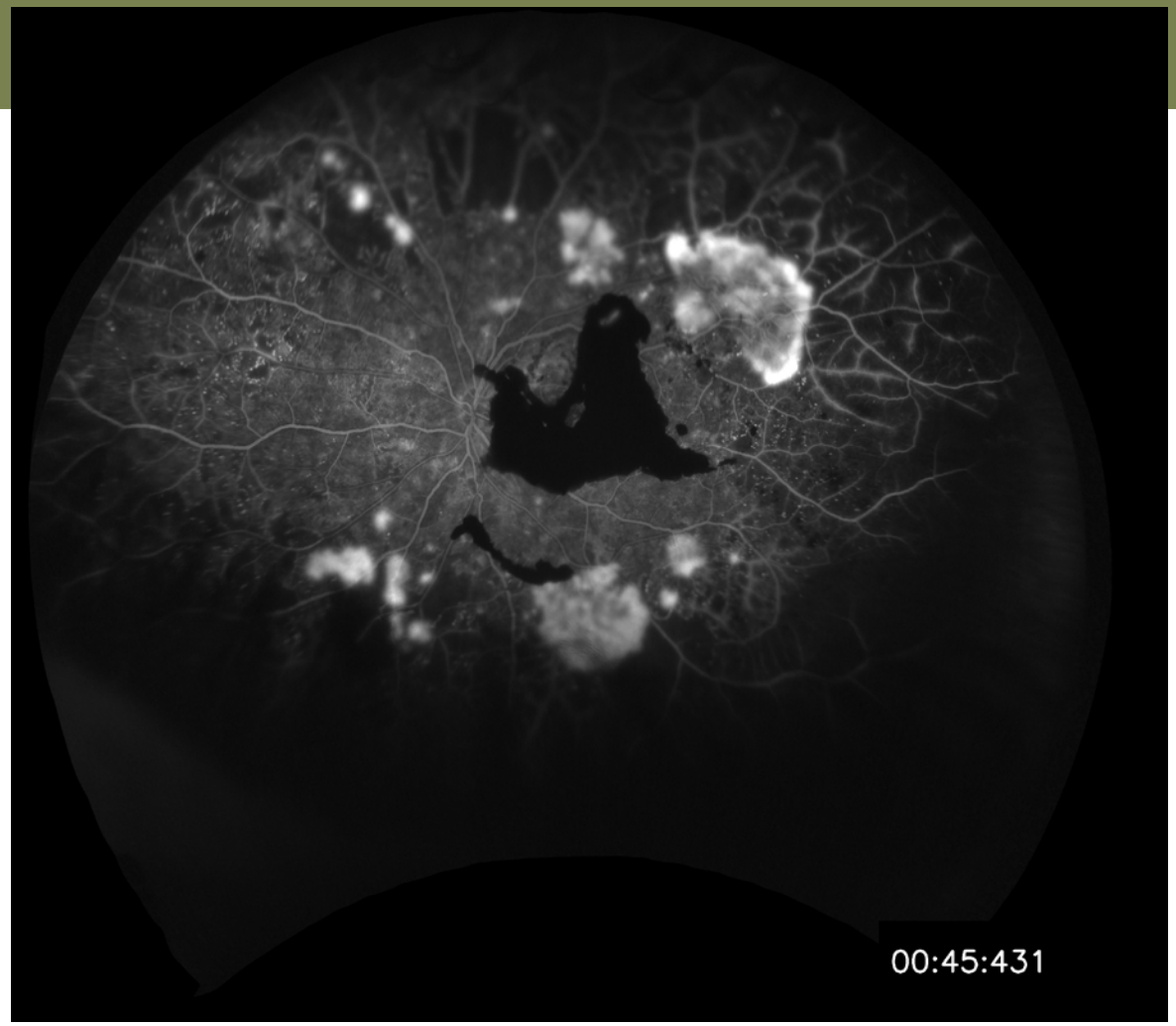

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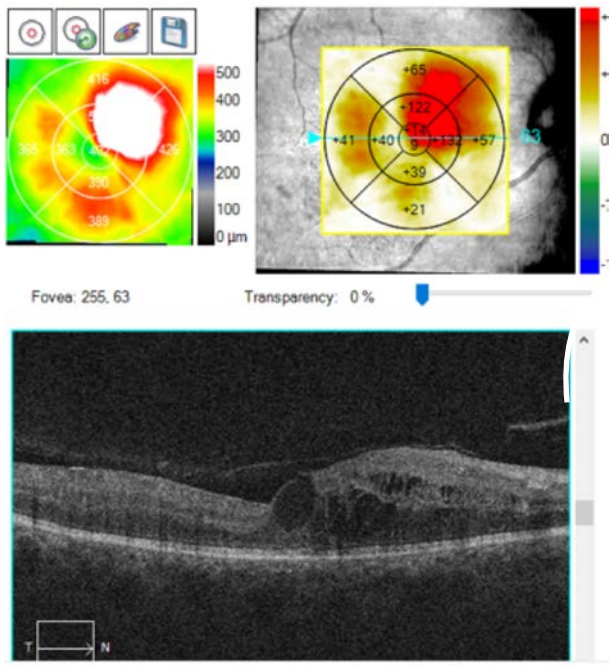
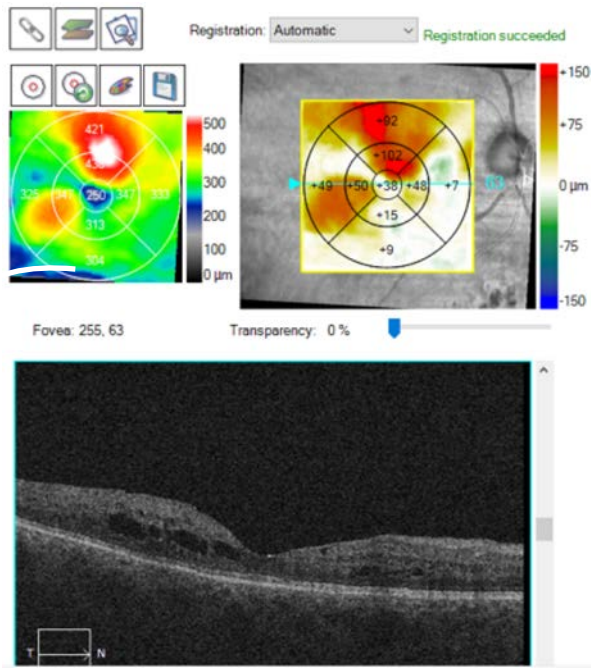
<u>03/01/2010</u>
MONTHLY RAN

