Greatest Posterior Segment Disease Talk - Ever!

Jay Haynie, OD, FAAO
Sound Retina
Tacoma WA

Brad Sutton, OD, FAAO
Professor, Indiana University College of Optometry
Atwater Clinic
Indianapolis, IN

Mark T. Dunbar, OD, FAAO
Director of Optometry
Bascom Palme Eye Institute
University of Miami, Miller School of Medicine
Miami, FL 33136

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Mark Dunbar: Disclosure

- Optometry Consultant
  - Carl Zeiss
  - Allergan
- Advisory Board for:
  - Allergan
  - Carl Zeiss
  - Regeneron
  - Genentech

Mark Dunbar does not own stock in any of the above companies

2

Jay M. Haynie, OD

- I have received honoraria or am on advisory board for the following companies:
  - Carl Zeiss Meditec
  - Reichert Technologies
  - Notal Vision
  - Thrombogenics

3

Disclosures: Brad Sutton

- No Disclosures

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Hot Topics

- Changing paradigm in the management of diabetic retinopathy
- Evolution of wide-field imaging
- AI
- OCT and OCTA
- AMD – will we have a Tx for dry
  - Will the new anti-VEGF drugs any better?
- Management of flashes/floaters
- Pigmented lesion of the fundus

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Diabetic Retinopathy

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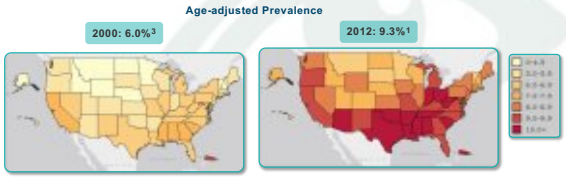
Prevalence of Diabetes Mellitus

- Affects 9.3% of the US population (29.1 million people)[1]
- Seventh cause of death in the US[1]
- By 2050 between 1 in 5 and 1 in 3 US adults (estimated) will be diabetic



	2000	2012
Diabetes Incidence (cases/1000)	6.0[4]	7.8[1]
Obesity Prevalence (%)	20.1[5]	27.6[6]

1. Centers for Disease Control and Prevention. http://www.cdc.gov/diabetes/pubs/statecontrol/national-diabetes-report-web.pdf. Accessed June 30, 2014.
2. Centers for Disease Control and Prevention. http://www.cdc.gov/diabetes/atlas/obesity/ri/atlas.html. Accessed July 25, 2014.
3. Centers for Disease Control and Prevention. http://www.cdc.gov/diabetes/statistics/prev/national/figpersub.htm. Accessed February 28, 2014.
4. Centers for Disease Control and Prevention. http://www.cdc.gov/diabetes/statistics/incidence/fig1.htm. Accessed February 28, 2014.
5. Centers for Disease Control and Prevention. http://apps.nccd.cdc.gov/brfss/list.asp?cat=OB&yr=2000&qkey=4409&state=All. Accessed February 28, 2014.

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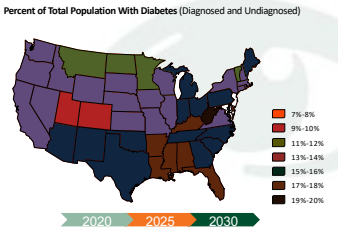
Future Prevalence Projections of Diabetes



Rowley WR, et al. *Popul Health Manag*. 2017;20(1):6-12.

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Diabetes by the Numbers

- Diabetes is increasing at epic proportions
- Optometrists are are on the front line as primary eye care providers
  - We play an important role as part of the healthcare team
- The rate of annual dilated eye examinations in people with diabetes is only approximately 50%
- Effective treatment is now available that can improve vision, not just slow disease progression
- If we can detect early and treat early, we can preserve and improve vision in many patients

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Diabetic Retinopathy 2019

- The diagnosis of DME has changed
- Anti-VEGF is the standard for treating DME
- We may need to refer before PDR
  - Earlier treatment may be beneficial (severe NPDR)
- How does the patient with PDR get treated?

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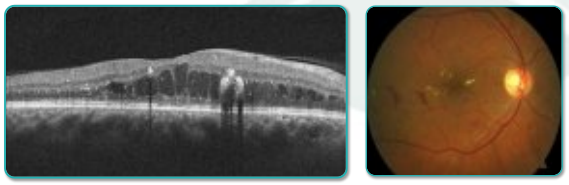
Diabetic Macular Edema (DME)



SD-OCT of a retina with DME

Color Fundus photo with DME

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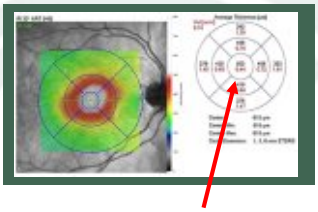
2017 DME Classification: Center Involved or Not?

- ETDRS definition of "clinically significant macular edema" modified in era of OCT
- Randomized clinical trials of anti-VEGF agents used presence of DME in **OCT central subfield**



Brown DM, et al. *Ophthalmology*. 2015;122(10):2044-52.
Nguyen QD, et al. *Ophthalmology*. 2012;119(4):789-801.

