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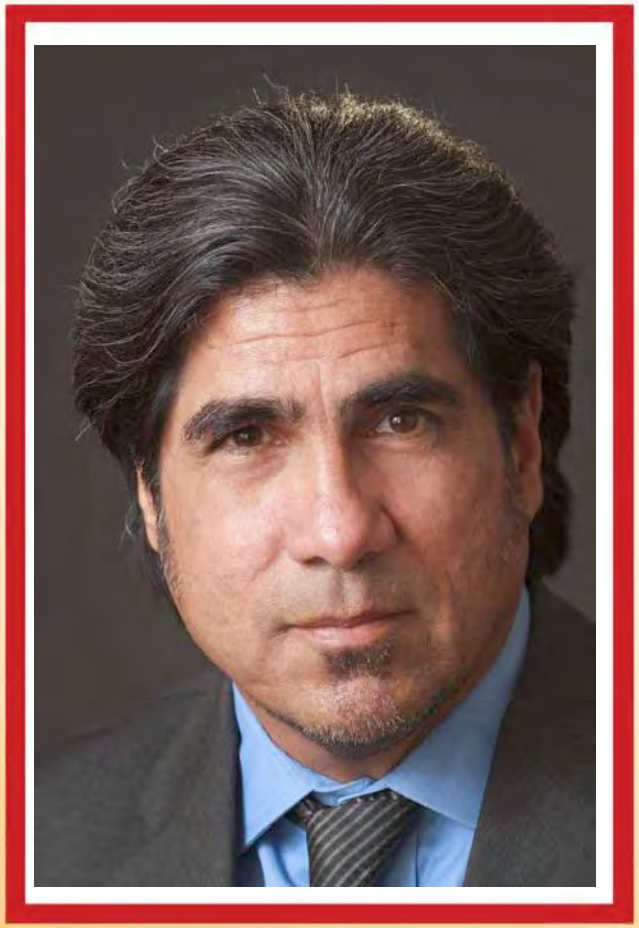
Bringing Americans to Eye Care

2018 Focus on Eye Health National Summit:
Research to Impact



Improving Access Through Telemedicine

--- moderator ---

Jorge Cuadros, OD, PhD
University of California, Berkeley
and EyePACS

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Improving Access Through Telemedicine

Graham E. Quinn, MD, MSCE
Children's Hospital of Philadelphia

Rajeev Ramachandran, MD, MBA
University of Rochester

Emily Y. Chew, MD
National Eye Institute

Lily Peng, MD, PhD
Google AI Healthcare

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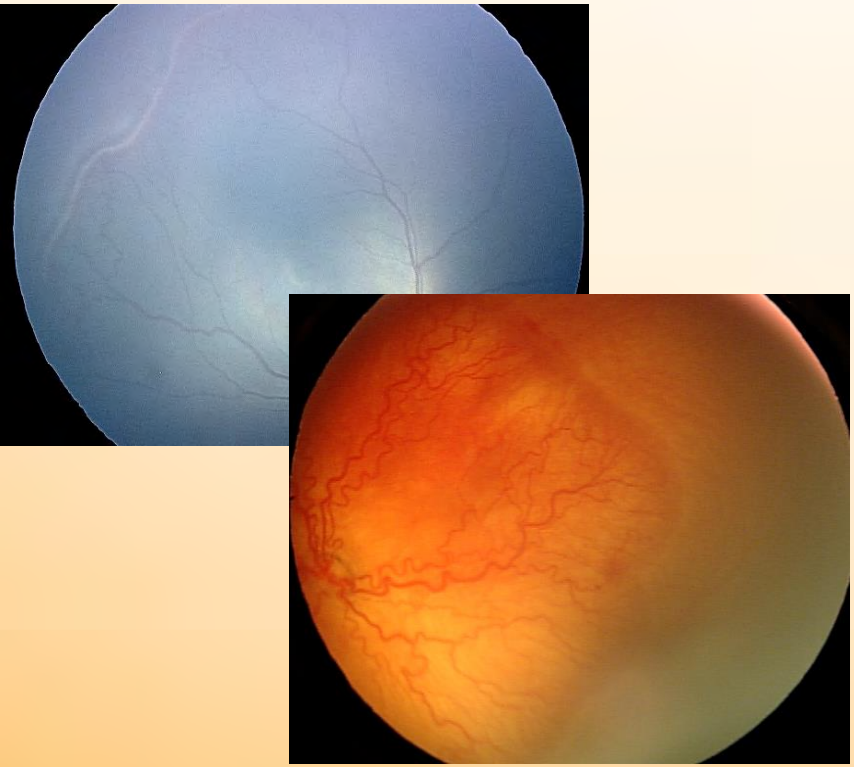
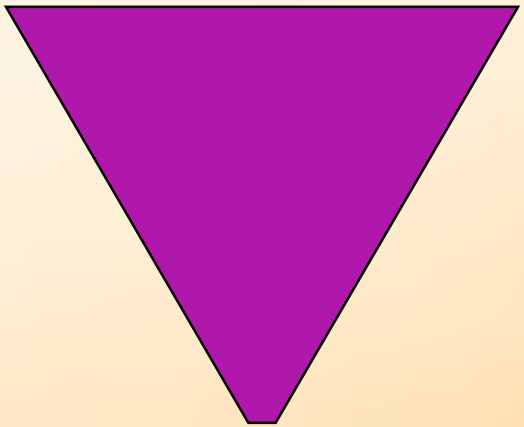
Telemedicine and ROP

Graham E. Quinn, MD, MSCE
Pediatric Ophthalmology
Children's Hospital of Philadelphia
University of Pennsylvania

What are the manpower demands for detection of serious ROP?



8200 babies ~20K exams



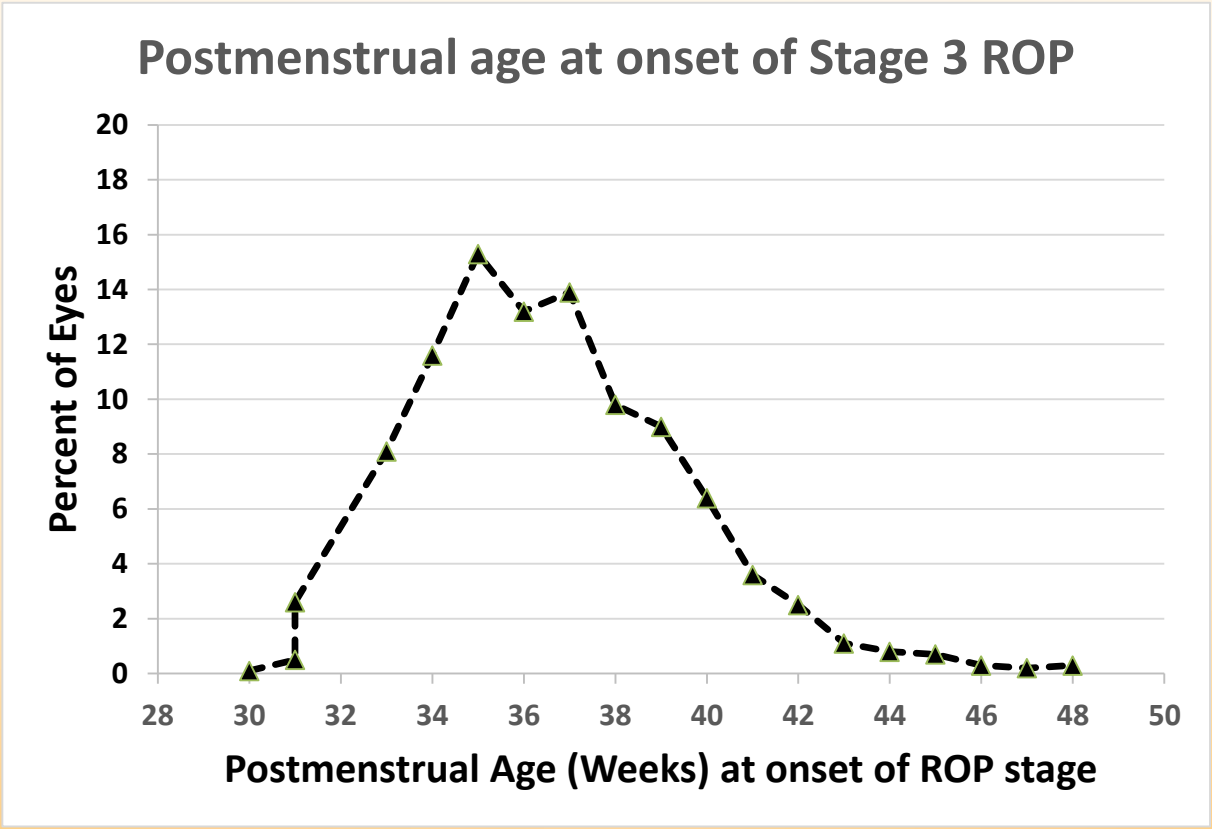
363 infants treated

A Fielder et al; 2002

UK cohort study 1997/8

Severe ROP to treatment – 1-3 DAYS

not weeks or months

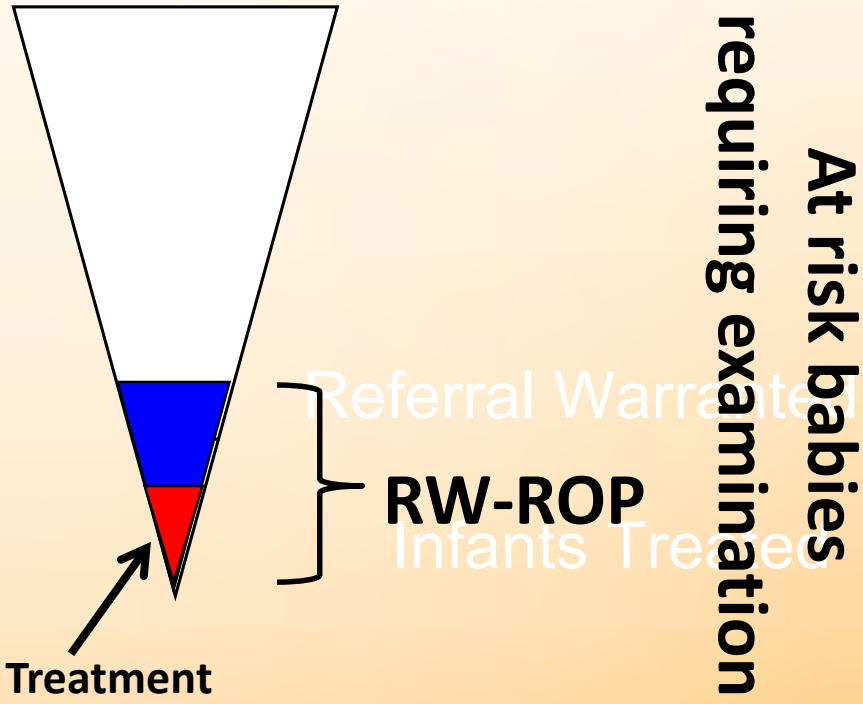


Shift from diagnostic exam to ROP screening

Referral-warranted ROP (Ells et al, 2003)

1) Any ROP in zone 1
2) Any stage 3
3) Presence of plus disease (2 or more quadrants)

Consistent with Type 1 + Type 2 ROP (based on results of ETROP trial)



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	#	Outcome	% Sensitivity	% Specificity
Schwartz et al, 2000	10	Plus	100 (81-100)	0 (0-98)
Yen et al, 2000	23	Predict prethresh at 32-34 wks PMA imaging	33	100
Ells et al, 2003	44	RW-ROP	100 (85-100)	96 (86-100)
Chiang et al, 2006	64	Type 2 or worse	77 (70-84)	96 (94-98)
Wu et al, 2006	43	Type 2 or worse	100 (16-100)	97 (87-100)
Chiang et al, 2007	67	Type 2 at 31-33 wks	76 (70-82)	96 (93-98)
PHOTO-ROP	51	Clinically significant ROP	92 (81-97)	37 (23-32)
Dhaliwal et al, 2009	81	Stage 3	57 (29-82)	68 (63-73)
Lorenz et al, 2009	1222	Suspect treatment req	100 (92-100)	-
Silva et al, 2011	230	Type 2 or worse	100 (66-100)	99.6 98-100)
Dai et al, 2011	108	Treatment requiring	100 (72-100)	98 (93-100)

At least 5 Level I studies (481 infants)

- **Sensitivity**:
  - **76**-100% for ≥Type-2 ROP
  - **87**-100% for ≥Type-1 ROP
  - (one 57% for stage 3)
- **Specificity**: 37-98%

3 Level III studies (1462 infants)

- **Sensitivity**: 100% (one N/A)
- **Specificity**: 99-100%

Ophthalmic Technology Assessment

Detection of Clinically Significant Retinopathy of Prematurity Using Wide-angle Digital Retinal Photography

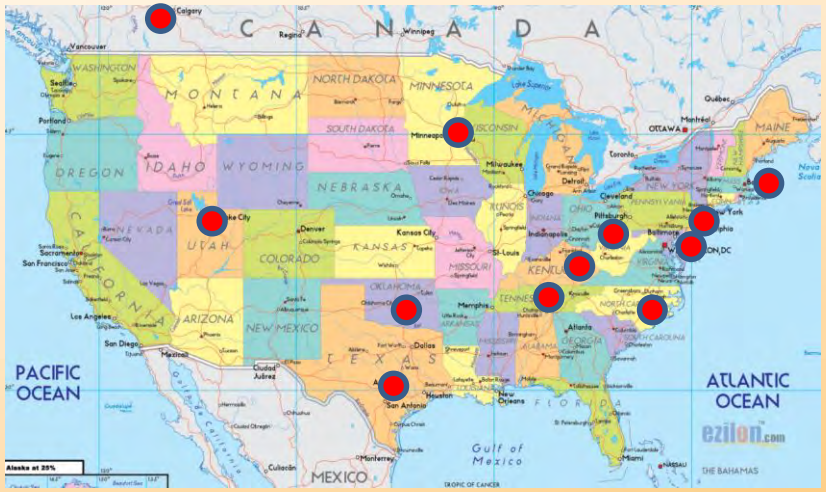
A Report by the American Academy of Ophthalmology