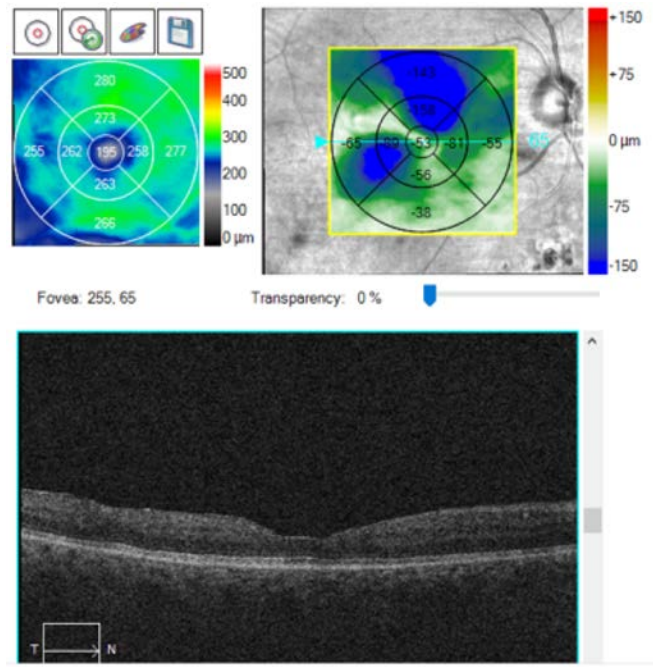
<u>04/29/2010</u>
RAN Q2M

<u>12/05/2014</u>
RAN Q2M

<u>06/23/2015</u>
AFL Q2M







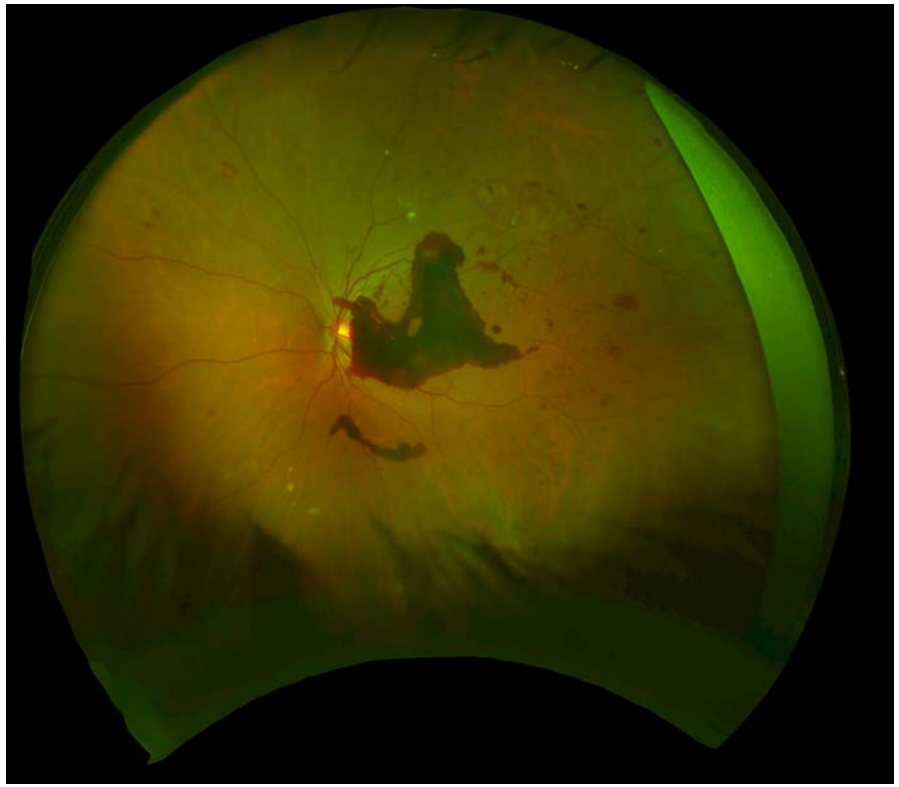
Attempted to extend RAN to 8 weeks

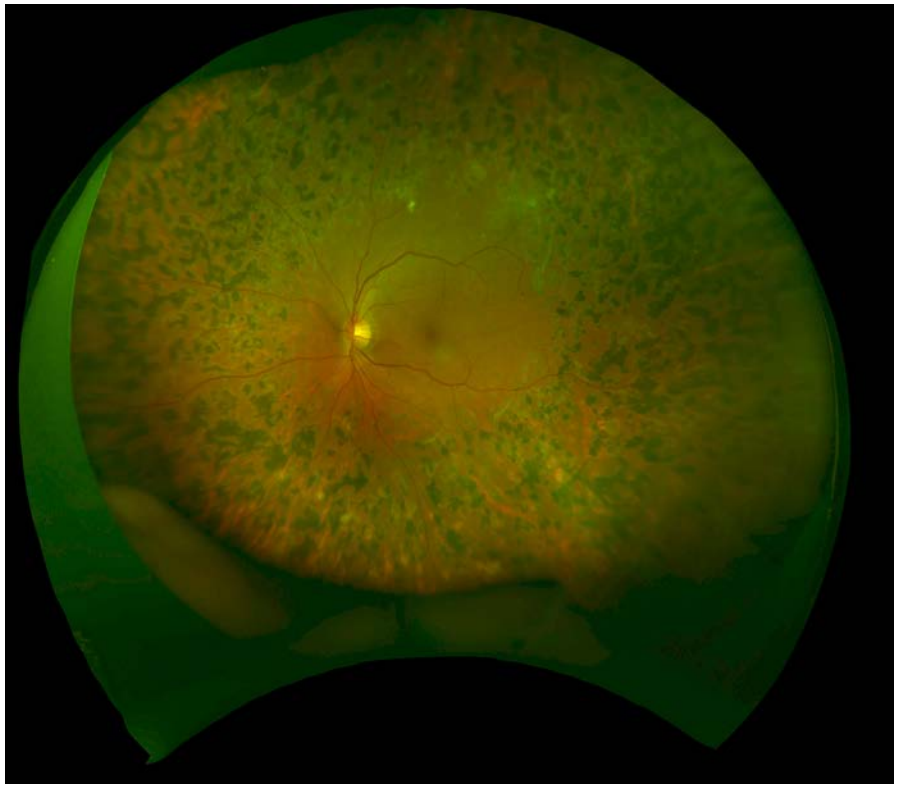
Attempted to extend RAN to 8 weeks

Switch to AFL monthly × 5 then Q2M

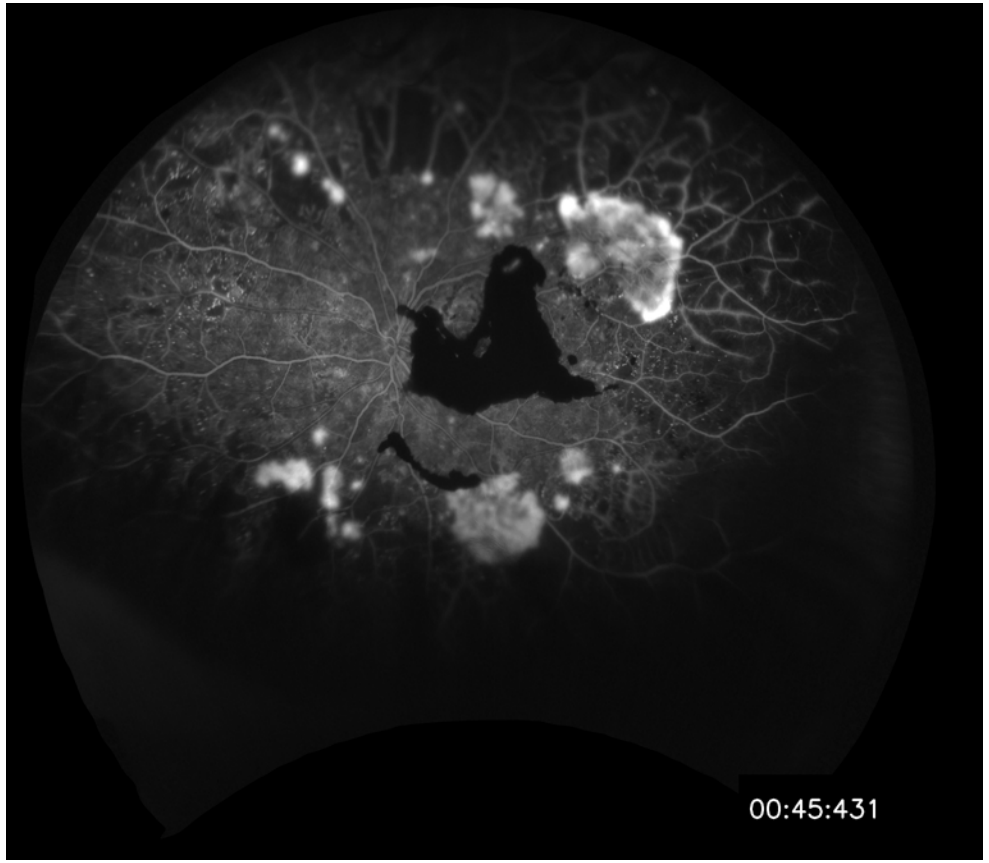
20/200 20/100 20/50

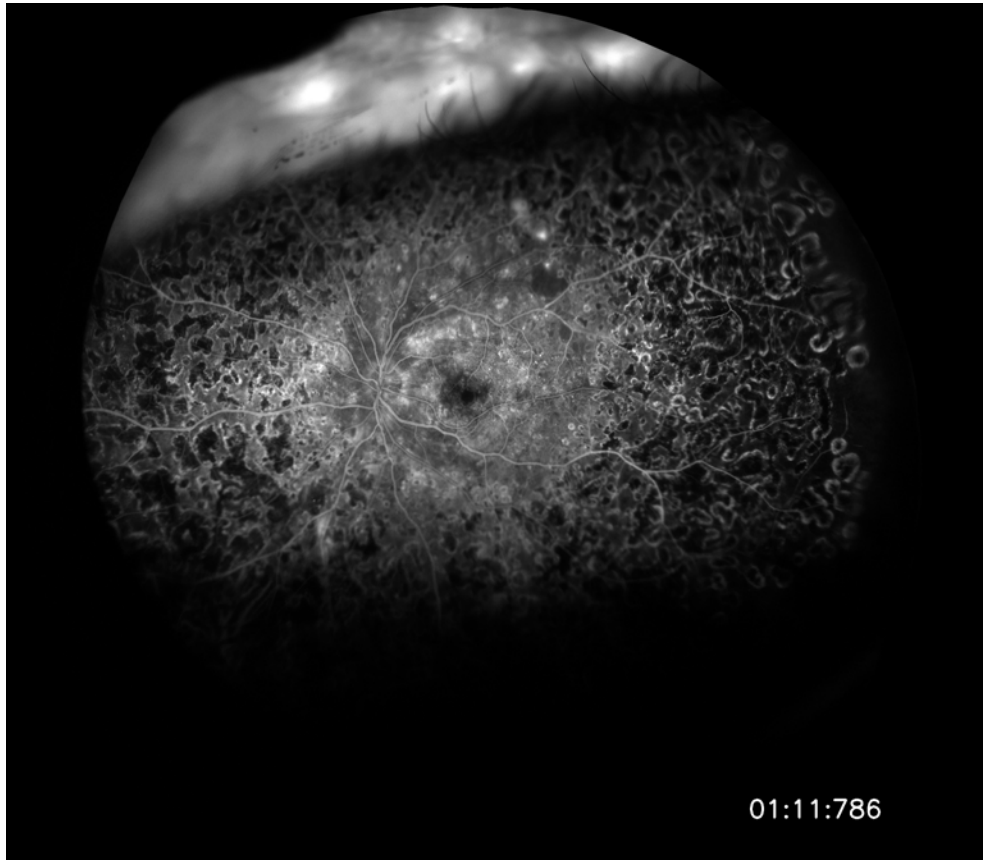