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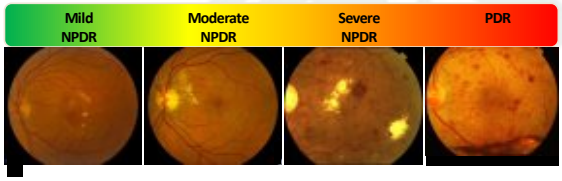
Diabetic Retinopathy Severity Scale



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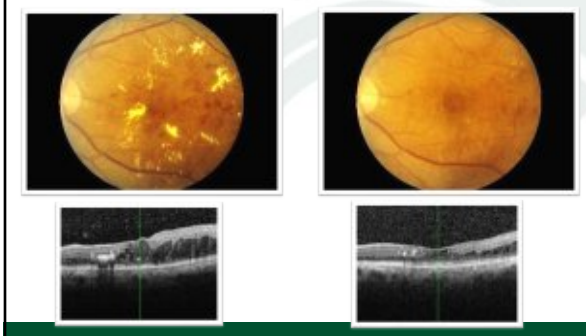
Anti-VEGF Drugs Affective in the Treatment of DME

DME Pre Treatment

DME Post Treatment



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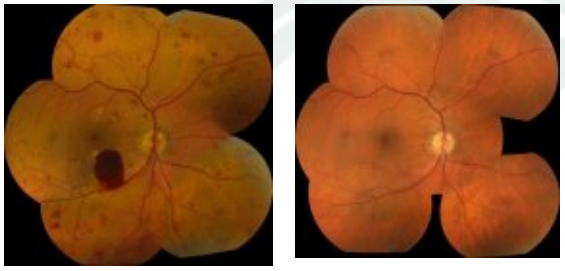
Retinopathy Regression

Screening
High-risk PDR (71A)

Month 24
Mild NPDR (35 E)



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The Debate…

- Is it better to treating early – before they develop PDR?
  - Would earlier treatment result in better visual outcomes?
  - Would it result in less # of injections?
  - Does the cost/burden of treatment warrant early treatment?

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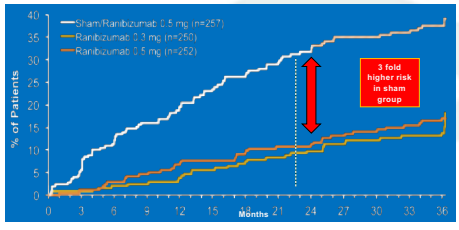
RISE/RIDE: Risk of PDR Outcomes in Sham vs Ranibizumab Groups

Time to First Progression to PDR Outcome



Cumulative probabilities calculated using the Kaplan-Meier method. Progression was defined by (1) progression from NPDR (DR severity level < 60) at baseline to PDR (DR severity level ≥ 60) at a later time point, (2) need for PRP laser, (3) vitreous hemorrhage (AE or slit lamp grade 0 at baseline to > 0 at a later time point, (4) cases identified by ophthalmoscopy, (5) vitrectomy, (6) iris neovascularization AE, or (7) retinal neovascularization AE. 1 month = 30 days. AE, adverse event; PRP, panretinal photocoagulation.

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"The Fate of 47…"

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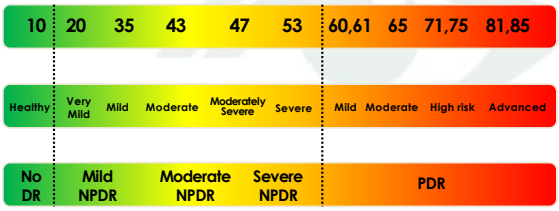
History of DR Severity Scales – ETDRS, Modified ETDRS, and International

ETDRS Grading Scale[1]



1. Early Treatment Diabetic Retinopathy Study (ETDRS) Research Group. *Ophthalmology*. 1991;98(5 Suppl):823-33. 2. Ip MS, et al. *Arch Ophthalmol*. 2012;130(9):1145-52.
3. American Academy of Ophthalmology. www.icoph.org/dynamic/attachments/resources/diabetic-retinopathy-detail.pdf. Accessed Nov 1, 2018.

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PANORAMA

- Phase 3 double-masked, randomized Prospective Study
- Efficacy and safety of intravitreal aflibercept (IAI) in patients with moderately severe to severe NPDR
  - DRSS 47 & 53
- Primary Endpoint:
  - Week 24
  - Proportion of patients improving ≥2 steps on DRSS
  - IAI groups combined
- Follow up through week 100

Wykoff, CC. Keypoints from the Phase 3 PANORAMA Study. (July 2018) American Society of Retina Specialists, Annual Meeting, Vancouver, BC, CA.

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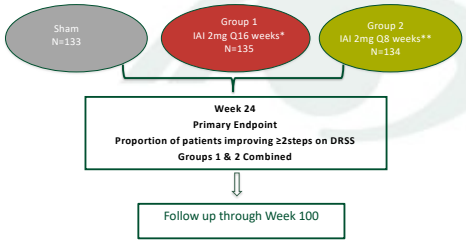
Phase 3 Double-masked, Randomized Prospective Study Efficacy and Safety of Intravitreal Aflibercept (IAI) in Patients with Moderately Severe to Severe NPDR (DRSS Level 47 and 53) N=402



*after 3 initial monthly doses and one Q8 week interval
**after 5 initial loading doses; flexible treatment schedule after week 52

Wykoff, CC. Key points from the Phase 3 PANORAMA Study. (July 2018) American Society of Retina Specialists, Annual Meeting, Vancouver, BC, CA.

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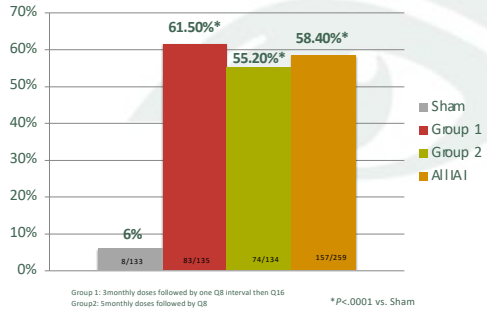
Proportion of Patients with ≥2-Step Improvement from Baseline in DRSS



Group 1: 3monthly doses followed by one Q8 interval then Q16
Group2: 5monthly doses followed by Q8

*P<.0001 vs. Sham

Wykoff, CC. Key points from the Phase 3 PANORAMA Study. (July 2018) American Society of Retina Specialists, Annual Meeting, Vancouver, BC, CA.