Michael F. Chiang, MD,[1] Michele Melia, ScM,[2] Angela N. Buffenn, MD, MPH,[3] Scott R. Lambert, MD,[4] Franco M. Recchia, MD,[5] Jennifer L. Simpson, MD,[6] Michael B. Yang, MD[7]

Ophthalmology 2012;119:1272–1280

Telemedicine in acute phase ROP – e-ROP

To evaluate a telemedicine <u>system</u> for detection of eyes of at-risk babies in need of exam by an ophthalmologist experienced in ROP



Funded by NEI/NIH 2010-16

ROP Treatment per Infant (N=855)

		Diagnostic examination findings of RW-ROP	
		Present	Absent
Image Evaluation of RW-ROP	+	159	137
	–	3	554

Sensitivity = 98.2%
(94.4-99.4%)
Specificity = 80.2%
(77.0-79.1%)
PPV = 44.3%
NPV = 99.6%

Single Session per Infant (N=855)

		Diagnostic examination findings of RW-ROP	
		Present	Absent
Image Evaluation of RW-ROP	+	215	24
	–	80	534

Sensitivity = 90.0%
(85.4-93.5%)
Specificity = 87.0%
(84.0-89.5%)
PPV* = 62.5%
NPV* = 97.3%

* Assumed RW-ROP rate of 19%

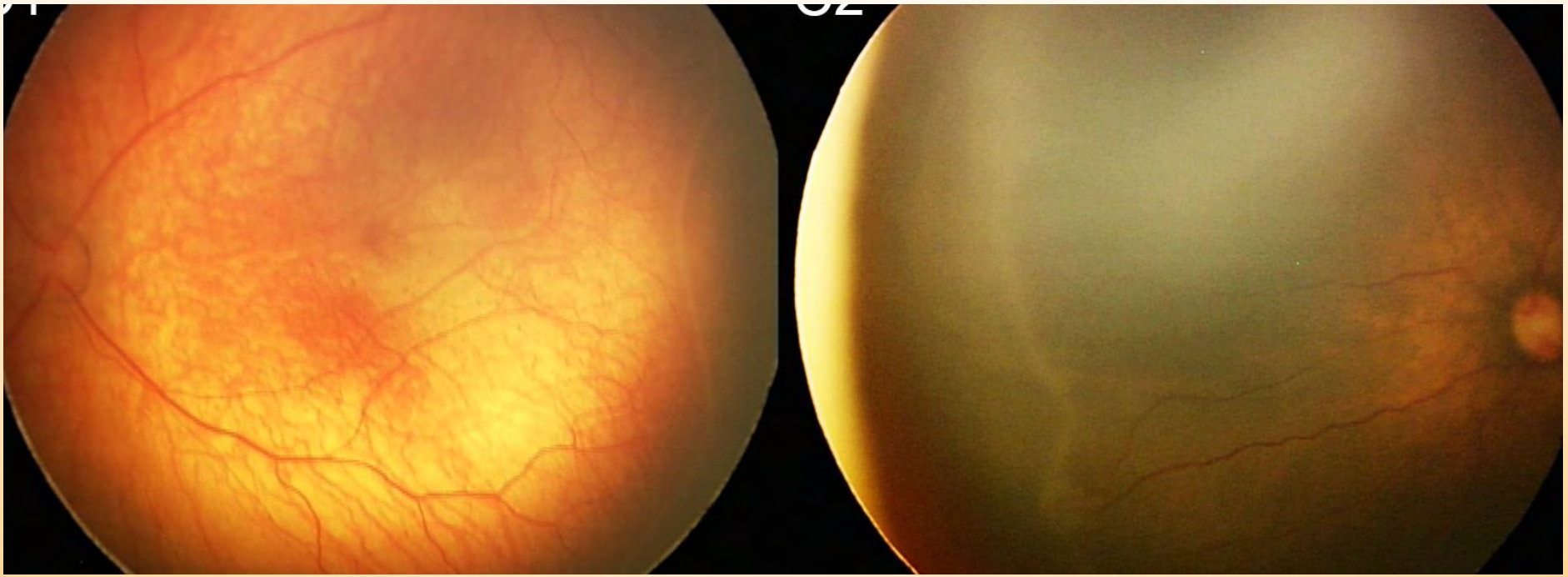
Image grading compared to exam results in e-ROP study

RW-ROP Status	Image grading +	Image grading -
Exam +	632 True positives	***161 False negatives***
Exam -	***854 False positives***	3703 True negatives

Image grading compared to exam results in e-ROP study

RW-ROP Status	Image grading +	Image grading -
Exam +	632 True positives	***161 False negatives***
Exam -	***854 False positives***	[illegible] True negatives

Stage 3 on exam: Grading -



Consensus review (40 image sets):

45% agree stage 3 on exam

Estimate of overall discrepant cases

- 161 G-/E+ (false negatives): estimate 46.5% would agree with **clinical exam** for the presence of RW-ROP
- 854 G+/E-: (false positives): estimate 70.0% would agree with **image graders**

Take home message:

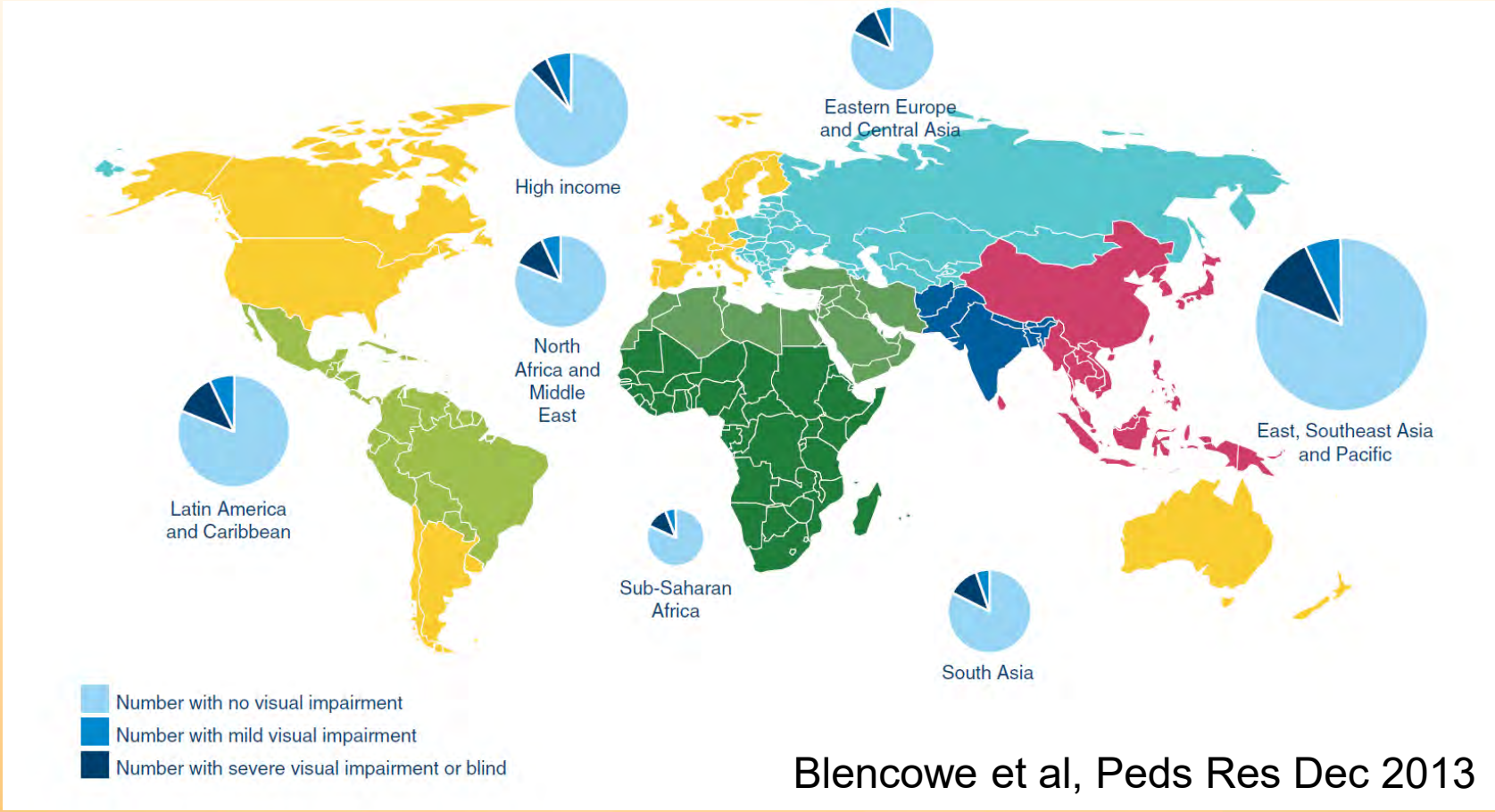
- Limitations and advantages of both remote evaluation and diagnostic examination
- 3 potential sources for error in detecting RW-ROP
  - Erroneous grading of images (grading includes recognizing inadequate images)
  - Seemingly adequate images that fail to show pathology
  - Erroneous diagnostic examination

Caution about ROP Telemedicine

- **Remote image evaluation is a supplement to, not a replacement for BIO by an experienced clinician.**
  - Current use has outstripped systematic evaluation
  - **Needed urgently!**
    - Standardization/validation of protocols
    - Performance standards
    - Clinical and cost-effectiveness of remote image evaluation

Fierson, Capone, Ophth Section AAP, AAO, AACO, Pediatrics, 2015

Visual impairment due to ROP in premature babies (2010 data)



Blencowe et al, Peds Res Dec 2013

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US Based Teleophthalmology:
Improving Access to Coordinated, Timely Care to Prevent Blindness in Diabetes

Rajeev S. Ramchandran, MD, MBA
Associate Professor of Ophthalmology,
Public Health Sciences, & Center for
Community Health & Prevention

Flaum Eye Institute, University of Rochester, NY

Disclosures

- **Image Grader and Subject Matter Expert :**
  - **Google & EyePACS, LLC**
- **Founded Tele-I-CARE – local program, U of Rochester, NY**

- **Funders:**
- **Greater Rochester Health Foundation**
- **Prevent Blindness America**
- **National Institute on Aging**
- **American Academy of Ophthalmology**
- **American Geriatrics Society**
- **Research to Prevent Blindness and the core grant NIH P30EY001319-35**

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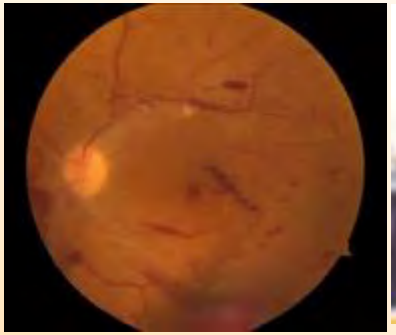
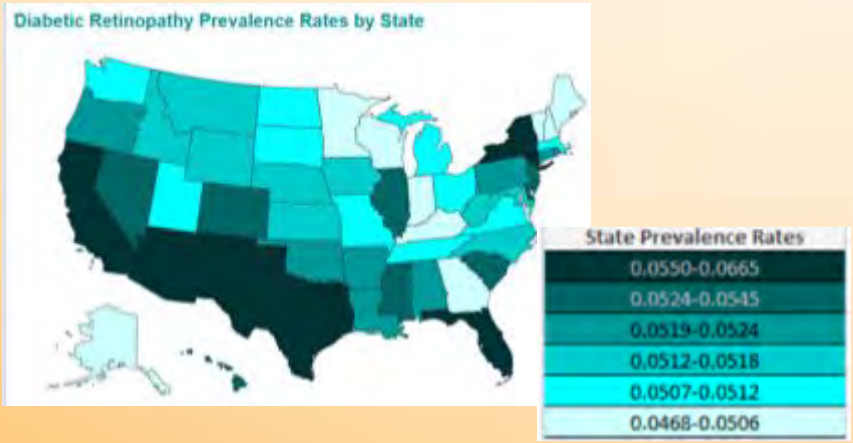
Diabetic Retinopathy – Leading Cause of Blindness among Ages 20-74 years in the US





- **~30 million with Diabetes**
  - inc 1.5 million/yr
- **~8 million with Diabetic Retinopathy (DR)**
  - 5% of US pop >40 yrs
  - 10,000 new cases of blindness/yr
- **Costs US $6.2 billion/yr**
- **NEI sponsored research:**
  - A yearly dilated eye exam with timely needed treatment prevents 90% of vision loss.

PBA http://visionproblemsus.org/diabetic-retinopathy.html Fong DS, Aiello LP, Ferris FL 3rd, Klein R. Diabetic retinopathy. Rein DB. Vision problems are a leading source of modifiable health expenditures. Invest Ophthalmol Vis Sci. 2013;54(14):Orsf18–22. Diabetes Care. 2004;27(10):2540–53. Singer DE, Nathan DM, Fogel HA, Schachat AP: Screening for diabetic retinopathy. Ann Int Med 116:660–671, 1992. National Eye Institute. Facts about diabetic eye disease. https://nei.nih.gov/health/diabetic/retinopathy. Accessed 7/7/18 Early Treatment Diabetic Retinopathy Study Research Group. Early photocoagulation for diabetic retinopathy: ETDRS report number 9. Ophthalmology. 1991;98(5):766–785.

