Improving Access Through Telemedicine

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Improving Access Through Telemedicine

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Children’s Hospital of Philadelphia

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National Eye Institute

Lily Peng, MD, PhD
Google AI Healthcare
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

Postmenstrual age at onset of Stage 3 ROP

Percent of Eyes

Postmenstrual Age (Weeks) at onset of ROP stage
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)
<table>
<thead>
<tr>
<th>#</th>
<th>Outcome</th>
<th>% Sensitivity</th>
<th>% Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>10 Plus</td>
<td>100 (81-100)</td>
<td>0 (0-98)</td>
</tr>
<tr>
<td>23</td>
<td>Predict prethresh at 32-34 wks PMA imaging</td>
<td>33</td>
<td>100</td>
</tr>
<tr>
<td>44</td>
<td>RW-ROP</td>
<td>100 (85-100)</td>
<td>96 (86-100)</td>
</tr>
<tr>
<td>64</td>
<td>Type 2 or worse</td>
<td>77 (70-84)</td>
<td>96 (94-98)</td>
</tr>
<tr>
<td>43</td>
<td>Type 2 or worse</td>
<td>100 (16-100)</td>
<td>97 (87-100)</td>
</tr>
<tr>
<td>67</td>
<td>Type 2 at 31-33 wks</td>
<td>76 (70-82)</td>
<td>96 (93-98)</td>
</tr>
<tr>
<td>51</td>
<td>Clinically significant ROP</td>
<td>92 (81-97)</td>
<td>37 (23-32)</td>
</tr>
<tr>
<td>81</td>
<td>Stage 3</td>
<td>57 (29-82)</td>
<td>68 (63-73)</td>
</tr>
<tr>
<td>1222</td>
<td>Suspect treatment req</td>
<td>100 (92-100)</td>
<td>-</td>
</tr>
<tr>
<td>230</td>
<td>Type 2 or worse</td>
<td>100 (66-100)</td>
<td>99.6 (98-100)</td>
</tr>
<tr>
<td>108</td>
<td>Treatment requiring</td>
<td>100 (72-100)</td>
<td>98 (93-100)</td>
</tr>
</tbody>
</table>
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%

*Ophthalmology 2012;119:1272–1280*
Telemedicine in acute phase ROP – e-ROP

To evaluate a telemedicine system 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)

<table>
<thead>
<tr>
<th>Image Evaluation of RW-ROP</th>
<th>Present</th>
<th>Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>159</td>
<td>137</td>
</tr>
<tr>
<td>-</td>
<td>3</td>
<td>554</td>
</tr>
</tbody>
</table>

Diagnostic examination findings of RW-ROP

- **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)

<table>
<thead>
<tr>
<th>Image Evaluation of RW-ROP</th>
<th>Present</th>
<th>Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>215</td>
<td>24</td>
</tr>
<tr>
<td>-</td>
<td>80</td>
<td>534</td>
</tr>
</tbody>
</table>

Diagnostic examination findings of RW-ROP

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

<table>
<thead>
<tr>
<th>RW-ROP Status</th>
<th>Image grading +</th>
<th>Image grading -</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exam +</td>
<td>632 True positives</td>
<td>161 False negatives</td>
</tr>
<tr>
<td>Exam -</td>
<td>854 False positives</td>
<td>3703 True negatives</td>
</tr>
</tbody>
</table>
Image grading compared to exam results in e-ROP study

<table>
<thead>
<tr>
<th>RW-ROP Status</th>
<th>Image grading +</th>
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<td>Exam -</td>
<td>854 False positives</td>
<td>3703 True negatives</td>
</tr>
</tbody>
</table>
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
2018 Focus on Eye Health National Summit:
Research to Impact
US Based Teleophthalmology: Improving Access to Coordinated, Timely Care to Prevent Blindness in Diabetes

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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
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.
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."
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%


PBA http://visionproblemsus.org/diabetic-retinopathy.html
HEDIS Metric Incentivization

- Health Care Effectiveness Data Information Set (NCQA)

- 2018 Annual Eye Exam Rate by Percentiles:
  - $90^{th}$: 68%
  - $75^{th}$: 59%
  - $50^{th}$: 50%
  - $25^{th}$: 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.)
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.
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


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
3. **Triage & Queue Patients** Needing Eye Care Appropriately

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

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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

Non Eye Care Setting (Primary care, Pharmacy, etc.)

Identify Patient in Need

Intake, Vision Assessment, Image Capture (Device Agnostic)

Reading Center

Remote Image reader (MD, OD, Trained Lay Graders, AI?)

Images

Report Generated: Presence & Severity of Pathology with suggested follow-up

Diabetic Retinopathy Screening/ Surveillance (DRS)

Actively Closing the Loop on Eye Care

Patient

Ophthalmologist Follow-up

Store

FORWARD

FORWARD

FORWARD

FORWARD

FORWARD

FORWARD
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 opthalmology

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

Rubric for Ophthalmology Referral

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>R0</td>
<td>No DR. None of the signs listed for the other grades. Isolated cotton-wool spots (≥1) in the absence of any microaneurysm or hemorrhage</td>
<td>Reevaluate in 12 mo with either eye care specialist or photographic screening</td>
</tr>
</tbody>
</table>
| R1    | Background DR 
≥1 Microaneurysm 
≥1 Retinal hemorrhage 
Any exudates caused by DR | Refer to eye care professional |
| R2    | Preproliferative DR 
Intra-retinal 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 
Preterinal or vitreous hemorrhage 
Preterinal 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**
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%

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EyePACS Performance in California

EyePACS Referral
• EyePACS consultant recommends referral

Referral Communicated to Patient
• Information EyePACS communicated to patient.