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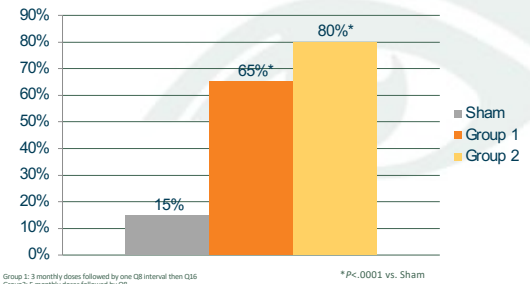
Proportion of Patients with ≥2-Step Improvement from Baseline in DRSS: 52 Weeks



Group 1: 3 monthly doses followed by one Q8 interval then Q16
Group2: 5 monthly doses followed by Q8

*P<.0001 vs. Sham

Aflibercept Improves Diabetic Retinopathy and Reduces Vision Threatening Complications in Phase 3 Trial; October 25, 2018. www.prnewswire.com

Wykoff, CC. Key points from the Phase 3 PANORAMA Study. (July 2018) American Society of Retina Specialists, Annual Meeting, Vancouver, BC, CA.

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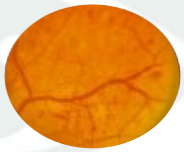
Diabetic Retinopathy Severity Score (DRSS)

Level*	ETDRS DRSS Severity	Description
1	10 and 12	DR absent
2	14, 15, 20	DR questionable, microaneurysms only
3	35	Mild NPDR
4	43	Moderate NPDR
5	47	Moderately severe NPDR
6	53	Severe NPDR
7	60, 61	Mild PDR
8	65	Moderate PDR
9	71	High-risk PDR
10	75	High-risk PDR



2-step improvement in DRSS
From DRSS level 53, Severe NPDR (level6)
To DRSS level 43, Moderate NPDR (level 4)

The Diabetes Control and Complications Trial. *Arch Ophthalmol*. 1995;113:36-51; Aiello LM. *Am J Ophthalmol*. 2003;136:122-135

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PANORAMA
Week 52 Results

- Vision threatening complications were reduced by 82% to 85% compared with sham injection
- Development of CI-DME was reduced by 68% to 74% compared with sham

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Ophthalmology Retina October 2018

Ranibizumab Induces Regression of Diabetic Retinopathy in Most Patients at High Risk of Progression to Proliferative Diabetic Retinopathy

Charles C. Wykoff, MD, PhD,[1] David A. Eichenbaum, MD,[2] Daniel B. Roth, MD,[3] Lauren Hill, MS,[4] Anne E. Fung, MD,[4] Zdenka Haskova, MD, PhD[5]

- The main objective of this exploratory post hoc analysis of the **RIDE and RISE clinical trials** was to examine DR outcomes in patients who were at highest risk for progressing to PDR (baseline DRSS levels 47/53).

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RISE AND RIDE POST HOC ANALYSIS
PATIENTS WHO HAD NPDR AND PDR WITH DME

Post hoc analysis:

- Included 746 patients (LUCENTIS 0.3 mg, n=245; LUCENTIS 0.5 mg, n=247; sham, n=254) who had DR with DME and were randomized for treatment in RISE & RIDE
- DR outcomes with LUCENTIS were evaluated in patients along the spectrum of the severity scale (baseline ETDRS levels 10–75)
- Patients with prior panretinal photocoagulation (PRP) were not included in this analysis

Wykoff et al. *Ophthalmology Retina*. 2018.

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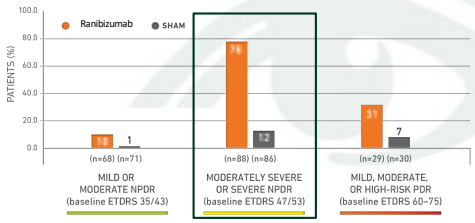
RISE AND RIDE POST HOC ANALYSIS
≥2-STEP REGRESSION IN DR AT 2 YEARS



Limitations of this analysis include that it is post hoc (ie, not prespecified in protocols). The statistical significance of these results cannot be determined, and the clinical significance of these results is unknown. Results between groups should not be compared.

Wykoff et al. *Ophthalmology Retina*. 2018.

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Ranibizumab induces Regression of Diabetic Retinopathy

Wycoff et al, Ophthalmology Retina October 2018

- At month 24, DR levels 47/53 **80% of eyes had a 2-step** improvement in ranibizumab treated eyes **vs 12% in the sham treated eyes**
- The regression of DR was not seen in earlier in less severe DR or in more severe DR
- **Study Conclusion**: In patients with baseline DR levels 47/53, ranibizumab treatment reduced the probability of patients experiencing a new proliferative event at month 36 by **3 X vs. sham Tx**

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JAMA Ophthalmology | Original Investigation

Effect of Intravitreous Anti–Vascular Endothelial Growth Factor vs Sham Treatment for Prevention of Vision-Threatening Complications of Diabetic Retinopathy

The Protocol W Randomized Clinical Trial

Raj K. Maturi, MD; Adam R. Glassman, MS; Kristin Josic, PhD; Andrew N. Antoszyk, MD; Barbara A. Blodi, MD; Lee M. Jampol, MD; Dennis M. Marcus, MD; Daniel F. Martin, MD; Michele Melia, ScM; Hani Salehi-Had, MD; Cynthia R. Stockdale, MSPH; Omar S. Punjabi, MD; Jennifer K. Sun, MD, MPH; for the DRCR Retina Network

CONCLUSIONS AND RELEVANCE In this randomized clinical trial, among eyes with moderate to severe NPDR, the proportion of eyes that developed PDR or vision-reducing CI-DME was lower with periodic aflibercept compared with sham treatment. However, through 2 years, preventive treatment did not confer visual acuity benefit compared with observation plus treatment with aflibercept only after development of PDR or vision-reducing CI-DME. The 4-year results will be important to assess longer-term visual acuity outcomes.