NEI Sponsored Research: Annual Dilated Eye Exams Save Vision

- 1993 - Frederick Ferris III, M.D., chief of NEI's clinical trials branch, *'continuing loss of sight from diabetic retinopathy is primarily because of failures to have regular eye examinations so the condition can be caught before vision is severely damaged.'*

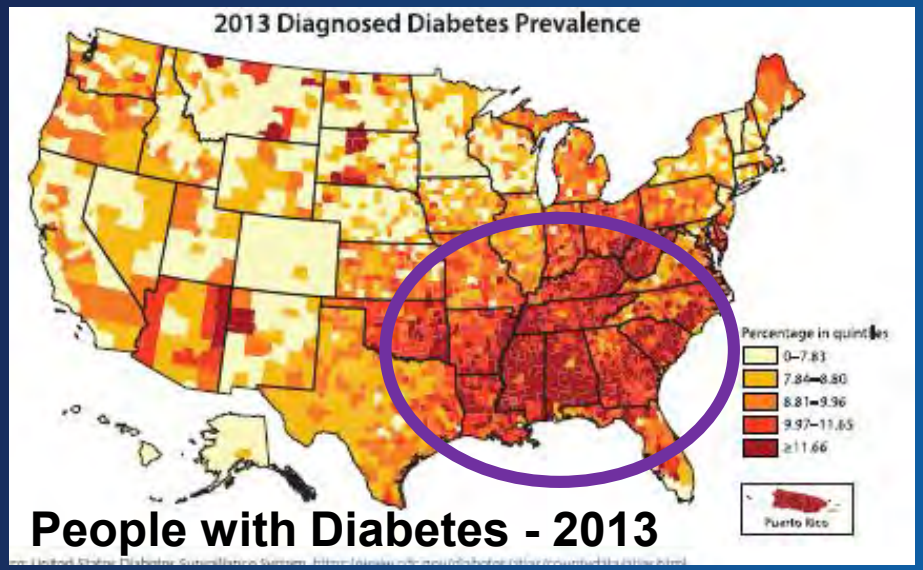
- 1993 - HHS Secretary Donna E. Shalala: "This finding underscores the *tremendous importance of all people with diabetes obtaining a dilated eye exam at least once a year to prevent vision loss.*"

ETDRS 5-Year Follow up Data Released, NEI Press Release National Institutes of Health National Eye Institute, March 9, 1993.

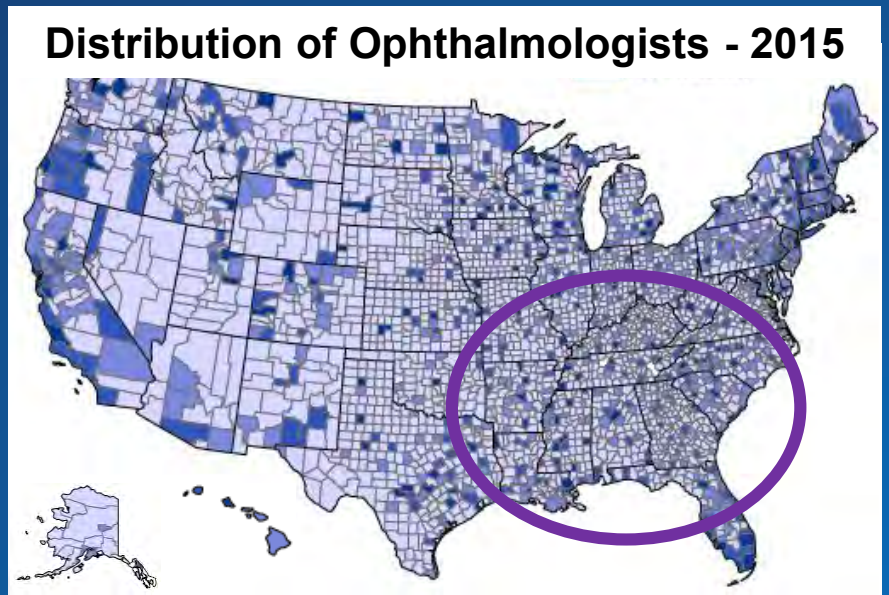
Annual Eye Exams Limited due to Lack of Eye Care Where Need is Greatest

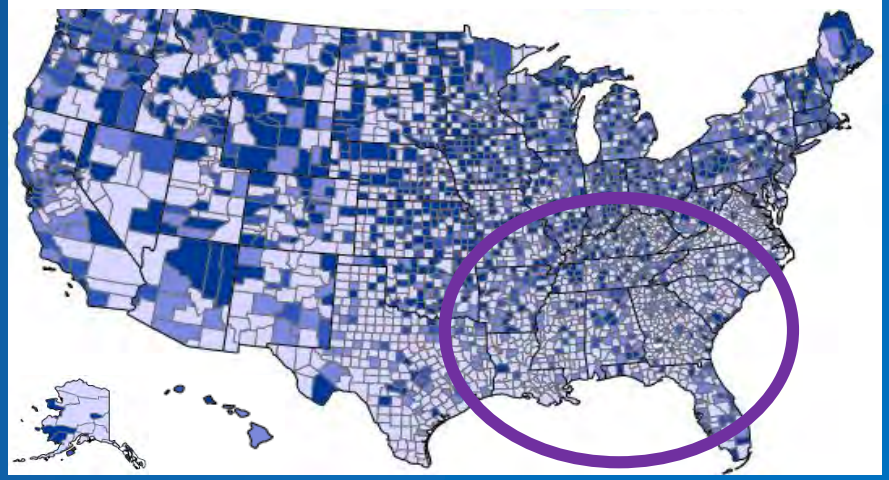
Current US Annual Diabetic Patient Eye Exam Rate Low:

- Insured: As low as 30-40%
- Un- or Underinsured:
  - As low as 10-20%



People with Diabetes - 2013


Distribution of Ophthalmologists - 2015


Distribution of Optometrists - 2015

https://www.cdc.gov/diabetes/data/statistics/statistics-report.html

PBA http://visionproblemsus.org/diabetic-retinopathy.html

Gibson, D. M. "The geographic distribution of eye care providers in the United States: implications for a national strategy to improve vision health." *Preventive medicine* 73 (2015): 30-36. Scanlon PH. The English National Screening Programme for diabetic retinopathy 2003-2016. Acta Diabetol. 2017; *BMJ open* 4.2 (2014): e004015. Lee PP et al.. Longitudinal rates of annual eye examinations of persons with diabetes and chronic eye diseases. Ophthalmology. 2003;110(10):1952–9. Mukamel BD et al. Ophthalmic Epidemiology, 1999, Vol. 6, No. 1 , Pages 61-72. *Ophthalmology 2003;110:1952–1959*

HEDIS Metric Incentivization

- Health Care Effectiveness Data Information Set (NCQA)

- 2018 Annual Eye Exam Rate by Percentiles:

  90th: 68% 75th: 59% 50th: 50% 25th: 46%

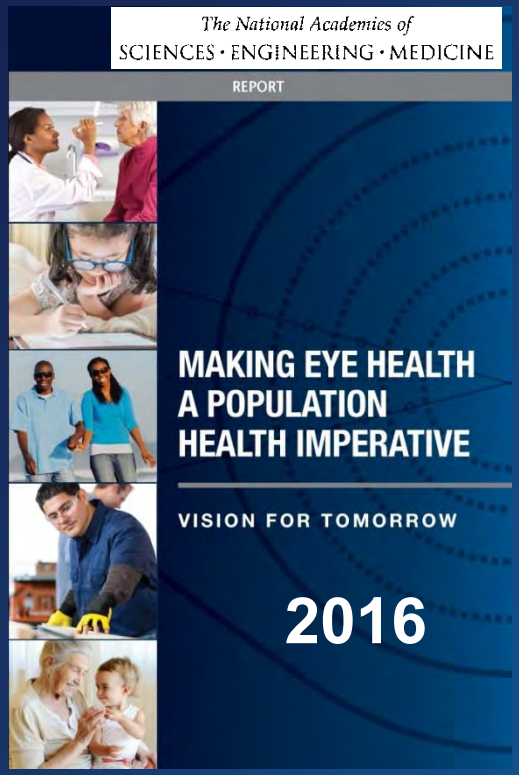
- **Financial Incentives to Primary Care Providers, Health Systems, and Insurers for achieving a higher percentile rank for annual eye exam rate.**
  - (Eye Care Providers are not graded on this metric.)

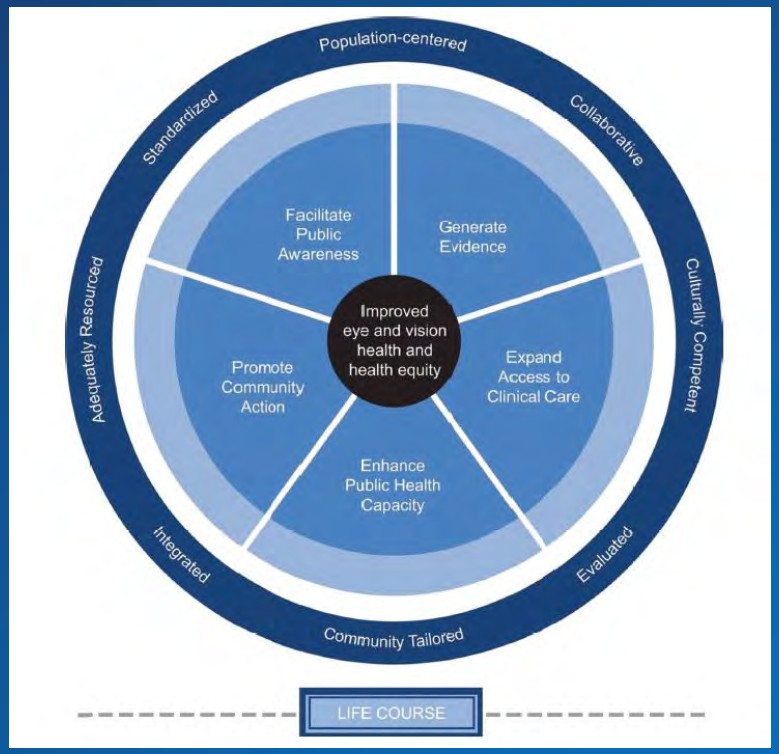
NCQA.org (2017). HEDIS Publications: Overview. [online] Available at: http://www.ncqa.org/HEDISQualityMeasurement/HED. Accessed 7/7/18.
NCQA.org. (2017). 2018 NCQA Health Plan Accreditation Requirements. [online] Maclennan PA, et al. Eye Care Use Among a High-Risk Diabetic Population seen in a public hospital's clinics. JAMA Ophthalmol. 2015;133(2):174–81.

Diabetes, NO longer the leading cause of blindness in the UK

- In the UK, Annual Eye Exam Rates are >90% due to:
  - Outreach & Public Health Campaigns
  - Population Health Registries, Surveillance
  - Camera Based Examination = Teleophthalmology integral Tool in Population Health Surveillance

Teleophthalmology Based Surveillance Meets Population Health Objectives





(NEI, PBA, CDC, et al. Sponsored Initiative)

Community-based intervention that proactively improves access to coordinated, accountable, and timely sight saving care especially in at risk and vulnerable populations.

National Academies of Sciences, Engineering, and Medicine. 2016. *Making eye health a population health imperative: Vision for tomorrow.* Washington, DC: The National Academies Press

Teleophthalmology Can Help Overcome Barriers for Annual Retinopathy Assessment in the US

Barriers to Detecting Retinopathy

1. PCP not equipped and may not have the know-how to adequately examine eyes

2. Patient: Other Priorities, Drops/Dilation, Asymptomatic Disease, Additional $$/Time Cost of Exam

3. US Eye Doctor (53K) Access issues: Supply limited & not well distributed
(29.1 M Diabetics – 2012)

4. Lack of Documentation Reaching PCP

Potential Solution:
Remote Imaging and Detection
(Teleophthalmology)

1. Non Eye Care Setting Staff operate FDA Approved **Non-mydriatic (No Dilation) Retinal Camera**.

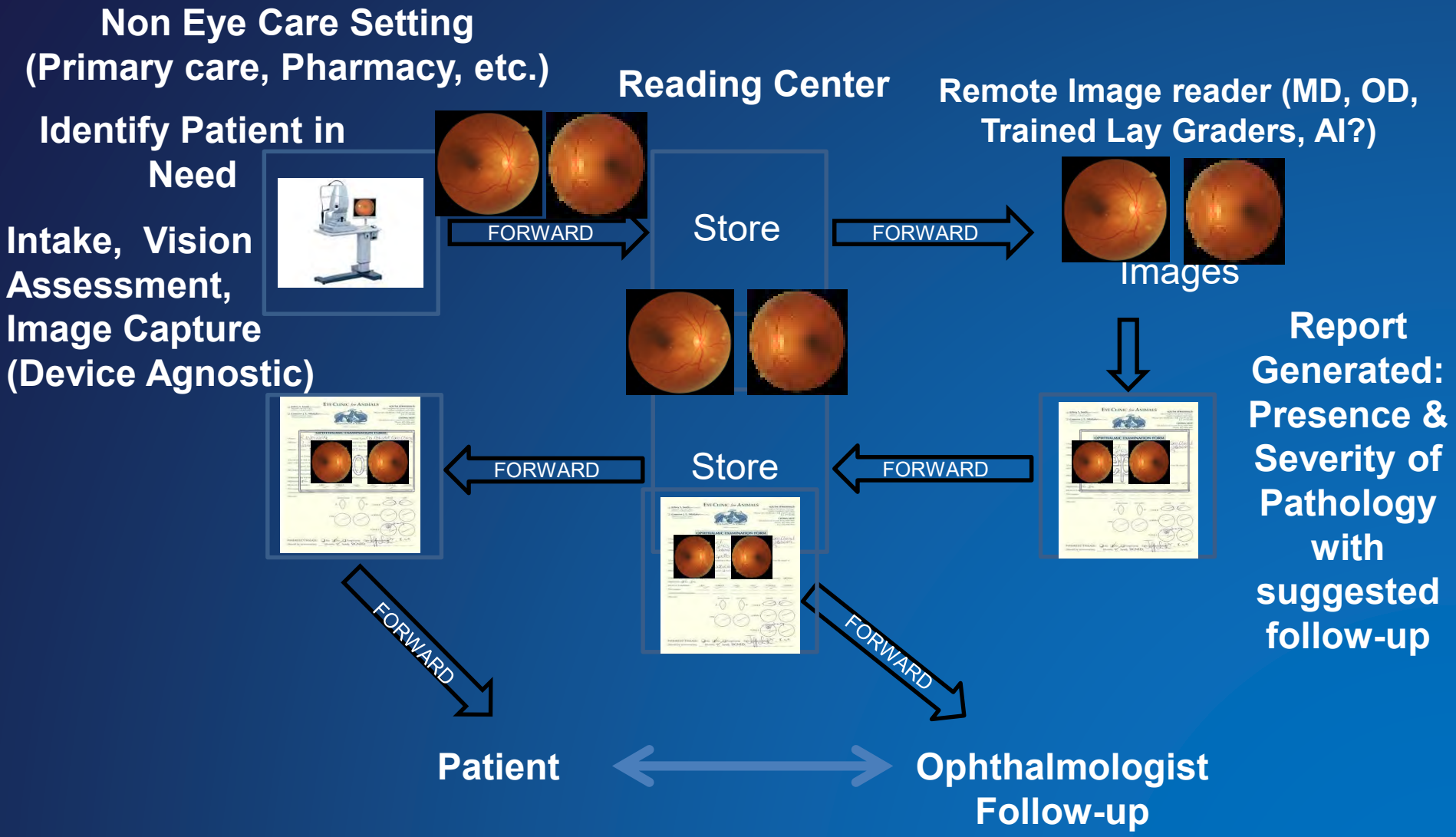
2. Via Reading Center, Eye Specialists Evaluate Images & **Report Findings to PCP on-line**

- Images Can **Educate Patients**
- **HEDIS Measure Met by Report**

3. Triage & Queue Patients Needing Eye Care Appropriately

Liu, Yao, and Rebecca Swearingen. "Diabetic eye screening: knowledge and perspectives from providers and patients." *Current diabetes reports* 17.10 (2017): 94.