Left Eye: Pre and Post Treatment



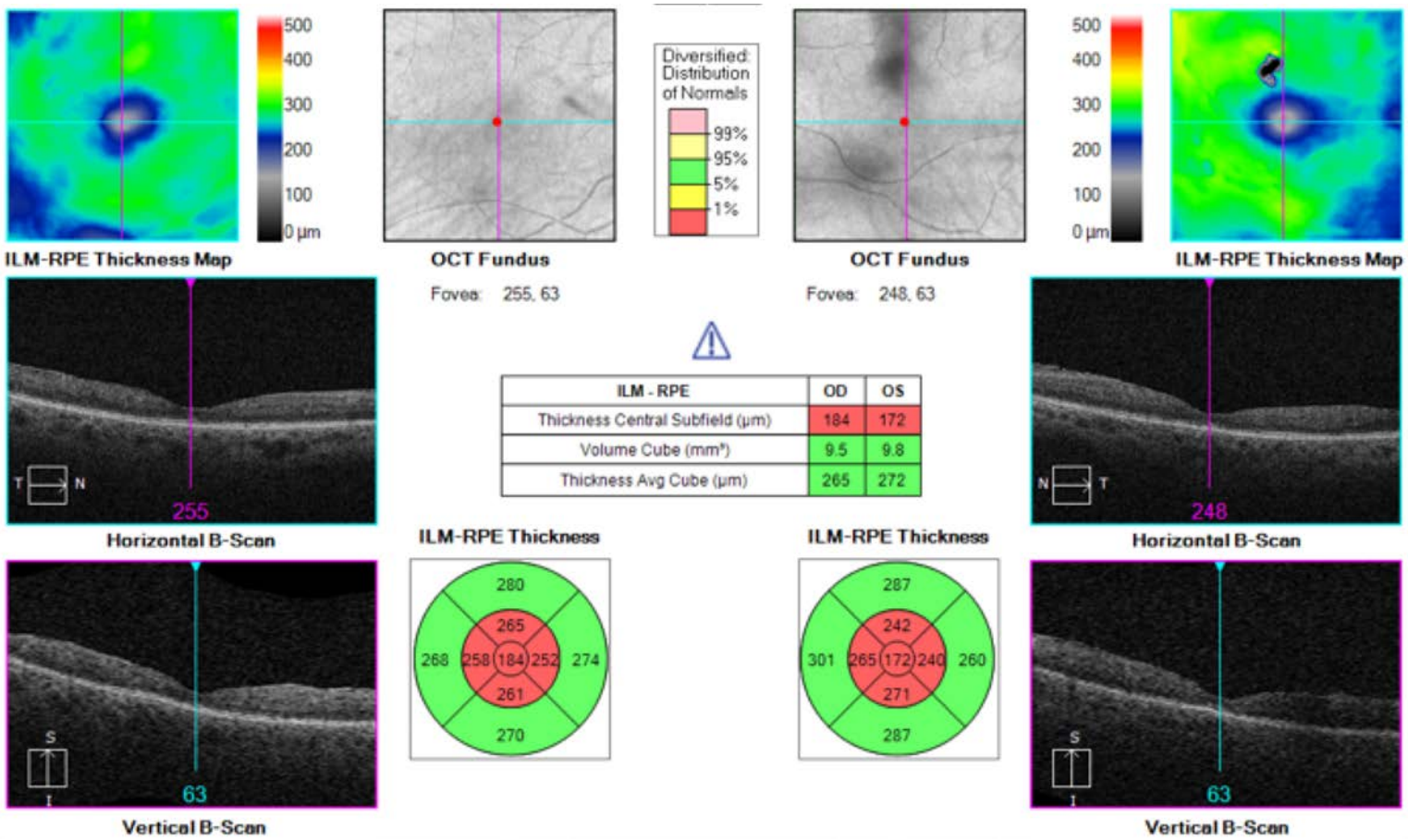


Left Eye Angiogram: Pre and Post Treatment





Maintenance With AFL Q10W OU



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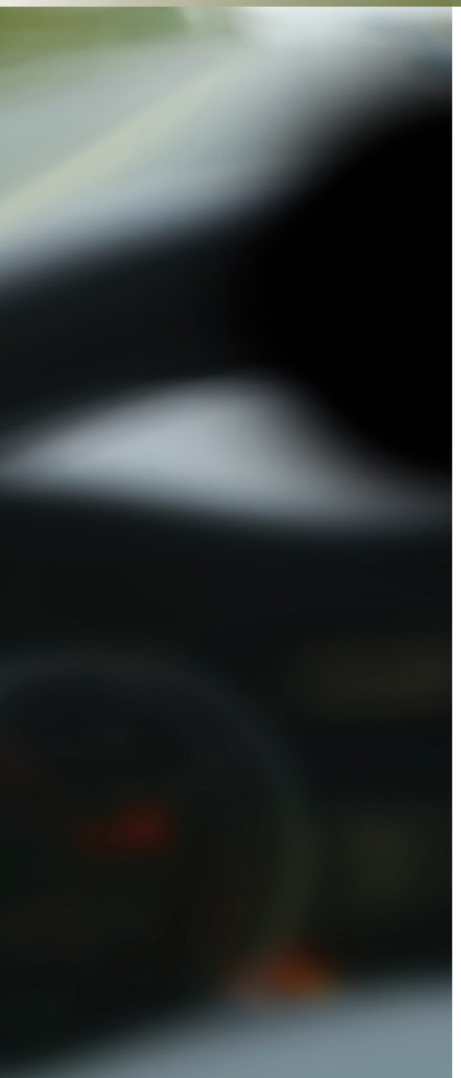
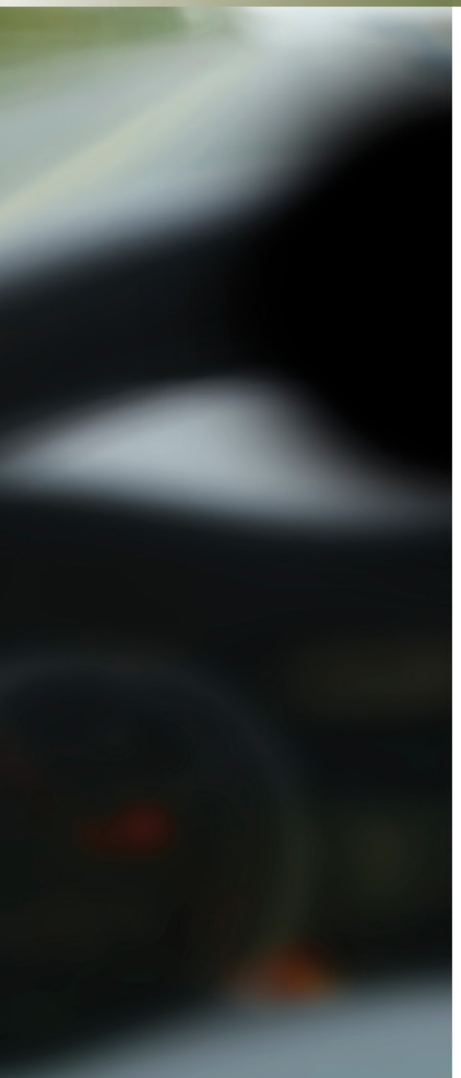
Learning Objective #4



- **Describe** age-related macular degeneration (AMD) and diabetic macular edema (DME) and their impact on patient quality of life