Jama Ophthalmology, March 30, 2021

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JAMA Ophthalmology | Original Investigation

Effect of Intravitreous Anti-Vascular Endothelial Growth Factor vs Sham Treatment for Prevention of Vision-Threatening Complications of Diabetic Retinopathy

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Jama Ophthalmology, March 30, 2021

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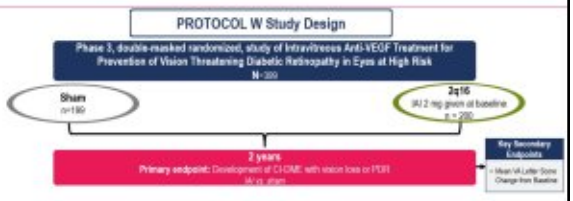
PROTOCOL W: EYLEA VS. SHAM IN MODERATE TO SEVERE NPDR (DRSS OF 43 – 53)



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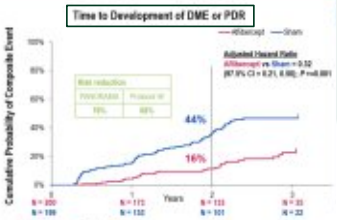
Protocol W: 2 Year Conclusions



- The 2-year data did not confer visual acuity benefit compared to sham group
  - Note: sham group received aflibercept once they developed DME or PDR

Jama Ophthalmology, March 30, 2021

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Is there a benefit from early Tx of Severe NPDR?

- So, what is the benefit of early treatment if it doesn't result in any visual acuity improvement?
- Does it matter that there is a regression in DR if when all and said and done the patient ends up with the same visual outcome?

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Discussion

- Does the data suggest patients with severe NPDR should be treated?
- How early should we refer patients with DR?
- Will the burden of early treatment be too overwhelming for ophthalmology?

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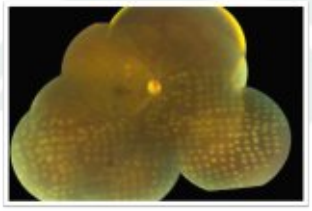
The Diabetic Retinopathy Clinical Research Network: Protocol S

Prompt PRP
versus
Ranibizumab + Deferred PRP
for PDR Study

Supported through a cooperative agreement from the National Eye Institute and the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Department of Health and Human Services EY14231, EY14229, EY018817



DRCR.net NIH National Eye Institute NIDDK

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Follow-up Schedule

Baseline to 1 Year

- **PRP group:** Visits every 16 weeks*
- **Ranibizumab group:** Visits every 4 weeks to assess for PDR treatment
- Both groups simultaneously evaluated for DME treatment

1 Year to 2 Years

- **PRP group:** Visits every 16 weeks*
- **Ranibizumab group:** Visits every 4wk to 16wk to assess for PDR treatment
- Interval is extended if injections for PDR and DME deferred ("Defer and Extend")

*Eyes with DME could be seen more frequently for DME treatment as needed.

Diabetic Retinopathy Clinical Research Network http://publicfiles.jaeb.org/S1ResultsSlideset_3_2_16.pptx

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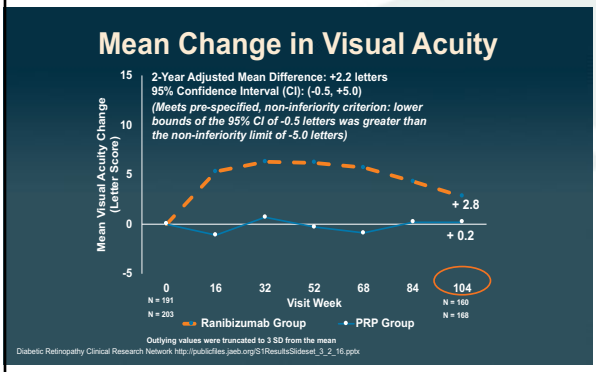
Mean Change in Visual Acuity



Retinopathy Clinical Research Network http://publicfiles.jaeb.org/S1ResultsSlideset_3_2_16.pptx

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DRCR.net: Protocol S

- At 2 years, VA improved by **2.8 letters** from baseline in the ranibizumab group vs. improvement of **0.2 letters** from baseline in the PRP group
- There was more peripheral VF loss and more vitrectomy's in the PRP group vs. Lucentis
  - VF Loss: 213 dB in the ranibizumab group vs. 531 dB in the PRP group
  - PPV: 15% with PRP vs. 4% with Lucentis
- When DME present, Lucentis did a better job treating

JAMA. 2015; 314(20):2137-2146. doi: 10.1001/jama.2015.15217 (Published).

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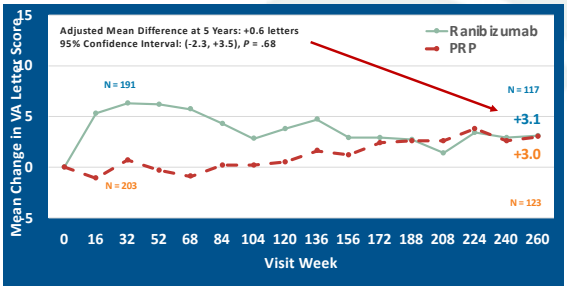
Mean Changes in VA From Baseline Over Time - Overall Cohort



Diabetic Retinopathy Clinical Research Network (DRCR.net).
http://drcrnet.jaeb.org/ViewPage.aspx?PageName=Presentations. Accessed October 26, 2018.

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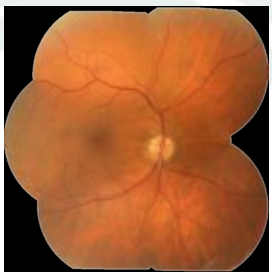
How Does this Patient Get Treated Today?