Teleophthalmology: Store and Forward Process



Diabetic Retinopathy Screening/ Surveillance (DRS)
Actively Closing the Loop on Eye Care

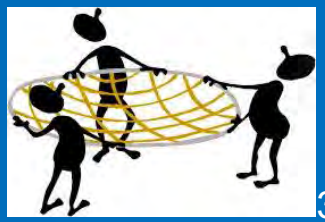
Increases Ability to Access and Screen Vulnerable Populations for Eye Disease

1. **US Urban & Rural Safety Net Clinics & Pharmacy**
   - **(Examples of 1 yr Cohort Studies)**

- **Nashville, TN:** 495 offered eye care, 293 screened - Annual DRS Rate INC (23-59%), 69% screened by camera, 48% referred for further eye care
- **Western NY:** 112 offered eye care, Annual DRS Rate INC (6-80%), 47% by camera, 53% by seeing eye doctor, 31% DR, 9% poor vision, 100% f/u
- **Philadelphia*, Winston-Salem, NC, Birmingham, AL, Miami:** 1,894 camera screened 22% with DR, 44% had other ocular pathology
- **LA County, CA:** 21,222 camera screened, Annual DRS Rate INC (41- 57%) DEC Wait Time 158 to 17 days, 20% with DR, 12% other pathology
- **NC DR Telemedicine Network:** 1787 screened, Annual DRS Rate INC (25.6-40.4%), 20.3% DR, 9.3% referred – 60% follow-up to ophthalmology

2. **Veteran Affairs**

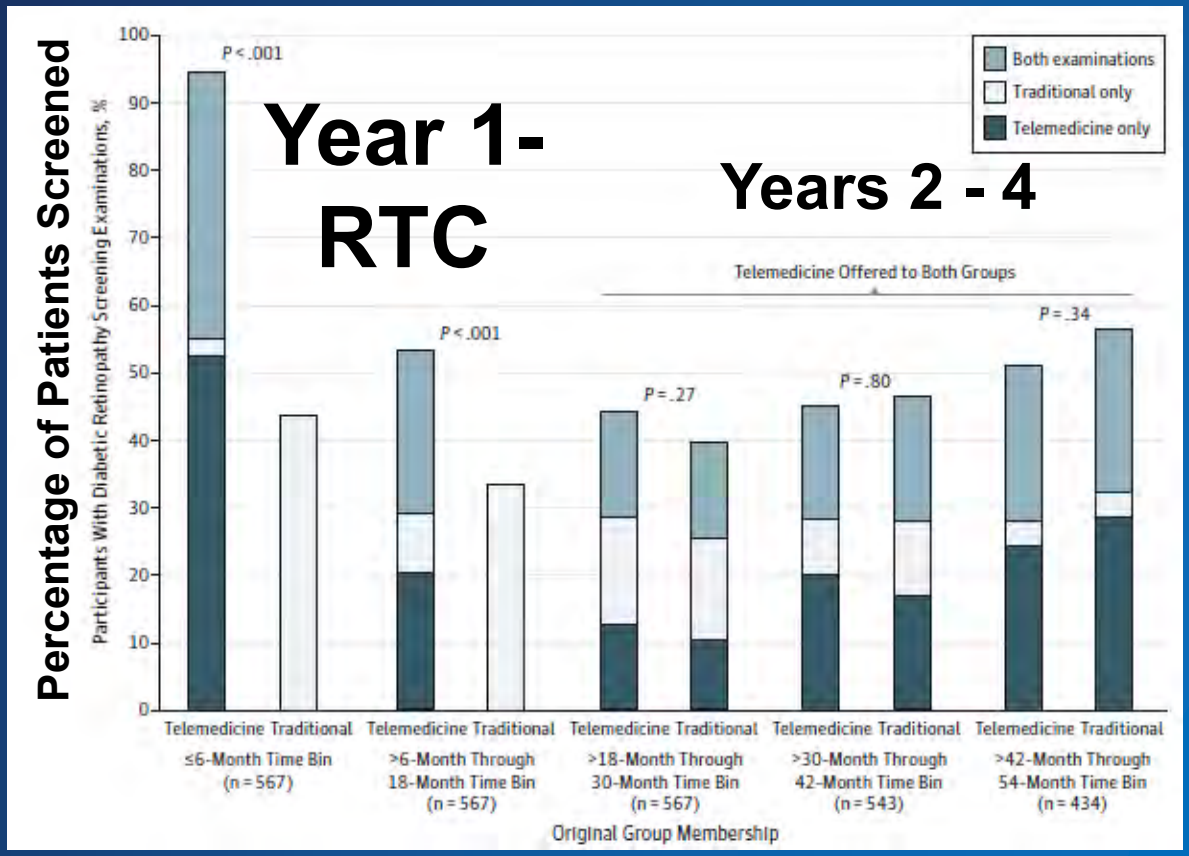
- One of the oldest programs, Joslin Vision Network
- 60% of eligible patients screened via teleophthalmology



Performance of Screening Over Time (Surveillance)

Indian Health Service and Tribal Communities

- IHS (Southwest US): DRS Rate INC from 50% to 75% 1999-2003
- Mansberger et al. Followed Native American Community for 5 years



Mansberger, Steven L., et al. "Long-term comparative effectiveness of telemedicine in providing diabetic retinopathy screening examinations: a randomized clinical trial." *JAMA ophthalmology* 133.5 (2015): 518-525

Efficient Triaging & Appropriate Queuing for Eye Care Follow-up

Rubric for Ophthalmology Referral

Table 1. Classifications Used to Grade DR Presence and Severity Based on the National Health Service Grading Classification System[a]

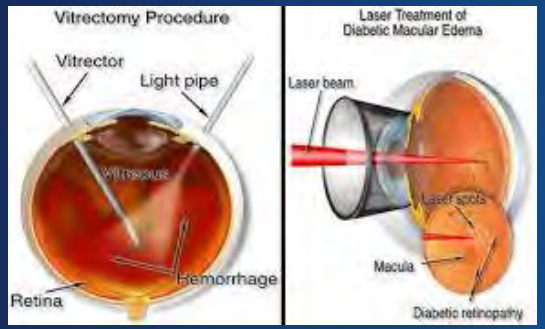
Grade	Description	Recommendation[b]
R0	No DR None of the signs listed for the other grades Isolated cotton-wools spots (≥1) in the absence of any microaneurysm or hemorrhage	Reevaluate in 12 mo with either eye care specialist or photographic screening
R1	Background DR ≥1 Microaneurysm ≥1 Retinal hemorrhage Any exudates caused by DR	Refer to eye care professional
R2	Preproliferative DR Intraretinal microvascular abnormality Venous beading Venous loop or reduplication Multiple deep, round, or blot hemorrhages	Refer to ophthalmologist promptly
R3	Proliferative DR New vessels on the disc New vessels elsewhere Preretinal or vitreous hemorrhage Preretinal fibrosis with or without tractional retinal detachment due to DR	Refer to ophthalmologist promptly
M	Maculopathy Exudate within 1 DD of the center of the fovea Circinate or group of exudates within the macula Any microaneurysm or hemorrhage within 1 DD of the center of the fovea only if associated with a best visual acuity of 20/40 or worse	Refer to ophthalmologist promptly
P	Photocoagulation Focal/grid to macula Peripheral scatter	Refer to eye care professional
U	Unclassifiable/ungradable Due to poor photographic location, focus, or contrast	Refer to eye care professional

Pathology Specific Based Referral Time to Eye Care

- 10-40% of Screened with Camera have DR
  - 15% or less have Vision Threatening DR immediate referral (1m)
  - Moderate DR with no DME, referral in 6m
  - Mild DR with no DME yearly referral/screening & comprehensive eye exam with eye care provider every 3 years?
- 20-60% have other pathology or poor vision requiring referral

American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern Guidelines. Diabetic Retinopathy. San Francisco, CA: American Academy of Ophthalmology. 2016.Available at: www.aao.org/ppp. Owsley C, McGwin G Jr, Lee DJ, Lam BL, Friedman DS, Gower EW, et al. Diabetes eye screening in urban settings serving minority populations: detection of diabetic retinopathy and other ocular findings using telemedicine. JAMA Ophthalmol. 2015;133(2):174–81.

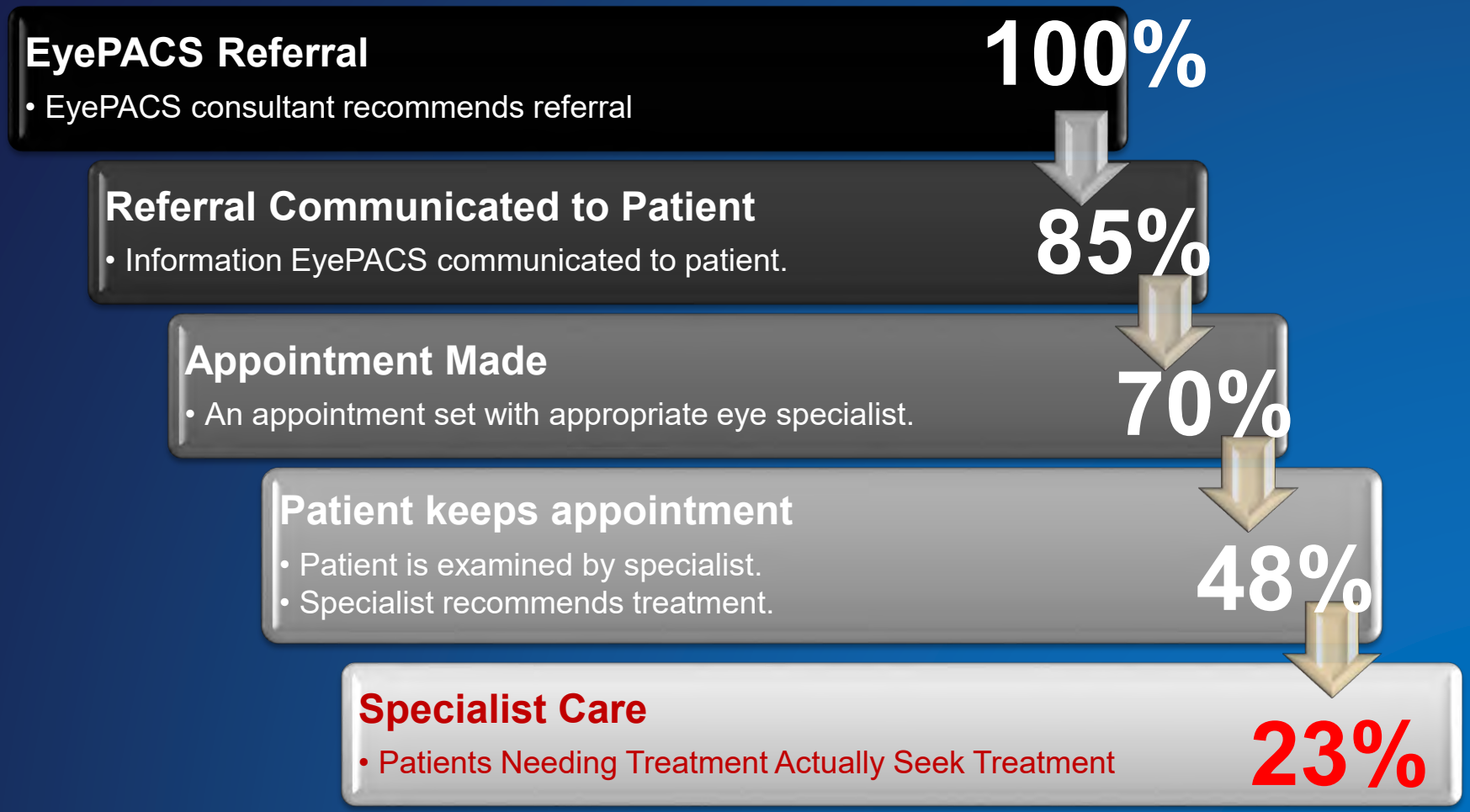
But After Screening Does Visit to Actual Eye Care Visit Happen?