- **Discuss** current and emerging treatment options for AMD and DME, including efficacy, safety, and relevant clinical trial data
- **Interpret** the rationale for using real-world evidence in treatment decision making for AMD and DME to optimize patient quality of life and outcomes
- **Recognize** approaches to assist in improving outcomes in AME and DME

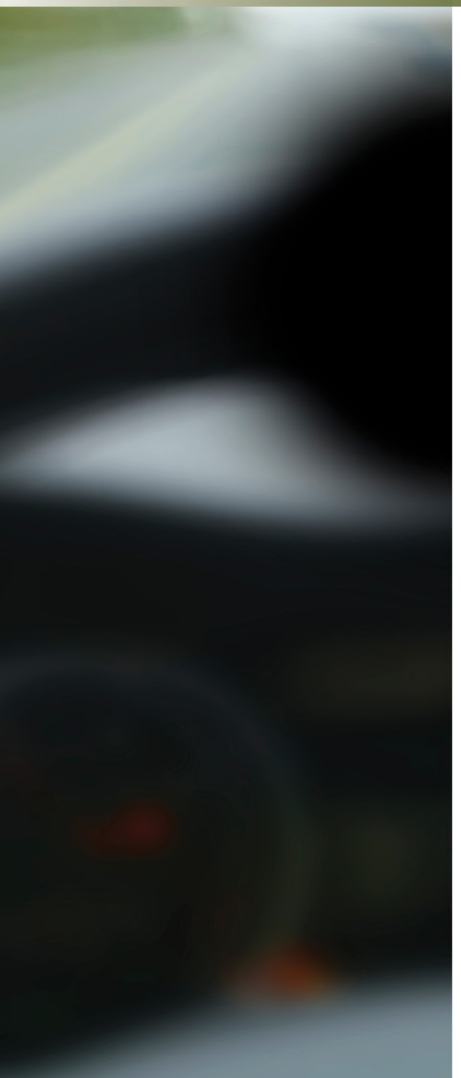
Pharmacist Considerations

Patient Education and Compliance Improvement



- Identify patients at risk
- Refer all patients with diabetes for complete, routine eye exams
- Encourage adherence to eye exam visit schedule for those with DR or DME
- Encourage treatment adherence
- Initiate preventive strategies
- Initiate patient education
- Evaluate treatment
- Assess adherence