High-risk PDR

Month 36
Mild NPDR



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Diabetic Retinopathy – Where Does that Leave Us?

- Should Anti-VEGF become the standard of care for PDR and NOT laser PRP?
- Should severe NPDR should be treated with anti-VEGF or wait until they progress to PDR?

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Retinal Imaging:

A Camera is a Camera…

Does it matter which one you have?

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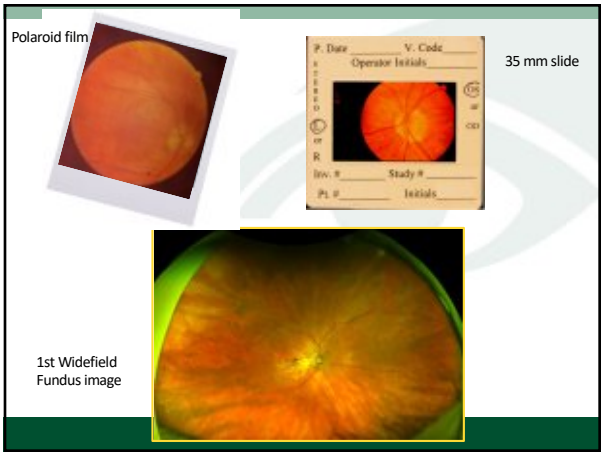

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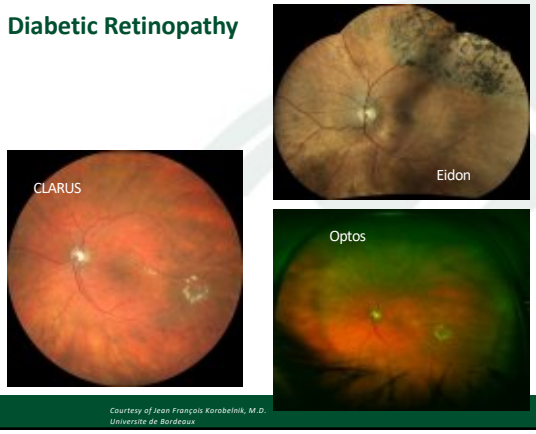
Diabetic Retinopathy



Courtesy of Jean François Korobelnik, M.D.
Université de Bordeaux

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Diabetic Retinopathy

Courtesy of Jean François Korobelnik, M.D.
Université de Bordeaux

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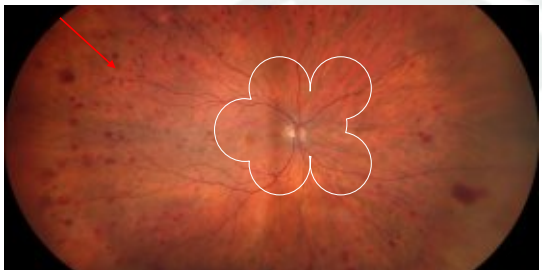
Identification of Additional Retinal Pathology

Retinal
Neovascularization >1/2
Disk Area



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Why does Wide-Field Fundus Imaging Matter?

- When do you do wide field imaging?
- Can it substitute for a dilated fundus exam?
- How do you see this technology evolving?

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In a primary eye care setting do we need to dilate every patient?

The reality:

- In a young patient population, the incidence of peripheral retinal pathology is exceedingly rare
  - You have to dilate a lot of patients to see any meaningful retinal pathology
- With changes in health care – there are greater demands to see more patient
- Is it an unreasonable medical expense?

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AMERICAN ACADEMY OF OPHTHALMOLOGY | EyeNet® Magazine

November 2017

Artificial Intelligence

AI is poised to revolutionize medicine.

50

IOVS Dec 2016

Retina

Improved Automated Detection of Diabetic Retinopathy on a Publicly Available Dataset Through Integration of Deep Learning

Michael David Abràmoff,[1-3] Yiyue Lou,[4] Ali Erginay,[5] Warren Clarida,[3] Ryan Amelon,[3] James C. Folk,[1,3] and Meindert Niemeijer[3]

[1]Department of Ophthalmology and Visual Sciences, University of Iowa Hospitals and Clinics, Iowa City, Iowa, United States
[2]Iowa City Veterans Affairs Medical Center, Iowa City, Iowa, United States
[3]IDx LLC, Iowa City, Iowa, United States
[4]Department of Biostatistics, College of Public Health, University of Iowa, Iowa City, Iowa, United States
[5]Service d' Ophtalmologie, Hôpital Lariboisière, APHP, Paris, France

Conclusions. A deep-learning enhanced algorithm for the automated detection of DR, achieves significantly better performance than a previously reported, otherwise essentially identical, algorithm that does not employ deep learning. Deep learning enhanced algorithms have the potential to improve the efficiency of DR screening, and thereby to prevent visual loss and blindness from this devastating disease.

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APR 12, 2018

AI device for detecting diabetic retinopathy earns swift FDA approval

By Kang Jin Lee
FDA

- Images captured by Topcon NW400 non-mydriatic retinal camera
- Images sent to a cloud-based server that utilizes the IDx-DR software and a 'deep learning' algorithm
- The technology was **87% sensitive and 90% specific** for detecting **more than mild** diabetic retinopathy
- The algorithm correctly identified **100% of with ETDRS level 43 or higher (moderate NPDR)**

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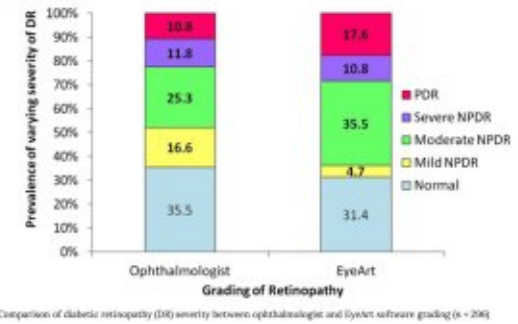
From: Automated diabetic retinopathy detection in smartphone-based fundus photography using artificial intelligence