- **F/u from Safety Net Clinics**
  (Affiliated eye care clinic in system)
  - **Letter/Call to Patient & PCP (UAB Prog):**
    49% f/u, 30% at rec. interval to eye care
  - **PCP asked to notify patient (Rochester, NY):**
    35% f/u to eye care, 80% rec. interval
  - **Eye Clinic Letter/Call to Patient (Roc, NY)**
    65% f/u to eye care, 80% rec. interval
- **F/u from Veteran's Clinic (Atlanta)**
  - **VA PCP notified: 70% f/u to eye care**
- **F/u From IHS Service (AZ)**
  - **Increased Treatment Rate by 50%**

American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern Guidelines. Diabetic Retinopathy. San Francisco, CA: American Academy of Ophthalmology. 2016.Available at: www.aao.org/ppp. Accessed 9-18-14, http://www.imcdxb.com/ophtha-retina.htm, http://maculacenter.com/eye-news/anti-vegf-vein-occlusion/

EyePACS Performance in California



Lack of Follow-up For Treatment due to Communication/Education/Access

Patient Education & Diabetes Knowledge

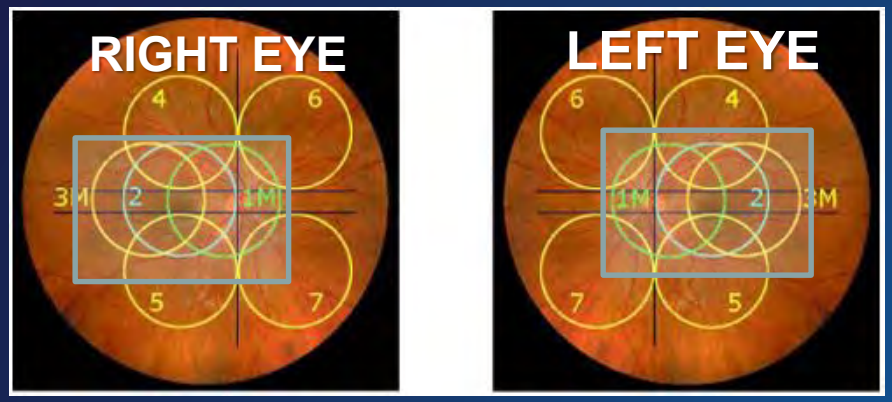
1. **Patient feel satisfied and value teleophthalmology**
   Quick, Convenient – 'One Stop Shop' in a familiar setting, Educational, Early Detection & ability for Timely Treatment

2. **Detection of Early Stages of Diabetic Eye Disease**
   - Early and Individualized Patient Education/Intervention
   - Early Behavior Modifications to improve Diabetes Management
   - Earlier Achievement of better glycemic control (Lower HbA1c)
   1.61 dec in HbA1c when counseling with images done in Endocrinology[1]

3. **Annual Screening = Re-emphasis**
- 'A Picture is worth a 1000 words.'
- Treatments Effective, But Cost $1,000s
- Prevention is Key

1. Salti H et al. Nonmydriatic retinal image review at time of endocrinology visit results in short-term HbA1c reduction in poorly controlled patients with diabetic retinopathy. Telemedicine and e-health. 2011; 17(6):415–419. Fonda, Stephanie J., et al. "The relationship of a diabetes telehealth eye care program to standard eye care and change in diabetes health outcomes." *Telemedicine and e-Health* 13.6 (2007): 635-644. Arthur Brisbane, newspaper editor, instructional talk to the *Syracuse Advertising Men's Club 1911, http://www.phrases.org.uk/meanings/a-picture-is-worth-a-thousand-words.html*

Advances in Technology Increase Access, But Ensuring Quality is Important



Fields 1,2,3, & 1 external photo
(30 or 45 Degrees), Nonmydriatic, Non-stereo

- 3-25% unreadable rate
- 89% Sensitive & 97% Specific vs ETDRS[1] 7 standard fields

Ultra Wide Field scanning laser cameras (Optos, plc, UK)

- **200 degree view, 3% ungradable images,**
- **Identifies 2x more DR vs standard nonmydriatic photos.[3]**

Handheld Digital Camera

- **Lower cost and more mobile.**
- **Ease of use and need for pupil dilation may affect image quality.**

1. Bursell SE, et al. Joslin Vision Network Research Team. Stereo nonmydriatic digital-video color retinal imaging compared with Early Treatment Diabetic Retinopathy Study seven standard field 35-mm stereo color photos for determining level of diabetic retinopathy. Ophthalmology. 2001;108(3):572–85. 2. Wilkinson CP, et al. Global Diabetic Retinopathy Project Group. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology. 2003:110(9):1677–82. 3. 2.Silva, Paolo S., et al. "Identification of diabetic retinopathy and ungradable image rate with ultrawide field imaging in a national teleophthalmology program." *Ophthalmology* 123.6 (2016): 1360-1367.

Advances in Technology Increase Access, But Ensuring Quality is Important

- **American Telemedicine Association Standards**
- **– Being Able to Differentiate Levels of DR**
- **UK NHS Criteria, EURODIAB Protocol[1]**
  - **Routine use of Image Quality Standard not seen in US**

- **Artificial Intelligence** – Automated Detection (IDx-DR, Iowa) of more than mild DR & diabetic macular edema (only)
  - **Exclusion**: persistent vision loss, blurred vision, floaters, previously diagnosed macular edema, severe non-proliferative retinopathy, proliferative retinopathy, radiation retinopathy, retinal vein occlusion or those with a history of laser treatment, surgery or injections in the eye
  - 1st FDA Approval
  - Detects worse than mild DR 87.4% of the time
  - Clinical use at University of Iowa Hospitals

1. EURODIAB Protocol: Aldington SJ, et al Methodology for retinal photography; the EURODIAB IDDM complications study. Diabetologia 38:437-444, 1995.
https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm604357.htm https://www.eyediagnosis.net

- Joslin Vision Network – Indian Health Service
  Also an Extensive Veterans Affairs Network

Wills Eye Telemedicine Department

EyeTel

Retasure

Welch Allyn-RetinaVue

IDx

AEON

GlobeCheck

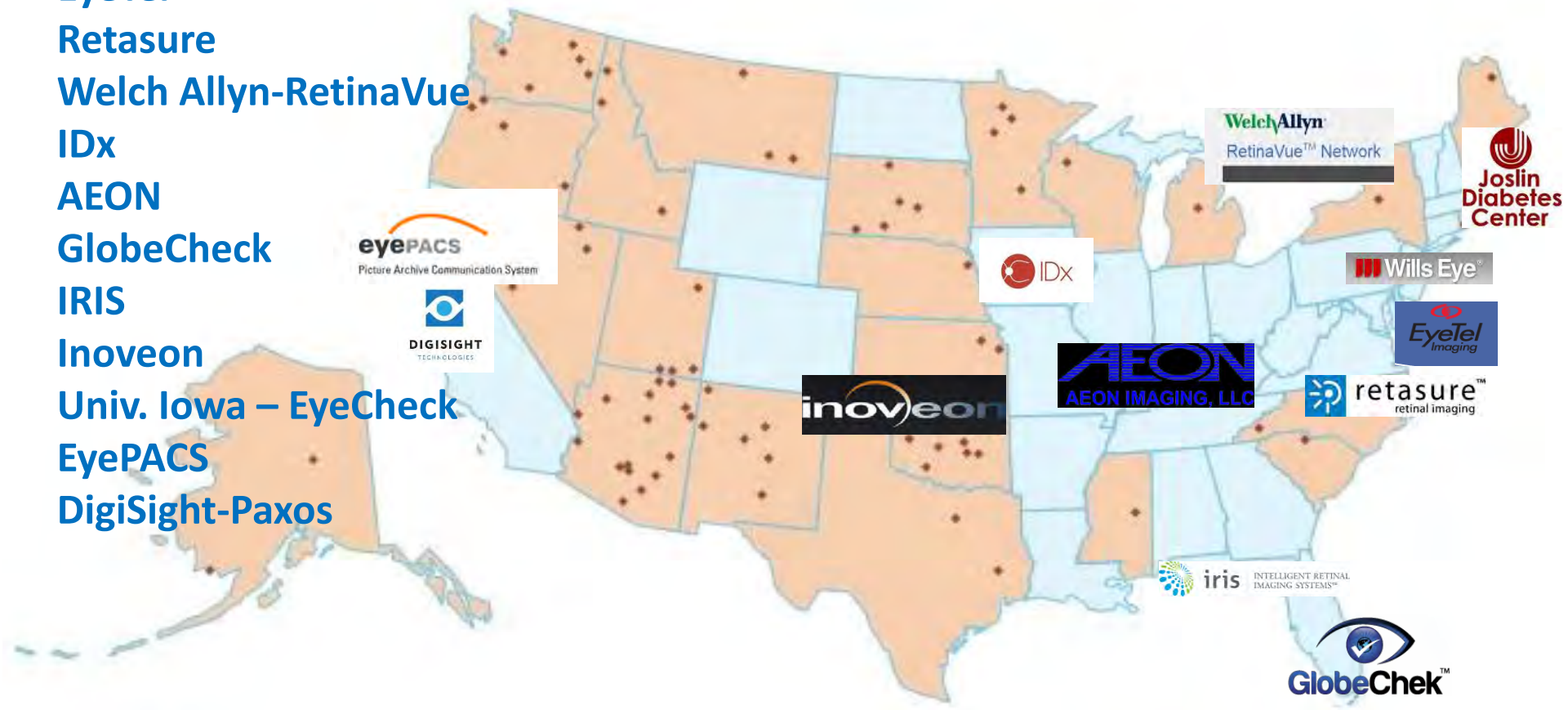
IRIS

Inoveon

Univ. Iowa – EyeCheck

EyePACS

DigiSight-Paxos

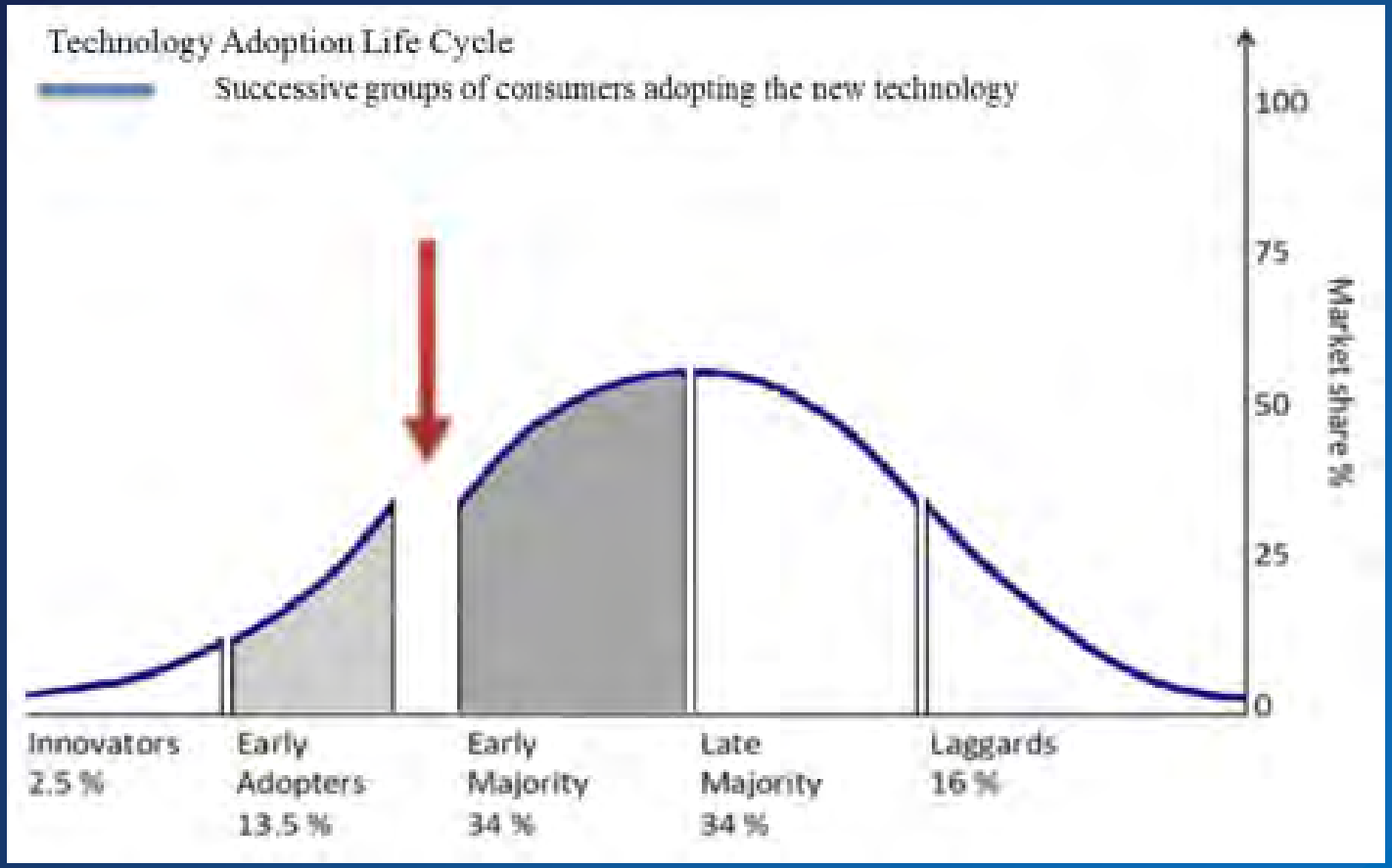


Sample of Organically Growing US Network of Teleophthalmology for DRS

Teleophthalmology: Successes & Challenges

- Successes:
  - Efficient population level screening for vision threatening disease, especially in low resourced settings
  - Improved communication and education of stakeholders
- Challenges:
  - Demonstrating surveillance and overall decrease in vision loss and disease burden overtime is needed. (Closing the loop of care)
  - Sustaining Programs
    - Inconsistent financial support – grants, contracts, insurance
    - High human resource turnover
  - Regulatory hurdles
  - Program coordination, oversight, and quality assurance

Rogers Diffusion of Innovation



Over 2000 Published Papers on Teleophthalmology since 2000.[1]

1/3 on DR[2]

Can Further Research Help Teleophthalmology Cross the Gap?

1.Kawaguchi, Atsushi, et al. "Tele-ophthalmology for age-related macular degeneration and diabetic retinopathy screening: a systematic review and meta-analysis." *Telemedicine and e-Health* 24.4 (2018): 301-308.
2. Bahaadinbeigy, Kambiz, and Kanagasingam Yogesan. "Advances in teleophthalmology: Summarising published papers on teleophthalmology projects." *Advances in Telemedicine: Applications in Various Medical Disciplines and Geographical Regions*. InTech, 2011.

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Boucher, Marie Carole, et al. "Teleophthalmology screening for diabetic retinopathy through mobile imaging units within Canada." *Canadian Journal of Ophthalmology/Journal Canadien d'Ophtalmologie* 43.6 (2008): 658-668.