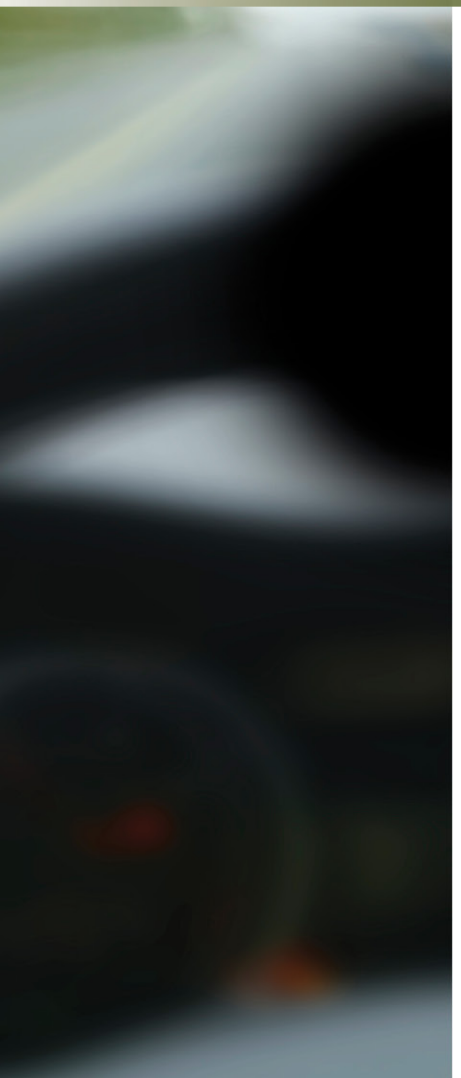
Coping Strategies for Vision Loss



- Low vision applications for mobile devices
- Special lighting
- Vision rehabilitation specialist
- Vision loss support groups

Patient Assistance Programs

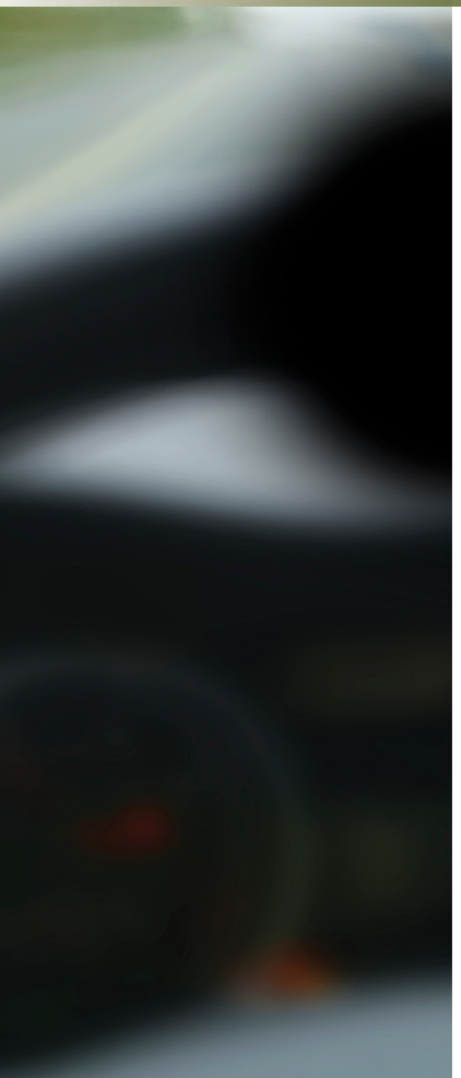
What Are Patient Assistance Programs?



- Most programs include:
  - Verification of patient-specific insurance benefits
  - Presubmission claims review and support
  - Prior authorization assistance
  - Coding and billing guidance
  - Payer research
  - Denied and underpaid claims assistance
  - Patient assistance program for qualified patients

National Comprehensive Cancer Network (NCCN). Virtual reimbursement resource room and app. https://www.nccn.org/business-policy/business/virtual-reimbursement-resource-room-and-app

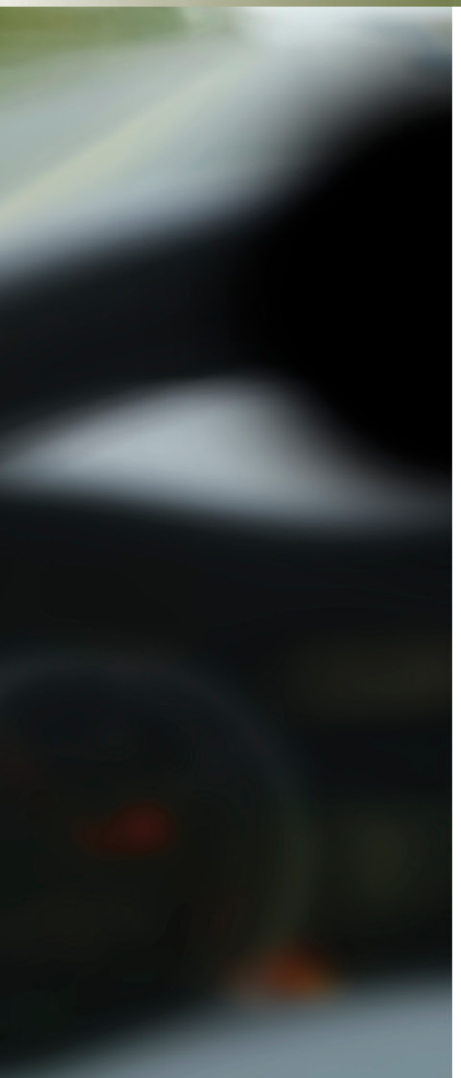
Programs and Resources



- **Patient Assistance Programs**
  - American Society of Retina Specialists (ASRS) https://www.asrs.org/patients/patient-assistance-resources
  - Good Days Assistance Program http://www.mygooddays.org/apply/
  - Patient Access Network (PAN) Foundation https://www.panfoundation.org/disease-funds/macular-diseases/