Comparison of diabetic retinopathy (DR) severity between ophthalmologist and EyeArt software grading (n = 296)

53

The Evolution of OCT Imaging

- OCT has changed how clinicians look at the retina
- The assessment of retinal abnormalities based on OCT imaging has advanced eye care
- OCT in Optometry practices ~ 20-40%
- As the technology has evolved -> prices continue to come down

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November 2016

ARVO
The Association for Research in Vision and Ophthalmology

New Videos, Resources Launch Outreach Campaign On Vision-Preserving Technology

Impact of optical coherence tomography on patients, general public revealed

OCT has become the predominant means of detecting and monitoring diseases like macular degeneration, diabetic retinopathy and glaucoma. Everyone over the age of 60 is recommended to get an OCT scan once a year.

"Everyone over the age of 60 is recommended to get an OCT scan once a year"

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Crossfire on OCT…

- Has OCT become "Standard of Care" in Optometry?
- Should OCT be done on "every" patient as a screening tool?
- Should OCT be done only when there is an indication?
  - Diabetes, macular degeneration

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The Challenge…

- Being able to correlate what you are seeing clinically with **what is happening anatomically – and then making the correct diagnosis**
  - Is there fluid or retinal thickening?
  - Where is the fluid?
- Being able to diagnose conditions that may not be seen with traditional ophthalmoscopy

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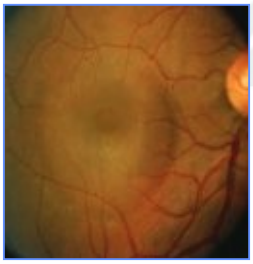
Advances in Diagnostic Technology can Help Establish a Diagnosis

58

Where is the Fluid?



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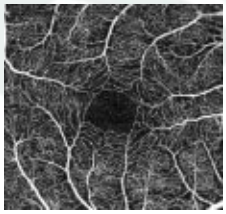
OCT Angiography: A New Way of Visualizing Vessels

- Identify retinal circulation using the intrinsic motion of blood cells in the vessel
- Functional and structural, information with en face projections
- No contrast medium, and the data are 3-dimensional and depth resolved



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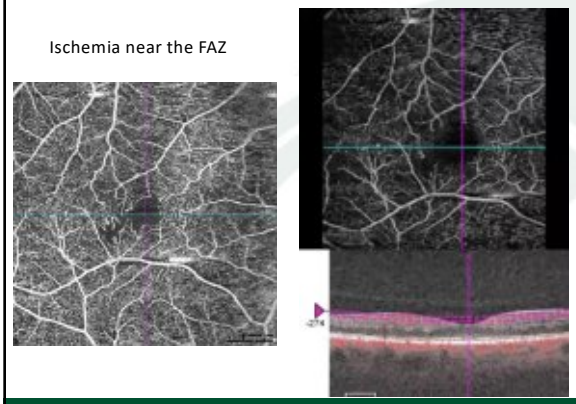
Ischemia near the FAZ



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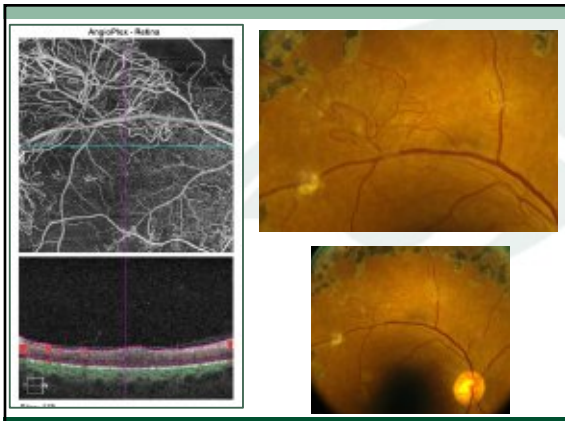

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Crossfire on OCT…

- Should every optometry practice have access to OCT?
- Has OCT become “Standard of Care” in Optometry?
- Should OCT be done on ”every” patient as a screening tool?
- Should OCT be done on every patient with diabetes or macular degeneration?

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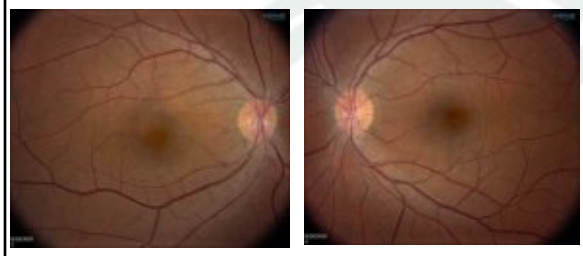
32 yo Hispanic Male

Blurry vision in the RE X 1 week



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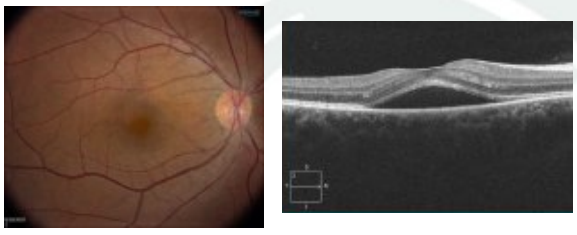

High Stress

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Management of CSR

- Reduce stress
- Observation
  - Often resolves without treatment
- Focal laser if isolated “hot” spot
- PDT recalcitrant or recurrent CSR
- Oral therapy: spironolactone
  - Diuretic to treat HTN

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British Journal of Ophthalmology

Spironolactone versus observation in the treatment of acute central serous chorioretinopathy

Xinghong Sun,[1] Yuanlu Shuai,[2] Wangyi Fang,[3] Jia Li,[3] Weizhong Ge,[2] Songtao Yuan,[3] Qinghuai Liu[3]

2018

Complete resolution of SRF was achieved in **55.6%** (10/18) and **8.3%** (1/12) of the eyes in the treatment group and the control group, respectively, **at 2 months**

Conclusions Oral spironolactone is more effective with a faster absorption of SRF than observations. It is a promising treatment for acute CSC.