B. Rajan, A. Seidmann, R. S. Ramchandran. “Teleophthalmology for Diabetic Patients: Saving Vision through IT.” *Proceedings of the 2014 47th Hawaii International Conference on System Sciences*. Pages: 4239-4243

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Owsley C, McGwin G Jr, Lee DJ, Lam BL, Friedman DS, Gower EW, et al. Diabetes eye screening in urban settings serving minority populations: detection of diabetic retinopathy and other ocular findings using telemedicine. JAMA Ophthalmol. 2015;133(2):174–81.

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Fonda, Stephanie J., et al. "The relationship of a diabetes telehealth eye care program to standard eye care and change in diabetes health outcomes." *Telemedicine and e-Health* 13.6 (2007): 635-644.

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Cavallerano, Anthony A., and Paul R. Conlin. "Teleretinal imaging to screen for diabetic retinopathy in the Veterans Health Administration." (2008): 33-39.

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Mansberger, Steven L., et al. "Long-term comparative effectiveness of telemedicine in providing diabetic retinopathy screening examinations: a randomized clinical trial." *JAMA ophthalmology* 133.5 (2015): 518-525.

Jani, Pooja D., et al. "Evaluation of diabetic retinal screening and factors for ophthalmology referral in a telemedicine network." *JAMA ophthalmology* 135.7 (2017): 706-714.

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2018 Focus on Eye Health National Summit:
Research to Impact

Home Monitoring for Age-Related Macular Degeneration (AMD)

Emily Y. Chew, MD
National Eye Institute/National Institutes of Health

No Financial Disclosures

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2018 Focus on Eye Health National Summit:
Research to Impact

HOme **M**onitoring Study of the **E**YE **(HOME)**

Age-Related Eye Diseases Study 2 (AREDS2)

The study was performed by the Age-Related Eye Disease Study 2 (AREDS2) investigators, and sponsored by Notal Vision, Inc, in collaboration with the National Eye Institute

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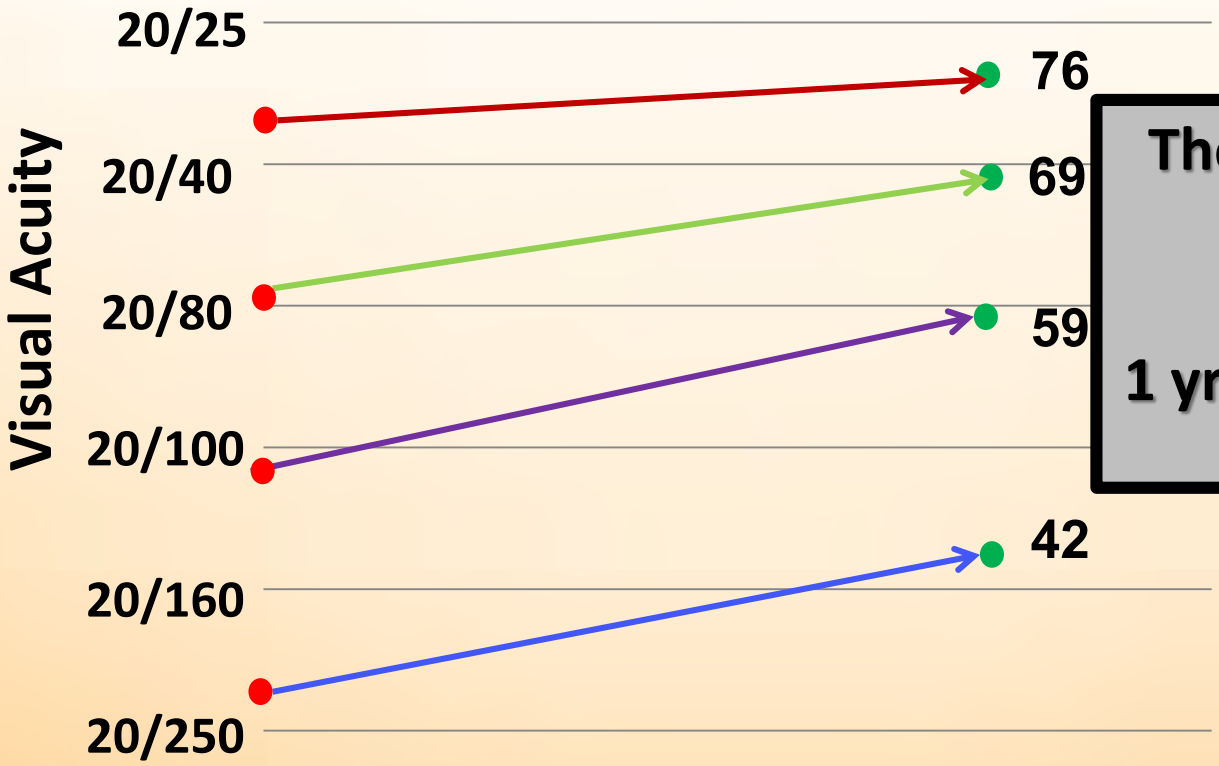
HOme Monitoring Study of the EYE (HOME) in AREDS2

Rationale & Study Design
Primary Results
Imaging Characteristics of Early CNV
Potential Clinical Impact

Intravitreal Injections of Anti-VEGF Therapies-Common Rx

Neovascular AMD

Predictor of Visual Outcome at 1 yr after Anti-VEGF RX



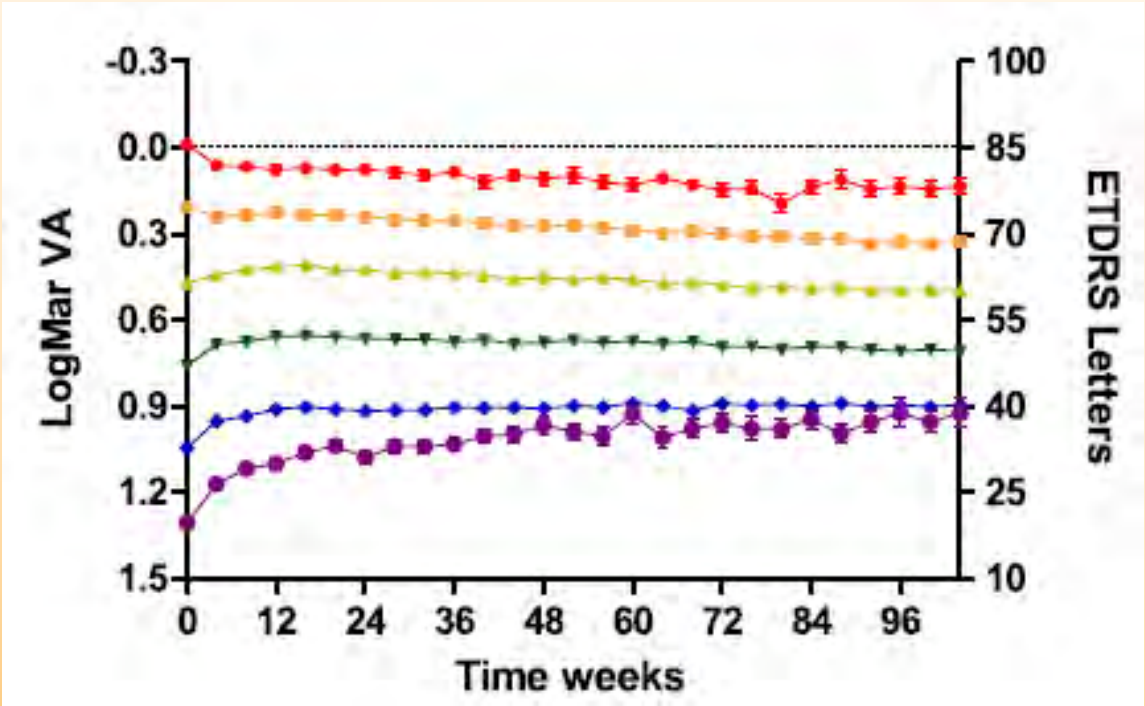
The better baseline visual acuity predicts 1 yr Vision Outcomes

CATT Study By Baseline Visual Acuity

Ophthalmology 2012

The UK Neovascular AMD EMR Database: Multicenter Study of 92,976 Ranibizumab Injections. (n=11,135 patients)

Mean(SE) VA Stratified by Baseline Acuity



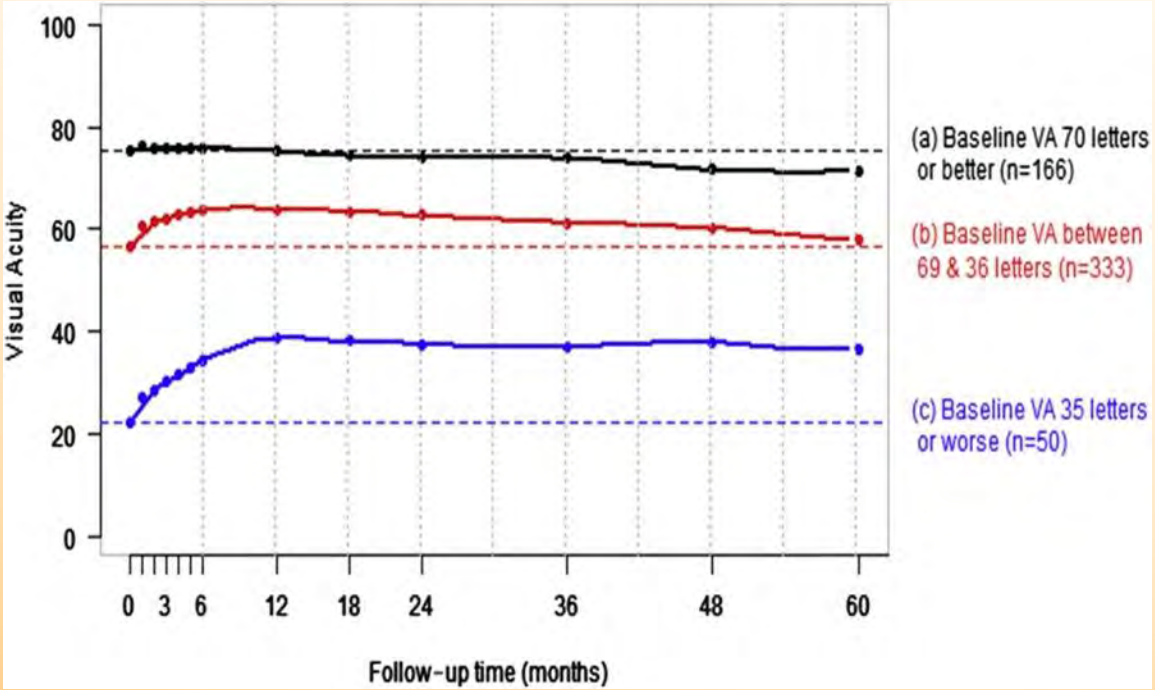
The better baseline VA is, the better the 2yr Outcome will be

Br J Ophthalmology 2015; (0): 1-6

Five Year Visual Acuity Data

Long-Term Outcomes of Treatment of Neovascular AMD

Data from an Observational Study (**n=1,212 eyes**)

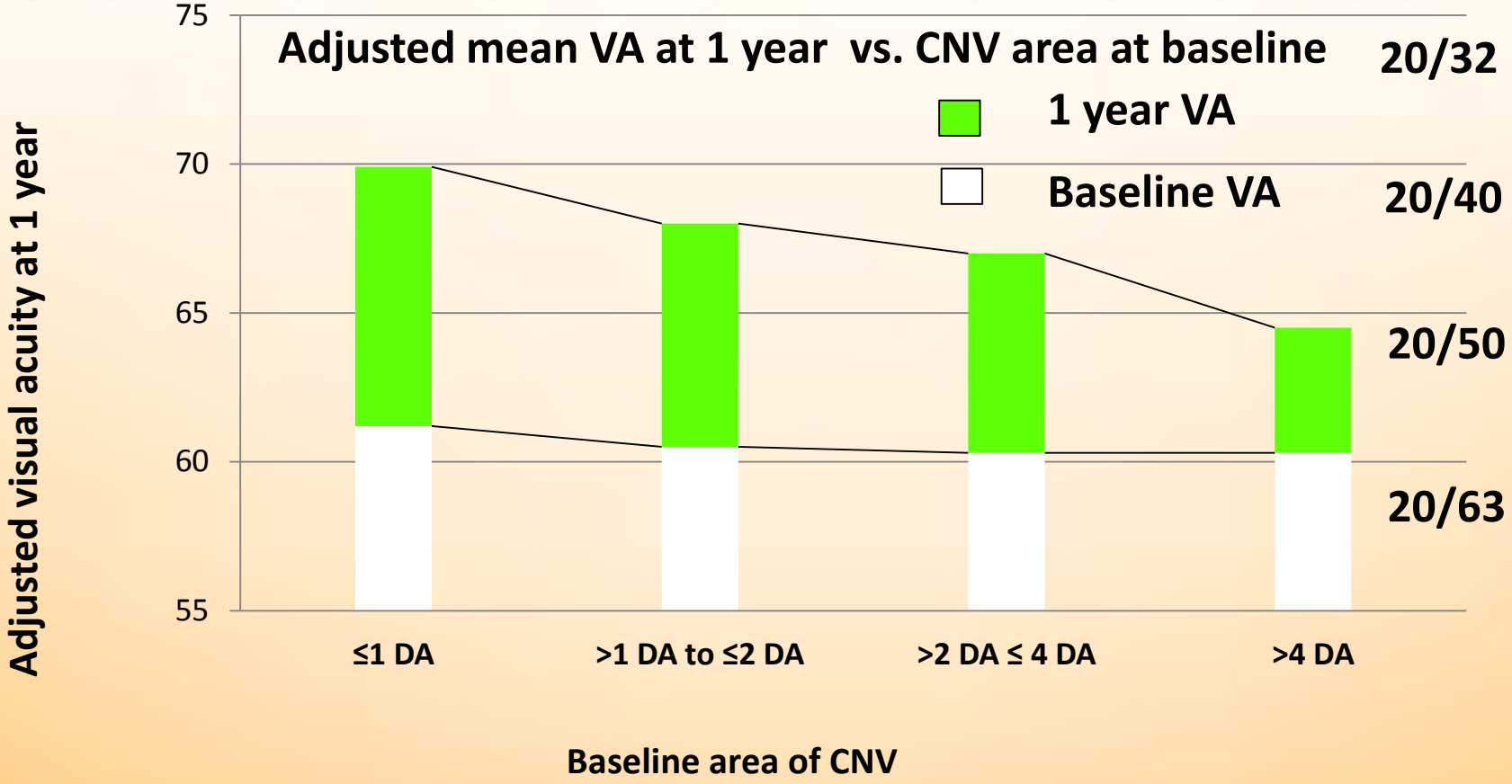


The better baseline VA is, the better the 5yr Outcome will be

Visual acuity Loss regression curves over 5 years stratified by baseline visual acuity