- **Patient Resources**
  - ASRS: Retina Health Information https://www.asrs.org/patients/retina-health-information
  - Prevent Blindness https://preventblindness.org/

Formulary and Payer Considerations



- Studies of anti-VEGF therapies need to translate to clinical practice
- Compliance with 9 injections during first year of treatment is difficult
- Ability to read 1 additional line on an eye chart may/may not have meaningful functional value
- Lack of evidence for treatment of nonresponders
- Necessary DME-related services (screening, diagnosis, treatment, ongoing care) may not be covered by insurance providers
- Precise data on DME financial impact to individual and society are needed to justify costs

International DME Expert Summit White Paper; June 2014.
https://www.angio.org/wp-content/uploads/2014/02/DME-Intl-Summit-White-Paper-Report.pdf

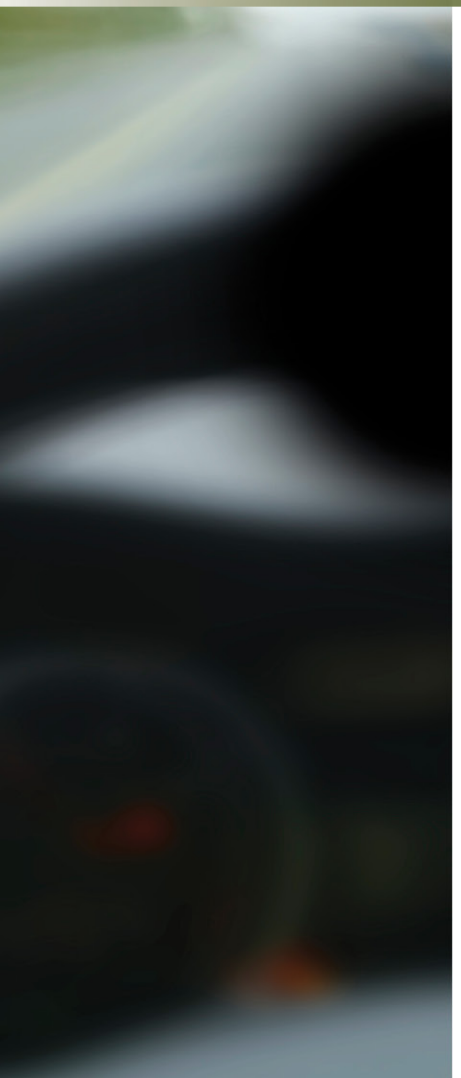
Formulary and Payer Considerations

- Cost (AWP[1]) of anti-VEGF therapies
  - Aflibercept 2.0 mg (Eylea) Q4W
    - $2,220 per 0.05 mL
  - Bevacizumab 1.25 mg (Avastin; used off label) Q4W
    - ~$50-$75 per dose ($73.20 for the Fagron Sterile Services product→)[2]
  - Brolucizumab 6.0 mg (Beovu) Q8/12W
    - $2,220 per 0.05 mL
  - Ranibizumab 0.5 mg (Lucentis) Q4W
    - $2,437 per 0.05 mL
  - Ranibizumab Port Delivery System Refill Q26 weeks
    - $9,600 per unit
- Copayments under Medicare Part B are typically 20% of drug plus physician services[3]

1. Average wholesale price (AWP). *Micromedex Red Book*. https://www.ibm.com/products/micromedex-red-book. Accessed June 9, 2022.
2. Bevacizumab (Avastin) injection solution. https://www.fagronsterile.com/avastin 3. Shah AR, et al. *Dev Ophthalmol*. 2016;55:376.

Prior Authorization

Consensus Statement on Improving the Prior Authorization Process



- Participants:
  - American Hospital Association (AHA), America's Health Insurance Plans (AHIP), American Medical Association (AMA), American Pharmacists Association (APhA), BlueCross BlueShield Association (BCBS), Medical Group Management Association (MGMA)
- Opportunities for improvement:
  - Selective application of prior authorization
  - Prior authorization program review and volume adjustment
  - Transparency and communication regarding prior authorization
  - Continuity of patient care
  - Automation to improve transparency and efficiency

Consensus statement on improving the prior authorization process. AMA. https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/arc-public/prior-authorization-consensus-statement.pdf

Selective Application of Prior Authorization

- **Encourage** the use of programs that selectively implement prior authorization requirements based on stratification of health care provider (HCP) performance and adherence to evidence-based medicine
- **Encourage:**
  1) Development of criteria to select and maintain HCPs in these selective prior authorization programs with the input of contracted HCPs and/or provider organizations; and
  2) Making these criteria transparent and easily accessible to contracted providers
- **Encourage** appropriate adjustments to prior authorization requirements when HCPs participate in risk-based payment contracts

Consensus statement on improving the prior authorization process. AMA.
https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/arc-public/prior-authorization-consensus-statement.pdf

Prior Authorization Program Review and Volume Adjustment

- **Encourage** review of medical services and prescription drugs requiring prior authorization on at least an annual basis, with the input of contracted HCPs and/or provider organizations
- **Encourage** revision of prior authorization requirements, including the list of services subject to prior authorization, based on data analytics and up-to-date clinical criteria
- **Encourage** the sharing of changes to the lists of medical services and prescription drugs requiring prior authorization via:
  1) Provider-accessible websites; and
  2) At least annual communications to contracted HCPs