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SPIRONOLACTONE FOR NONRESOLVING CENTRAL SEROUS CHORIORETINOPATHY

A Randomized Controlled Crossover Study

Journal of Ophthalmology

Mineralocorticoid Receptor Antagonist Treatment for Steroid-Induced Central Serous Chorioretinopathy Patients with Continuous Systemic Steroid Treatment

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Why it might work

- Strong relationship between exogenous cortisol and CSR
- Mineralocorticoid receptor (MR) pathway may play a role in the disease pathogenesis
- Aldosterone controls retinal fluid homeostasis through upregulating the ion and water channel, which is expressed in the apical region of RMGs

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55 yo Caucasian Male

- **Presents with sudden onset of floaters RE**
  - "Feels like I am looking through an oil slick or water"
- BCVA: 20/20 each eye
- CVF: FTFC OU
- Dilated patient with 1% Tropicamide, 2½% Neo
- Examines with 90 D and peripheral retina with BIO and 20 D lens
- Notes Weiss Ring and attached retina

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55 yo Caucasian Male

- Diagnosis: PVD
- Educated regarding signs and symptoms of retinal detachment
- Explains need to **return immediately** if he should see these symptoms
- RTC 1 yr

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Crossfire…

- Did the OD manage this patient correctly?
- Was there anything else they **should have** done?
- Was he obligated to do scleral depression?
- Should he have referred this patient to a retinal specialist?

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OPTOMETRIC CLINICAL PRACTICE GUIDELINE

American Optometric Association

Care of the Patient with

Retinal Detachment And Related Peripheral Vitreoretinal Disease

Approved by the AOA Board of Trustees April 27, 1995(1st ed).
Reviewed April 1998, Revised June 1999, Reviewed 2004

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II. CARE PROCESS

This Guideline describes the optometric care provided to a patient with a retinal detachment or related peripheral vitreoretinal disease. The components of patient care described are not intended to be all inclusive. Professional judgment and individual patient symptoms and findings may have significant impact on the nature, extent, and course of the services provided. Some components of care may be delegated.

A. Diagnosis of Retinal Detachment and Related Peripheral Vitreoretinal Disease

Evaluation of patients with retinal detachment or related peripheral vitreoretinal disease includes the elements of a comprehensive eye and vision examination.[4] It may include, but is not limited to, the following areas:

1. Patient History

The clinician should review the patient's present and past history of ocular and systemic disease and elicit information regarding:

- Loss of vision
- Sudden, recent onset of floaters
- Flashing lights
- Loss of peripheral visual field
- Family members with loss of vision or history of retinal disease
- History of trauma

2. Ocular Examination

The examination for retinal detachment and related peripheral vitreoretinal disease may include, but is not limited to:

- Best corrected visual acuity
- Pupillary responses
- Biomicroscopy
- Binocular indirect ophthalmoscopy with scleral indentation if indicated
- Tonometry
- Visual field screening (confrontation)
- Retinal drawing or photodocumentation, if indicated

3. Supplemental Testing

The interpretation of data obtained during the examination may indicate the need for additional testing which may include, but is not limited to:

- Fundus fluorescein angiography with fluorescein contact lens, or other precorneal condensing lens
- Ultrasonography
- Fluorescein angiography
- Formal visual field testing

Binocular indirect ophthalmoscopy with pupillary dilation is generally necessary for diagnosis of a peripheral retinal break or detachment. During ophthalmoscopy, the undetlying chorioidal detail is obscured by the detached retina, a helpful sign in detecting the presence of a retinal detachment. Scleral depression may be needed to detect small, asymptomatic peripheral retinal detachments. The biomicroscope can be used to search for breaks in detachments using a mirrored fundus contact lens, a hand-held precorneal fundus lens, or a wide-field fundus contact lens. A search for all possible retinal breaks should be performed, and any breaks discovered should be accurately drawn on the patient's chart or photodocumented.

The biomicroscopic examination can also be useful in detecting a rhegmatogenous retinal detachment or a retinal tear without a significant associated detachment by the observation of pigment cells floating in the anterior vitreous cavity immediately behind the lens (Shaffer's sign or "tobacco dust").[5,6] These pigment cells can migrate from the uncovered

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the detached retina, a helpful sign in detecting the presence of a retinal detachment. Scleral depression may be needed to detect small, asymptomatic peripheral retinal detachments. The biomicroscope can be used to search for breaks in detachments using a mirrored fundus contact lens, a hand-held precorneal fundus lens, or a wide-field fundus contact lens. A search for all possible retinal breaks should be performed, and

75

65 yo Caucasian Male PVD

The rest of the story…

- Patient return about 5 weeks later complaining he can't see out of his right eye for th past 4 days
- Has a macula-off RD
- RD repaired but VA 20/200

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Crossfire Topics

- Should optometrists should refer all patients with flashes and floaters because the risk of having a retinal tear is too great?
- The standard of care for evaluating a patient with flashes and floaters is **scleral depression**

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PVD

- Retinal tears occur 8-15% of eyes with symptomatic PVD
  - 90% are superior
- VH occurs in 13-19% of symptomatic PVD's
- VH + PVD -> 70% will have a retinal break
- PVD No VH -> 2-4% will have retinal break

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Lattice Degeneration as a Routine Finding?

Is this any cause for concern?

How do you manage it?