Gillies, MC; Campain, A; Barthelmes, D, et al. Long-Term Outcomes of Treatment of Neovascular Age-Related Macular Degeneration, *Data from an Observational Study.* Ophthalmology 2015; XX(XX): 1-9

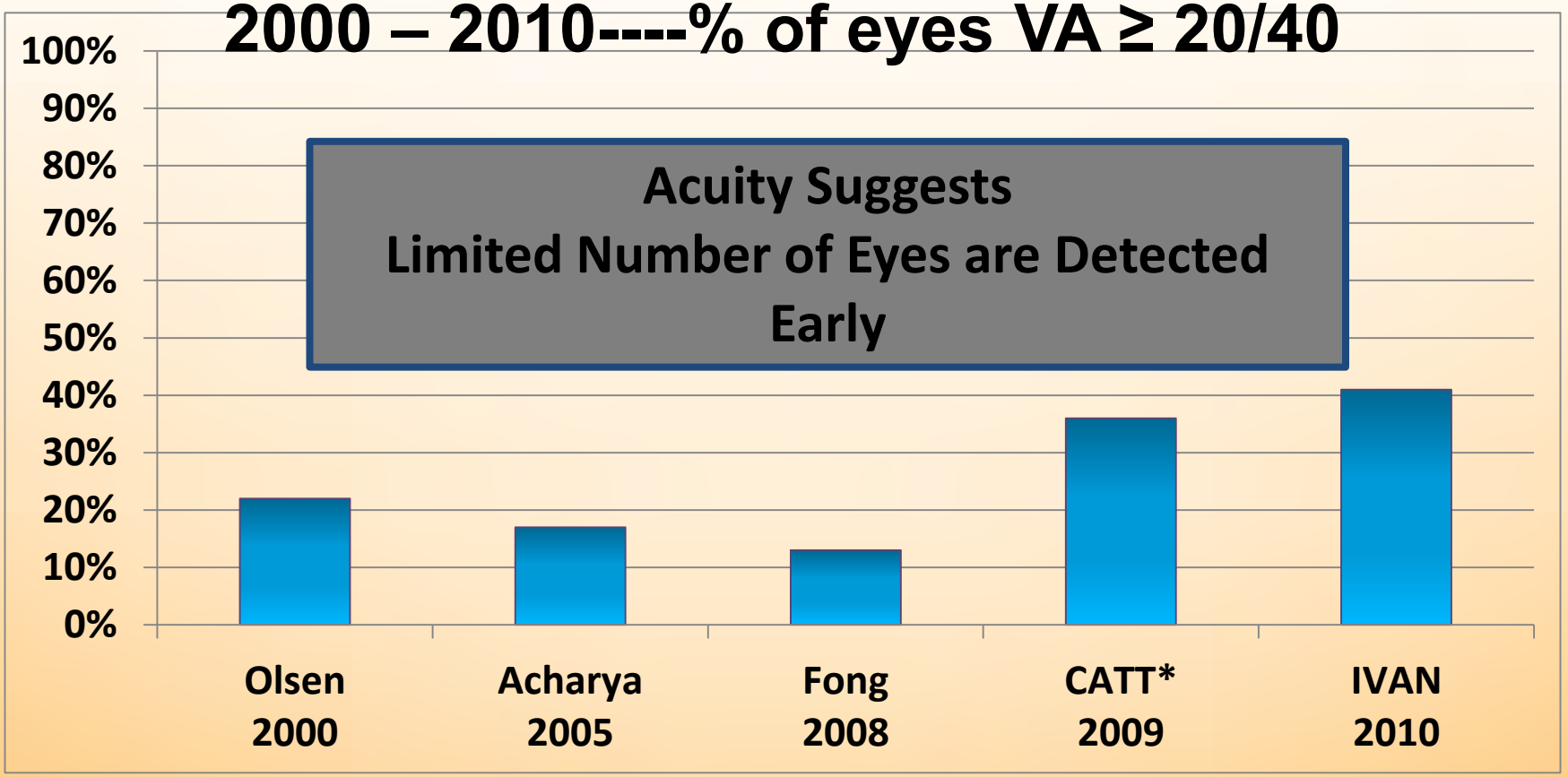
One Year CNV Area Data –CATT Baseline Predictors



CATT: The smaller the lesion at diagnosis the better the VA at 1 year

Baseline Predictors for One-Year Visual Outcomes with Ranibizumab or Bevacizumab for Neovascular AMD. Ophthalmology 2012

Baseline VA at CNV Diagnosis Studies Performed 2000 – 2010----% of eyes VA ≥ 20/40



*All but CATT included eyes with VA of 20/20 or worse (CATT included ≤20/25)

AREDS2 - HOME Study

Objective: A randomized trial to determine if home monitoring improves detection of progression to choroidal neovascularization (CNV)

Home Study Population: 1520 participants

AREDS2 + non-AREDS2 participants

1 or 2 study eyes with:

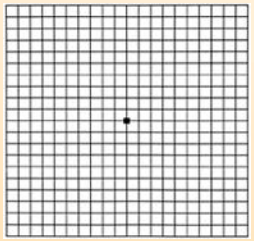
- **≥ 1 large drusen (≥125 microns)**
- **VA at least 20/60 (ETDRS-EVA equivalent)**
- **Absence of advanced AMD**

AREDS2 HOME Study Design

Randomization

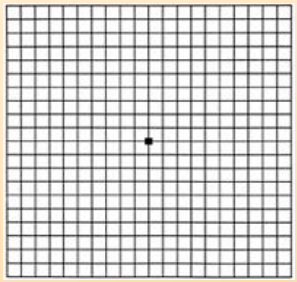
Device* + Std Care

+



May include Amsler Grid

Standard care



May include Amsler Grid

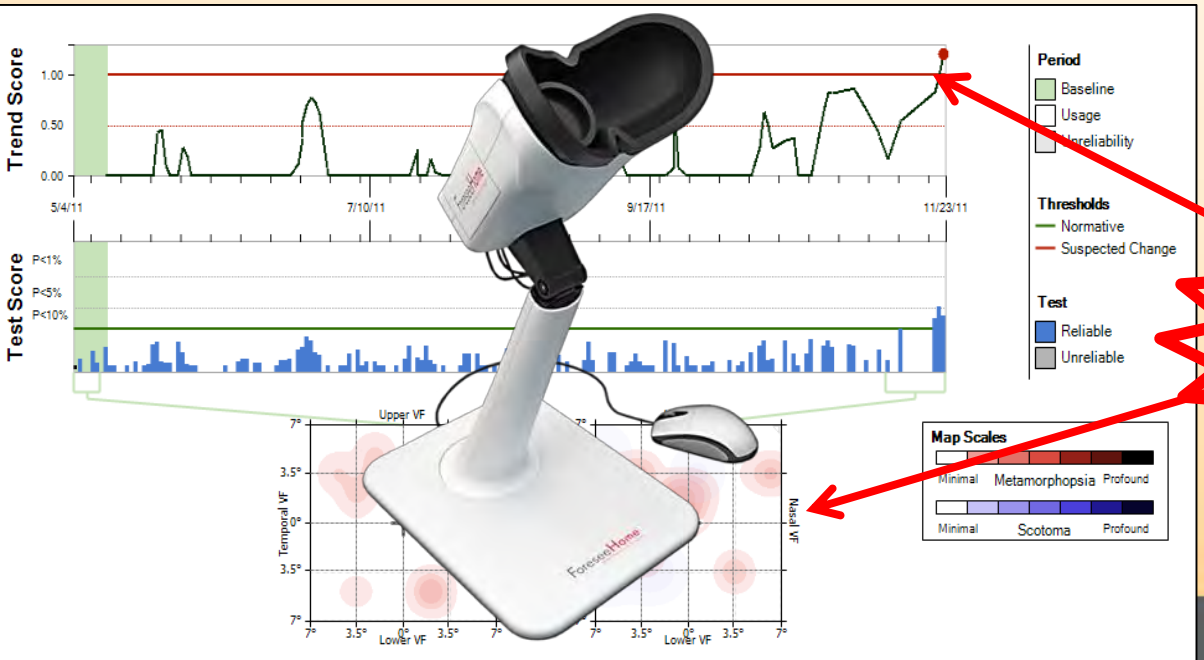
*Device—telemonitoring….testing transmitted to a data center

- **Hyperacuity Testing**
- **Telemonitoring**

ForeseeHome Device

ForeseeHome: Testing, the Report, an Alert

Hyperacuity Visual Field Test
About 3 minutes / eye



1520 participants randomized

Standard Care

757 participants

31 CNV events

Device + Standard Care

763 participants

51 CNV events

Mean follow-up (SD)
1.4 yr ± 0.6 yr
Mean VA at entry
20/25*

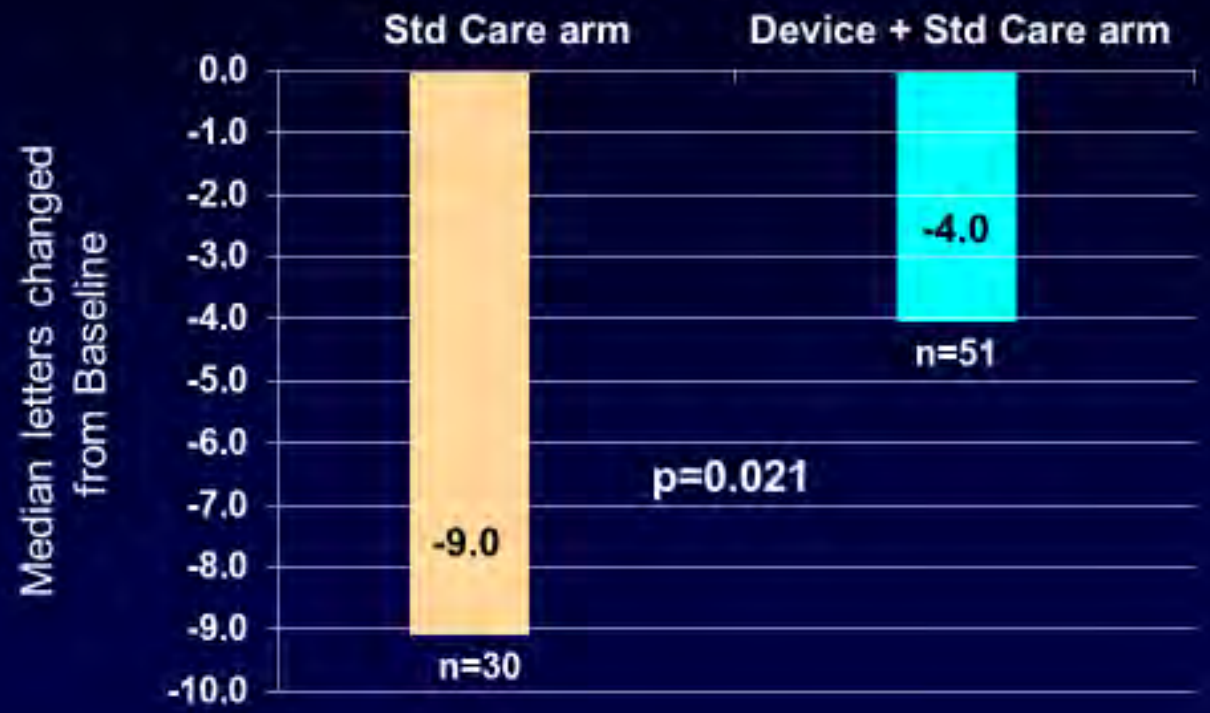
HOME Study - Results

*Snellen equivalent

The HOME Study

Primary Outcome:

Median VA change from Baseline



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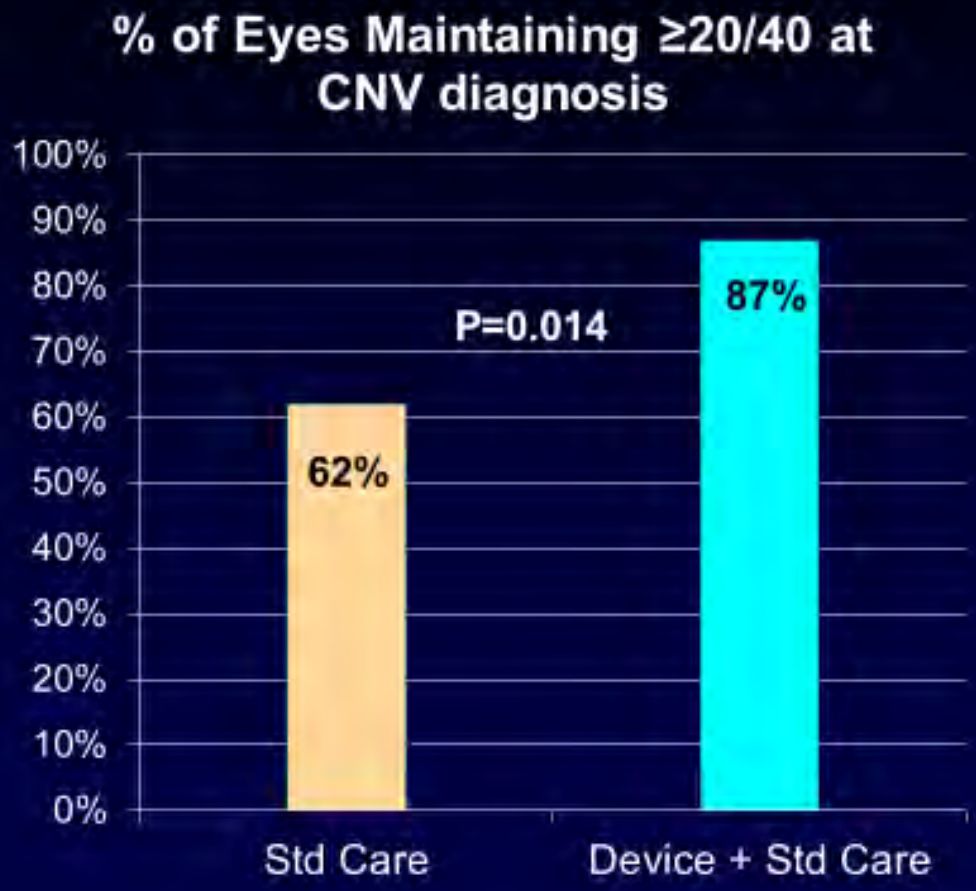
HOME Study Primary Outcome Results