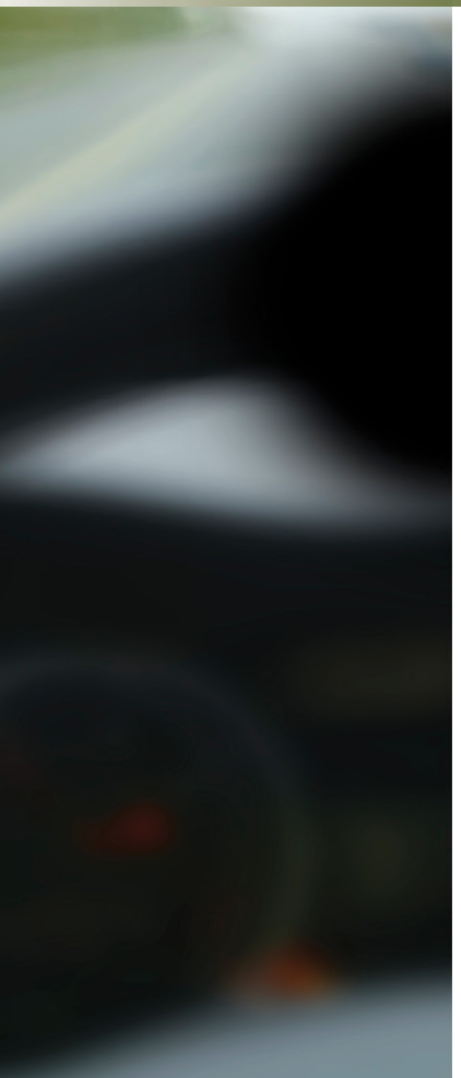
Consensus statement on improving the prior authorization process. AMA.
https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/arc-public/prior-authorization-consensus-statement.pdf

Transparency and Communication Regarding Prior Authorization

- **Improve** communication channels between health plans, HCPs, and patients
- **Encourage** transparency and easy accessibility of prior authorization requirements, criteria, rationale, and program changes to contracted HCPs and patients/enrollees
- **Encourage** improvement in communication channels to support:
  1) Timely submission by HCPs of the complete information necessary to make a prior authorization determination as early in the process as possible
  2) Timely notification of prior authorization determinations by health plans to impacted HCPs (both ordering/rendering physicians and dispensing pharmacists) and patients/enrollees

Consensus statement on improving the prior authorization process. AMA. https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/arc-public/prior-authorization-consensus-statement.pdf

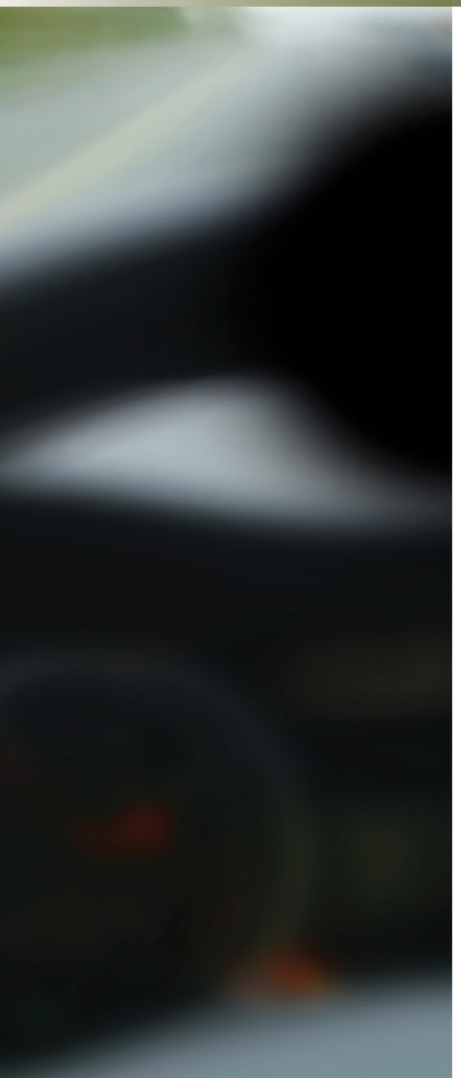
Continuity of Patient Care



- **Encourage** sufficient protections for continuity of care during a transition period for patients undergoing an active course of treatment when there is a formulary or treatment coverage change or change of health plan that may disrupt their current course of treatment
- **Support** continuity of care for medical services and prescription medications for patients on appropriate, chronic, stable therapy through minimizing repetitive prior authorization requirements
- **Improve** communication between HCPs, health plans, and patients to facilitate continuity of care and minimize disruptions in needed treatment

Consensus statement on improving the prior authorization process. AMA. https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/arc-public/prior-authorization-consensus-statement.pdf

Automation to Improve Transparency and Efficiency



- **Encourage** HCPs, health systems, health plans, and pharmacy benefit managers to accelerate use of existing national standard transactions for *electronic prior authorization* (ie, National Council for Prescription Drug Programs ePA transactions and X12 278)
- **Advocate** for adoption of national standards for the electronic exchange of clinical documents (ie, electronic attachment standards) to reduce administrative burdens associated with prior authorization

Consensus statement on improving the prior authorization process. AMA. https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/arc-public/prior-authorization-consensus-statement.pdf

Automation to Improve Transparency and Efficiency

- **Advocate** that HCP and health plan trading partners, such as intermediaries, clearinghouses, electronic health records (EHR), and practice management system vendors, develop and deploy software and processes that facilitate prior authorization automation using standard electronic transactions
- **Encourage** the communication of up-to-date prior authorization and step therapy requirements, coverage criteria and restrictions, drug tiers, relative costs, and covered alternatives:
  1) To EHR, pharmacy system, and other vendors to promote the accessibility of this information to HCPs at the point-of-care via integration into ordering and dispensing technology interfaces
  2) Via websites easily accessible to contracted HCPs

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Questions & Answers