What is the Risk for developing a retinal tear or RD

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Lattice Degeneration

- Present 5-20% of the general population
- Localized area of retinal thinning associated with a fluid pocket in the overlying cortical vitreous

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Lattice Degeneration and Risk of RD

- RD develop in **0.7%** of eyes with lattice degeneration followed for 10.8 yrs
- Eyes with lattice that developed tractional retinal tears
  - 40% occurred in areas not associated with lattice…normal-appearing retina

Byer NE. Ophthalmology. 1989; 96:1401-1402

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Macular Degeneration

- One of the most common causes for vision loss in the elderly population
- 85% with dry AMD; 15% with Wet AMD
- Nutritional supplements have been shown to decrease the risk of progression to wet AMD
- Newer Anti-VEGF treatments have greatly improved the visual outcome
  - Earlier detection of CNV results in even better visual come
- We now understand there is a strong genetic link to AMD
  - There is a genetic test commercially available – ArticDx

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The evolution of Anti-VEGF

- Lucentis
- Avastin
- Eylea

New drugs in the pipeline (phase III)

- Brolucizumab – Novartis: quarterly treatment
- Abicipar – Allergan: quarterly treatment

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Potential Treatments for Geographic Atrophy

- **APL-2: C3 inhibitor by Apellis**
- May have a wide range of possibilities for complement –mediated disease
- Blocks all the pathways of complement activation
- Being studies in GA, paroxysmal nocturnal hemoglobinuria (PNH)

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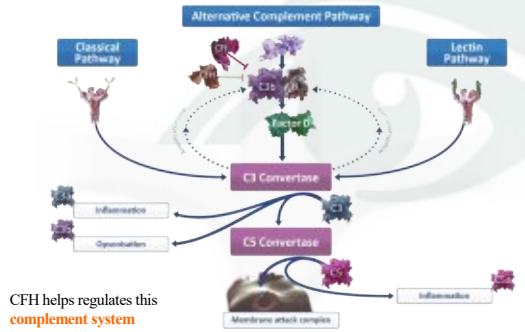
Pathways for Complement Activation

Required for the initiation and amplification of the alternative complement pathway



CFH helps regulates this **complement system**

Figure based on the scientific information from the following sources: Owen J., Punt J. and Stranford S. (2013) Kuby Immunology 7th edition, New York: W.H. Freeman and Co Ltd; Walport MJ. N Engl J Med 2001;344:1058–66

85

85

Filly 2 Trial

- APL-2 is a synthetic cyclic peptide conjugated to a polyethylene glycol polymer that binds to C3 and C3b, blocking the pathways of complement activation
- Theory: by inhibiting C3, you can slow/stop the rate of degeneration
- Phase 2 FILLY trial: showed a 29% reduction in the growth of geographic atrophy lesions after 12 months in the monthly treatment group, and a 20% reduction in the every-other-month treatment group

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18 Month Data

February 2018

- "The 18-month results of the FILLY trial support the positive effect seen at 12 months. In the FILLY trial, APL-2 significantly reduced the growth of GA, and may for the first time offer these patients hope of preserving their vision. We eagerly anticipate the start of the Phase 3 trials."

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Technologies Involved in the Early Detection of AMD

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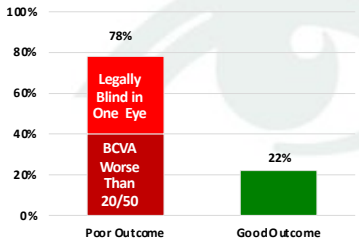
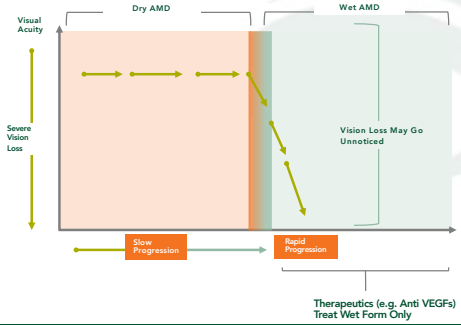
Too Many AMD Patients Are Diagnosed After Vision Loss Has Already Occurred



Cervantes-Castañeda RA, et al. Eye (Lond). 2008;22(6):777-781.
Olsen TW, et al. Ophthalmology. 2004;111(2):250-255.

89

Vision Loss in AMD



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The Challenge:

Detect Wet AMD Before Severe Vision Loss Occurs

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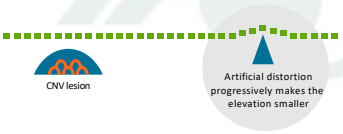
Preferential Hyperacuity Perimetry



When the elevation caused by CNV is larger than the artificial distortion, the patient will preferentially pick this spot of true distortion

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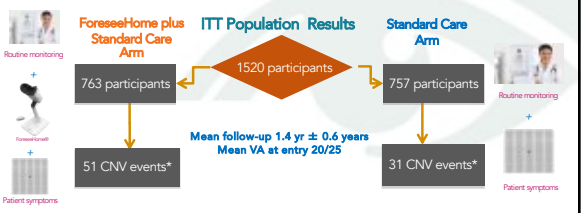
NEI Sponsored AREDS2 Home Study



Primary Outcome: Change in Best Corrected Visual Acuity from Baseline to CNV Detection

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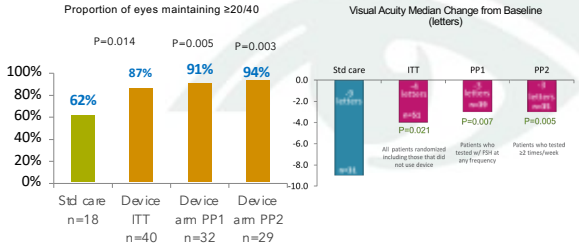
Maintenance of Vision



Testing with FSH 2x/week led to 51% more eyes maintaining 20/40 and fewer letters lost

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