Change in Visual Acuity Score from Baseline at CNV Detection (ITT Cohort)

		Control arm	Device arm	Difference	P Value
Participants		30*	51		
VA change	Mean (SD)	-12.6 (16.5)	-7.4 (11.4)	5.2	
	Median (IQR)	-9.0 (-14 to -4)	-4.0 (-11 to -1)	5	0.021

*Excluded 1 eye with no VA data at time of event

The HOME Study



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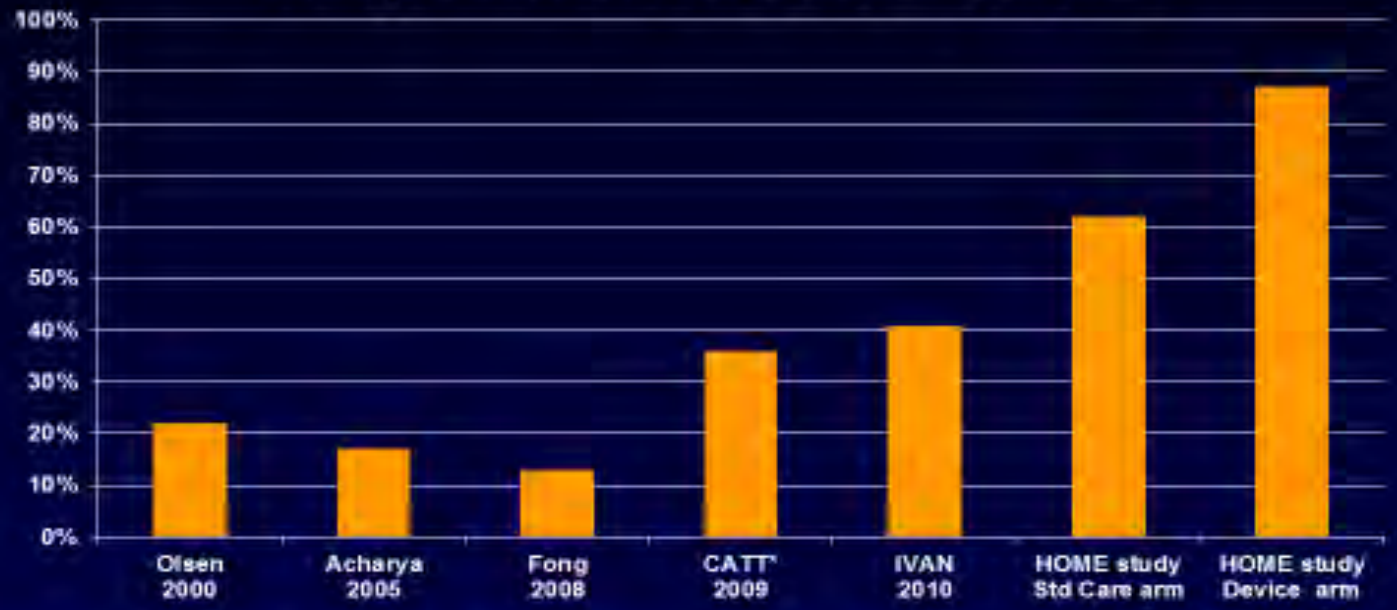
Visual Acuity at CNV Presentation

% of eyes with VA ≥ 20/40 at CNV Detection



*All but CATT included eyes with VA of 20/20 or worse (CATT included ≤20/25) at baseline.

Goals of Imaging Study

- **To validate VA gains -- "Did the ForeseeHOME Device pick up smaller CNV lesions?"**
- **Describe early lesion location/composition**
- **Compare CNV lesion characteristics between eyes assigned to the device arm with those in the standard care arm**

Analysis Cohort:
CNV events in Primary Report*

82 Investigator Diagnosed CNV events

7/82 (8%) no CNV per the RC
8/82 (10%) missing or cannot grade

67/82 (82%) CNV events confirmed by RC

67 eyes confirmed on FA and/or OCT

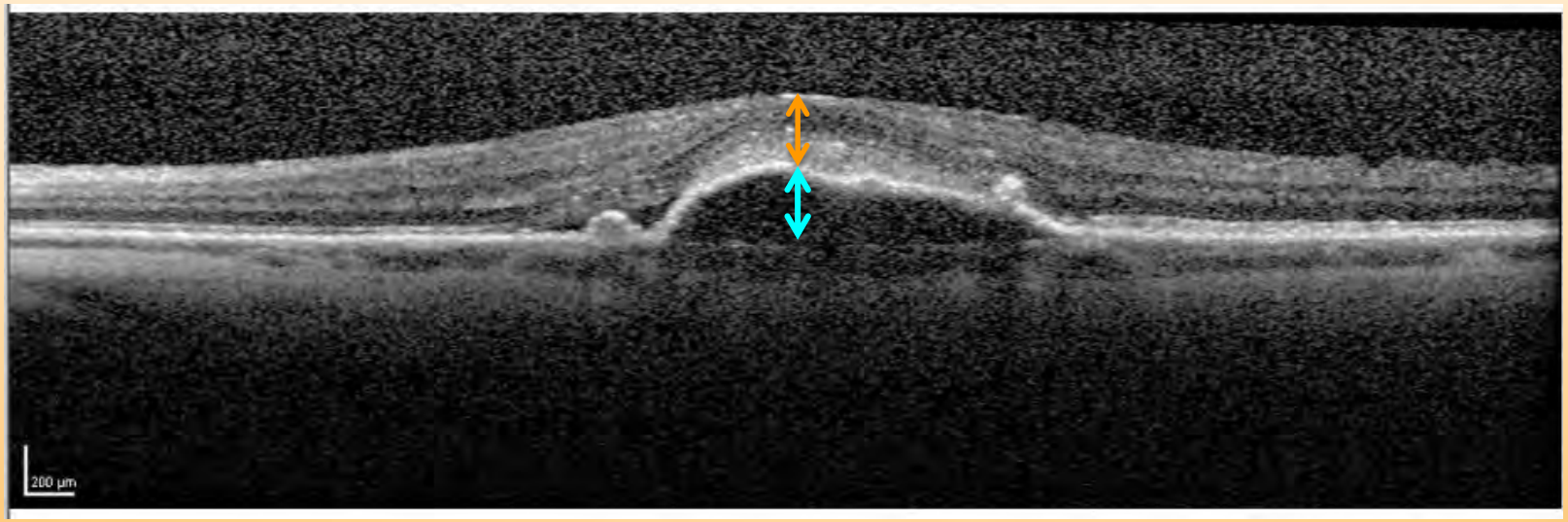
	Device (n=39)	Std Care (n=23)	P-Value*
CNV area (DA) median	0.17	0.6	**0.05**
Lesion size (DA) median	0.23	0.7	**0.05**
VA loss	-4	-10	**0.004**

Fluorescein angiogrpahic Characteristics

Among CNV Events Confirmed on FA by RC

Lesion Characteristics Median	Device monitoring (n = 23)	Standard Care (n = 19)	P-value*
CNV Area (DA)	0.48	0.65	0.23
Lesion area (DA)	0.69	0.99	0.31
VA loss (letters)	-4	-12	0.006

Measurements of OCT Lesion Components by the Reading Center

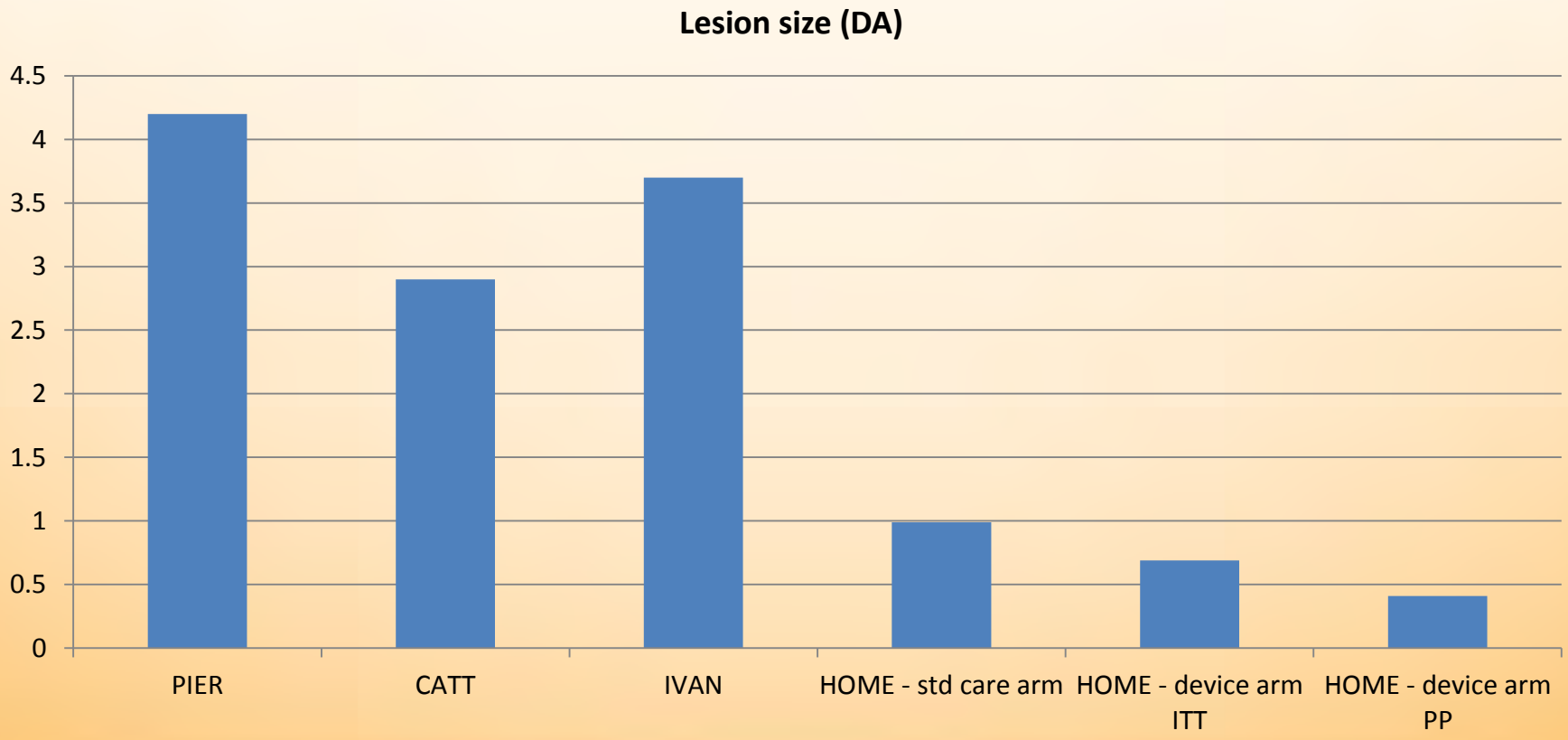


Results – OCT Characteristics

Among 59 CNV Events Confirmed on OCT by RC

Centerpoint measurements Median (μ)	Device Monitoring (n=37)	Standard Care (n=22)	P-value*
Retinal thickness	209	229	0.24
Subretinal fluid height	76	77.5	0.41
RPE lesion complex	76	155	0.04
VA loss (letters from BL)	-3	-9	0.005

Lesion Characteristics
Clinical trials vs. ForeseeHome



Summary of Imaging Study

- **Both arms of study led to detection of early CNV**
- **Lesions characteristics associated with early Dx:**
  - **Very small lesions**
  - **Few to none with additional characteristics: lipids, serous PED, fibrosis, RPE tear, RAP**

HOME Study: Performance

Specificity: Annual Device False Positive Rate

- The annual false positive rate was 24%
  - Extrapolated to an average of one false positive device alert per 4.2 monitoring years for every device user

79% of device participants had no device false alert

Estimate of target population Based on AREDS Simple Scale

2013 estimated population of people ≥65 with AMD:

- **18.5 million with AMD**
- **9 million with Intermediate AMD**
- **1.6 million with AREDS Simple Scale score 4***
- **1 million with AREDS Simple Scale CNV***

*Estimated based on prevalence of AMD as reported by the Eye Disease Prevalence Research Group (EDPRG), applied to 2013 US Census estimates and AREDS prevalence, incident and progression rates calculated from AREDS patients data.

U.S. Intermediate AMD Population at Risk for Developing CNV

2.6 million at highest risk (Simple Scale Score 4 + CNV)

1.3 million may progress, ~50% 5 year Advanced AMD rate

150,000 avoid late AMD: ~50% of recommended use of AREDS/AREDS2 supplement

1.15 million expected to progress

767,000 (2/3) will develop CNV in 5 y

Summary

If all patients in the US, who are at high risk for developing CNV, and can use this type of monitoring, an estimate between 100,000 – 315,000 additional patients would avoid functional vision loss over the next 5 years

The potential impact on public health in the United States can be considerable

Conclusions: AREDS2 - HOME Study

- **Patients would benefit from home monitoring with the device to detect CNV at an earlier stage with fewer letters lost compared with baseline.**
- **Better preservation of their visual acuity at CNV detection, including 87% 20/40 or better**
- **Smaller CNV lesions at detection of CNV-both arms**

Conclusions: AREDS2 - HOME Study

- **HOME monitoring increased likelihood of maximizing visual acuity results after intravitreal therapy with anti-VEGF agents.**
- **Has public health implications**
- **Further research into monitoring would be warranted**

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