Appointment Made
• An appointment set with appropriate eye specialist.

Patient keeps appointment
• Patient is examined by specialist.
• Specialist recommends treatment.

Specialist Care
• Patients Needing Treatment Actually Seek Treatment

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

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

Advances in Technology Increase Access, But Ensuring Quality is Important

- 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.

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

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https://www.fda.gov/news-events/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
Over 2000 Published Papers on Teleophthalmology since 2000.¹
1/3 on DR²

Can Further Research Help Teleophthalmology Cross the Gap?

References


Home Monitoring for Age-Related Macular Degeneration (AMD)

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

No Financial Disclosures
HOME Monitoring Study of the EYE (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.
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
CATT Study By Baseline Visual Acuity

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

- **Mean VA at 12 months with Anti-VEGF (CATT)**

The better baseline visual acuity predicts 1 yr Vision Outcomes

- **VA at Treatment Initiation**

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)

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

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

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

Adjusted mean VA at 1 year vs. CNV area at baseline

- 1 year VA
- Baseline VA

Baseline area of CNV

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

Acuity Suggests
Limited Number of Eyes are Detected Early

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

*Device—telemonitoring....testing transmitted to a data center
• Hyperacuity Testing
• Telemonitoring

ForeseeHome Device
ForeseeHome: Testing, the Report, an Alert

Hyperacuuity Visual Field Test
About 3 minutes / eye
HOME Study - Results

- **Standard Care**
  - 757 participants
  - 31 CNV events
  - Mean follow-up (SD): 1.4 yr ± 0.6 yr
  - Mean VA at entry: 20/25* (Snellen equivalent)

- **Device + Standard Care**
  - 763 participants
  - 51 CNV events

- Total participants randomized: 1520 participants

*Snellen equivalent*
The HOME Study
Primary Outcome:

Median VA change from Baseline

- **Std Care arm**
  - Median letters changed from Baseline: -9.0
  - n=30

- **Device + Std Care arm**
  - Median letters changed from Baseline: -4.0
  - n=51

p=0.021
HOME Study Primary Outcome Results

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

<table>
<thead>
<tr>
<th></th>
<th>Control arm</th>
<th>Device arm</th>
<th>Difference</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>30*</td>
<td>51</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VA change</td>
<td>Mean (SD)</td>
<td>-12.6 (16.5)</td>
<td>-7.4 (11.4)</td>
<td>5.2</td>
</tr>
<tr>
<td></td>
<td>Median (IQR)</td>
<td>-9.0 (-14 to -4)</td>
<td>-4.0 (-11 to -1)</td>
<td>5</td>
</tr>
</tbody>
</table>

N=51

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

% of Eyes Maintaining ≥20/40 at CNV diagnosis

- Std Care: 62%
- Device + Std Care: 87%

P = 0.014
Visual Acuity at CNV Presentation

% of eyes with VA $\geq 20/40$ at CNV Detection

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

<table>
<thead>
<tr>
<th></th>
<th>Device (n=39)</th>
<th>Std Care (n=23)</th>
<th>P-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNV area (DA) median</td>
<td>0.17</td>
<td>0.6</td>
<td>0.05</td>
</tr>
<tr>
<td>Lesion size (DA) median</td>
<td>0.23</td>
<td>0.7</td>
<td>0.05</td>
</tr>
<tr>
<td>VA loss</td>
<td>-4</td>
<td>-10</td>
<td>0.004</td>
</tr>
</tbody>
</table>
Fluorescein angiographic Characteristics
Among CNV Events Confirmed on FA by RC

<table>
<thead>
<tr>
<th>Lesion Characteristics Median</th>
<th>Device monitoring (n = 23)</th>
<th>Standard Care (n = 19)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNV Area (DA)</td>
<td>0.48</td>
<td>0.65</td>
<td>0.23</td>
</tr>
<tr>
<td>Lesion area (DA)</td>
<td>0.69</td>
<td>0.99</td>
<td>0.31</td>
</tr>
<tr>
<td>VA loss (letters)</td>
<td>-4</td>
<td>-12</td>
<td>0.006</td>
</tr>
</tbody>
</table>
Measurements of OCT Lesion Components by the Reading Center
# Results – OCT Characteristics

*Among 59 CNV Events Confirmed on OCT by RC*

<table>
<thead>
<tr>
<th></th>
<th>Centerpoint measurements Median (µ)</th>
<th>Device Monitoring (n=37)</th>
<th>Standard Care (n=22)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinal thickness</td>
<td>209</td>
<td>229</td>
<td></td>
<td>0.24</td>
</tr>
<tr>
<td>Subretinal fluid height</td>
<td>76</td>
<td>77.5</td>
<td></td>
<td>0.41</td>
</tr>
<tr>
<td>RPE lesion complex</td>
<td><strong>76</strong></td>
<td><strong>155</strong></td>
<td></td>
<td><strong>0.04</strong></td>
</tr>
<tr>
<td>VA loss (letters from BL)</td>
<td>-3</td>
<td>-9</td>
<td></td>
<td>0.005</td>
</tr>
</tbody>
</table>
Lesion Characteristics

Clinical trials vs. ForeseeHome

Lesion size (DA)
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